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BUSINESS, CONSUMER SERVICES AND HOUSING AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
GOVERNOR EDMUND G. BROWN JR.

ENFORCEMENT AND COMPOUNDING COMMITTEE
MEETING MATERIALS
JUNE 1, 2016

Amy Gutierrez, PharmD, Chair, Board President
Greg Lippe, Public Member, Vice Chair
Stan Weisser, Professional Member
Allan Schaad, Professional Member
Greg Murphy, Public Member

II. PUBLIC COMMENT FOR ITEMS NOT ON THE AGENDA/AGENDA ITEMS FOR FUTURE MEETINGS

Note: The committee may not discuss or take action on any matter raised during this public comment section that is not included on this agenda, except to recommend whether to place the matter on the agenda of a future meeting. [Government Code Sections 11125, 11125.7(a)]

III. ENFORCEMENT MATTERS

a. Update by the University of California, San Diego on Its Pilot Program to Permit Patients to Access Medication from an Automated Storage Device Not Immediately Adjacent to a Pharmacy

Attachment 1

At the Board of Pharmacy's April 2015 Board Meeting, the board approved an 18-month pilot study under the auspices of the University of California, San Diego (UCSD) School of Pharmacy involving use of an automated storage device for prescription medication from which staff of Sharp Hospital in San Diego and their families, who opted in, could pick up their outpatient medications. Consultation would be provided via telephone before medication could be dispensed to a patient.

This study was planned to start in June or July, 2015; however, at the September 9, 2015 Enforcement Committee meeting, Dr. Jan Hirsch, BS Pharm, PhD, spoke via telephone and anticipated the pilot study would not begin until December.

At the December 14, 2015 Enforcement Committee meeting, Dr. Hirsch, reported that they would launch the device, enroll patients and refine data collection tools and processes during the first and second quarters of 2016, collect and review the data during the third quarter of 2016, and report back to the board with their results during the last quarter of 2016.

Also at the December meeting, the committee recommended that the board ask UCSD to collect drug classification data as part of the study. The board approved this recommendation at the February 2016 board meeting.

At the March 2, 2016 Enforcement Committee meeting, Dr. Hirsch reported that the study had launched on January 20, 2016 and 120 patients had enrolled to use the automated device. The committee recommended that the board ask UCSD for the number of employees and the work hours of those who utilize the device. At the April 28, 2016 board meeting, the board approved the recommendation.

At this meeting, Dr. Hirsch will provide an update via telephone and respond to questions from the committee. A copy of her presentation is provided in **Attachment 1**.

Reports on this study will be provided at each quarterly Enforcement and Compounding Committee meeting while the study is underway.

b. Update on the CURES 2.0 Prescription Monitoring Program

The Department of Justice (DOJ) announced that beginning January 8, 2016, the upgraded prescription drug monitoring program was available and all current registrants were required to update their registration in the new 2.0 environment to ensure access to the system.

According to DOJ, CURES 2.0 is available to all registrants that use Microsoft Internet Explorer Version 11.0 or greater, or the latest versions of Mozilla FireFox, Google Chrome, or Apple's Safari when accessing the system. Registrants that do not currently have access to one of those specified internet browsers will be able to continue to access the prior version of CURES until the legacy system's retirement, at which time an updated browser must be used.

The board is working with DOJ to develop "Frequently Asked Questions" to assist registrants with understanding CURES 2.0. The board will send out updates via its subscriber alert system as it learns additional information from DOJ.

On February 8, 2016, the board sent post cards to all licensed California pharmacists as a reminder that California law requires all individuals holding an active California pharmacist license to register with CURES by July 1, 2016.

According to reports generated by the CURES system, 30,544 pharmacists have registered for CURES 2.0, an increase of 22 percent from the March Enforcement Committee Meeting when 25,132 pharmacists had registered. Additionally, over 344,000 patient activity reports (PARs) were run in the last 30 days by pharmacists, indicating pharmacists are using CURES.

The board is currently preparing a mailing to the non-CURES registered pharmacists reminding them of their obligation to apply for registration in CURES. There are 14,330 active pharmacists who are not registered to access CURES. Of these pharmacists, 8,143 have California addresses of record, 5,985 have other US addresses of record and 202 have foreign addresses of record. The board is currently mailing a reminder letter to all of these pharmacists of their obligation to apply for registration in CURES by July 1, 2016.

At this meeting, Ms. Herold, who sits on the DOJ/DCA Change Control Board for CURES, will provide an update on the CURES 2.0 program.

c. Consideration of the Proposed Regulation Relating to Reconciliation and Inventory Reports of Controlled Substances (Currently, to Add Title 16 California Code of Regulations Section 1715.65

Attachment 2

At the July 2015 Board Meeting, the board approved initiation of a rulemaking to establish inventory requirements for controlled drugs for pharmacies and clinics. The regulation would require perpetual inventories of all federal Schedule II drugs, with a physical count every 90 days. Additionally, the board would establish a list of one or several additional controlled drugs from Schedules III – V that are reported as frequently stolen to the board and/or the DEA.

The regulation was released for the required 45-day public comment period between October 16, 2015 and November 30, 2015. At the February 2016 Board Meeting, the board referred the regulation back to the Enforcement Committee for review and consideration of the comments submitted.

Comments received by the board and a copy of the proposed regulation are provided in **Attachment 2**.

At this meeting, the committee will evaluate the regulation. To focus the discussion, Board President Gutierrez and Executive Officer Herold developed a new draft of the regulation which is also provided in **Attachment 2.**

d. Consideration of the Department of Consumer Affairs Contract and Audit of the DCA Diversion Programs Provided by Maximus Health Services

Attachment 3

The California Business and Professions Code provides that various healthcare licensing boards, under the auspices of the Department of Consumer Affairs (DCA), may establish a

program to identify and rehabilitate licensees whose competency might be impaired due to substance abuse or mental illness. The board is one of several DCA boards that have implemented such programs; however, the board's program differs from those of other DCA boards in that it does not divert licensees from discipline -- it uses the program as a monitoring program for its participants before, during and after discipline is being secured.

In 2003, DCA began contracting with Maximus Health Services, Inc., to provide what DCA calls "Diversion Program services." In October 2015, an audit of Maximus was conducted for the contract period January 1, 2010 through December 31, 2014. This report was referenced in the board's 2015 Sunset Report, but never shared with the board specifically.

A copy of the audit is provided in **Attachment 3.**

e. Consideration of the Food and Drug Administration's Required Class-Wide Safety Labeling Changes for Opioid Pain Medications

Attachment 4

On March 22, 2016, the U.S. Food and Drug Administration (FDA) announced required class-wide safety labeling changes for immediate-release opioid pain medications. Among the changes, the FDA is requiring a new boxed warning about the serious risks of misuse, abuse, addiction, overdose, and death. The FDA is also now requiring a warning that chronic maternal use of opioids during pregnancy can result in neonatal opioid withdrawal syndrome (NOWS), which can be life-threatening. Provided below is a sample of how the new black box warning label might appear:

ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME

Addiction, Abuse, and Misuse
[TRADENAME] exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk prior to prescribing [TRADENAME], and monitor all patients regularly for the development of these behaviors or conditions *[see Warnings and Precautions (5.X)]*.

Life-Threatening Respiratory Depression
Serious, life-threatening, or fatal respiratory depression may occur with use of [TRADENAME]. Monitor for respiratory depression, especially during initiation of [TRADENAME] or following a dose increase *[see Warnings and Precautions (5.X)]*.

Accidental Ingestion
Accidental ingestion of even one dose of [TRADENAME], especially by children, can result in a fatal overdose of [active moiety] *[see Warnings and Precautions (5.X)]*.

Neonatal Opioid Withdrawal Syndrome
Prolonged use of [TRADENAME] during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available *[see Warnings and Precautions (5.X)]*.

In addition, the FDA is requiring several safety labeling changes across all prescription opioid products to include additional information on the risks of these medications.

Copies of the FDA's News Release and Safety Announcement are provided in **Attachment 4.**

f. Consideration of the Centers for Disease Control and Prevention's Guideline for Prescribing Opioids for Chronic Pain

Attachment 5

On March 15, 2016, the Centers for Disease Control and Prevention (CDC) released 12 recommendations for primary care clinicians who are prescribing opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care.

The recommendations are grouped into three areas:

- Determining when to initiate or continue opioids for chronic pain
- Opioid selection, dosage, duration, follow-up, and discontinuation
- Assessing risk and addressing harms of opioid use

The categorization of the recommendations was based on the following:

- No evidence shows a long-term benefit of opioids in pain and function versus no opioids for chronic pain with outcomes examined at least one year later
- Extensive evidence shows the possible harms of opioids (including opioid use disorder, overdose, and motor vehicle injury)
- Extensive evidence suggests some benefits of nonpharmacologic and nonopioid pharmacologic treatments compared with long-term opioid therapy, with less harm

A copy of the CDC Guideline and the board's January 13, 2016 letter of support are provided in **Attachment 5.**

This guidance is in addition to guidance provided by other agencies on opioid prescribing. In November 2014, the Medical Board of California produced its *Guidelines for Prescribing Controlled Substances for Pain*. According to the Medical Board's executive officer, the Medical Board is in the process of comparing its guidelines with those of the CDC. Board staff will continue to monitor this review and its outcome. The Medical Board's guidelines are available from its website at www.mbc.ca.gov.

g. Proposal to Add Statutory Authority Relating to the Registration with the Board of Automated Delivery Systems for Dispensing of Medication

Attachment 6

At the February 2016 Board Meeting, the board considered a draft proposal to establish a registration requirement for pharmacies that operate automated delivery systems. During the meeting, the board discussed creating inventory requirements for the devices and the need to clarify some of the terminology used in the draft language. The board also heard public comment in which the board was asked to modify the requirements for hospitals that use the automated delivery systems. The board asked staff to modify the language and bring it back to the committee for further discussion. Subsequent to that meeting, staff worked with the board president and vice-president to refine the language (provided below).

Proposal to Add Section 4105.5

(a) For purposes of this section, an automated drug delivery system includes a device as defined in Health and Safety Code Section 1261.6(a)(1).

(b) Every pharmacy that owns or provides dangerous drugs dispensed through an automated drug delivery system shall provide the board in writing with the location of each device within 30 days of installation of such a device, and on an annual basis as part of the license renewal. The pharmacy shall also advise the board in writing within 30 days if the pharmacy discontinues operating an automated drug delivery system.

(c) Every pharmacy that uses such a system may only do so if all of the following conditions are satisfied.

1. *Use of the device is consistent with legal requirements.*
2. *Policies and procedures include appropriate security measures and monitoring of the inventory to prevent thefts and diversion. <u>The inventory shall be done at least quarterly.</u>*
3. *Drug losses from the device are reported to the board as required by law.*
4. *The pharmacy license is in good standing with the board.*
5. *<u>The device is located within a seventy-five mile radius of the pharmacy</u>.*

(d) The board may prohibit a pharmacy from using a system if it determines that the conditions provided in subdivision (c) are not satisfied. If such a determination is made, the board shall provide the pharmacy with written notice including the basis for the determination. The pharmacy may request an office conference to appeal such a decision within 30 days of receipt of the written notice. The executive officer or designee may affirm or overturn the prohibition as a result of the office conference.

(e) <u>A device used in a licensed hospital for doses administered in the hospital is exempt from subdivision (b).</u>

At the April 27-28 Board Meeting, the board discussed the proposed language, and asked questions regarding the level of security that the board should require for the locations of the machines, especially if the machine would be located 75 miles from the pharmacy.

Supervising Inspector Janice Dang explained how the automated drug delivery systems are used in skilled nursing facilities and noted that in rural areas the machines may actually be located farther than 75 miles from the pharmacy.

The board determined that requiring the registration of the automated drug delivery systems would provide the board with important information regarding the use of the machines; however, they elected to send the proposed language back to the Enforcement Committee so that sections (c) and (d) (which detail the specific requirements for the use of the machines) could be further vetted.

At this meeting, the committee will review and discuss sections (c) and (d) of the proposed regulation language.

An excerpt from the discussion of these devices from the February board meeting minutes is provided in **Attachment 6.**

h. Consideration of a Proposal to Conduct Inspections of All Pharmacies Every Four Years

Attachment 7

The board's charge to regulate the pharmacy profession necessitates routine inspections of licensed facilities to confirm adherence to or identify failures in adherence to the requirements of pharmacy law. Failure to perform such inspections makes that the board's enforcement program reactive rather than proactive because inspections are currently done when the board is investigating potential violations of pharmacy law from a complaint or other information that would trigger an investigation.

For a number of years, the board's policy has sought to inspect all facilities every three or four years. The board has been unable to complete these routine inspections of all facilities with any regularity, and in recent years has had to substantially reduce such inspections because the board's first priority is investigation of complaints and performance of mandated annual sterile compounding inspections. While thousands of inspections are completed, inspections occur generally as part of the investigative process, prior to issuance or renewal of a sterile compounding license or as part of probation monitoring.

All Inspections FY11-12 thru FY14-15 by Visit Type

Number of Inspections Inspection Type	FY11-12	FY12-13	FY13-14	FY14-15	Total
Routine	1730	1010	287	342	3369
Investigation	743	896	875	926	3440
Probation/PRP	258	228	139	227	852
Sterile Compounding	268	276	996	1067	2607
Other	34	39	32	26	131
Grand Total	**3033**	**2449**	**2329**	**2588**	**10399**

Mandatory inspections on a routine but random basis would enable the board to perform compliance inspections to educate licensees about pharmacy law as well as identify problems early to prevent more serious consumer issues from developing. Like all inspections, such inspections would be unannounced.

Compliance inspections provide an opportunity for board staff to answer questions about pharmacy law and to complete follow up inspections of facilities previously issued either citations or letters of admonishment to confirm compliance.

Establishing a policy of mandatory inspections of each pharmacy every four years would supplement our current practice of conducting inspections principally to investigate problems (or inspect sterile compounders).

The board currently has 6,614 community pharmacies licensed in California. Some of these pharmacies have never been inspected by the board. The creation of a policy directing the board to perform inspections of all pharmacies every four years would require approximately 1,650 routine inspections annually. Over the last two years, the board completed an average of 1,215 inspections annually (routine plus investigation inspections).

At the December 14, 2015 Enforcement Committee meeting, the committee recommended creating a statutory mandate to complete random, unannounced routine inspections of resident pharmacies once every four years.

At the February 24-25, 2016, Board Meeting, the board referred the matter to Enforcement Committee for additional discussion about ways to ensure more compliance inspections are performed.

At this meeting, the enforcement committee will resume its discussion.

An excerpt from the previous discussion on this topic at the February 2016 board meeting is provided in **Attachment 7.**

IV. COMPOUNDING MATTERS

a. Update on the Status of the Board's Sterile Compounding Regulations, Title 16 California Code of Regulations, Sections 1735 et seq., and 1751 et seq.

Attachment 8

On May 8, 2015, the board initiated a formal rulemaking to update California's compounding regulations. The chronological timeline for the regulation is:

Board approved proposed the text for rulemaking:	April 21, 2015
Regulation Hearing:	June 25, 2015
45-day comment period:	May 8 – June 22, 2015
15-day comment period:	July 31 – August 15, 2015
15-day comment period:	November 20 – December 5, 2015
Board approved the final text:	January 19, 2016
File submitted to DCA for review:	March 10, 2016

The board set the effective date of the regulation as January 1, 2017. The file is currently being reviewed by DCA.

At this meeting, Ms. Herold will provide an update on the status.

A copy of the regulation is provided in **Attachment 8.**

b. Presentation by the Office of Statewide Health Planning and Development Regarding its Process for Reviewing Structural Modifications Needed in Healthcare Facilities

At this meeting, Glenn Gall, Supervisor in the Facilities Development Division of the Office of Statewide Health Planning and Development, will make a presentation on the process for reviewing structural modifications in healthcare facilities. A copy of the presentation will be provided at the meeting.

c. Consideration of the Process for Pharmacies Seeking Waivers in Anticipation of the New Requirements in Title 16 California Code of Regulations, Sections 1735 et seq., and 1751 et seq.

The final version of the proposed regulations contains a waiver provision for some of the structural requirements. As proposed in the regulation (as subdivision 1735.6(f) and in 1751.4(l)), the waiver request shall:

1. be made in writing
2. identify the provision(s) requiring physical construction, alteration, or improvement
3. contain a timeline for any such change

Staff has developed a proposed process for pharmacies to request waivers. **At this meeting**, this process will be discussed and refined.

A copy of the proposed waiver application form will be provided at the meeting.

d. Consideration of The Pew Charitable Trust Reports: "Best Practices For State Oversight of Drug Compounding" and "National Assessment of State Oversight of Sterile Drug Compounding"

Attachment 9

Recently, the Pew Charitable Trust published reports on the best practices for drug compounding. The goal of these reports is to establish a baseline describing state policies today, and promote best practices in order to ensure that patients are safeguarded regardless of the state in which they receive treatment.

- ***Best Practices for State Oversight of Drug Compounding*** proposes best practices that are most meaningful to patient safety and the most achievable -- while recognizing that state funding may place limits on oversight systems
- ***National Assessment of State Oversight of Sterile Drug Compounding*** looks at the compounding landscape across the states to see how regulation and oversight vary in a number of categories (e.g., inspection, tracking, licensing)

Executive Officer Herold served on this task force representing this board and California.

A copy of both reports is provided in **Attachment 9.** More information regarding The Pew Charitable Trust organization can be found at: http://www.pewtrusts.org/en/projects/drug-safety-project.

e. Consideration of the Food and Drug Administration's Guidance Documents on Standards for Compounding Drugs Under Sections 503A and 503B of the Federal Food, Drug, and Cosmetic Act

In April 2016, the FDA released three draft guidance documents for public comment involving compounding or outsourcing of human drugs. Each of these documents is listed below for discussion at this meeting. The board may choose to submit comments, which would be due by mid-July, on some or all of these guidance documents as the FDA develops policy for compounding and outsourcing facilities in the USA.

1) Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act

Attachment 10

According to this guidance document, the guidance in this document addresses:

- Compounding AFTER the receipt of a prescription for an identified, individual patient,
- Compounding BEFORE the receipt of a prescription for an identified individual patient (anticipatory compounding), and
- Compounding for office use.

This guidance document states the value of compounding for individual patients by pharmacies, outsourcing facilities and physician offices when clinically necessary for a patient. The FDA states that when a product is compounded by a pharmacy or physician for an individual patient, the compounding entity is usually not registered with the FDA, and that the FDA is not usually aware of problems with compounded drug products unless it receives a report of serious adverse event or visible contamination.

The FDA also states it has identified many pharmacies that compound drug products under insanitary conditions that ship numerous products, sometimes in large amounts, across the country. "The longer a compounded sterile drug product that has been contaminated is held by a pharmacist or physician before distribution, or held in inventory in a health care facility before administration, the greater the likelihood of microbial proliferation and increased patient harm."

As such, the FDA states that compounding by 503A facilities (pharmacies) necessitate the following tenants:

1. Compounding is for an identified individual patient (after a patient-specific prescription is received)
2. Drugs compounded in advance of receiving prescriptions are compounded only in limited amounts (anticipatory compounding),
3. Drugs are distributed pursuant to a patient-specific prescription

The guidance document encourages the use of the following statement when a prescriber is prescribing a compounded drug product for a patient:

Per [type of communication] with [name of prescriber] on [date], [name of prescriber] has advised that compounded [name of drug] is necessary for the treatment of [name of patient].

The guidance states that unless anticipatory compounding is done for a limited quantity of compounded products, a prescription for a specific patient is first required before compounding occurs.

Anticipatory compounding may occur:

- Based on a history of the licensed pharmacy receiving a valid prescription order,
- If the orders have been generated solely within an established relationship between the pharmacist and prescriber,
- The compounder holds for distribution no more than a 30-day supply,
- The amount of supply is based on the number of valid prescriptions received by the compounder for identified individual patients in a 30-day period over the past year

The guidance draws a distinction in the activities performed by an outsourcer versus a pharmacy in that because the outsourcer is held to a higher standard of facility requirements and reporting obligations for adverse events and other factors, "outsourcing facilities can compound and distribute sterile and non-sterile non-patient-specific drug products to hospitals, clinics, and health care practitioners for office use."

2) Facility Definition Under Section 503B of the Federal Food, Drug, and Cosmetic Act

Attachment 11

This guidance document was developed for entities registered or considering registering as outsourcing facilities, and whether the "at one address means" whether multiple suites used for compounding constitute separate locations.

According to the guidance, outsourcing facilities may or may not receive a prescription for a compounded drug product, and are not subject to interstate distribution restrictions as are 503A facilities, but are required to compound all products under Current Good Manufacturing Practices (CGMPs), label all products as compounded, and be subject to adverse event reporting.

The FDA goes on to discuss that any product compounded in an outsourcing facility must be compounded pursuant to CGMP conditions, and not those of a pharmacy. Thus the FDA concludes that there can be no comingling of products (those compounded under 503A conditions and those compounded under 503B outsourcing conditions) in the same facility. All compounding in such facilities must be done under outsourcing facility requirements.

If implemented, this policy would require California licensed sterile compounding pharmacies that produce large quantities of non-patient specific compounded product to be generally regulated as outsourcers, not as pharmacies. As such, the guidance supports enactment of the board's SB 1193 to permit separate regulation of outsourcers and pharmacies.

The guidance also addresses the co-location of a manufacturer and an outsourcing facility and concludes:

> *"When a facility both manufactures conventional drug products and compounds drug products under section 503B, the policies described in this guidance would apply to the facility's compounded drug products except with respect to CGMP requirements that must be implemented throughout a manufacturing facility and cannot be applied differently to different drug products in the same facility, such as environmental monitoring and pressure differential monitoring requirements."*

The guidance states that approved drug products manufactured by a manufacturer would be easily differentiated from the outsourcing-produced products due to the differing labeling requirements between outsourcing facility-produced drugs and manufactured drugs.

3) Hospital and Health System Compounding Under the Federal Food, Drug, and Cosmetic Act

Attachment 12

This guidance states that outsourcing facilities are not required to be licensed as pharmacies, they may compound products in large quantities, they will be inspected by the FDA on a risk-based assessment, and they may compound with or without having a patient-specific prescription.

The FDA notes that compounding in hospitals can occur under various forms: some hospitals compound only those products the hospital needs for its patients (e.g., inpatients and emergency department), while other hospitals compound for other facilities within their health system (clinics, infusion centers, long-term care) for administration or dispensing.

According to this guidance document, hospitals can compound pursuant to a patient-specific prescription as well perform anticipatory compounding for future use. Hospitals can also buy compounded products from outsourcers for use within their facilities. Additionally, some hospitals have registered as outsourcing facilities.

The FDA goes on to repeat messages from the other two proposed guidance documents that it does not routinely regulate compounding by pharmacists or

physicians, and thus is not aware of substandard compounding practices until an adverse event occurs. If compounding is done in an outsourcing facility, then because the FDA has regulatory oversight and the facility must adhere to CGMPS, higher production of compounded products can occur with longer beyond use dates without the risks inherent in compounding pharmacies. The FDA further states that compounded products should be used only when commercial products will not fit the medical needs of a patient.

The guidance states that in hospital pharmacies, compounding must be done in accordance with all provisions of regulations governing 503A pharmacies, and such pharmacies may be subject to regulatory action for violations of new drug approval, adequate directions for use and CGMP requirements.

The guidance goes on to state that in a hospital or health system, compounding may occur after receipt of a valid order for an identified, individual patient, or be done in limited quantities in advance of receipt for an identified, individual patient.

The FDA indicates that it does not intend to take action when a hospital pharmacy distributes compounded drug products without first receiving a patient-specified drug order if:

1. The drug products are distributed only to healthcare facilities that under common ownership of the hospital pharmacy and that are located within a 1 mile radius of the compounding pharmacy;
2. The drug products are only administered within healthcare facilities to patients within the healthcare facilities, pursuant to a patient specific prescription or order; and
3. The drug products are compounded in accordance with all other provisions of section 503A, and any other applicable requirements of the FD&C Act and FDA regulations (e.g., the drug products are not made under insanitary conditions or misbranded).

The FDA states that the 1 mile radius is necessary because a health system pharmacy that compounds drug products without patient-specific prescriptions for facilities within its health system across a broader geographic area could function as a large manufacturing operation, but without the necessary standards to assure drug quality. If such a pharmacy contaminates or otherwise adulterates or misbrands a compounded drug, the drug has the potential to harm many patients.

The FDA instead offers that outsourcing facilities, which are subject to CGMP requirements and other conditions that help to assure drug quality, can compound and distribute drug products to healthcare facilities nationwide without first receiving prescriptions for identified individual patients.

The FDA states that a hospital compounding pharmacy can register as an outsourcing facility if it intends to provide compounded drugs to facilities such as other hospitals or

clinics outside the 1 mile radius of the pharmacy in which the drug is compounded without first obtaining a prescription for an identified individual patient.

Noted: This guidance conflicts with the regulatory provisions enacted under Business and Professions Code section 4128 et seq. under which the board licenses centralized hospital packaging pharmacies. Centralized packaging pharmacies allow hospitals under common ownership to secure unit-dose packaged medications from a centralized pharmacy if the pharmacies are located within 75 miles of the licensed packaging pharmacies.

f. Overview of Compounding Inspections Performed and Violations Noted

At this meeting, Supervising Inspector Christine Acosta will present data compiled from board inspections of licensed compounding pharmacies.

A copy of Dr. Acosta's presentation will be provided at the meeting.

IV. MEETING DATES FOR 2016

The Enforcement Committee will meet on the following dates during 2016:

- August 31, 2016
- December – TBD (once a date is finalized, it will be posted on the board's website)

Attachment 1

Study of Expanded Use of an Automated Delivery Device

UPDATE 06-01-16

Jan D. Hirsch, BPharm, PhD

UCSD Skaggs School of Pharmacy & Pharmaceutical Sciences

UC San Diego
HEALTH SCIENCES

Update

- ScriptCenter Kiosk
  - Operations Update
- Update on Study
  - Reminder: Research Design & Questions
  - IRB Amendment
  - Study Timeline Requested Revision

UC San Diego
SKAGGS SCHOOL OF PHARMACY AND PHARMACEUTICAL SCIENCES

ScriptCenter Kiosk
Sharp Memorial Hospital

GO LIVE DATE
January 20th, 2016

Located at Sharp Memorial Hospital
Employee entrance on ground floor.
Secure access only.

Location Change
June 2016

First Floor Lobby Sharp Memorial Hospital

- Original location deemed hazardous because located in a fire exit corridor (unclear why this wasn't discovered at the original inspection/approval)
- New location is alcove near information desk first floor.
- Site to have 24/7 security cameras and on-site monitoring.

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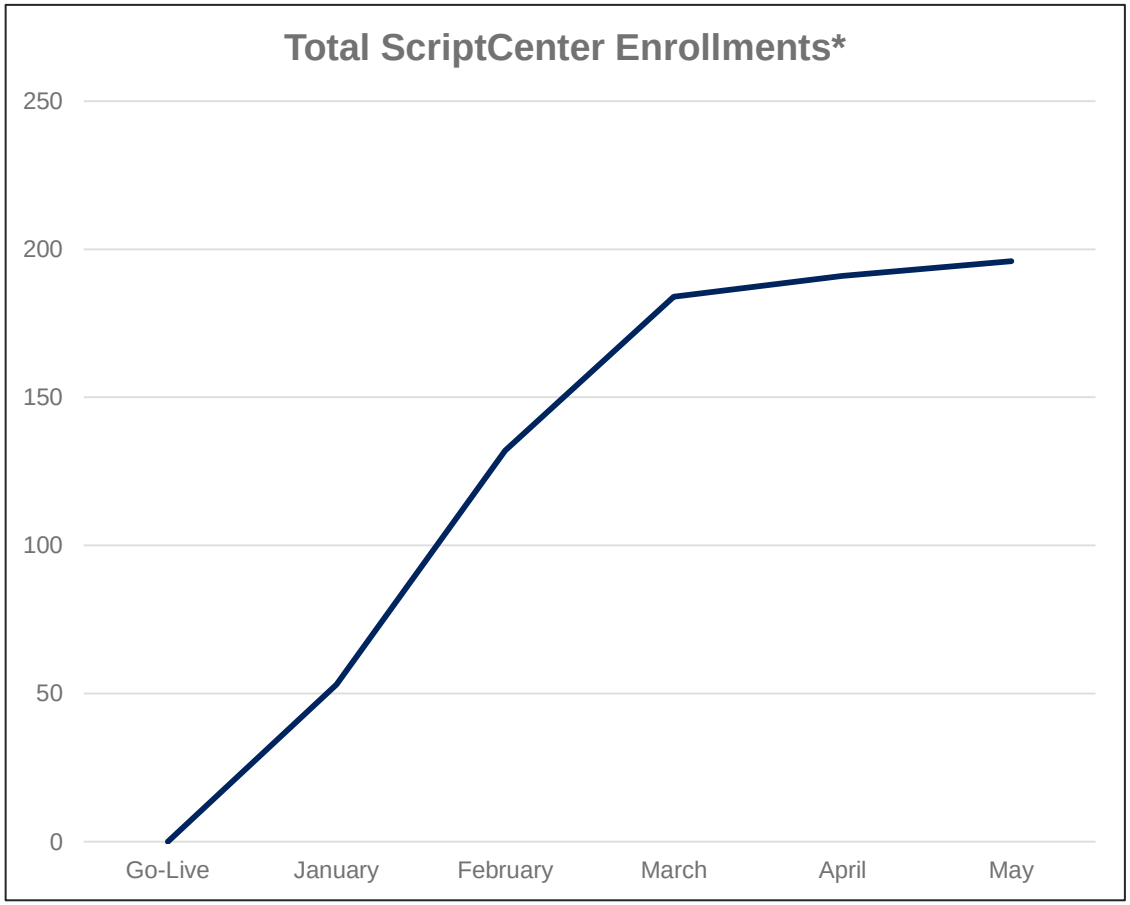
ScriptCenter Kiosk
Activity 1/20/16 through 5/9/16

ENROLLMENT



About 200 users
(*4% Campus Employees)*

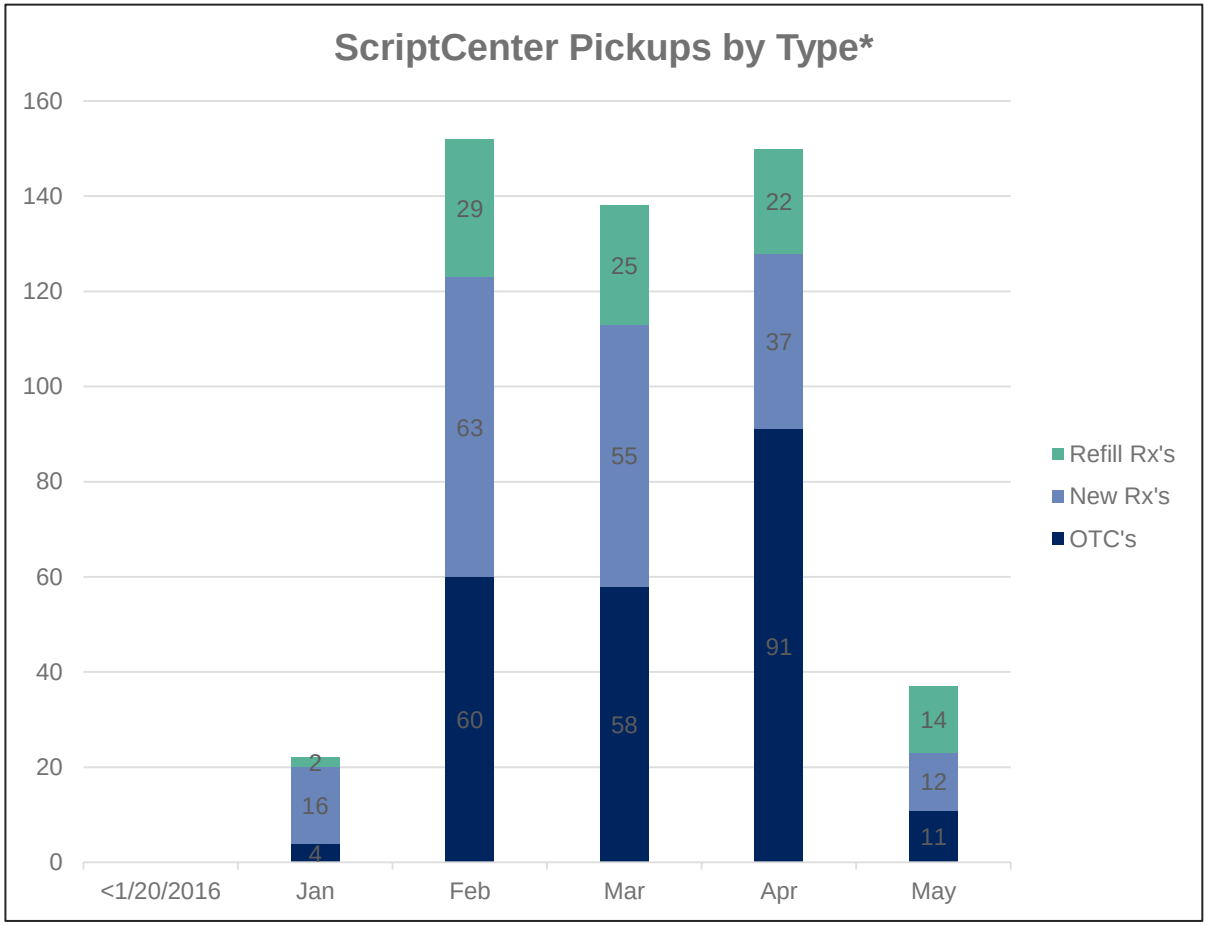
Total Campus Employees
4,820
Day Shift = 2,592
PM+ Variable = 2,228

If estimate 2 per household
= 9,640

UC San Diego
Skaggs School of Pharmacy and Pharmaceutical Sciences

ScriptCenter Kiosk Activity 1/20/16 through 5/9/16

Pick-ups by Type



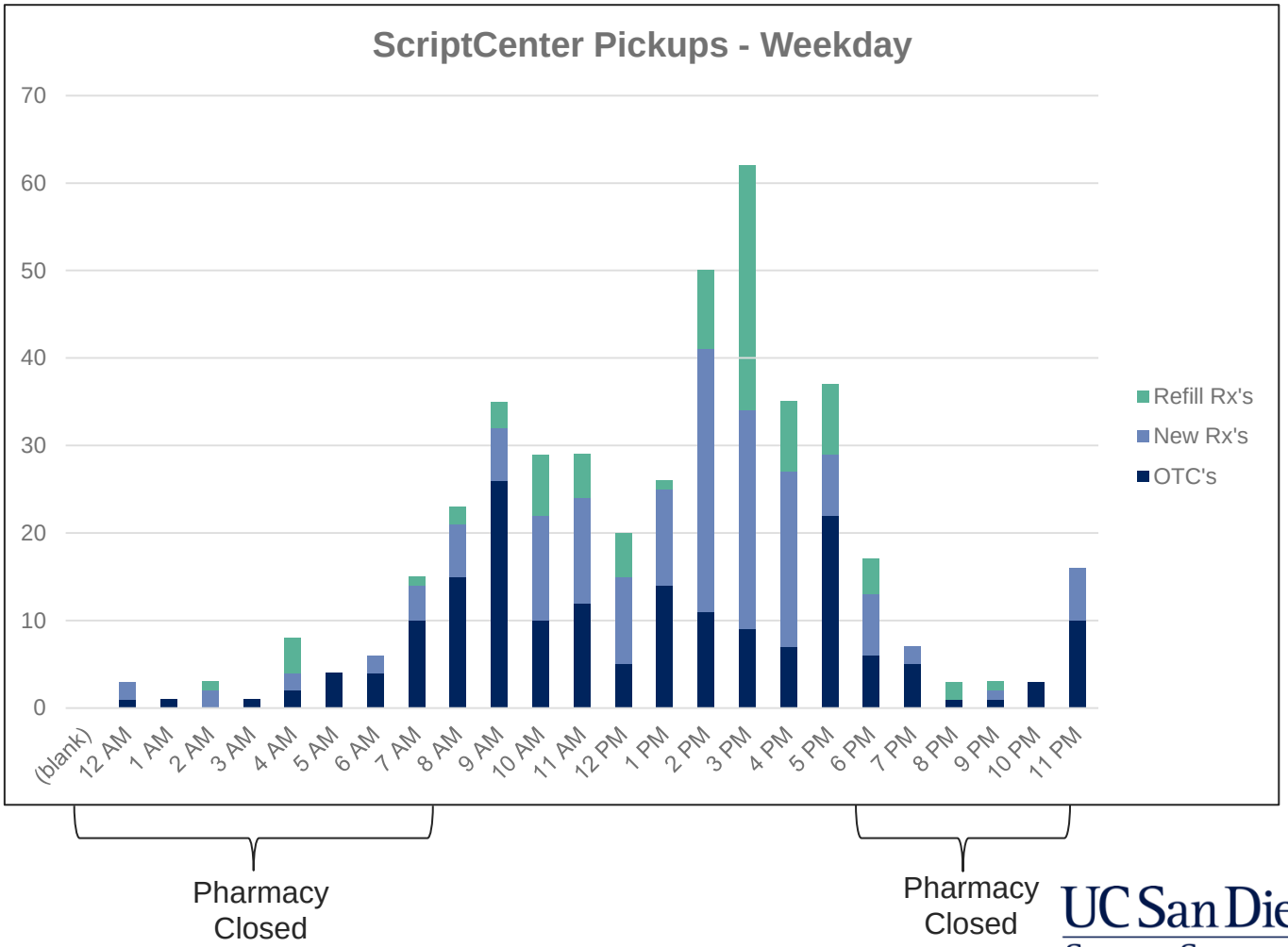
- Need 140 Rx pickups per month to hit 820 target for primary variable RTS
- If have about 80 per month need 10 months
  - Original plan was 6 months
- Requesting extension to collect March - December

Note: Higher 'new prescriptions' in the early months are due to a higher number of prescription transfers when went live. Many of these prescriptions are being turned into refills as time passes.

UC San Diego
Skaggs School of Pharmacy and Pharmaceutical Sciences

ScriptCenter Kiosk Activity 1/20/16 through 5/9/16

Pick-ups by Time Weekday



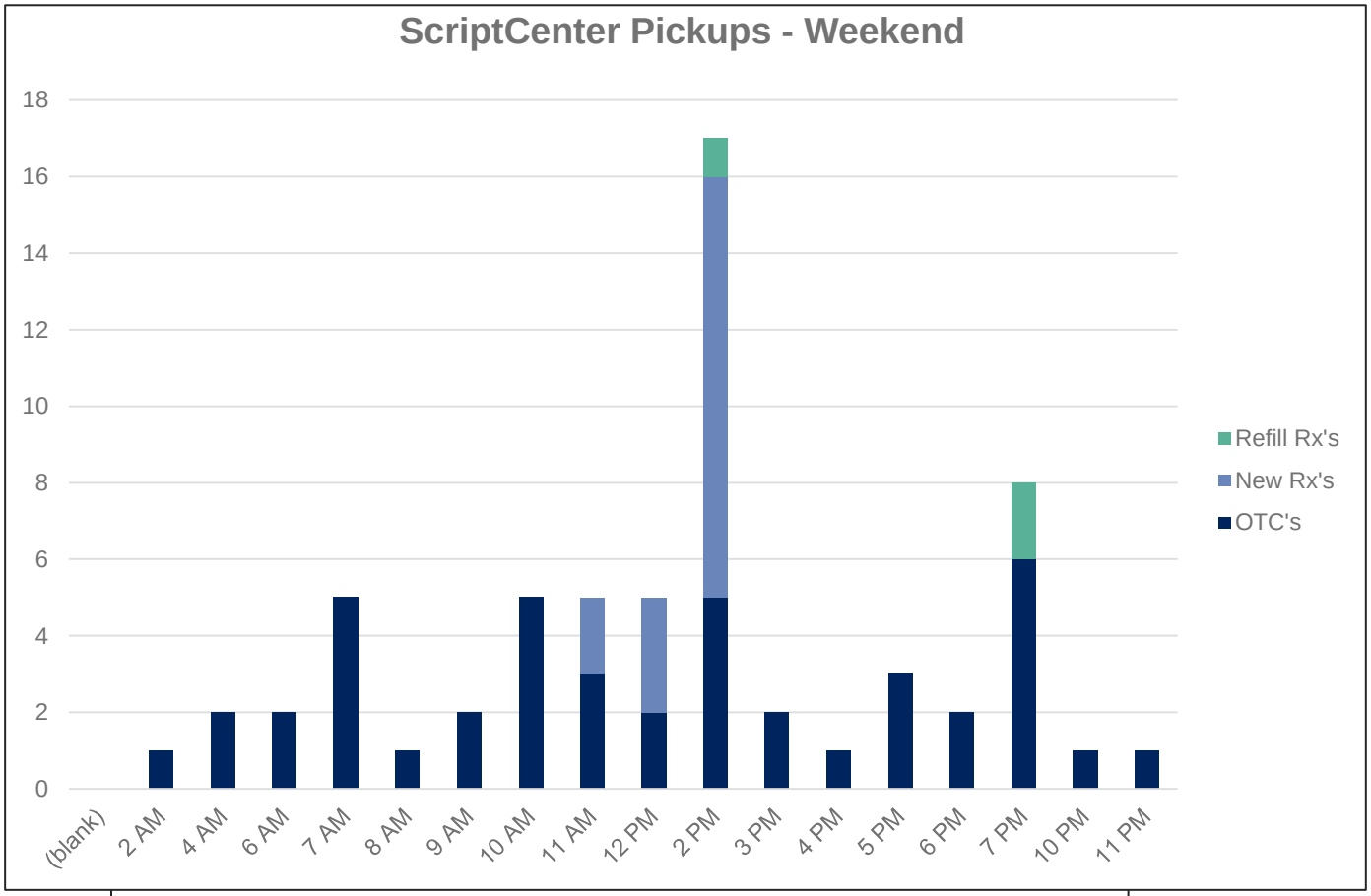
Day Shift
2,592

PM + Variable
2,228

UC San Diego
Skaggs School of Pharmacy and Pharmaceutical Sciences

ScriptCenter Kiosk Activity 1/20/16 through 5/9/16

Pick-ups by Time Weekend



Pharmacy Closed

Day Shift
2,592

PM + Variable
2,228

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ScriptCenter Kiosk
During vs. After Hours Pick-Up

524 Total Pickups

334 (64%) During pharmacy hours
190 (36%) After pharmacy hours

191 New Rx Pickups

139 (73%) During pharmacy hours
52 (27%) After pharmacy hours

99 Refill Rx Pickups

77 (78%) During pharmacy hours
22 (22%) After pharmacy hours

234 OTC Pickups

118 (50%) During pharmacy hours
116 (50%) After pharmacy hours

Day Shift 2,592

PM + Variable
2,228

Data is through noon on 5/17/16.
After hours includes weekday & weekend times pharmacy is closed.

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Study Design

Quasi-experimental with non-randomized control group

- *Pre-Kiosk Implementation Survey (Sharp Employees)*

Kiosk Start

6 months pre-kiosk
(September 2015 – February 2016)

Regular Counter

- RTS rate*

Month 1 *(March)*

Kiosk

- RTS rate
- Consultation Log
- Time to Pick-up
- Kiosk Patient Satisfaction

Regular Counter

- RTS rate*
- Consultation Log *(MAY 23rd: 1 week sample new Rxs)*
- Time to Pick-up*

Month 6
(August)

RTS = Return to Stock

* For employees and dependents

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IRB Amendment: Therapeutic Categories
Amendment Submitted

- December Enforcement Committee meeting
  - Requested to add analyses by therapeutic category

	Return to Stock Rate		Time to Pick Up		Number/Nature Questions for Pharmacist during Consultation		Patient Satisfaction
Therapeutic Category	Script Center	Regular Counter	Script Center	Regular Counter	Script Center	Regular Counter	Script Center Only
Anti-diabetics							
Anti-infectives							
Pain							
Anti-hypertensive							
Respiratory							
Mental Health							
Dermatology							
Etc.							

  - Can accomplish for “Return to Stock” and “Time to Pick Up”
  - Consultation and Satisfaction may be for multiple types of prescriptions

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Projected Study Timetable

- Q4 2015 — Pre-kiosk 6-month data collection phase begins
- Q1 2016 — Implement Kiosk device (1/20/16)
  Refine data collection tools & process
  Deployment of program/enroll patients
- Q2 & Q3 2016
  March – August — Post-kiosk implementation
  Data collection and analysis
- Q4 2016 — Report Results to Board

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Proposed REVISED Study Timetable

- Q4 2015 — Pre-kiosk 6-month data collection phase begins
- Q1 2016 — Implement Kiosk device (1/20/16)
  Refine data collection tools & process
  Deployment of program/enroll patients
- Q2 & Q4 2016
  March – December — Post-kiosk implementation
  Data collection and analysis
- Q1 2017 — Report Results to Board

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Questions?

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Code Section	Commenter	Comment
1715.65(a)	**BJ Bartleson** **CHA** **and** **Dignity Health**	"Every pharmacy, and every clinic licensed under sections 4180 or 4190, shall perform periodic reconciliation and inventory functions, defined by policy, to prevent the loss of controlled substances." California hospitals and health system pharmacies have stringent individualized standardized practices in place to prevent, detect, and mitigate controlled substance diversion. Because of the broad variability in types of facilities, and, medication administration resources, hospitals each define their individualized system in specific policies, as well as, perform periodic controlled substance inventory. All hospitals perform the required CMS biennial inventory of controlled substances and a monthly physical inventory of the respective pharmacy vault. While most hospitals have automated dispensing cabinets (ADC's), the types and utilization are variable, depending on available resources. Thus the most important aspect of this regulation should be the requirement for periodic reconciliation based on individualized hospital policy that defines the specific controlled substance procurement and administration process inventory and reconciliation process.
1715.65(a)	**Kaiser**	Section 1715.65 (a} says "Every pharmacy...". This terminology is unclear as it does not differentiate between Community/Retail, Central Fill, Mail Order and other pharmacies licensed as "PHY" pharmacies and Hospital pharmacies that are licensed as "HSP" pharmacies. It does not reflect the discussion at the Board of Pharmacy meetings that the risk and history of diversion of large of amounts of controlled substances was substantially greater by many fold from Community ("PHY") pharmacies than it has been or is likely to be from Hospital ("HSP") licensed pharmacies. This section should be modified to indicate that the regulation only applies to "PHY" licensed pharmacies or to "PHY" pharmacies and controlled substances stored centrally in "HSP" pharmacies. In hospitals only small amounts of controlled substances are stored in each patient care areas away from the pharmacy, e.g. in nursing station,surgery related suites, "crash carts", etc. Storage in patient care areas are inside very secure equipment with sophisticated access and record keeping controls,e.g. "Pyxis" and similar dispensing equipment. Cost Impact: Without a regulatory language change reflecting the differentiation specified above regarding periodic physical inventory requirements in patient care areas vs. within the hospital's pharmacy the Board's predicted cost impact of the regulation on hospitals, including State,County and municipal hospitals,substantially under stated.
1715.65(a)	**Michael Tou** **Providence Health**	"Every pharmacy, and every clinic licensed under sections 4180 or 4190, shall perform periodic reconciliation and inventory functions to prevent the loss of controlled substances."

Code Section	Commenter	Comment
1715.65(b)	**BJ Bartleson CHA** **and** **Dignity Health**	"The pharmacist-in-charge or designee, or consultant pharmacist for a clinic shall review periodic reconciliations and inventories taken, and establish and maintain secure methods to prevent losses of controlled substances. Written policies and procedures shall be developed for performing the reconciliation and inventory reports required by this section." All hospitals have standardized procedures to assign designee status in situations where they do not have direct supervision over providers. Those standardized reconciliation and inventory activities are done periodically per hospital policy.
1715.65(b)	**Michael Tou Providence Health**	"The pharmacist-in-charge or designee of a pharmacy or consultant pharmacist for a clinic shall review periodic reconciliations and inventories taken, and establish and maintain secure methods to prevent losses of controlled drugs. Written policies and procedures shall be developed for performing the reconciliation and inventory reports required by this section." Providence believes this section may also apply to unresolved orders for overrides of controlled substances. Pharmacists-in-charge are caught between end-users, such as nurses and physicians, of whom PICs do not have supervision over.
1715.65(b), (c), (e)	**Lauren Berton CVS** **Also provided at Hearing**	CVS Health maintains a perpetual inventory for all Schedule II controlled substances and also completes a physical count of these medications once a month. By maintaining the perpetual inventory, we are able to identify potential losses and investigate discrepancies on a regular basis. We strongly urge the board to consider adding language for pharmacies that maintain a perpetual inventory of Schedule II controlled substances to be deemed compliant with 1715.65(b), (c), and (e). Full reconciliations, as required by 1715.6(e) will take a substantial amount of time and focus for the pharmacist to complete by reviewing all acquisition invoices and dispensing records to determine the expected stock and then comparing to the balance on hand. Also, Pharmacists may not be able to perform cognitive services such as MTM or furnishing of hormonal contraceptives as well as experiencing difficulty to perform mandatory counseling as they will be focused on completing these reconciliations if maintaining a perpetual inventory is not deemed compliant.

Code Section	Commenter	Comment
1715.65(c)	**BJ Bartleson CHA** **and** **Dignity Health**	"Perform a Periodic Inventory: An Inventory Report of specific controlled substances at least every three months. The compilation of this Inventory Report shall require a physical count, not an estimate, of all quantities of federal Schedule II controlled substances *(within the inpatient pharmacy only if a licensed hospital) and at least one additional controlled substance which may be specified by the Board each year as based upon loss reports made to the Board in the prior year. The Inventory Report shall be dated and signed (electronic signature acceptable) by the individual(s) performing the inventory, and countersigned by the pharmacist-in-charge or consultant pharmacist." CHA agrees that periodic inspection of controlled substances in the inpatient pharmacy is necessary; in fact, hospitals routinely perform a monthly physical inventory of the inpatient pharmacy vault. Most also do "blind counts" to verify they match the total in their software systems, if computerized software tracking software systems are in place. If a physical inventory count was required of all dispensing cabinets throughout the hospital by the Inpatient Pharmacy, an undue burden of resources would be incurred. A California health care system with over 30 hospitals and 700 ADC's would need four hours of labor per machine to count all schedule II controlled substances at an annual cost of $300,000. Extrapolate that to 400 plus California hospitals and this regulation will conservatively cost over $3 million annually. The physical inventory of ADC's should be optional if organizations have explicit alternatives in place to inventory and reconcile controlled substance diversion. As discussed, this is an unnecessary financial burden, as other safeguards listed below are examples of activities implemented in hospitals that utilize ADC's e.g. blind counts, robust discrepancy resolution process, review of ADC overrides, and periodic inventory of the ADCs by nurses, etc. Hospitals deploy stringent ADC reconciliation procedures depending on the type and quantity of ADC resources, as well as available reconciliation technology.

Code Section	Commenter	Comment
1715.65(c)	**BJ Bartleson CHA** **and** **Dignity Health** **(Also provided at Hearing)**	Examples of automated dispensing cabinets (ADCs) inventory practices utilized in various facilities: • Use of biometric identification to access ADCs • Use of "blind counts" when removing controlled substances which eliminates the possibility of confirmation bias in the counting process and automatically records any discrepancies • Use of "blind counts" when restocking the ADCs • Required resolution of any controlled substance discrepancies on a daily basis by the nurses, and verification (oversight) by pharmacy that the process has been completed (including reviewing the rationale documented during the resolution process) • Physical inventory of controlled substances in the ADCs on a regular basis by the nurses utilizing "blind counts." • Daily monitoring ADC overrides to ensure there is a valid prescriber order for the medication that was removed • Regular review of oversight reports, e.g. ADC Users created; Cancelled transactions, to detect suspicious activity and prevent diversion • Use of specialized computer software (Pandora) to analyze patterns of controlled substances removal from ADCs and identify suspicious activity and/or users to prevent diversion • Perpetual inventory of all controlled substances in the pharmacy utilizing specialized computer software (C-II Safe). This software also tracks all controlled substances removed from the pharmacy and stocked in the ADCs and communicates with the ADCs to verify the controlled substances that left the pharmacy were subsequently stocked in the ADCs. • Review and approval of all Pharmacy orders for controlled substances from wholesalers/suppliers by a Pharmacy Manager • Verification by a Pharmacy Manager that all controlled substances received in the Pharmacy from a wholesaler/supplier are entered in to the specialized tracking software • Use of "blind counts" when adding and/or dispensing controlled substance from the Pharmacy inventory specialized computer tracking software As evidenced by the aforementioned numerous examples, each hospital, depending on size and resource availability must devise its individualized policy and plans for controlled substance reconciliation and inventory outside the inpatient pharmacy vault.
1715.65(c)	**Grace Magedman**	In subsection (c), it states that a physical count must be done of all Schedule II controlled substances (CS) during this quarterly inventory. In our organization, the charge nurse and another nurse witness do a weekly physical count of the CS in their automated dispensing cabinets (Pyxis). This is a blind count, so it would force a physical count of the CS. Would this suffice as part of the required quarterly physical count for the Schedule IIs stored outside of the pharmacy department when compiling information? It would also be electronically "signed" and timed/dated, as access details are typically captured when this activity occurs and could then be countersigned by the PIC after review.

Code Section	Commenter	Comment
1715.65(c)	**John Gallegos**	As the pharmacy consultant, other than verification that the DEA schedule II count is done twice daily and that there is no shrinkage involved, am I responsible for more than documenting due diligence on the part of the surgery clinic staff as a result of my quarterly audits? I generate a multi-page report every quarter that covers my responsibilities listed under surgical clinic consultant pharmacist. My question was do I have any additional responsibilities under the proposed regulation as it applies to the quarterly controlled substances audit
1715.65(c)	**John Grubbs** **UC Davis**	As worded, Subdivision (c) would require my staff to complete an inventory of all Schedule II controlled substances plus one other Schedule III-V controlled substance every three months and for me as the Pharmacist-in-Charge to sign these inventories. At my hospital we have more than two thousand (2,000) locations where Schedule 11 controlled substances are stored, including all of the automated dispensing machines. Using a conservative estimate of two minutes per location, this inventory would take at least 1 33 hours to complete.
1715.65(c)	**Kaiser**	Section 1715.65 (c) again does not differentiate between hospital pharmacies,which have much stronger controlled substance inventory control procedures than other categories of pharmacies. Thus,this section's proposed requirement for physical inventories of Schedule II and other controlled substances specified by the Board, is unclear as it does not differentiate between controlled substances maintained in the pharmacy vs.controlled substances distributed throughout the patient care areas of a hospital,as specified above. The proposed regulation would place a disproportionate burden on hospitals in relation to the history and future risk of major controlled substance diversion from hospitals vs non-hospital licensed facilities. Hospital pharmacies are also governed by the California Department of Public Health {CDPH} and inspected by CDPH for compliance with CDPH regulations and all other California and federal law, including proper accounting for and security of,controlled substances. CDPH also inspects hospitals for compliance with federal CMS Conditions of Participation. Hospitals are also accredited by several deemed status organizations, such as The Joint Commission, on behalf of government and other payers for compliance,quality and safety. Because of these standards and the standards of practice for hospitals, much more strict procedures are employed by hospitals to secure controlled substances and usually include not only daily perpetual physical inventory counts of controlled substances in patient care areas, but the majority hospitals perform such counts several times per day upon nursing shift changes.

Code Section	Commenter	Comment
1715.65(c)	**Kaiser**	Section 1715.65(c) also does not reflect the difference in preponderance of use of different non- Schedule II controlled substances between Hospital (HSP) and Community (PHY) licensed pharmacies. Hospitals administer very few controlled substances intended for symptomatic relief, such as benzodiazepines and codeine containing cough preparations than do Community pharmacies. Therefore,the substantially diminished diversion risk for such "outpatient" controlled substances should be recognized in the regulation by language that indicates that the additional non-Schedule II inventory control requirements may not apply to Hospitals, as determined by the Board.
1715.65(c)	**Kaweah Delta**	Please consider the following revisions: Remove requirement that Inventory Reports be signed and dated by the individual performing the inventory and the PIC or consultant pharmacist. Instead allow for a report showing electronic access and remove requirement for countersignature of PIC or consultant pharmacist. At Kaweah Delta Health Care District, an inventory of all controlled substances is performed at each automated drug delivery machine weekly by two registered nurses using an inventory function. Each RN accesses the ADM using their sign on and password. The ADM records the access and this acts as an electronic signature. Change time frame requirement from every 3 months to quarterly.
1715.65(c)	**Lauren Berton CVS** **Also provided at Hearing**	We also request that the board limit the additional controlled substance identified in 1715.65(c) to be inventoried to one additional controlled substance. The current language leaves this open to the board adding on an infinite number of controlled substances to be inventoried, which can become very onerous for the pharmacies to complete. Current discussion includes Alprazolam and Promethazine with Codeine as the additional controlled substances. Alprazolam has multiple strengths and a pharmacy could possibly stock more than one manufacture, so this already requires at least 5 additional medications to be included in the count. Suggested Language: (c) Perform a Periodic Inventory: A pharmacy or clinic shall compile an Inventory Report of specific controlled substances at least every three months. The compilation of this Inventory Report shall require a physical count, not an estimate, of all quantities of Schedule Ii controlled substances and at least one additional controlled substance which may be specified by the board each year as based upon loss reports made to the board in the prior year.

Code Section	Commenter	Comment
1715.65(c)	**Mary Staples** **NACDS**	In Section 1715.65, the Board seeks to require pharmacies to provide quarterly inventories of Schedule II drugs and "at least one additional controlled substance which may be specified by the board every year based upon loss reports." While we have no objection to the Schedule II drug inventories, we have concerns regarding the scope of the latter provision. More specifically, our members will have difficulty meeting the inventory requirements for non-Schedule II drugs if the state does not provide enough notice of the specific "additional controlled substances" to be inventoried or does not effectively communicate which non-Schedule II drug or drugs will require quarterly inventories. In addition to this lack of specificity in the Proposed Rule, we are concerned that this provision could be used to overburden pharmacies and their inventory capabilities. While we understand the need to curb diversion and abuse of controlled substances, we believe that overly burdensome and time consuming quarterly inventories of non-Scheduled II controlled substances hinders the ability for pharmacists to focus on other needed patient care activities. We believe and have full confidence in other mechanisms that are currently in place to monitor and inventory these substances, which ultimately allows pharmacists to devote adequate time to patient care activities such as counseling patients, performing medication therapy management, providing disease management programs, engaging in other important pharmaceutical patient care services and conferring with other health care professionals, thus permitting a higher level of service to patients that ultimately improve patient outcomes. In light of the lack of specificity discussed above and the potential for a wide scope of non-Schedule II drugs subject to inventory, we ask the Board to adopt one of the following proposals. First, and our strongest preference, is for the Board to remove the provision for "at least one additional [non-Schedule II] controlled substance" to be inventoried. Second, as an alternative, in order to prevent undue inventory burdens on pharmacies, we ask the Board to limit how many non-Schedule II controlled substances can be identified each year. As a third alternative approach, we request that, with regard to non-Schedule II drugs, only pharmacies that have reported a theft or loss of the Board identified drug be required to do the quarterly audit and to do so for only one year following the reported loss. In conclusion, at a minimum, we are asking for more parameters regarding inventories of non-Schedule II drugs and we would prefer that such drugs not be subject to quarterly inventories.
1715.65(c)	**Rita Shane** **Cedars-Sinai**	Recommendation: Revise proposed regulations to: "Perform a Periodic Inventory: A pharmacy or clinic shall compile an Inventory Report of specific controlled substances at least every three months. The compilation of this Inventory Report shall require a physical count, not an estimate, of all quantities of federal Schedule II controlled substances and at least one additional controlled substance which may be specified by the board each year as based upon loss reports made to the board in the prior year. The Inventory Report shall be dated and signed by the individual(s) performing the inventory, and countersigned by the pharmacist-in-charge or consultant pharmacist. Alternatively, a pharmacy or clinic may utilize automated drug delivery systems in lieu of performing a periodic inventory." As defined under 4186 (h), automated drug delivery systems (ADDs) collect, control and maintain all transaction information to accurately track the movement of drugs into and out of the system for security, accuracy, and accountability. Since ADDs provide perpetual inventory of controlled substances, pharmacies should be allowed to utilize these systems to fulfill the requirements of the proposed regulation.

Code Section	Commenter	Comment
1715.65(c)(1)	**Grace Magedman**	In regards to subdivision (c)(1) and (e), will electronic copies of the signed CS inventory report as well as other records used in reconciliation be acceptable? It would be much more readily retrievable and it would cut down on the costs of increasing document storage requirements and retrieval.
1715.65(c)(1)	**Kaiser**	Section 1715.65 (c) (1) regarding record retention for "three years" "in the...pharmacy" without mention of the current ability for pharmacies to store records outside the pharmacy on the premises, and, with the Board's permission, offsite for the balance ofthe three years is vague and confusing. Historical storage of such records as allowed outside a hospital or community pharmacy space has not been discussed by the Board as being a significant problem or risk that would justify the additional space allocation and expense for storage inside the pharmacy.
1715.65(c)(1)	**Michael Tou Providence Health**	Providence requests clarification from the Board as to whether records can be stored off-site for licensed facilities that inventory more frequently than every 90 days.
1715.65(c)(2)(A)	**Lauren Berton CVS** **Also provided at Hearing**	Current proposed language in 1715.65(c)(2)(A) indicates that the biennial inventory of controlled substances required by federal law may serve as one of the periodic inventories, provided that a physical count of all controlled substances is performed. This is more stringent than DEA regulation 21 CFR 1304.11(e)(6)(i) and (ii) which allows for a registrant to estimate Schedule III to V, unless the container holds more than 1,000 tablets or capsules. We request that the board clarify this section that requires only an exact physical count for the additional controlled substance identified by the board as opposed to all controlled substances. Suggested Language: (A) A physical count of controlled substances in Schedule II and the additional controlled substance identified by the board to be inventoried periodically is performed, with an estimated count of all other Schedule III to V controlled substances as allowed by 21 CFR 1304.11.
1715.65(d)	**Kaiser**	Section 1715.65 (d) is vague as it does not reflect whether the requirement for a "new pharmacist-in-charge" to complete and inventory applies to an "interim pharmacist-in-charge", as specified in B&P Code section 4113(e). Further, for hospitals, is the required physical count limited to only what is stored inside the hospital pharmacy. Again, if the physical inventory is required for every patient care area storage unit,the burden is understated.

Code Section	Commenter	Comment
1715.65(e)	**BJ Bartleson CHA** **and** **Dignity Health**	"Reconciliation with Inventory Report: The pharmacy or clinic shall review, based on policy, all acquisitions and dispositions of controlled substances as part of the inventory process (within other inpatient pharmacy only if a licensed hospital or clinic) as part of the inventory process to determine the expected stock of each controlled substance on hand, based on the prior Inventory Report. Records used to compile each reconciliation shall be maintained in the pharmacy or clinic for at least three years in a readily retrievable form." As per section 1715.65(c), CHA proposes this regulation apply only to inpatient pharmacies of a licensed hospital, and allow individualized reconciliation and inventory policies be applied to hospitals that utilize ADC's or other mechanisms for narcotic administrative practice. If a physical inventory count was required of all dispensing cabinets throughout the hospital by the inpatient pharmacy, an undue burden of resources would be incurred. This is unnecessary as other individualized stringent safeguards are implemented, such as, blind counts; robust discrepancy resolution process, review of ADC overrides, periodic inventory of the ADCs by nurses, etc. (See more specific examples in section 1715.65(c).
1715.65(e)	**John Grubbs UC Davis**	Subdivision (e) requires reconciliation between the on-hand inventory and all acquisitions and dispositions of controlled substances. At my hospital, we dispense approximately 50,000 CII doses per month. In addition, we perform approximately 5,000 refills. It would be difficult to estimate the time required to reconcile the acquisitions and dispenses against the inventory, but it's likely to be at least a full time job.
1715.65(e)	**Kaiser**	Section 1715.65 (e) is vague or incomplete because it does not reflect the discussion by staff and Board members of the problem found that reconciliation processes were not well understood by pharmacists. Further it does not reflect the Board's discussion that reconciliation should and be performed against Accounts Payable records rather than just relying on packing lists or invoices to determine what the actual total amounts of a controlled substances acquired by the pharmacy during the starting and ending physical count period. The Board's discussion indicated the entity (pharmacy or hospital) would be held responsible for what was "paid for" (or otherwise acquired) not just what was listed on packing lists or invoices that reached the pharmacist-in-charge.
1715.65(e)	**Michael Tou Providence Health**	Providence requests clarification from the Board on the following issues: Does this requirement take into account stock fluctuations based on demand, as well as facilities that ramp up purchases due to anticipated shortages? Does the language need to specify that this inventory report is meant to determine expected stock on hand? If the stock on hand has doubled for a legitimate reason, does it conflict with the proposed requirement?

Code Section	Commenter	Comment
1715.65(e)	**Rita Shane** **Cedars-Sinai**	Recommendation Revise proposed regulations to add: "Alternatively, organizations may use Automated Drug Delivery systems (ADDs) to perform ongoing perpetual inventory of all controlled medications that includes reconciliation of acquisitions and dispositions. Comments: As defined under 4186 (h),automated drug delivery (ADDs) systems collect,control and maintain all transaction information to accurately track the movement of drugs into and out of the system for security,accuracy, and accountability. Organizations which utilize these systems perform reconciliation on an ongoing basis which meets the intent of this section and therefore should be included in the regulations as recommended above.
1715.65(e)(2)	**Michael Tou** **Providence Health**	Providence requests clarification from the Board on the following issues: Should overages be documented in the inventory report? Does this require dual- signature by the pharmacist- in-charge and another licensed pharmacist/technician?
1715.65(e)(3)	**BJ Bartleson** **CHA** **and** **Dignity Health**	"Should the reconciliation identify controlled substances which had been in the inventory of the pharmacy or clinic during the prior six-month period, but for which there is no stock at the time of the physical count, and, if the pharmacist-in-charge or consultant pharmacist determines there has been a loss of these controlled substances, then the losses shall be reported in the manner specified by paragraph 1." Suggestions for language clarification
1715.65(e)(3)	**Kaweah Delta**	Please consider the following revision: Should the reconciliation identify controlled substances which had been in the inventory of the pharmacy or clinic during the prior six-month period, but for which there is no stock at the time of the physical count, and there is no matching disposition, the pharmacist-in-charge or consultant pharmacist shall determine there has been a loss of these controlled substances.
1715.65(e)(3)	**Michael Tou** **Providence Health**	"Should the reconciliation identify controlled substances which had been in the inventory of the pharmacy or clinic during the prior six-month period, but for which there is no stock at the time of the physical count, and, if the pharmacist-in-charge or consultant pharmacist determines there has been a loss of these controlled substances, then the losses shall be reported in the manner specified by paragraph 1."

Code Section	Commenter	Comment
1715.65(g)	**BJ Bartleson CHA** **and** **Dignity Health**	Language clarification and change of 14 to 30 days per title 16, Division 17 section 1715.6, Reporting Drug Loss California regulations currently require pharmacies to report loss associated with pharmacy personnel within 14 days. All other losses are required to be reported to the board within 30 days. ADC's located in hospital or nursing home would be more susceptible to losses associated with nursing or medical personnel, more so than pharmacy personnel. This is because nursing and medical personnel access the machines on a more frequent basis than pharmacists who restock or replenish the supply. The actions of the non-pharmacy personnel are not under the direct supervision of the pharmacist or the pharmacist in charge. It may take greater than 14 days upon discovery of an inappropriate access or removal to perform an appropriate inquiry or investigation. It may be discovered that the access or removal was not actually "inappropriate" and over reporting could occur in an effort to meet the 14 day time period. CHA suggest changing the time frame to 30 days as allowed for an actual irreconcilable loss of controlled drugs as presently in regulations.
1715.65(g)	**Candace Fong (Hearing)**	Allow the pharmacist-in-charge to delegate the reconciliation and inventory.
1715.65(g)	**Dale Costantino**	I would like to comment on the proposed changes to 1715.65. My comments are specific to paragraph "g' below. Hundreds and sometimes thousands of doses of controlled substances are removed from automated drug delivery systems daily at many California hospitals for patients administration. This obligation to review each record would be overwhelming if not impossible. One person, a PIC in this case, may be able to review approximately 50 records a day. (g) The pharmacist-in-charge of a hospital pharmacy or of a pharmacy servicing skilled nursing homes where an automated drug delivery system is in use shall review at least once each month all controlled substances removed from or added into each automated drug delivery machine operated by the pharmacy. I believe that oversight and audits are needed. However, please consider revising this proposed text.

Code Section	Commenter	Comment
1715.65(g)	**John Grubbs UC Davis**	Subd ivision (g) requires monthly reviews of all removals and additions of controlled substances to automated drug delivery systems and investigation and reporting of unusual accesses or discrepancies. Does this review supersede the inventory and reconciliation requirements of Subdivisions (c) and (e)? Also, what would constitute acceptable proof of this review? I suggest that the Board allow hospitals utilizing automated drug delivery systems to implement alternative processes to identify and prevent controlled substance diversion. Some examples of such processes would include monthly analysis of staff who are removing more controlled substances than their peers, daily investigation of all discrepancies in the inventories of controlled substances, and review of all removals of controlled substances that were made on "override" (ie emergent situation when physician 's order has not been verified by pharmacist) to ensure the remova l is appropriate. All inappropriate accesses or removals identified by these processes would be reported to the Board. Additionally, some hospitals have formed multi-disciplinary commi ttees charged with reviewing all audits of controlled substance use, for overseeing investigations into potentially inappropriate use, for ensuring appropriate reporting when theft or diversion has occurred and for implementing changes to prevent future occurrences. This would be another alternative process that hospitals could use instead of the requirements of Subdivisions (c) and (e). I feel that the alternative processes that I 've described above would be much more effective at preventing controlled substance diversion than the requirements of Subdivision (c) and (e). Hospitals that implement such alternative processes should not be subject to these new requ irements. The language in Subdivision (g) should be modified to allow for such alternative processes and should specify that hospitals that have these processes in place are exempt from the requirements of Subdivisions (c) and (e)
1715.65(g)	**Kaiser**	Section 1715.65 (g) is vague as it applies to hospital pharmacies in that it uses a term "review" for the duties of the pharmacist-in-charge regarding records of controlled substances "removed from or added into each automated drug delivery machine". It is unclear:1)because it is not clear whether this monthly task could serve as substitute for the tri-monthly physical inventory and reconciliation of such controlled substance in such secure storage devices as is implied by Sections 1715.65 (a)&(c) above,2) because it is not clear whether the reporting of "inappropriately accessed or removed" means would only be required if the removal resulted in a "loss" or diversion from the hospital,and 3) how this reporting responsibility corresponds to reporting a loss within 30 days in Regulation 1715.6. Allow the pharmacist to delegate to another staff person the inventory requirement.

Code Section	Commenter	Comment
1715.65(g)	**Kaweah Delta**	The text as proposed seems to imply that the pharmacist-in-charge would be required to review all transactions, including removal for a specific patient need, from every automated drug delivery machine. A more effective method to identify diversion would be the use of software to identify anomalous activity. Please consider softening the language to allow for the use of software to identify anomalous activity and change the requirement to state that the pharmacist-in-charge shall review any activity determined to be anomalous. Please consider clarifying if there is required documentation for the review that was performed. Additionally, please consider the following revision: Controlled drugs inappropriately accessed or removed from the automated delivery shall be reported to the Board within 14 days of discovery. If the pharmacist-in charge is reviewing controlled substances removed from or added to each automated drug delivery machine monthly, it is possible that inappropriately accessed or removed medication would not be discovered within 14 days of access or removal. This would place the pharmacy immediately out of compliance.
1715.65(g)	**Lauren Berton CVS (Hearing)**	Allow some delegation of the inventory review and investigation of automated delivery systems. Is quarterly review mandatory of the machines.
1715.65(g)	**Michael Tou Providence Health**	"The pharmacist-in-charge of a hospital pharmacy or of a pharmacy servicing skilled nursing homes where an automated drug delivery system is in use shall review at least once each month all controlled substances removed from or added into each automated drug delivery machine system operated by the pharmacy. Any discrepancy or unusual access identified shall be investigated. Controlled drugs inappropriately accessed or removed from the automated delivery drug system shall be reported to the Board within 14 30 days." California regulations currently require pharmacies to report losses associated with pharmacy personnel within 14 days. All other losses are required to be reported to the board within 30 days. Automated Dispensing Systems (ADS), which are located in a hospital or nursing home, would be more susceptible to losses associated with nursing or medical personnel, more so than pharmacy personnel. Nursing and medical personnel access the machines to remove doses of controlled substances on a more frequent basis than the pharmacy personnel, who access the inventory to restock or replenish the supply. Additionally as the actions of these non-pharmacy personnel are not under the direct supervision of the pharmacy or pharmacist-in-charge, it may take greater than 14 days upon discovery of an inappropriate access or removal to perform an appropriate inquiry or investigation. Many occurrences may be resolved satisfactorily upon investigation. It may be discovered that the access or removal was not actually "inappropriate" after all.

Code Section	Commenter	Comment
1715.65(g)	**Michael Tou** **Providence Health**	The timeframe required by the Board should allow sufficient time for investigation first, and then, unresolved inappropriate access or removals should be reported. Pharmacies are being prompted to report every discrepancy to the Board prior to performing a diligent investigation in order to make that 14-day time period. This could create over-reporting and difficulty identifying actual events versus miscounts and typographical errors. The timeframe of 14 days for an inappropriate access or removal does not seem proportionate to the 30-day timeframe allowed for an actual irreconcilable loss of controlled drugs, as stated in Section 1715.65(h). Providence urges the Board to provide further clarification as to the definition of “inappropriately access or removed” in the proposed rule. Errors on the patient’s medication record may not be the result of an actual loss or diversion. Providence requests clarification from the Board as to how it plans to take action against non-pharmacy personnel associated with a reported loss or discrepancy. Has the Board engaged with the Medical Board of California and Board of Registered Nursing on the proposed rule to ensure effective compliance with the requirements across disciplines?
1715.65(g)	**Rita Shane** **Cedars-Sinai**	Recommendations: Revise proposed regulations as follows: "The pharmacist-incharge of a hospital pharmacy or of a pharmacy servicing skilled nursing homes where automated drug delivery systems (ADDs) are used shall ensure that: a) All controlled substances added to an automated drug delivery system are accounted for; b) Access to automated drug delivery systems is limited to authorized facility personnel; c) An ongoing evaluation of discrepancies or unusual access associated with controlled substances is performed; and d) Confirmed losses of controlled substances are reported to the board." Comments: 1. The intent of the proposed regulations is to identify losses of controlled substances. Performing a monthly review of all controlled substances removed from or added into each automated drug delivery machine operated by the pharmacy will not meet this goal. Having policies in place to ensure effective use of ADDs and leveraging the capabilities of these systems to identify discrepancies/unusual access and investigating them in real time allow pharmacies to identify and follow up on discrepancies or unusual access. Of note, larger institutions such as Cedars Sinai Medical Center add and remove approximately 80,000 controlled substance doses each month. 2. Inappropriate access or removal of controlled substances does not always result in loss of controlled substances. A thorough investigation needs to be performed to confirm loss of controlled medications before reports are submitted to the board. This will minimize the number offalse positive reports submitted to the board and provide a more accurate estimate of the number of controlled substances lost due to employee pilferage.

Code Section	Commenter	Comment
1715.65(g)	**William Mcguire**	I am writing to ask for clarification on Ca. code of Regulations in section 1715.65(g) and also some comments. According to the proposed regulation, it states either the PIC or pharmacy consultant shall review at least once a month all controlled substances removed or added to the ADC. Questions; a. Can this function be delegated to another pharmacist or than the PIC or consultant pharmacist-like an assistant Mgr or lead pharmacist? Seems very onerous. b. Is this rule only for institutions with ADC's? It clearly states for those sites with ADC's so does that mean it is not mandatory for non-automated sites? If not mandated for non-automated sites-why? There are more chances of diversion without automation.
1715.65(h)	**BJ Bartleson CHA** **and** **Dignity Health**	Strike," including installation of cameras, relocation of the controlled drugs to a more secure location within the pharmacy, or daily inventory counts of the drugs where shortages are continuing", and replace with "take additional steps to improve the security of the controlled substances to prevent losses". Hospitals need to have flexibility in what resources are used to address narcotic loss.
1715.65(h)	**Kaiser**	Section is vague as it does not indicate which action or actions have priority. The installation of cameras is mentioned first and seems to indicate that should be tried first before the "relocation of the controlled substance to a more secure location" or the implementation of "daily inventory counts". It is likely that the delay for the camera installation and the capture of good identification may result in further significant or substantial losses/diversions. Conversely, the implementation of a storage change or additional physical counts may alert the individual or individuals to the hospital's or pharmacy's awareness of the losses and thus prevent the identification of the individuals responsible for,or the methods employed, that resulted in the loss. The Board should provide guidance as to which is more important - apprehending the responsible individual{s) or protecting the public and patients immediately from further diversion. The Board's guidance has not been consistent on this point historically. Perhaps the Board's guidance on this point could be related to the US Drug Enforcement Administration's (DEA) multi-faceted guidance on when a loss is considered "significant" for reporting.
1715.65(h)	**Michael Tou Providence Health**	"A pharmacy or clinic identifying losses of controlled drugs but unable to identify the cause within 30 days shall take additional steps to identify the origin of the losses, including installation of cameras, relocation of the controlled drugs to a more secure location within the pharmacy, or daily inventory counts of the drugs where shortages are continuing, until the cause is identified and resolved."

Code Section	Commenter	Comment
1715.65(h)	**Rita Shane Cedars-Sinai**	Recommendation: Revise proposed regulations to: "A pharmacy or clinic identifying losses of controlled drugs but unable to identify the cause within 30 days shall take additional steps to identify the origin of the losses, which may include installation of cameras, relocation of the controlled drugs to a more secure location within the pharmacy, or daily inventory counts of the drugs where shortages are continuing. Comments: The pharmacist- in- charge should evaluate and determine which strategy will prevent further loss of controlled medications .
Overall	**Chad Signorelli**	Is there an allowance or exception allowed for those facilities that keep the entirety of their C-II inventory stock in perpetual inventory machines? In our facility, our C-II stock is in either the Pyxis C-II Safe or a Pyxis ADM with “Blind Count On” thereby allowing an inventory count to be completed every time the medication is removed. If counts are not correct there is an immediate discrepancy created that must be followed up on and acted upon. We therefore inventory our medications much more frequently than every 3 months and asking us to physically inventory the stock every 3 months would be unnecessary and unneeded. I can understand the importance of this process in non-perpetual inventory locations but do not see the need in a location such as ours.
Overall	**Hilary Ward**	Our humble opinion from Tahoe Forest is that increasing the frequency of narcotic inventory audits is not going to deter diversion effectively. Counts may be off for any number of reasons which are infrequently diversion, yet a diverter can operate in many ways that would never be detected by just looking at inventory counts. If the Board truly feels more frequent inventory audits will be beneficial, we believe doing every 6 month counts would be operationally feasible, but every 3 months is just excessive.

Code Section	Commenter	Comment
Overall	**Jeremish Joson**	This is another "reactive" action by the Board that does not solve the problem but further burdens already burdened pharmacists and their staff. This has happened with the New England Compounding Center debacle; the Board became overzealous with their regulations to the point that mixing three ingredients to make Magic Mouthwash was considered compounding. This level of bureaucratic insanity does nothing to protect the public (please, explain to me how preventing me from mixing 3 ingredients and letting the patient do it themselves is supposed to protect them) but only further complicates an already complicated and stressed profession. For one, opioids are just one class of abused prescription drugs (http://www.pdmpexcellence.org/drug-abuse-epidemic). According to the PDMP Center of Excellence, the "rise in the misuse and abuse of prescription drugs, opiates in particular, has been attributed to their increased availability over the last decade, a result of increased prescribing." Many deaths are due to heroin, due to its low cost, easy availability, and the fact that it can be smoked or snorted. Compounding the profession with excessive, ineffective regulations will only lead to increased robberies, threatening our livelihoods, as is also referenced by the PDMP. According to Okie, NEJM 2010, "more than 40% of opioid prescriptions are written by general or family practitioners, osteopaths or internists..." As studies by the State Departments of Health for Florida, Kentucky, and Ohio have shown, the vast majority of deaths were due to pain clinic over prescribing and oxycodone. When Kentucky and Florida decided to go after these "pill mills," their death rates were reduced drastically. They also increased drug abuse programs. Dr. Frieden of the CDC, published a report in 2014 stating that the drug abuse epidemic is caused largely by prescribers. His study, along with an LA Times investigation, showed that physician prescribing was a key contributor to the crisis of addiction (http://www.latimes.com/local/la-me-rx-source-20140304-story.html#axzz2v0MEW9Sh). Why are we asked to count all our Schedule II medications every three months when we are, by law, required to keep a perpetual inventory maintained daily? Furthermore, we are required to have policies & procedures in place addressing diversion. Furthermore, we are required to report theft or loss to the Board as well as the DEA via form 106. This is another attempt by the Board to "brown nose" the public, to put on a performance so as to assure them that it is doing everything in its power to protect the public from the drug epidemic, when in fact, it is just forcing its pharmacists to exercise futile maneuvers and to collect payment from them for "gotcha" non-compliance. Drug diversion within pharmacies is already well regulated and plays a minor part in the overall scheme of drug overdose deaths. As mentioned in many reports and studies (something the Board should undertake before jumping to conclusive actions), the greatest problem to the epidemic is PHYSICIAN PRESCRIBING.

Code Section	Commenter	Comment
Overall	**Jeremish Joson**	Thanks to the Board, and case law, State of California v. Thang Tran, pharmacists are already burdened with filling controlled substances, checking CURES, and acting as gate-keepers, fighting with patients and sometimes their prescribers. The burden of liability rests solely on pharmacists and nothing is being done to address the real problem, physician over-prescribing and/or inappropriate prescribing. This has opened up more paperwork, time spent filling prescriptions, hostility from patients toward pharmacists, and as has been already reported, increased gun-point robberies. Physicians should be required to staple a current CURES report with each opioid prescription they write before a patient leaves their office. It is my professional opinion that if the Board truly believes that the "protection of the public shall be the highest priority," it would work with the California Medical Association, CDPH, and the State DEA to conduct a study and set forth recommendations as did the states of Florida, Kentucky, Ohio, and Tennessee, all of whom were successful in reducing drug deaths. As a matter of fact, none of those states required their pharmacists to count their Schedule II prescriptions every 3 months. Also, counting every Schedule II (e.g., Adderall, Concerta, Vyvanse, Duragesic), a vast majority of which are not implicated in the epidemic, is another waste of time and energy. In addition, the Board should remove penalties of any kind for the self-reporting of controlled substance losses unless those losses were deemed intentional or have already been addressed in a previous infraction. Getting pharmacists and pharmacies to feel more comfortable with reporting diversion requires removing punishment the Board hands out to its pharmacists-in-charge. As has been known for a long time by the Institutes of Medicine, medication error reporting dramatically increases when employees know that no punitive action will be taken against them (https://www.ismp.org/Tools/whitepapers/concept.asp). It is ridiculous for the Board to make examples of its pharmacists and it does not help in the protection of the public, much like medication underreporting does not either. In summary: 1. No, do not require a Schedule II inventory every 3 months with more burdensome paperwork to fill out 2. Understand the true nature of the problem before creating a useless, ill-advised regulation that does not protect the public or address the problem. Create a taskforce with other key-institutions and come up with real solutions. 3. Physicians should be required to print a current CURES report and attach it to any controlled substance prescription they write 4. Codify that pharmacists-in-charge will not be punished by the Board for any reports of diversion or missing pills, within reason

Code Section	Commenter	Comment
Overall	**K. Scott Guess**	The need for a CS inventory monitoring system has been clearly demonstrated by the numbers of lost drug being reported. However, I feel this regulatory requirement will be too stringent, too time consuming, and too overly burdensome to the practice pharmacy, as well as for the Board. Surely the Board does not have the resources to account for every 'lost' tablet in the state? This level of accounting will require the documentation of every dropped pill, every broken tablet found in every bottle, and every over or under fill by a manufacturer. Diversion by internal theft in the retail or outpatient setting does not generally happen in counts of 1-10, but by the bottle, counts of 100, 500 or 1000. The institutional setting is quite different. That setting can and does loose full bottles as well as single doses to internal theft; setting tighter CS inventory controls may be necessary in the institutional setting. I will respectfully disagree with the Board's financial impact assessment. A full CS physical count using estimated values for C3-5 (as permitted by current rules) is roughly a 3-hour process at my stores. A full manual count of C-2 drugs is also a 3-hour project. Collating that data and comparing it to purchase data can take 10-15 hours. This is a sensitive job and should only be done by the PIC or owner, 13 hours of PIC labor will minimally cost the pharmacy $1200 in total payroll costs. In our current economic environment with ever-dwindling profit margins and third party reimbursements this is level of scrutiny and labor investment is not cost efficient. For general retail pharmacy a simple In-Out audit is all that is necessary. Compare monthly purchases to monthly dispensing; then look for the discrepancies that are greater than 1 package size (100, 500, 1000) for further research and documentation.
Overall	**K. Scott Guess**	A much more efficient mechanism, and just as capable of detecting diversion, if not more so would be: • Collect purchase data reports directly from the vendor either as a printed or downloaded report. Do not use invoices; the diverter can destroy invoices. • Collect sales data directly from the pharmacy software system. • Compare line items sorted by NDC number (more exacting than drug name). o If the difference is greater than 1 package size, documenting the on-hand inventory should balance the equation. o If not then a more exacting count and audit process is needed. • Mandating the use of a perpetual inventory for C-2 drugs is another tool that can be employed to catch inventory discrepancies in timely manner. It is well documented in the press, Board posted accusations and actions, and Law enforcement investigations the internal retail pharmacy diversion involves full bottles, not random hands full of drug. The full inventories for PIC change must remain as a hard data point for the staffing change. The Biennial inventory is mandated by Federal regulation and currently accepts count estimates for schedules C III-V for packages of 1000 or less. Retail and institutional pharmacy are vastly different, with different inventory management systems and needs. The above comments are directed towards the retail setting. As the practice of pharmacy becomes more and more specialized it is not unreasonable to develop separated inventory monitoring programs for retail (including institutional out patient) and institutional (inpatient) settings. Furthermore this regulation MUST apply to EVERY pharmacy licensed by the California Board of Pharmacy, hospital inpatient, retail (including institutional out-patient), LTC, central fill, and mail order (in or out of state). The Board can fulfill their mission of protecting the public without burdening the practice of pharmacy with down-to-the-tablet accounting.

Code Section	Commenter	Comment
Overall	**Kaiser Doug O'Brien (Hearing)**	Large losses unusual in California because of oversight by the Board and CDPH. Lots of controls in Hospitals with automated dispensing machines. Realtime discrepancy detection, blind counts, biometric ID access, and tracers. Hospitals have the tightest controls in California. Hospitals experience little loss of controlled substances. Target outpatient / community pharmacies as that is where most of the drug loss occurs. This regulation will not improve oversight in Hospitals. Do a Risk Based Approach.
Overall	**Robert Shmaeff Joyce E. Keefer Med Center**	I am the Director of Pharmacy Services of a hospital pharmacy providing services to 239 skilled nursing beds and 10 gero-psychiatric beds. The pharmacy employs two pharmacists, two technicians and a biller. During my tenure of over eight years we have not had a loss of any controlled substance. It is my belief that hospital pharmacies do not contribute significantly to the diversion problem. Mandating four controlled inventories annually would be over kill. The inventory process here is time consuming and would result in a waste of resources. It is my considered opinion that four controlled substance inventories per year is not necessary. Thank you for your consideration
Overall	**Terry Cater**	I am commenting on the proposed adoption of Section 1715.65 of Article 2 of Division 17 of Title 16 of the CCR (requirements for reconciliation and inventory of controlled substances) which, among other requirements, would require pharmacies to perform a physical inventory count of all Schedule II controlled substances every 3 months. This proposed regulation does not increase the protection of the public. It may actually take away from the public safety. This is one more non-patient centered activity that takes pharmacist's time and attention away from patient medication safety. The DEA currently requires a complete CS inventory every two years. The State of California regulations should either "mirror" the federal requirement or consider amending the current proposal from taking an inventory every three months to once a year.

Title 16. Board of Pharmacy
Proposed Text

Adopt section 1715.65 in Article 2 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1715.65. Reconciliation and Inventory Report of Controlled Substances

(a) Every pharmacy, and every clinic licensed under sections 4180 or 4190, shall perform reconciliation and inventory functions to prevent the loss of controlled substances.
(b) The pharmacist-in-charge of a pharmacy or consultant pharmacist for a clinic shall review all reconciliations and inventories taken, and establish and maintain secure methods to prevent losses of controlled drugs. Written policies and procedures shall be developed for performing the reconciliation and inventory reports required by this section.
(c) Perform a Periodic Inventory: A pharmacy or clinic shall compile an Inventory Report of specific controlled substances at least every three months. The compilation of this Inventory Report shall require a physical count, not an estimate, of all quantities of federal Schedule II controlled substances and at least one additional controlled substance which may be specified by the board each year as based upon loss reports made to the board in the prior year. The Inventory Report shall be dated and signed by the individual(s) performing the inventory, and countersigned by the pharmacist-in-charge or consultant pharmacist.
    (1) The original or copy of the signed controlled substances Inventory Report shall be kept in the pharmacy or clinic and be readily retrievable for three years.
    (2) The biennial inventory of controlled substances required by federal law may serve as one of the mandated inventories under this section in the year where the federal biennial inventory is performed, provided:
        (A) A physical count of all controlled substances is performed, not an estimated count of how much medication is in a container.
        (B) The federal Drug Enforcement Administration biennial inventory was taken no more than three months from the last inventory required by this section.
(d) A new pharmacist-in-charge of the pharmacy shall complete an inventory as required by subdivision (c) within 30 days of becoming pharmacist-in-charge. Whenever possible an outgoing pharmacist-in-charge should complete an inventory as required in subdivision (c).
(e) Reconciliation with Inventory Report: The pharmacy or clinic shall review all acquisitions and dispositions of controlled substances as part of the inventory process to determine the expected stock of each controlled substance on hand, based on the prior Inventory Report. Records used to compile each reconciliation shall be maintained in the pharmacy or clinic for at least three years in a readily retrievable form.
    (1) Losses shall be identified in writing and reported to the board and, when appropriate, to the Drug Enforcement Administration.
    (2) Likely causes of overages shall be identified in writing and retained.

(3) Should the reconciliation identify controlled substances which had been in the inventory of the pharmacy or clinic during the prior six-month period, but for which there is no stock at the time of the physical count, the pharmacist-in-charge or consultant pharmacist shall determine there has been a loss of these controlled substances. These losses shall be reported in the manner specified by paragraph 1.

(f) Adjustments to the Inventory Report shall be made following reconciliation, only after the reporting and documenting of any losses or accounting made for overages.
   (1) Each adjustment to the Inventory Report made to correct the stock on hand count shall be annotated to show any adjustment in the number of controlled substances on hand in the pharmacy or clinic, and who made the annotation, and the date.
   (2) The pharmacist-in-charge or consultant pharmacist shall countersign the adjusted Inventory Report.
   (3) The original Inventory Report and amended Inventory Report following reconciliation shall be readily retrievable in the pharmacy or clinic for three years.

(g) The pharmacist-in-charge of a hospital pharmacy or of a pharmacy servicing skilled nursing homes where an automated drug delivery system is in use shall review at least once each month all controlled substances removed from or added into each automated drug delivery machine operated by the pharmacy. Any discrepancy or unusual access identified shall be investigated. Controlled drugs inappropriately accessed or removed from the automated delivery shall be reported to the board within 14 days.

(h) A pharmacy or clinic identifying losses of controlled drugs but unable to identify the cause within 30 days shall take additional steps to identify the origin of the losses, including installation of cameras, relocation of the controlled drugs to a more secure location within the pharmacy, or daily inventory counts of the drugs where shortages are continuing.

Authority cited: Section 4005, Business and Professions Code. Reference: Sections 4081, 4104 and 4332, Business and Professions Code.

Proposed New Draft
5/25/2016

PROPOSED NEW DRAFT 5/25/16

1715.65. Reconciliation and Inventory Report of Controlled Substances

a) Every pharmacy, and every clinic licensed under sections 4180 or 4190, shall perform periodic inventory and inventory reconciliation functions to detect and prevent the loss of controlled substances.
b) The pharmacist-in-charge of a pharmacy or consultant pharmacist for a clinic shall review all inventory and inventory reconciliation reports taken, and establish and maintain secure methods to prevent losses of controlled drugs. Written policies and procedures shall be developed for performing the inventory reconciliation reports required by this section.
c) A pharmacy or clinic shall compile an Inventory Reconciliation Report of all Schedule II controlled substances at least every three months. This compilation shall require:
    a. A physical count, not an estimate, of all quantities of federal Schedule II controlled substances. The biennial inventory of controlled substances required by federal law may serve as one of the mandated inventories under this section in the year where the federal biennial inventory is performed, provided the biennial inventory was taken no more than three months from the last inventory required by this section.
    b. A review of all acquisitions and dispositions of Schedule II controlled substances since the last Inventory Reconciliation Report.
    c. Comparison of (a) and (b) to determine if there are any variances.
    d. All records used to compile each reconciliation shall be maintained in the pharmacy or clinic for at least three years in a readily retrievable form.
d) Losses shall be identified in writing and reported to the board and, when appropriate, to the Drug Enforcement Administration. Likely causes of overages shall be identified in writing and incorporated into the Inventory Reconciliation Report.
e) The Inventory Reconciliation Report shall be dated and signed by the individual(s) performing the inventory, and countersigned by the pharmacist-in-charge, and be readily retrievable in the pharmacy or clinic for three years.
f) A new pharmacist-in-charge of a pharmacy shall complete an inventory within 30 days of becoming pharmacist-in-charge as identified in subdivision (c). Whenever possible an outgoing pharmacist-in-charge should complete an inventory as required in subdivision (c).
g) For inpatient hospital pharmacies, a separate Inventory Reconciliation Report shall be required for Schedule II controlled substances stored within the pharmacy and for each pharmacy satellite location.
h) The pharmacist-in-charge of an inpatient hospital pharmacy or of a pharmacy servicing onsite or offsite automated drug delivery systems shall ensure that:
    a. All controlled substances added to an automated drug delivery system are accounted for;

b. Access to automated drug delivery systems is limited to authorized facility personnel;
c. An ongoing evaluation of discrepancies or unusual access associated with controlled substances is performed;
d. Confirmed losses of controlled substances are reported to the board; and
e. A pharmacy or clinic identifying losses of controlled drugs but unable to identify the cause within 30 days shall take additional steps to identify the origin of the losses and improve security of controlled substance access to prevent losses.

Authority cited: Section 4005, Business and Professions Code. Reference: Sections 4081, 4104 and 4332, Business and Professions Code.

Attachment 3

CPS HR CONSULTING

FINAL REPORT

Department of Consumer Affairs

Contract and Performance Audit of the DCA Diversion Program provided by Maximus Health Services

February 18, 2016

SUBMITTED BY:

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Your Path to Performance

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Executive Summary

The California Business and Professions Code provides enabling legislation to various health care licensing Boards under the auspices of the Department of Consumer Affairs (DCA) to identify and rehabilitate licensees whose competency may be impaired due to substance abuse and/or mental illness. In part, this legislation establishes a Diversion Program as a voluntary alternative approach to traditional disciplinary actions. The Boards that have implemented Diversion Programs include: Dental, Osteopathic Medicine, Physical Therapy, Physician Assistant, Pharmacy, Registered Nurses and Veterinary Medicine.

Since 2003, DCA has contracted with Maximus Health Services, Inc. (Maximus) to provide Diversion Program services for approximately 700 licensee participants.

Business and Profession Code Section 156.1 (c) authorizes the DCA Director or Chief Deputy Director to request an examination and audit by the Department's internal auditor of all performance under the contract. In January 2010, the DCA Internal Audit Office (IAO) audited the period from July 1, 2003 through December 31, 2009 and found that overall, Maximus is effectively and efficiently providing the program services.

In October 2015, the DCA IAO engaged CPS HR Consulting (CPS) to conduct an audit of the Diversion Services provided by Maximus for the contract period from January 1, 2010 through December 31, 2014. This audit was performed in compliance with Uniform Standard 15 that requires an external independent audit at least once every three years.

Overall Conclusion

Overall, this audit found Maximus is effectively and efficiently managing the various Board diversion programs and recommends the program be continued under the vendor. This audit identifies a variety of non-compliant instances and opportunities for improvement, but nothing of a systemic nature that materially affects program effectiveness and efficiency.

Findings and Recommendations

This report includes a program description section that covers the Diversion Program goals, enabling legislation, uniform standards, and distinguishing program elements; and an audit section that presents findings and 30 recommendations in the following areas:

Historical Program Statistics, Trends and Costs

- Over the audit period, approximately 67% of the program participants were female; 80% were Caucasian, and the average age increased from 30-34 years old to 45-49 years old.
- Approximately 67% of the participants entered the program through a Board referral.
- Slightly over 50% successfully completed the program.
- Most relapses were in the first year of the program and primarily due to abuse of alcohol, narcotics and other opiates, and benzodiazepine. The relapse rate has improved over time.

- Only seven of the 20 DCA healing arts licensing Boards are included in the Diversion Program, and the Board of Registered Nursing (BRN) does not include nurses on probation in the program.
- Some program participants lose their health insurance, but there are insurance benefits available for substance abuse and mental health treatment.

Recommendations

1. If applicable and warranted, other DCA healing arts Boards should consider participating in the Diversion Program, and in particular, the Medical Board of California and Board of Vocational Nursing and Psychiatric Technicians.
2. The BRN should consider making probationers attend the Diversion Program as a condition of probation.
3. Maximus should identify a program staff member whose sole responsibility is to become knowledgeable about health insurance coverage benefits and referral sources, and periodically update the Clinical Case Managers and Compliance Monitors.
4. Program participants should assume personal responsibility to contact and research coverage options and costs with the health insurance companies listed on the Covered California website.

Diversion Program and Shared Services Staffing

No negative findings or recommendations.

Diversion Program Manager Survey Results

- In lieu of observing DEC and Board Participant Review meetings, CPS surveyed the DPMs and attended a monthly DPM meeting resulting in the following observations:
  - All receive information timely from Maximus before a meeting.
  - They all have remote access to the Max-CMS and most reported the information is generally complete and accurate, and the system is easy to use.
  - Decisions and outcomes are well documented based on standardized templates.
  - They receive materials timely (within 7 days) after the meetings.
  - The DPMs rated as high: Program effectiveness for licensees, Maximus knowledge and expertise, and Program efficiency.
  - The DPMs offered a number of improvement recommendations.

Recommendation

5. Maximus should consider and evaluate all of the Diversion Program Manager (DPM) recommendations and, at a minimum, provide the DPMs with recovery training.

Treatment Provider Survey and Credential File Audit Results

- Treatment Providers (Clinical Assessors, Health and Nurse Support Group Facilitators and Worksite Monitors) were surveyed to identify obstacles/challenges that hinder their program role and recommendations to improve the program.
- In addition, the auditors reviewed a sample of credential files for compliance with Uniform Standards and found partial compliance.

Recommendations

6. Maximus should consider and evaluate all of the stated Treatment Provider obstacles/ challenges, then prioritize and implement the recommendations accordingly.
7. As evidenced by the success of the auditor's online survey, Maximus should periodically reach out to Treatment Providers and other stakeholders to identify ongoing issues and opportunities for continuous improvement.
8. Maximus and the Boards should ensure each credential review is completed in compliance with the Uniform Standards, including evidence of: a license, experience and insurance; do not accept licensees with whom they have had a personal, financial and business relationship within the last year; and Board approval.
9. Per healthcare standards, perform and document an OIG clearance for each Treatment Provider at https://exclusion.oig.hhs.gov
10. Per healthcare standards, require all Treatment Providers with access to records to sign HIPPA confidentiality statements.

Participant File Audit Results

- The auditors reviewed a statistically-valid random sample of participant files for compliance with applicable Uniform Standards and found a variety of non-compliant instances and opportunities for improvement.

Recommendations

11. Maximus should consider hiring a part-time CCM to cover vacations, illness and time away at DEC meetings, etc. This will improve the management of multiple calls.
12. Maximus program staff should continue to document reasons for assessment completion delays.
13. All program staff should take advantage of the improved spelling and grammar check feature in the upgraded Max-CMS.
14. The Project Manager should review and revise closing notes as necessary.
15. Use the participant's first or last name rather than pronouns only to prevent misunderstandings with case log entries.

16. Maximus should develop and implement a written policy for making deletions and retractions to case logs. The American Health Information Management Association website (http://www.ahima.org) has examples and sample policies Maximus could use.
17. Maximus program staff should track and trend the reasons for program withdrawal to determine the number of participants who withdrew for financial and other reasons.

18-20. Maximus program staff should improve or modify the Program Handbook in a variety of ways to provide participants with more valuable information.

21. Maximus should include medicine disposal information from the USFDA website in the Program Handbook.
22. Maximus should consider advising participants to seek out Mental Health Services from their local county government Adult System of Care, when appropriate.
23. Maximus should contact the California Chapter of the American Organization of Nurse Executives and California Hospital Association to speak at a regional or state-wide meeting regarding the prevention and detection of nurses diverting drugs.
24. The Board's should collectively consider identifying an acceptable, but less frequent, random testing schedule that would accomplish the goal and reduce participant cost and loss, then modify Uniform Standard 4 accordingly.
25. The non-DEC Board's should consider evaluating the effectiveness of the participants' non-attendance at Board review meetings, and consider ways to improve interpersonal interaction by Skype, Face Time or other forms of communication.

Drug Test File Audit Results

- The auditors reviewed a statistically-valid random sample of 114 participant drug testing files on the FirstLab website for compliance with applicable Uniform Standards and found all but four participants in the files. The drug test files include the participant name, license number, organization, test start and end dates, testing frequency, whether observed and current status.

Recommendation

26. The Maximus Quality Analyst should periodically audit the FirstLab website files to ensure all program participants being drug tested are included in the database.

Program Effectiveness Reporting

- Each Board is required to report specific information on a yearly basis to the DCA and the Legislature as it relates to licensees with substance abuse problems who are either in the Diversion Program or on Board probation. The auditors identified some minor issues and made the following recommendations for these specific reporting items.

Recommendations

27. Maximus should revise the intake report accordingly to eliminate the confusion between monthly and year-to-date reporting.
28. Maximus should consider tracking and trending major violations and actions taken, and report this information in the annual report.
29. Maximus should consider tracking and trending successful returns to work on a monthly and annual basis, and report this information in the annual report.
30. Participating Boards should attempt to monitor long range participant outcomes after program completion.

Planned Technical Improvements

No negative findings or recommendations.

The auditee responses to these findings and recommendations are contained in Appendix 6. Any inaccuracies the auditees noted in the draft report have been corrected in this final report.

Introduction

The following provides a brief background about the Maximus Diversion Program since its inception; presents the program staffing as of December 31, 2015, project scope, objective and methodology, constraints and data qualifications; and acknowledges the important role all of the audit participants.

Background

The DCA Diversion Program provided by Maximus is a voluntary, statewide, confidential, comprehensive, substance abuse disorder and mental illness monitoring and referral program for impaired health care professionals. It is not a treatment program. The primary role of Maximus is to provide case management for program participants during their recovery and to serve as a liaison with the Boards to which they are affiliated. As of December 2014, there were approximately 700 licensee participants in the program.

In 2003, DCA selected Maximus to provide Diversion Services on behalf of six health care licensing Boards and one Committee that fall under DCA administrative authority.

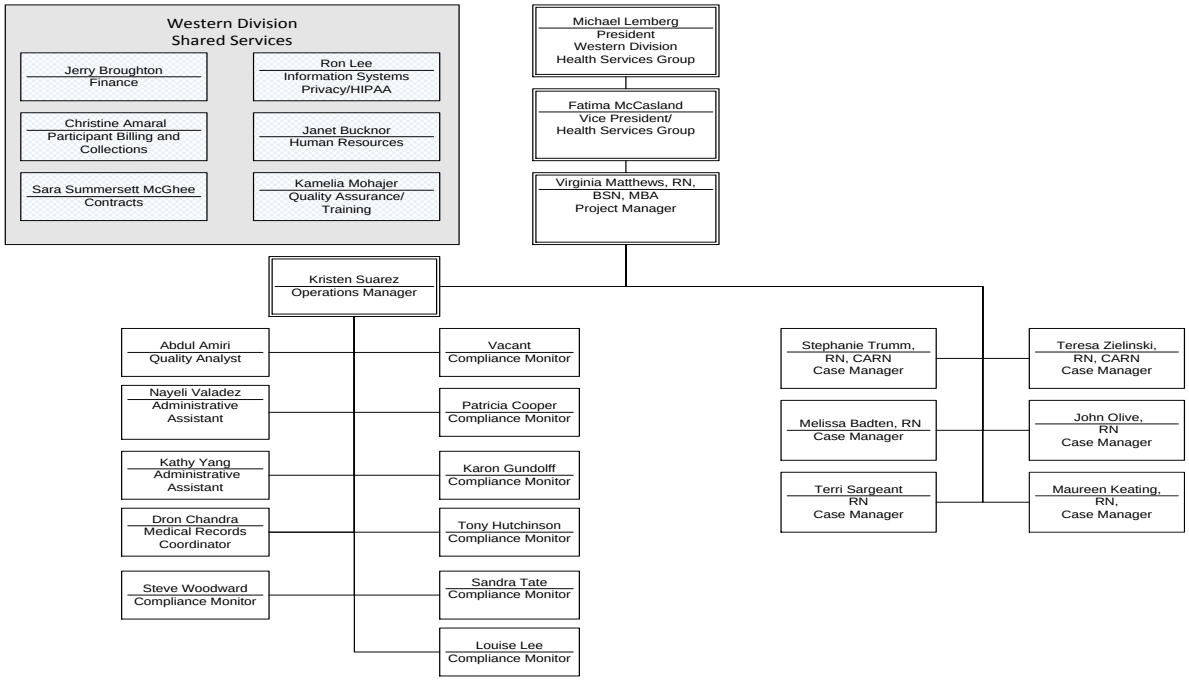
In 2009, the DCA Internal Audit Office (IAO) audited the DCA contract with Maximus to fulfill the audit requirement in Senate Bill 1441, chaptered September 28, 2008. The audit test period covered was July 1, 2007 through June 30, 2009. Overall, the DCA IAO audit concluded Maximus was effectively and efficiently managing the various Board diversion programs and recommended the program be continued with some opportunities for improvement.

In October 2015, the DCA engaged CPS HR to conduct a contract and performance audit of the DCA Diversion Program with an audit test period from July 1, 2010 through December 31, 2014 for up to approximately 700 eligible participants. The Diversion Program contract value for this audit period was $10,672,884. This audit was performed in compliance with Uniform Standard 15 that requires an external independent audit at least once every three years.

Maximus Program and Shared Services Staffing

Figure 1 displays the 19 authorized Maximus Diversion Program staff positions (including one vacancy) and the six Western Division Shared Services organizations supporting the program as of December 31, 2015. The staff roles and tasks are discussed in detail in the Audit Results section of this report.

Figure 1
Maximus Diversion Program Organization Chart as of 12/31/15



Project Scope, Objective and Methodology

The scope of this engagement focused on auditing the DCA Diversion Program services provided by Maximus from July 1, 2010 through December 31, 2014 to eligible licensee participants of the following seven Boards:

- Dental Board of California (+ Hygiene Committee) (DBC)
- Osteopathic Medical Board of California (OMB)
- Board of Pharmacy (BOP)
- Physical Therapy Board of California (PTB)
- Physician Assistant Board (PAB)
- Board of Registered Nursing (BRN)
- Veterinary Medical Board of California (VMB)

The project objective is to provide DCA management and the California Legislature with an external audit of the Maximus Diversion Program's compliance, effectiveness, efficiency and overall performance as required by Senate Bill 1441.

The CPS HR methodology included the following approach:

- Conducted off-site and onsite document reviews of the DCA-Maximus contract and drug screening administer contract (FirstLab); pertinent California program legislative mandates and regulations; Maximus staffing and organization charts, job descriptions, personnel

files, policies, procedures, performance metrics, flowcharts, forms and operating statistics.

- Converted applicable standards to compliance criteria checklists.
- Conducted staff interviews and group facilitation with Maximus program and shared services staff to better understand duties and workload, the as-is business processes used within the program, and document compliance with their own procedures.
- Surveyed Board/Review Committee Program Managers and reviewed applicable meeting minutes.
- In addition, CPS surveyed online:
  - Clinical Assessors to better understand their roles and responsibilities, and review their credential files and assessments.
  - Health Support Group Facilitators (HSGF) and Nurse Support Group Facilitators (NSGF) to better understand their roles and responsibilities, and review their credential files and reports.
  - Work Site Monitors (WSM) to better understand their roles and responsibilities, and review their credentials and reports.
- Audited the treatment program referrals for licensure and accreditation, and licensee participant records per the applicable standards at a statistically valid sample size (attribute sampling with expected error rate not over 5% at a confidence level of 95% with a precision of plus or minus 4%) using the Maximus MAX-CMS case management system.
- Surveyed FirstLab regarding licensure/accreditation; drug screening and laboratory services provided to program participants; audited a statistically valid sample (attribute sampling with expected error rate not over 5% at a confidence level of 95% with a precision of plus or minus 4%) of applicable records for contract compliance and quality controls; and conducted site visits of local laboratory subcontractors.
- Briefed DCA and Maximus periodically as requested.
- Prepared incremental deliverables, monthly status reports, draft and final reports.

The audit as conducted in accordance with:

- The terms and conditions of contract REQ0003674 approved December 27, 2009, including but not limited to, General Requirements (Section 4), Board Specific Requirements (Sections 5-11), Functional Requirements (Section 12), Administrative Requirements (Section 19), and all provisions listed in the Appendices (Section 19); and Amendment #1 approved December 27, 2012 and Amendment #2 approved December 31, 2013, including, but not limited to, section B. Revisions to the Agreement.
- The DCA Uniform Standards as stipulated in Senate Bill 1441, April 2011, and the California Attorney General Decision on Uniform Standards dated April 8, 2015; and

- The US General Accounting Office Government Auditing Standards for performance reviews of government agencies and programs.
- Finally, the audit was managed according to the best practices of the Project Management Institute.

Constraints and Data Qualifications

CPS relied on information received from Maximus staff, Board staff, and program service providers. With the exception of audited Maximus information, conclusions were drawn from unaudited information provided by these other sources.

Acknowledgment

CPS wishes to thank all participants at Maximus Health Services, especially the Program Manager, Operations Manager and the Quality Assurance function that gave so willingly of their time and expertise. In addition, CPS wishes to thank Professional Health Consulting Services (PHCS) for their invaluable health care expertise and services.

Maximus Diversion Program Services

The following describes the Diversion Program, including a summary of the program goals and enabling legislation; budgeted program participants; program length, entry and confidentiality; program intake and clinical assessment; treatment programs; program requirements, uniform standards and distinguishing program elements; and program billing and reporting.

Program Goals and Enabling Legislation

The primary Diversion Program goal is to protect the public by early identification of affected health care professionals and immediate access to appropriate intervention programs and treatment services. The secondary goal is to assist licensee participants with their recovery without losing their license to practice. The program intent is not to punish but to rehabilitate and return the health care professional to safe practice.

Table 1 summarizes the California statutes within Division 2 of the Business & Professions Code enable the Diversion Program for the health care licensing boards within the scope of this audit.[1]

Table 1: Diversion Program Enabling Legislation

Participating Board	Business & Professions Code Section Division 2
Dental Board of California (+ Hygiene Committee)	Chapter 4, Article 4.7, Section 1695
Osteopathic Medical Board of California	Chapter 5, Article 15, Sections 2360-2370
Physical Therapy Board of California	Chapter 5.7, Article 5.5, Sections 2662-2669
Board of Registered Nurses	Chapter 6, Article 3.1, Sections 2770-2770.14
Physician Assistant Board	Chapter 7.7, Article 6.5, Sections 3534-3534.10
Board of Pharmacy	Chapter 9, Article 21, Sections 4360-4373
Veterinary Medical Board	Chapter 11, Article 3.5, Sections 4860-4873

Budgeted Program Participants

Table 2 displays the number of program participants, unit cost and total amount budgeted in the DCA contract and two amendments with Maximus for managing the Diversion Program during the audit period. The table indicates total budgeted participants declined over the audit period from 686 to 658, BRN licensees comprised more than 70% of the program participants, the monthly unit cost increased 3% per fiscal year, and the total budgeted cost was $10,672,884.

[1] Appendix 1 contains, in part, the applicable Business & Professions Code sections.

Table 2: Diversion Program Participants Budgeted by Board

FY	FY 2010-11			FY 2011-12			FY 2012-13			FY 2013-14			FY 2014-15 (7/1/14-12/31/14)		
Board	# Part.	Mo. Unit Cost	Amt	# Part.	Mo. Unit Cost	Amt	# Part.	Mo. Unit Cost	Amt	# Part.	Mo. Unit Cost	Amt	# Part.	Mo. Unit Cost	Amt
BRN	509	$ 280.16	$1,711,217.28	509	$ 288.56	$1,762,524.48	480	$ 297.22	$1,711,987.20	485	$ 306.14	$1,781,734.80	485	$ 315.32	$917,581.20
BOP	79	$ 280.16	$265,591.68	79	$ 288.56	$273,554.88	75	$ 297.22	$267,498.00	80	$ 306.14	$293,894.40	80	$ 315.32	$151,353.60
DBC	48	$ 280.16	$161,372.16	48	$ 288.56	$166,210.56	36	$ 297.22	$128,399.04	40	$ 306.14	$146,947.20	40	$ 315.32	$75,676.80
PAB	22	$ 280.16	$73,962.24	22	$ 288.56	$76,179.84	25	$ 297.22	$89,166.00	20	$ 306.14	$73,473.60	20	$ 315.32	$37,838.40
PTB	12	$ 280.16	$40,343.04	12	$ 288.56	$41,552.64	15	$ 297.22	$53,499.60	15	$ 306.14	$55,105.20	15	$ 315.32	$28,378.80
OMB	10	$ 280.16	$33,619.20	10	$ 288.56	$34,627.20	12	$ 297.22	$42,799.68	12	$ 306.14	$44,084.16	12	$ 315.32	$22,703.04
VMB	6	$ 280.16	$20,171.52	6	$ 288.56	$20,776.32	10	$ 297.22	$35,666.40	6	$ 306.14	$22,042.08	6	$ 315.32	$11,351.52
Totals	686		$2,306,277.12	686		$2,375,425.92	653		$2,329,015.92	658		$2,417,281.44	658		$1,244,883.36

Source: DCA contracts

Program Length, Entry and Confidentiality

The length of participation in the program depends on the licensee participant's compliance with program requirements and demonstrated recovery progress. There are essentially two program phases: recovery and transition. Most participants remain in the program for three to five years. At a minimum, during the recovery phase participants must demonstrate full compliance with program requirements before they may petition their respective Board to enter the transition phase. However, transition is not guaranteed at the two-year mark. The transition phase lasts at least one year and is designed to ease participants into accepting full responsibility for their recovery. Participants are given more autonomy and responsibility with fewer program requirements and restrictions.

Depending on Board policy, licensee applicants can enter the program in the following ways defined in the contract:

- Board Referral: a licensee referred to the Diversion Program by the Board, based on information or complaint received by the Board, indicating the licensee may be impaired due to a substance abuse disorder or mental illness. (66.6% of referrals)[2]
- Self-Referral: a licensee who voluntarily seeks admission into the Diversion Program may apply to the program directly by calling a 24 hour/7 day a week toll-free phone number [(800) 522-9198]. (19.7% of referrals)
- Probation Referral: a licensee referred to the Diversion Program by their applicable Board as a condition of a Board-imposed disciplinary action. (9.2% of referrals)
- Informal Referral: a licensee of the Dental Board of California (DBC) and/or Board of Pharmacy (BOP) who may have a Board investigation pending, and upon recommendation of a Board inspector/investigator, may voluntarily apply to the program. (4.0% of referrals)
- In Lieu of Discipline: a licensee the BOP investigated and referred into the program to be assessed in order to determine if the licensee has a substance abuse disorder. In cases of a

[2] Based on Diversion Program Annual Reports from FY 2010-11 through FY 2014-15.

serious violation, the BOP may refer to the program in addition to discipline. Approximately 0.5% of program participants are this type of referral. (0.5% of referrals)

Participant confidentiality is protected by law. Licensees become participants after they are accepted into the program. Any and all information gathered to assist in developing a recovery plan, and all other information in their record, is confidential. In general, when participants successfully complete the Diversion Program, their program records are destroyed. However, except for BOP participants, if a participant does not successfully complete the program, the original complaint, if any, is investigated by the respective Board's Enforcement Program.

Program Intake and Clinical Assessment

After verifying the eligibility of the applicant, the assigned Compliance Monitor (CM) contacts the licensee and schedules an initial intake interview with the assigned Clinical Case Manager (CCM). Within 10 days of applying for entry into the program, the CCM conducts an in-depth telephone interview with the licensee. Following the interview, the CCM prepares and mails a Pre-Entry Agreement and recovery plan which may include some or all of the following recovery activities:

- Random drug testing
- 12-step meeting attendance
- Support group meeting attendance
- Outpatient or inpatient treatment
- Psychiatric evaluation
- Individual psychotherapy
- Medication management
- Medical evaluation
- Nephrology evaluation
- Submission of monthly self-reports
- Work site monitor reports
- Temporary work suspension
- Periodic reviews with Board Evaluation Committees or Board Diversion Evaluation Committees

Within five days of completing the intake interview, an Administrative Assistant mails the applicant an application packet. The applicant has 10 days from the intake to complete and return the application.

Within 10 days after completing the intake interview, the CM schedules the applicant to meet with a licensed clinician near their home for a Clinical Assessment. There are 34 Clinical Assessors statewide.

Before the clinical assessment, the applicant completes a self-assessment and takes it to the appointment. The clinician conducts a comprehensive assessment and discusses treatment options with the applicant. The clinician has 30 calendar days to prepare and submit the Clinical Assessment with treatment recommendations to the CCM. However, if the clinician determines there is a safety

concern with an applicant, s/he must notify the CCM within one day and the CCM contacts the applicant for entry into care. Otherwise, upon receipt of the assessment, the CCM notifies the applicant and the applicable Board to schedule the applicant for a Board Review or Diversion Evaluation Committee meeting.

Appendix 2 displays a high level flowchart of initial participant contact, program roles and tasks.

Treatment Programs

Participants discuss outpatient or other treatment options with their Clinical Assessor and CCM. There are literally hundreds of nonmedical alcoholism, drug recovery or treatment facilities licensed and/or certified by the California Department of Health Services (CDHS) covering all 58 counties to choose from.

Program/facility types include, but are not limited to:

- RES and RES-DETOX– 24-hour residential nonmedical alcoholism or drug abuse recovery or treatment facility licensed by the Department of Alcohol and Drug Programs (ADP).
- NON – nonresidential program certified by ADP.
- DETOX – free standing, 24-hour nonmedical detoxification facility licensed by ADP.
- DHS – medical alcohol and drug recovery or treatment facilities licensed by CDHS and certified by ADP. Typically, these are Chemical Dependency Recovery Hospitals.
- DSS – residential facilities licensed by the Department of Social Services and certified by ADP. Typically, these are group homes.

However, the CCM must approve the treatment program the participant selects before s/he can attend. Participants must complete and sign a Consent to Exchange Information for the treatment provider and send it to Maximus.

Maximus cannot require participants to go to any one specific program, a stance influenced by Medicare guidelines that prohibit hospitals from referring to a single provider. Participants must ultimately select from the CDHS list of approved facilities.

Program Requirements, Uniform Standards and Distinguishing Elements

Participants must comply with the following rigorous ongoing requirements incorporated into 16 Uniform Standards implemented in 2011 to successfully complete the program:

- After reading the Diversion Program Handbook, sign and return the signature page to Maximus.
- Call the CCM: weekly at first then monthly after formal acceptance into the program by the appropriate Board PRM or DEC.
- Always notify the CCM of any address or telephone number changes and be reachable.
- Complete a self-assessment, give a copy to the Clinical Assessor and mail the original to Maximus.

- Ensure outpatient or other treatment programs are approved by the CCM.
- Prepare and submit a monthly self-report to Maximus by the 10th of the following month.
- Arrange for treatment providers to submit monthly progress reports to Maximus by the 10th of the following month.
- Attend appropriate 12-step meetings, obtain one signature per day, and submit the attendance card to Maximus by the 10th of the following month.
- Attend the appropriate health or nurse support group and ensure the group facilitator submits a monthly attendance report by the 5th of the next month. There are 21 health support groups and 45 nurse support groups statewide.
- Follow individual restrictions on practice, including submitting a Return to Work request, approved by the respective Board.
- Obtain a Maximus-approved worksite monitor before starting work, ensure the monitor files the required consent forms and monthly reports the first three months, then quarterly thereafter with Maximus. There are 436 worksite monitors statewide.
- Participate in the random drug testing program, including registration within five days of the intake interview, check-in daily online or by phone, provide observed specimens at a local collection site, enter post test data online, respond appropriately to test results, and pay for the cost of the test plus collection fee.
- Abide by the unapproved medication list and remains free of mind-altering substances (unless prescribed by a physician for a specific diagnosis and approved by the Board).
- Pay the monthly program fee to Maximus based on applicable Board policy.
- Petition for and be accepted by the applicable Board PRM or DEC into the program's Transition phase, meet the minimum conditions of this phase, complete the Transition Packet and be approved by the CCM, PRM or DEC for successful completion. If approved by the PRM/DEC, the CCM recommends and prepares a successful completion letter within 10 days of the PRM/DEC meeting.

In 2011, Senate Bill 1441 (Ridley-Thomas) established in the Department of Consumer Affairs the Substance Abuse Coordination Committee. This committee was comprised of the 20 Executive Officers of the Department's healing arts licensing boards and a designee of the State Department of Alcohol Drug Programs. The committee no longer exists. The bill required the committee to formulate uniform standards in specified areas that each healing arts board would be required to use in dealing with substance-abusing licensees. The following briefly summarizes the 16 Uniform Standards the committee formulated and implemented in April 2011. There must be:

1. Specific requirements for a clinical diagnostic evaluation of the licensee, including, but not limited to, required qualifications for the providers evaluating the licensee.
2. Specific requirements for the temporary removal of the licensee from practice, in order to enable the licensee to undergo the clinical diagnostic evaluation described in subdivision (a) and any treatment recommended by the evaluator described in subdivision (a) and approved by the board, and specific

criteria that the licensee must meet before being permitted to return to practice on a full-time or part-time basis.

3. Specific requirements that govern the ability of the licensing board to communicate with the licensee's employer about the licensee's status or condition.
4. Standards governing all aspects of required testing, including, but not limited to, frequency of testing, noticing the licensee, number of hours between the provision of notice and the test, standards for specimen collectors, procedures used by specimen collectors, the permissible locations of testing, whether the collection process must be observed by the collector, backup testing requirements when the licensee is on vacation or otherwise unavailable for local testing, requirements for the laboratory that analyzes the specimens, and the required maximum timeframe from the test to the receipt of the result of the test.
5. Standards governing all aspects of group meeting attendance requirements, including, but not limited to, required qualifications for group meeting facilitators, frequency of required meeting attendance, and methods of documenting and reporting attendance or nonattendance by licensees.
6. Standards used in determining whether inpatient, outpatient, or other type of treatment is necessary.
7. Worksite monitoring requirements and standards, including, but not limited to, required qualifications of worksite monitors, required methods of monitoring by worksite monitors, and required reporting by worksite monitors.
8. Procedures to be followed when a licensee tests positive for a banned substance.
9. Procedures to be followed when a licensee is confirmed to have ingested a banned substance.
10. Specific consequences for major and minor violations. In particular, the committee shall consider the use of a "deferred prosecution" stipulation described in Section 1000 of the Penal Code, in which the licensee admits to self-abuse of drugs or alcohol and surrenders his or her license. That agreement is deferred by the agency until or unless licensee commits a major violation, in which case it is revived and license is surrendered.
11. Criteria a licensee must meet in order to petition for return to practice on a full time basis.
12. Criteria a licensee must meet in order to petition for reinstatement of a full and unrestricted license.
13. If a Board uses a private-sector vendor that provides diversion services, there must be (1) standards for immediate reporting by the vendor to the board of any and all noncompliance with process for providers or contractors that provide diversion services, including, but not limited to, specimen collectors, group meeting facilitators, and worksite monitors; (2) standards requiring the vendor to disapprove and discontinue the use of providers or contractors that fail to provide effective or timely diversion services; and (3) standards for a licensee's termination from the program and referral to enforcement.
14. If a Board uses a private-sector vendor that provides diversion services, the extent to which licensee participation in that program shall be kept confidential from the public.
15. If a Board uses a private-sector vendor that provides diversion services, a schedule for external independent audits of the vendor's performance in adhering to the standards adopted by the committee
16. Measurable criteria and standards to determine whether each board's method of dealing with substance-abusing licensees protects patients from harm and is effective in assisting its licensees in recovering from substance abuse in the long term.

The following discusses other essential and distinguishing program elements concerning random drug testing, health and nurse support groups, and worksite monitors.

Random Drug Testing

According to the American Society of Addiction Medicine (ASAM)[3], the nation's largest organization of physicians specializing in the prevention and treatment of addiction, drug testing is a primary prevention, diagnostic, and monitoring tool used to identify the presence or absence of drugs of abuse or therapeutic agents related to addiction management in multiple settings.

The ASAM encourages wider and "smarter" use of drug testing within the practice of medicine and broadly within American society. Smarter drug testing means:

- Increased use of random testing rather than scheduled testing;
- Testing not only urine but also other substances such as blood, oral fluid (saliva), hair, nails, sweat and breath; and
- Testing based upon clinical indication for a broad and rotating panel of drugs rather than only testing for the traditional five-drug panel designed by the federal government for government-mandated testing such as that required of commercial drivers.
- Improved sample collection and detection technologies to decrease sample adulteration and substitution, including designing appropriate steps to respond to the efforts of individuals trying to subvert the testing process.
- Giving careful consideration of the financial costs of testing in relationship to the value and in many cases, medical necessity, of the test results. It means considering the advantages and limitations of the many testing technologies available today.

Maximus has contracted with First Hospital Laboratories, Inc. (FirstLab), a third party laboratory administrator, to provide qualitative urine substance abuse testing for each program participant. In turn, FirstLab has subcontracted the laboratory services to DrugScan, a laboratory certified by the US Department of Health and Human Services (DHHS), and to almost 700 program collection sites in California.

Health and Nurse Support Groups

Depending on the participant's license, each participant is required to attend either a weekly Health Support Group (HSG) or a Nurse Support Group (NSG). According to the contract, HSGs are facilitated by a California licensed registered nurse, marriage family therapist, licensed clinical social worker, psychologist or psychiatrist who has a minimum of three years of experience providing chemical dependency and mental health treatment for health care professionals. The NSGs are facilitated by a California licensed registered nurse with similar experience. HSG's typically charge more than NSG's because they are usually led by a licensed clinician.

[3] Drug Testing: A Whitepaper of the American Society of Addiction Medicine, October 26, 2013

The audit scope of work included observing several HSG and NSG meetings. However, due to participant confidentiality concerns, CPS was unable to observe these meetings but understands the process involves, and is not limited to:

- Facilitating or co-facilitating a weekly hourly group meeting with program participants. Keeps the group focused on the day-to-day professional issues and recovery process and applies interpersonal interaction group process while giving priority to recovery.
- Observing and reporting to Maximus staff any behavior, attitude, demeanor or appearance which may suggest a relapse within twenty-four (24) hours of the observation.
- Recording and reporting weekly attendance to Maximus staff by the 5th of every month. If the participant does not show, or if the excused absence is unreasonable, the facilitator must report to Maximus staff within twenty-four (24) hours.
- Reporting relapses to Maximus staff within twenty-four (24) hours.
- Being accessible to participants twenty-four (24) hours a day for crisis intervention or referral.
- Provides input and recommendations at any time to Maximus staff regarding a participant's recovery.

Worksite Monitors

Worksite monitors (WSMs) assist licensed health professionals return to work in a controlled and safe manner. According to the contract, WSMs observe participants at least once a week or up to a maximum of 100%, verify participant attendance, review work performance, monitor/detect substance abuse, submit monthly worksite monitor reports to Maximus, and report any non-compliant work-related issues or changes in behavior and signs of relapse. The worksite monitoring percentage can be reduced to zero in the transition phase.

WSMs must be have knowledge of the provisions or requirements of the applicant/participant's recovery contract and be approved by the Diversion Program's CCM, Board's DPM and/or DEC. WSMs maintain continual communication with the assigned CCM. They are required to notify Maximus within one hour of noticing any signs of relapse or suspicious behavior and submit a written report within 48 hours of the occurrence. In addition, WSMs submit a written monthly or quarterly reports to Maximus by the 10th of the following month.

Participant Review Process

Depending on the Board, the initial and recurring participant review process varies. For example, the BRN, DBC, OMB and VMB use a Diversion Evaluation Committee (DEC) meeting to evaluate initial applicants for program entry, approve Recovery Agreements, review participant progress, make Agreement revisions, and approve program discharges for recurring participants. DECs are unique because they also review participants in person. The DEC composition is mandated by law and is typically composed of three to four Board-appointed members who are licensed by the same Board as the participant, a physician and a public member. The CCM and a Board representative also attend

the meetings. The BRN (has 14 DECs located throughout the state), DBC and OMB DEC meetings are held quarterly. The VMB DEC meets every four months.

The BOP, PAB and PTBC use Board Participant Review Meetings (PRM) instead of DECs to review applicants for entry and on a routine recurring basis, but do not meet with participants in person. Typically, a Board representative meets with the CCM to review participant progress, revise the Recovery Agreements and approve program discharges. BOP meetings are held monthly, PTBC meetings are held quarterly, and PTBC meetings are held semi-annually.

In between the various Board meetings and until program completion, six teams of paired CMs and CCMs monitor ongoing participant compliance with the program requirements and specific Board uniform standards to ensure timely, successful completion. The CM/CCM teams will actively monitor for compliance all of the above tasks included in the initial and revised Recovery Agreements in accordance with each Board's uniform standards. Participants must sign and return the Recovery Agreements within 10 days of receipt. The CM monitors each participant daily and submits noncompliance issues to the CCM and the PRM/DEC within five days of discovery. When teams identify non-compliance, they contact participants by phone or email then mail them non-compliance letters within five days. Participants must respond timely to the compliance letters or be subject to program termination.

Appendix 3 displays a high level flowchart of the recurring participant and program responsibilities and tasks.

Program Billing and Reporting

Maximus bills and accounts for the Board and participant administrative co-pay fees on a monthly basis. Boards are billed individually based on their own specific requirements in arrears $338.15 per participant a month by the 10th day of the following month. This expense increases by three percent (3%) annually on January 1. Maximus provides each Board Diversion Program Manager (DPM) with a monthly report of all administrative fees collected from participants, an aged receivable report, and a monthly audit schedule.

Table 3 shows depending on the respective Board requirements, Maximus bills participants varying administrative co-pay amounts by the 20th of the current month ranging from $25 to $338.15 a month or from $1,000 to $2,000 for a one-time fee that may be paid in quarterly installments. Participants may pay by check, cashier's check, credit card, money order or ATM debit with no service charges. Participants are charged fees for non-sufficient funds. Maximus credits the collected participant fees against the fee balance paid by each Board the following month.

Table 3: Participant Administrative Co-Pay Fees

Board	Participant Co-Pay	Frequency	Comments
BOP	$100.00	Monthly	
BRN	$25.00	Monthly	
DBC (+ Hygiene)	$100.00	Monthly	
PTBC	$338.15	Monthly	Increases 3% annually on Jan. 1
PAB (Board referral)	$338.15	Monthly	Increases 3% annually on Jan. 1
PAB (Self referral)*	$253.61	Monthly	Increases 3% annually on Jan. 1
OMB**	$1,600.00	1-Time	Can be paid in qtrly installments
VMB	$2,000.00	1-Time	Can be paid in qtrly installments
Source: Maximus			
* A regulatory change in 2011 provided a 25% reward for participant self-referral to the program.			
** Plans to make participants pay the full program fee of $338.15.			

FirstLab bills each participant directly for each drug test performed. Participants are responsible for paying the collection site specimen collection and drug testing fees at the time service is rendered. These fees can range up to $125.

Audit Results

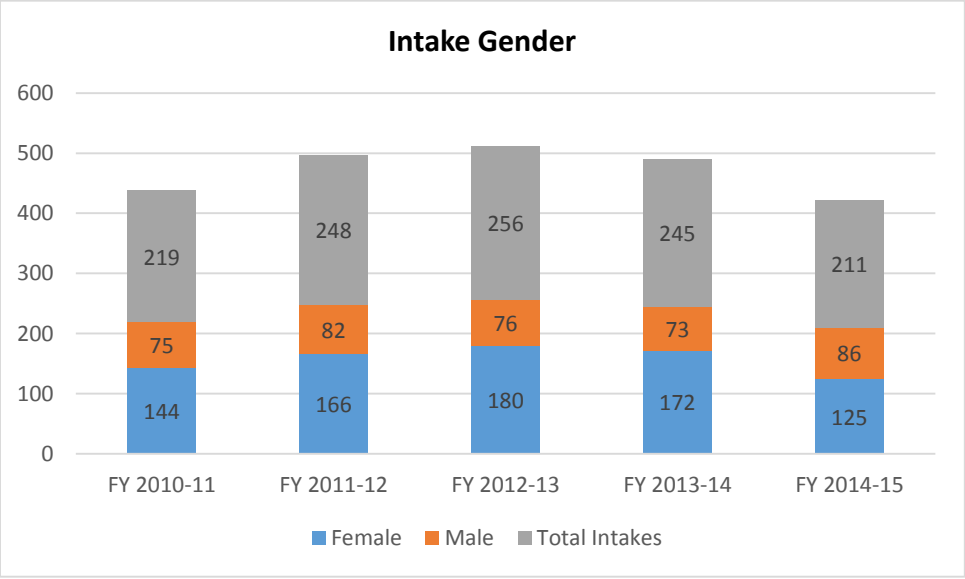
This section of the report presents audit observations, findings and recommendations for improvement based on interviews and information gathered and analyzed from: Maximus Program and Shared Services staff; Board Diversion Program Managers; Treatment Providers (Client Assessors, Health and Nurse Support Group facilitators and Worksite Monitors); drug testing subcontractor FirstLab; and licensee participant and drug test files.

The following presents historical program statistics, trends and costs; Diversion Program staffing, roles and tasks; Shared Services roles and responsibilities; Diversion Program Manager survey results; Treatment Provider survey and credential file audit results; results of participant file and drug test file audits; Program effectiveness reporting and planned technical improvements.

Program Statistics, Trends and Costs

Based on the Maximus California Diversion Program Annual Reports for FY 2010-11 through 2014-15 (six months beyond the scope of this audit), there were 1,179 intakes (top of stack) into the program. Approximately 66.8% (787) were female (bottom of stack) and 33.2% (392) were male (middle of stack). Figure 2 graphically displays the program intakes by gender and reveals intakes began dropping after FY 2012-13. The program experienced its lowest overall intake level in FY 2014-15 with a significant drop in female intakes.

Figure 2

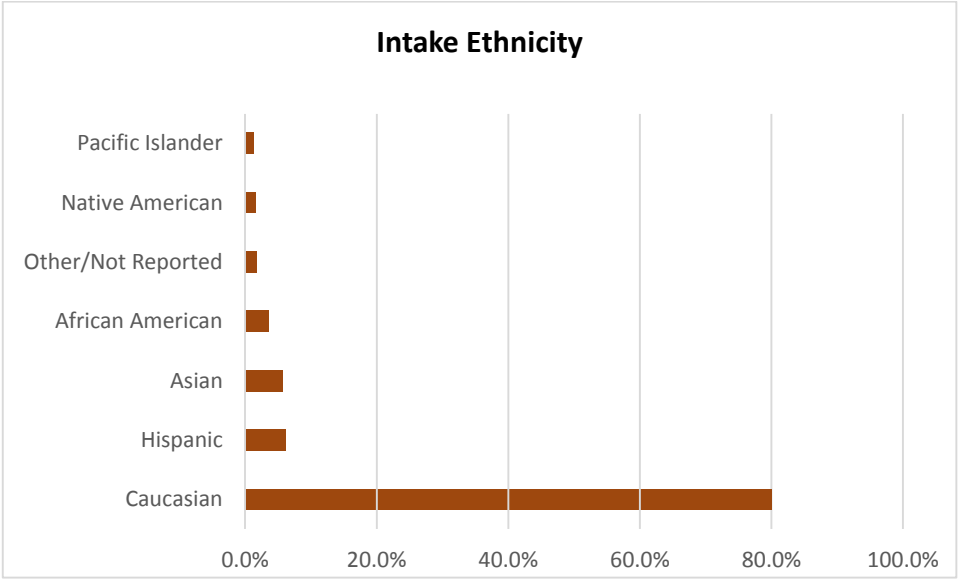


Source: Diversion Program Annual Reports

The average program intake for the five fiscal years by the following ethnicities is shown in Figure 3:

- Pacific Islander (average 1.4%)
- Native American (1.6%)
- Other/Not Reported (1.8%)
- African-American (3.5%)
- Asian (5.6%)
- Hispanic (6.1%)
- Caucasian (80.1%)

Figure 3



Source: Diversion Program Annual Reports

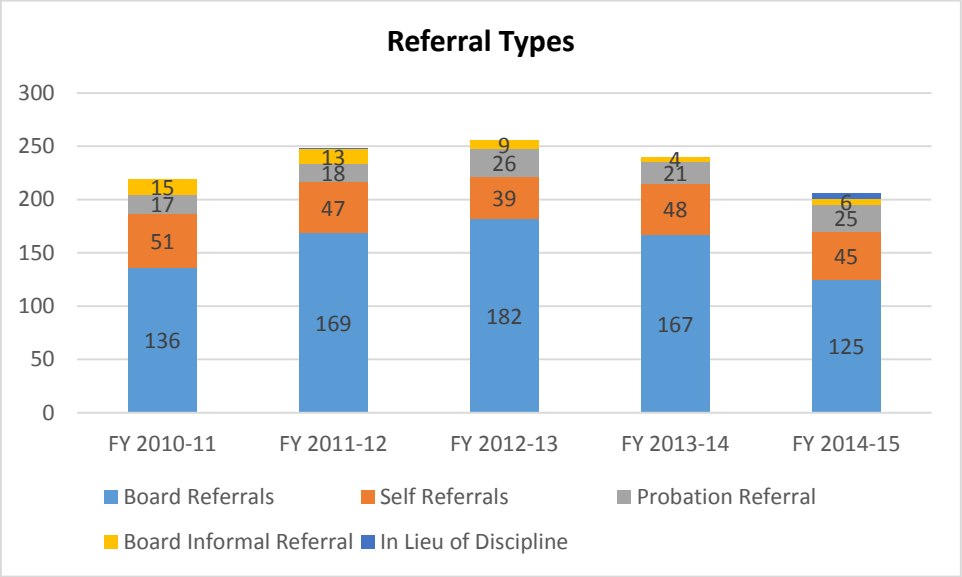
A particularly interesting trend has been the increase in the average age of program participants. In FY 2010-11, the average age range was from 30-34 years old. In FY 2014-15, the average age range increased to 45-49 years old. This is primarily due to the fact most of the program participants are registered nurses who are aging. According to the National Council of State Boards of Nursing, the average age of a nurse is 50 years old and 53% are over the age of 50.

Over the past five fiscal years, program entry has been through the following types of referrals. The leading referral types are Board, self and Probation referrals:

- Board referrals (66.6%)
- Self-referrals (19.7%)
- Probation referrals (9.2%)
- Board informal referrals (4.0%)
- In lieu of discipline referrals (0.5%)

Figure 4 displays the breakdown of referral types over the five fiscal years.

Figure 4



Source: Diversion Program Annual Reports

The Program Annual Reports also present information on 15 program closure types and relapses by eight different substances for the audit period. Table 4 reveals slightly over 50% of participants successfully completed the program, while the rest were terminated for a wide variety of reasons. A closure type that should be considered and is conspicuously absent is financial hardship.

Table 4: Closure Types

	Closure Type	FY 2010-11	FY 2011-12	FY 2012-13	FY 2013-14	Totals	% Total
1	Successful Completion	104	127	144	122	497	50.1%
2	Terminated-Public Risk	32	32	19	23	106	10.7%
3	Applicant Withdrawn-Pre DEC	22	34	21	29	106	10.7%
4	Terminated-Non Compliant	22	14	12	12	60	6.0%
5	Applicant Public Risk	14	20	11	13	58	5.8%
6	Withdrawn-Post DEC	10	20	13	13	56	5.6%
7	Clinically Inappropriate-Pre DEC	6	6	12	14	38	3.8%
8	Terminated-Failure to Derive Benefit	7	9	2	2	20	2.0%
9	Applicant Not Accepted by DEC	4	6	5	3	18	1.8%
10	No Longer Eligible-Post-DEC	3	3	4	3	13	1.3%
11	Clinically Inappropriate-Post DEC	2	2	1	4	9	0.9%
12	No Longer Eligible Pre-DEC	2	1	2	0	5	0.5%
13	Expired	1	1	0	2	4	0.4%
14	Terminated – Moved	0	1	1	0	2	0.2%
15	Sent to Board- Post DEC	0	0	0	0	0	0.0%
	Total Number of Closures	**230**	**276**	**247**	**240**	**993**	**100.0%**

Source: Diversion Program Annual Reports

Table 5 shows over the audit term the number of program participants decreased, but the relapse rate improved over time, with an average relapse rate of 10.6% per fiscal year.

Table 5: Program Participants and Relapse Rates over the Audit Term

Program Indicators	FY 2010-11	FY 2011-12	FY 2012-13	FY 2013-14	FY 2014-15	Avg.
Program participants (high)	682.0	650.0	645.0	652.0	650.0	655.8
Program participants (low)	667.0	632.0	630.0	625.0	571.0	625.0
Program participants (avg)	674.5	640.3	635.8	630.3	611.8	638.5
Total relapses	81.0	76.0	68.0	68.0	47.0	68.0
Relapse rate based on participant avg	12.0%	11.9%	10.7%	10.8%	7.7%	10.6%

Source: Diversion Program Annual Reports

According to a 2012 research guide prepared by the National Institute on Drug Abuse,[4] the disease of substance abuse disorders is estimated at 10 to 14% of the general population and has a relapse rate similar to other chronic diseases. For example, the relapse rate for drug addiction is 40% to 60% versus 30% to 50% for type I diabetes, and 50% to 70% for hypertension and asthma. As table 5 reveals, the DCA Diversion Program average relapse rate is almost four times better than the expected relapse rate of the general public.

Table 6 indicates most relapses reflect the use of alcohol, narcotics and other opiates, and benzodiazepine (drugs primarily used for treating anxiety).

Table 6: Relapses by Substance

Relapses by Substance	FY 2010-11	FY 2011-12	FY 2012-13	FY 2013-14	FY 2014-15	Avg*
Alcohol	29.8%	26.0%	47.0%	31.0%	38.3%	34.4%
Narcotics and other opiates (hydrocodone)	30.6%	26.0%	22.0%	28.0%	25.5%	26.4%
Benzodiazepine	6.0%	9.0%	15.0%	10.0%	19.1%	11.8%
Other	9.5%	12.0%	7.0%	7.0%	2.1%	7.5%
Tramadol	10.5%	2.0%	7.0%	5.0%	12.7%	7.4%
Amphetamines	1.0%	7.0%	3.0%	7.0%	2.1%	4.0%
Marijuana	1.5%	2.0%	4.0%	6.0%	2.1%	3.1%
Cocaine	0.8%	4.0%	4.0%	1.0%	0.0%	2.0%

* Total do not equal 100% but provides a reasonable indication of the most abused substances

Source: Diversion Program Annual Reports

In summary, most program participants are Caucasian females that enter the program through Board referrals. Approximately half successfully complete the program and most of the relapses involve the use of alcohol, narcotics and other opiates, and benzodiazepine.

[4] Principles of Drug Addiction Treatment: A Research-Based Guide, National Institute on Drug Abuse, December 2012

Board Participation

It is interesting to note that only eight of the 20 DCA healing arts licensing Boards are included in the program. Notable exceptions with large licensee populations include the Medical Board of California (medical doctors) and Board of Vocational Nursing and Psychiatric Technicians (LVNs and PTs).

In addition, BRN probationers are not included in the Diversion Program as a condition of probation like some other Boards. As of December 2015, BRN had 425 program participants and approximately 1,420 probationers, including 1,125 active and 305 in tolled status which are out of state and require minimum monitoring. It can be reasonably assumed a percentage of the probationers probably suffer from substance abuse or mental issues and do not receive the medical attention the program participants receive. Like other Boards, BRN probationers would probably benefit if they were included in the Diversion Program.

Recommendations

1. If applicable and warranted, other DCA healing arts Boards should consider participating in the Diversion Program, and in particular, the Medical Board of California and Board of Vocational Nursing and Psychiatric Technicians.
2. The BRN should consider making probationers attend the Diversion Program as a condition of probation.

Program Costs

Table 7 presents a representative breakdown of the participant monthly cost elements and total program costs by Board for the full five year term. Costs are not exact because every participant is treated based on their individual needs.

Costs vary by Board and, in general, non-nursing Board participants pay substantially more than BRN participants. For example, in Year 1 the range of costs for a BRN participant ranges from $5,980 to $27,620, while the low cost for other Board participants start at $8,800 to $11,658 and range up to $31,800 to $46,400. The total estimated five-year cost for BRN participants ranges from $18,700 to $60,900, while the costs for other Board participants range from a low of $30,400 to a potential high of $104,289.

Table 7 indicates the primary cost differences between Boards are the participant co-pay fees and the monthly support group fees. The BRN subsidizes most of the participant co-pay fee while the other Boards do not subsidize any portion, or subsidize a smaller portion of the total fee. In addition, the Nurse Support Groups are facilitated by a nurse while the Health Support Groups are facilitated by a licensed therapist, which typically costs significantly more.

Table 7: Participant Cost Differential by Board for 5 Years

Year	BRN		BOP		DBC		PTBC		PAB		OMB		VMB	
Year 1	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**
3-day clinical assessment*	$0	$0	$0	$15,000	$0	$15,000	$0	$0	$0	$15,000	$0	$0	$0	$0
Participant co-pay fee varies from $25/mo and up**	$300	$300	$1,200	$1,200	$1,200	$1,200	$4,058	$4,058	$4,058	$4,058	$1,600	$1,600	$2,000	$2,000
Drug testing: 52-104 times @ $100 per	$5,200	$10,400	$5,200	$10,400	$5,200	$10,400	$5,200	$10,400	$5,200	$10,400	$5,200	$10,400	$5,200	$10,400
Nurse Support Group @ from $40 to $160/mo	$480	$1,920	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Health Support Group 1x-2x/wk@ $200-$400/mo	$0	$0	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800
Treatment cost: $0 - $15,000	$0	$15,000	$0	$15,000	$0	$15,000	$0	$15,000	$0	$15,000	$0	$15,000	$0	$15,000
Estimated Year 1 Costs	***$5,980***	***$27,620***	***$8,800***	***$46,400***	***$8,800***	***$46,400***	***$11,658***	***$34,258***	***$11,658***	***$49,258***	***$9,200***	***$31,800***	***$9,600***	***$32,200***
Year 2	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**
Participant co-pay fee varies from $25/mo and up**	$300	$300	$1,200	$1,200	$1,200	$1,200	$4,058	$4,058	$4,058	$4,058	$1,600	$1,600	$0	$0
Drug testing: 24-36 times @ $100 per***	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600
Nurse Support Group @ from $40 to $160/mo	$480	$1,920	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Health Support Group 1x-2x/wk@ $200-$400/mo	$0	$0	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800
Treatment cost: $0 - $5,000	$0	$5,000	$0	$5,000	$0	$5,000	$0	$5,000	$0	$5,000	$0	$5,000	$0	$5,000
Estimated Year 2 Costs	***$3,180***	***$10,820***	***$6,000***	***$14,600***	***$6,000***	***$14,600***	***$8,858***	***$17,458***	***$8,858***	***$17,458***	***$6,400***	***$15,000***	***$4,800***	***$13,400***
Year 3	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**
Participant co-pay fee varies from $25/mo and up**	$300	$300	$1,200	$1,200	$1,200	$1,200	$4,058	$4,058	$4,058	$4,058	$1,600	$1,600	$0	$0
Drug testing: 24-36 times @ $100 per***	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600
Nurse Support Group @ from $40 to $160/mo	$480	$1,920	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Health Support Group 1x-2x/wk@ $200-$400/mo	$0	$0	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800
Treatment cost: $0 - $2,000	$0	$2,000	$0	$2,000	$0	$2,000	$0	$2,000	$0	$2,000	$0	$2,000	$0	$2,000
Estimated Year 3 Costs	***$3,180***	***$7,820***	***$6,000***	***$11,600***	***$6,000***	***$11,600***	***$8,858***	***$14,458***	***$8,858***	***$14,458***	***$6,400***	***$12,000***	***$4,800***	***$10,400***
Year 4	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**
Participant co-pay fee varies from $25/mo and up**	$300	$300	$1,200	$1,200	$1,200	$1,200	$4,058	$4,058	$4,058	$4,058	$1,600	$1,600	$0	$0
Drug testing: 24-36 times @ $100 per***	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600
Nurse Support Group @ from $40 to $160/mo	$480	$1,920	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Health Support Group 1x-2x/wk@ $200-$400/mo	$0	$0	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800	$2,400	$4,800
Treatment cost: $0 - $2,000	$0	$2,000	$0	$2,000	$0	$2,000	$0	$2,000	$0	$2,000	$0	$2,000	$0	$2,000
Estimated Year 4 Costs	***$3,180***	***$7,820***	***$6,000***	***$11,600***	***$6,000***	***$11,600***	***$8,858***	***$14,458***	***$8,858***	***$14,458***	***$6,400***	***$12,000***	***$4,800***	***$10,400***
Year 5	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**
Participant co-pay fee varies from $25/mo and up**	$300	$300	$1,200	$1,200	$1,200	$1,200	$4,058	$4,058	$4,058	$4,058	$1,600	$1,600	$0	$0
Drug testing: 24-36 times @ $100 per***	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600	$2,400	$3,600
Nurse Support Group @ from $40 to $160/mo	$480	$1,920	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Health Support Group (Transition not required)	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0	$0
Treatment cost: $0 - $1,000	$0	$1,000	$0	$1,000	$0	$1,000	$0	$1,000	$0	$1,000	$0	$1,000	$0	$1,000
Estimated Year 5 Costs	***$3,180***	***$6,820***	***$3,600***	***$5,800***	***$3,600***	***$5,800***	***$6,458***	***$8,658***	***$6,458***	***$8,658***	***$4,000***	***$6,200***	***$2,400***	***$4,600***
5 Year Total Estimated Costs	**$18,700**	**$60,900**	**$30,400**	**$90,000**	**$30,400**	**$90,000**	**$44,689**	**$89,289**	**$44,689**	**$104,289**	**$32,400**	**$77,000**	**$26,400**	**$71,000**

*3-day clinical assessments are only required when a more comprehensive evaluation is needed.
**See Board Participant administrative co-pay fees (Table 3).
***12 times per year for mental health diagnosis otherwise 36-104 times per year; 24 times per year for non-working only.
Treatment cost is only required if a participant requires treatment, and mostly at the initial program enrollment or if a participant relapses while in the program.

Table 7 shows the Diversion Program may be cost prohibitive for some, and especially for non-nursing participants. Without insurance or financing, Board subsidies or waivers, it may be financially impossible for some to participate in the program. With some Boards, such as the BOP and PAB, the fee may be waived, reduced or deferred by the DPM if the participant demonstrates financial hardship. Under certain conditions, it would be in the best interest of participants if other Boards consider granting such waivers.

Insurance Benefits for Substance Abuse and Mental Health Coverage

Effective January 1, 2014, the federal Affordable Care Act (ACA) expanded coverage for treatment of substance abuse addictions. Insurance plans are governed by the federal Mental Health Parity and Addiction Equity Act of 2008. In California, the coverage includes both inpatient (residential) and outpatient (day-treatment, individual and group counseling) services.

Those on Medi-Cal that make less than $16,000 per year are also eligible under the ACA. Under Medi-Cal there is a separately funded program for substance abuse known as DMC, or Drug Medi-Cal, which offers inpatient detox, residential treatment, methadone maintenance, and outpatient counseling. At the state level, the Department of Health Care Services (DHCS) administers the DMC and certifies treatment providers. There are over 1,400 DMC-certified treatment facilities statewide. At the local level, county alcohol and drug programs (Adult System of Care) determine applicant eligibility and are reimbursed by DHCS for the cost of those activities.

The website for the US Centers for Medicare and Medicaid Services (CMMS) (https://www.healthcare.gov/coverage/mental-health-substance-abuse-coverage/) indicates all health plans in the health insurance marketplace must cover substance abuse disorder and mental health services, including behavioral health treatment such as counseling and psychotherapy, prescription drugs and laboratory services. Furthermore, marketplace plans cannot deny coverage or charge more for a pre-existing condition. Moreover, marketplace plans cannot put yearly or lifetime dollar limits on coverage of any essential health benefit, including substance abuse disorder and mental health services.

A review of the Covered California website (http://www.coveredca.com) shows there are 12 health insurance companies that are required to provide coverage in compliance with the ACA. A telephone survey of the six largest companies reveals that all provide ACA coverage for substance abuse disorder and mental health treatment. However, under Laboratory Services, the following conditions typically apply to having the cost of random drug testing covered:

- The participant must be a patient of a specific health insurance company/provider that provides such coverage, and
- A physician of the health insurance provider must order a claimable service, and
- The physician must be able to monitor the participant's performance.

The auditors found that all sales agents were not equally knowledgeable about these benefits. Therefore, it behooves program participants to be persistent about getting their questions about Laboratory services covered answered correctly.

Recommendations

3. Maximus should identify a program staff member whose sole responsibility is to become knowledgeable about health insurance coverage benefits and referral sources, and periodically update the Clinical Case Managers and Compliance Monitors.
4. Program participants should assume personal responsibility to contact and research coverage options and costs with the health insurance companies listed on the Covered California website.

Diversion Program Staffing, Roles and Tasks

Based on a review of job descriptions, interviews and observations, CPS confirmed the accuracy of the following Diversion program staff roles and tasks and the six Western Division Shared Services organizations supporting the program

The **Project Manager**, a licensed registered nurse and former hospital administrator, holds a MBA with significant related experience. She is responsible for, but not limited to:

- Ensuring MAXIMUS complies with all applicable contractual requirements, state, and federal regulations.
- Coordinates development of project performance goals, objectives, policies and procedures, and monitors achievements.
- Supervises Clinical Case Managers to ensure requirements are met or exceeded.
- Oversees the Diversion quality assurance program.
- Maintains relationships with the Department of Consumer Affairs (DCA) and the seven Health Professional Boards and Committees
- Maintains effective communications with Clinician Assessors, laboratory subcontractors, and health and nurse support group facilitators.
- Attends, presents and/or chairs meetings and educational programs including, but not limited to: the Diversion Evaluation Committee (DEC) and review committee, the Diversion Liaison Committee, the Diversion Discipline Committee, Board meetings, Quality Improvement Committee, orientations, conferences, and presentations.
- Approves time cards, work plans and schedules, deliverables, contracts, correspondence, billings and invoices, and evaluates staff.
- Performs other corporate responsibilities as required.

The **Operations Manager**, a former Compliance Monitor with substantial program experience, is responsible for day-to-day operations, which include, but are not limited to:

- Assists the Project Manager and ensures the availability of all staff, resources, and Diversion services, are effectively and efficiently delivered throughout California.
- Supervises Administrative Assistants, Compliance Monitors, Quality Assurance, Administrative Assistants and the Medical Records Coordinator.
- Maintains relationships with the Department of Consumer Affairs (DCA) and the seven Health Professional Boards and Committee.
- Maintains effective communications with Clinician Assessors, laboratory subcontractors, and health and nurse support group facilitators.
- In the absence of the Project Manager, attends, presents and/or chairs meetings and educational programs, approves deliverables and signs correspondence.
- Conducts Quality Assurance Testing on the Maximus Case Management System (CMS).
- Updates Diversion Program policies and procedures and provides training as needed.
- Prepares Monthly Status Report, Quarterly Report and Annual Diversion Program Report, and conducts research for special studies.
- Performs other program and corporate responsibilities as required.

The **Clinical Case Managers** (CCMs) are licensed registered nurses with at least three years of experience working in the treatment of substance abuse and/or mental illness. Their educational backgrounds include addiction, psychology and chemical dependency. Until December 2015, they were short-handed one position. CCMs are paired with Compliance Monitors who jointly serve a geographic and Board-specific caseload of up to 130 participants and are responsible for, but not limited to:

- Through continuous communication by phone, mail and email, CCMs manage applicants/participants through intake into the program, clinical assessment, overseeing preparation of initial program entry and recurring recovery agreements, continually monitoring recovery activities and treatment recommendations, and liaising with Boards to ensure overall program compliance and completion success.
- Conduct remote, telephonic assessment and reassessments of impaired licensees to evaluate their overall compliance with program requirements and progress in recovery. Using a standardized template, CCM's conduct a thorough applicant intake telephone interview. In their first contact it is important to set the stage right from the beginning. Participants are generally upset and don't always retain the information given to them the first time. It takes a lot of reinforcement, support and encouragement. After the intake interview, it requires ongoing communications and scheduling of appointments.
- Respond to incoming calls on the toll-free line, as needed, and after-hour, weekend, and holiday calls on a rotating basis with other Diversion Program staff. CCMs are on call

for a week at a time about every 5-6 weeks from Monday to Monday. Most calls are related to lab issues, ER visits or medications.

- Meet with applicant/participant telephonically weekly until seen by the Diversion Evaluation Committee (DEC), and monthly thereafter, to review compliance and progress in recovery. CCMs verbalize the importance of keeping up with all the non-compliant issues daily and the necessity of reviewing all reports daily. In addition, it is necessary to communicate daily with their Compliance Monitor and with the DEC/Diversion Program Manager (DPM) when indicated. All CCMs agree that aside from leaving voice messages and playing phone tag, their biggest obstacle is not having personal interaction face-to-face with a new participant.
- Evaluate incoming information submitted by treatment providers, facilities, participants, and labs to monitor participant's progress and compliance with recovery agreements.
- Ongoing communications with the participant, the appropriate Board/Committee (or their designee) or treatment providers, facilities and labs in response to participant non-compliance with their recovery agreement.
- Enter information into the Maximus CMS (Max-CMS). Compiles, produces, reviews and ensures timely distribution of the History and Profile (H&P) reports before submitting to the DPMs. There is an abundance of paper work compiled several weeks ahead of time. All of the CCM's and CM's are looking forward to the Boards having access to all information on-line so there won't be a need to compile massive paper packets.
- Review Monthly Compliance/Non-Compliance reports and letters, as well as other reports and correspondence, as required. The CCMs' agree it is an ongoing daily process and that the upgraded Max-CMS will be a time saver since all the information will be within one tracking system.
- Produce other reports and letters as requested, including the "Letter of Successful Completion."
- Serve as liaison for assigned Board/Committee and their designee (DPM), DEC Case Consultant, DEC Chair and provide clinical case input.
- Perform other program and corporate responsibilities as required.

The **Compliance Monitors** (CMs) are college-educated with three-to-five years of experience in a behavioral health care setting related to chemical dependency, recovery, and/or mental illness. Their educational backgrounds include biology, chemistry, psychology and pharmacy. They constantly communicate with their paired CCM and are responsible for, but not limited to:

- Respond to incoming calls from participants regarding their program participation, applicants regarding entry into the program, and licensees regarding general program information. Contact participants for additional relevant information.

- The CM's mail the new applicant's package of information within five days of the initial intake and from there the process begins. After the CCM completes the telephone intake and schedules the clinical assessment and first DEC meeting, the CM's begin daily tracking. The CM's all rely on the Maximus daily tracking system that tracks the timelines of due dates of all items to be sent or to be received and lab correspondence. In addition, all mailed and faxed documents are scanned into the record immediately. As a result, the CCMs and CMs are able to access the Case Logs to review up-to-date documentation.
- Prepare initial entry agreements and recurring recovery agreements based on participant case history and forward to the CCM for review and approval.
- Collect and analyze incoming data and reports from participants, treatment providers, labs, and other team members to determine the participant's level of compliance and enter necessary information into the Max-CMS. The CM's check all documents received to ensure they are timely and complete. If items are missing, late, or incomplete, the CM informs the CCM and the issues is entered onto the case log. They also check to see if there are any missed calls into the lab or if there are late fees, etc. They call the participants to inform them of potential violations as related to their agreement. If participants are non-compliant, the CM's reports the non-compliance to the CCM to determine the compliance level. The CM writes a non-compliance letter and the Administrative Assistant mails the documents to the participants and to the Boards. The CMs then enter the findings into the case log and notify the participants. The CM's manage the paper work and CCM's manage the participant's systematic recovery process.
- Make follow-up calls to respond to non-compliance data from providers.
- CMs produce monthly compliance/non-compliance reports and letters based on analysis of information received from participants, treatment providers and the laboratory. The Recovery Contracts are updated at each DEC or Board meeting and more often if needed. The update information is written into the DEC/ Committee minutes by the CCM's. The CM's revise the Recovery Agreement based on the DEC/Committee recommendations. Information is entered into the template and reviewed with CCM's before forwarding the revised contract to administrative assistant for mailing to the participants and the Board.
- Compile, produce, and timely distribute the H&P reports to CCM, Client DPMs, and DEC members.
- Perform other program and corporate responsibilities as required.

The **Administrative Assistants** and **Medical Records Coordinator** possess at least an Associate's degree with at least two years of experience in behavioral health care, call center and/or crisis intervention. They are responsible for, but not limited to:

- Respond to incoming calls from licensees, Boards/Committee and their designee,

applicants/participants and other inquiries. Apply standardized protocol to identify cases requiring immediate crisis or clinical intervention.

- Process incoming faxes and incoming U.S. mail.
- Provide necessary administrative support, including handling correspondence.
- Perform limited direct participant services under supervision.
- Manage and file documents and correspondence received from and sent to participants.
- Maintain participant records in hard copy file format, scan and index documents.
- Prepare H&Ps for mailing.
- Maintain and prepare orders for office supplies for department.
- Perform other program and corporate responsibilities as required.

In summary, the Project Manager reports all assigned work is getting completed but due to a CCM vacancy, CCM/CM workload has increased and will until the position is filled (the position was filled in mid-December 2015). The Project Manager emphasized how critical the CCM/CM teamwork is to program success.

Shared Services Roles and Responsibilities

Based on interviews and documentation reviews, CPS confirmed Diversion Program staff are supported effectively and efficiently by the following Maximus Western Services Division departments displayed in the Figure 1 organization chart. The Project Manager recognizes the cost effective benefits of having full-time departments support this small program which would otherwise be unaffordable. The following briefly discusses the services each department provides, staffing levels, and information CPS reviewed.

Quality Assurance/Training Department

The Quality Assurance/Training Department has a central role in ensuring project operations, quality assurance and training adhere to ISO 9001:2008 standards, resulting in program success. There are 14 Quality Analysts in this department, including one QA Analyst dedicated to the Diversion Program. The QA responsibilities cover eight Maximus programs, including the Diversion Program.

The Maximus Quality Manual, Quality Assurance Plan (QAP) and other written procedures provide the integrated framework and detailed work instructions to ensure contract provisions and quality standards are met, information is reported, corrective and preventive actions are taken, and the process is continually improved. The QA function has its own system (ITG) for identifying, tracking, correcting and reporting on QA problems. The QAP is reviewed and updated annually.

According to the Quality Assurance Plan, ISO 9001:2008 requirements stipulate inspections and testing of critical process inputs and outputs. Inspections take place at four levels: individual, supervisory or quality control, quality assurance, and ISO 9001:2008 audits.

- Quality control is a failure detection system that uses observation techniques and activities to identify and correct errors in products or services to ensure they meet defined requirements.
- Quality assurance is a failure prevention system that uses planned and systematic activities like defined processes and procedures to ensure products or services delivered will be of good quality.

The first level of Quality Control (QC) monitoring activities start with individual staff members. Each employee is required to inspect his or her own work in accordance with the established procedures and standards. Each individual inspects the inputs they receive from another process before sending it forward for further processing.

The second level of QC inspection involves the Program Manager and/or Operations Manager who review and evaluate process outputs based on established requirements and standards. They document their monitoring results and take immediate corrective action for any unacceptable results.

Quality Assurance (QA) Analysts are responsible for the third level of inspection which starts the quality assurance process. They are primarily responsible for sampling processes on a scheduled, monthly basis to ensure Quality Management System controls are operating correctly and that all requirements and standards are met. The analysts retrieve samples from the MAX-CMS using a sampling formula that ensures a 95% confidence level and 5% error rate unless otherwise noted in the Maximus Sampling Procedure.

The monthly QA evaluations use checklists based on criteria extracted from contract requirements, state law and regulations, business rules and internal process standards. The analysts document the evaluation data for trending, research, and quality improvement purposes in the Monthly Quality Management Performance Report per the required procedure.

The following 13 processes or products are subject to monthly QA evaluations.

Process/Product	Evaluation Criteria	QC Sample	QA Sample	Reporting
Initial Intake	Timeliness, accuracy	None	100% of sample	Standard QA Report
Worksite Monitor	Timeliness, accuracy	None	Standard sample	Standard QA Report
Random Drug Test	Timeliness, accuracy	1 positive result per CCM/CM team monthly randomly selected	Standard sample	Standard QA Report & Standard Business Unit Report
Recovery Agreement	Timeliness, accuracy	5/month randomly selected	Standard sample	Standard QA Report
Non-Compliance Letters	Timeliness, accuracy	4/month per CM randomly selected	Standard sample	Standard QA Report

Monthly Reports/Contacts	Timeliness, accuracy	None	Standard sample	Standard QA Report
Document Scanning	Timeliness, accuracy	10 documents/week randomly selected	Standard sample	Standard QA Report
Billing (Premium) Processing	Timeliness, accuracy	None	Standard sample	Standard QA Report
Physical Therapy Board	Accuracy	None	1 intake/quarter	Monthly Business Unit Report
Call Monitoring	Various call aspects	None	Min of 3 staff/week	Standard QA Report
Case Closures	Info ok and verified	100% of files with public risk	None	Standard Business Unit Report
Clinical Assessors	Various appointment aspects	None	3 per month	Monthly Business Unit Report
Lab Test Results	Cut off levels	1 result daily		Monthly Business Unit Report

Source: Maximus Quality Assurance Plan, DPP-12-01

One result of the work of the QA Analyst is a Monthly Quality Management Performance Report that summarizes and provides details on the results of the 13 processes or products evaluated during the month. This includes a breakdown of the number of items reviewed, errors found, a trend analysis against the specific goal, and a root-cause analysis of the top errors. Monthly meetings are held with the Diversion staff to discuss the findings and corrective action required.

In addition, the QA Analyst monitors and reports monthly on the performance of 45 specific contract provisions (see Appendix 5, Contract Performance Standards Measured). The Diversion Program Performance Standards Analysis Report is referred to as the "red-green" report because items meeting standards are shaded in green while those that are not are shaded in red.

The December 15, 2015 red-green report covers from December 2014 through November 2015. Table 8 shows the number of contracts standards measured every month for the past year varied from month to month, but overall compliance with the standards averaged 94% per month.

Table 8: Contract Standards Compliance from December 2014 through November 2015

Month/Year	12/14	1/15	2/15	3/15	4/15	5/15	6/15	7/15	8/15	9/15	10/15	11/15	Avg
Contract Stds Measured	45	45	45	45	45	45	45	45	45	45	45	45	45.0
Contract Stds Not Measured	11	10	9	13	14	9	14	10	7	12	11	9	10.8
Number of Contract Stds Met	31	33	35	32	29	34	30	32	35	32	33	31	32.3
Compliance Rating	**91%**	**94%**	**97%**	**100%**	**94%**	**94%**	**97%**	**91%**	**92%**	**97%**	**97%**	**86%**	**94%**

Source: Maximus

Both of these monthly reporting activities demonstrate how thorough, yet prescriptive and administrative-intense the ISO process is. The samples are drawn and analyzed from the Maximus CMS which is efficient and paperless.

In the past before the new scanners were deployed, there was a document scanning backlog. However, the backlog did not impact program participants because staff and used original

hardcopy documents. With the implementation of new scanning equipment and electronic document policy, there is no longer a document scanning backlog.

The fourth level of inspections is an Internal Quality Audit per the required procedure. The purpose of these audits is to verify whether quality activities and related results comply with requirements and to determine the effectiveness of the quality system. The Internal Audit department may conduct 4-5 operational reviews a year of the program based on its policies and procedures. Finally, Bureau Veritas conducts a two-day surveillance audit once a year and an in-depth, end-to-end ISO audit every three years.

The program has been primarily aimed at tracking activities performed and timeliness, and outcomes such as successful completions, terminations and relapses. The QA analyst continually tests for procedural untimeliness that is corrected through the Corrective and Preventive Action (CAPA) Procedure, DPP-12-03 and tracked in the QA ITG database.

All staff receive mandatory corporate training for HIPAA, safety and sexual harassment. The Quality Analysts participate in a formal training program and receive additional in-house on-the-job training based on their education and experience. Maximus also offers a professional development program and staff can request outside training, which is typically granted. Maximus is also taking action to train or hire more certified internal auditors and project managers.

Administrative Services Department

The Administrative Services Department provides the Diversion Program with the following services: budgeting, forecasting, accounting, accounts payable, accounts receivable, and contracts. These services incorporate three of the shared services boxes on the organization chart.

The Senior Director of Administrative Services has one direct report and three other non-direct reports. In addition to the Diversion Program, this unit supports 13 other Maximus programs and projects.

Boards pay Maximus a participant fee and participants pay Maximus a co-pay that is credited back to the Boards. Depending on the Board, Maximus may or may not have a financial risk. Accounts Receivable (AR) bills the Boards (by the 10th calendar day of the month) and participants (by the 20th calendar day) according to the contract requirements. Payments are received and accounted for through a bank lockbox.

AR also performs the collection function which includes establishing payment plans for delinquent participants. If a participant is delinquent, AR notifies the program and CMs prepare and send non-compliance letters. The Quality Assurance (QA) Analyst ensures non-compliance letters were sent to participants that are more than 60 days in arrears with their payments. The Annual Reports for the last Fiscal Years 2010-11 through 2014-15 reveal there have been about three delinquent participants per fiscal year.

CPS reviewed comprehensive policies and procedures concerning Project Financial Management that include the accounting system of record; budgets, forecasting and variance analysis; accounts receivable (billing and collection) and accounts payable; contracting and management reporting. Execution of these policies and procedures, including billing compliance, is continually monitored by the Quality Assurance Analyst. The only financial performance metrics concern timely billing of the Boards and participants. The QA Analyst reported there are no financial process delays or operational issues with the participant billing process.

To verify the program's financial reporting process and its financial condition, CPS reviewed end-of-calendar year monthly Project Status Reports as of January 1, 2010, 2011, 2012, 2013 and 2014. Also reviewed were income statements and accounts receivable aging reports for the same time periods.

In our opinion, the monthly Project Status Reports provide the Project Manager with complete and timely information to manage the project. The reports summarize total funded, billed to date and balance due, and track current period revenue and expenses, year to date and contract to date actuals. The reports also contain detailed line items that capture total revenue, labor and non-labor expenses, overhead allocations, total expenses and profit.

The following table 9 shows a summary income statement covering Calendar Years (CY) ending in 2011 through 2014. Since CY 2011, program revenue has been stable but profitability has varied substantially as the number of program participants, direct labor, direct costs and allocations have fluctuated.

Table 9: Summary Income Statement*
CYs 2011 – 2014

	12/31/10	12/31/11	12/31/12	12/31/13	12/31/14	Totals	% Total Revenue
Revenue	**$2,190,579**	**$2,187,733**	**$2,186,800**	**$2,241,025**	**$2,249,313**	**$11,055,450**	**100.0%**
Direct Labor	1,176,211	1,358,249	1,218,332	1,352,691	1,389,331	6,494,814	58.8%
Direct Costs	219,435	276,371	302,080	315,322	285,992	1,399,200	12.7%
Overhead, G&A	315,777	337,521	308,777	310,668	323,936	1,596,679	14.4%
Total Costs	**$1,711,423**	**$1,972,141**	**$1,829,189**	**$1,978,681**	**$1,999,259**	**$9,490,693**	**85.9%**
Profit	$479,156	$215,592	$357,611	$262,344	$250,054	$1,564,758	14.1%
% Profit	21.9%	9.9%	16.4%	11.7%	11.1%	14.1%	

Source: Maximus (numbers are rounded)*

As a publicly traded company, Maximus has multiple layers of internal and external controls. In addition to continual review by the QA Analyst, there is a Maximus internal audit team and an outsourced PriceWaterhouseCoopers internal audit team. The external auditors include Ernst & Young and Bureau Veritas (ISO auditor).

The Contracts Unit consists of three staff that maintain copies of subcontract and Clinical Assessor agreements, provide updates to Diversion ISO procedures and policies that pertain to contracts, and compile monthly Supplier Performance Evaluations from various departments. The Diversion Program consumes minimal time.

The unit has detailed written policies and procedures that are subject to the continual QA review process to ensure contract policies, procedures, legal and compliance provisions are being met. The unit manager and the QA Analyst confirmed there are no persistent financial management process delays or operational issues.

Information Systems Department

The Information Systems Department (ISD) supports the Diversion Program Maximus CMS, a mission-critical program component. The Maximus CMS is planned to be updated to further improve operational effectiveness and efficiency in 2016.

The Director of ISD has five staff including two in application development & testing and three in infrastructure, database management and data warehousing. Staff spend less than half their time supporting the Diversion program as they also support a Michigan healthcare project, a Federal background check project, and a Hawaii call center.

The most important performance metric for this department is 100% percent uptime. During 2015, the application, database and web servers' average uptime was 100%, and the Max-CMS database average uptime was 99.5%.

ISD is not required to comply with ISO standards but must comply with the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and security policies. CPS reviewed the HIPAA policy contained within the Corporate Employee Manual. CPS found the policy establishes compliance with the national standards for privacy of individually identifiable health information designed to meet HIPAA and contract requirements.

CPS also reviewed the comprehensive Maximus Information Security Policy which covers confidential information handling, storage, reproduction, transport and destruction; system access and privileges; internet connections; use of Maximus electronic communications systems; application development; business continuity and disaster recovery; encryption; portable computers and remote printing; privacy and personal use; software copying; physical security and violations. CPS found the policy meets contract requirements.

In addition, CPS reviewed the Maximus Server Security Policy, Application Security Statement and Physical Security Policy and found them to be comprehensive and compliant with contract requirements. CPS did not test the effectiveness or efficiency of the various policies.

Furthermore, CPS reviewed the master services agreement with Iron Mountain to provide storage of records and media, document scanning and shredding services, and found it to be compliant with contract requirements.

Human Capital Department

The Human Capital (HC) Director manages three professional and three support positions. The department supports all HC functions for the Diversion Program including:

- **Recruitment/Selection** - maintains recruiting database including job postings, resumes, background checks, offer letters, and electronic on-boarding, etc. Trend data for CY 2014 shows program turnover at less than one percent annualized. New positions are posted internally first. Program administrative positions are commonly filled by internal candidates. Recruitment/selection issues for Program openings include highly specific skillset for RNs which requires specialized sourcing of nurses more suited to the alcohol/chemical dependency aspects of this program.
- **Classifications** - Personnel Requisitions are submitted to the corporate compensation team to confirm selected classification/job titles, etc. Maximus does not "impose" corporate-wide job descriptions/classifications on work sites with differing needs.
- **Employee Relations** - Human Capital Director works directly with Project Manager and/or Operations Manager to address employee matters.
- **Performance Management** – The annual review of employees is done in April and they are eligible for quarterly bonuses.
- **Benefits Administration** – The local HC supports open enrollment and answers questions while Corporate Total Rewards administers the benefit program.

HC training responsibilities include: state-mandated sexual harassment training (AB 1825) for management and mandatory annual supervisor training for: EEO Compliance, Corporate Compliance Refresher, Employee Disclosure, and Workplace Harassment Refresher. HC provided CPS with a compliance training matrix showing that Diversion Program staff received required training.

Diversion Program Manager Survey Results

In lieu of observing DEC and Board Participant Review meetings, CPS surveyed the DPMs and attended a monthly DPM meeting resulting in the following opinions and observations.

The DPMs represented both DEC (4) and PRM Non-DEC (3) Boards. The DPMs averaged almost eight years of experience in the position and ranged from nine months to 30 years on the job. The survey results indicated the following:

- All receive information timely from Maximus before a meeting.
- They all have remote access to the Max-CMS but only 4 of 7 use the system extensively.

- Of those using the Max-CMS, all experienced a high (>98%) percentage of uptime and most reported the information is generally complete and accurate, and the system is easy to use.
- Decisions and outcomes are well documented based on standardized templates (100%).
- They receive materials timely (within 7 days) after the meetings.
- On a scale of 1 to 5 with 5 being the highest, the DPMs rated the following:
  - Program effectiveness for licensees: average 4.6
  - Maximus CCM knowledge and expertise: average 4.6
  - Program efficiency: average 4.8
- Some DPMs felt cost was not a factor, but most indicated the total program cost to the participant is expensive.

As a result of the DPM meeting, CPS learned the following:

- Issues or obstacles that affect program efficiency include phone "tag" between program staff and participants, lost paperwork and participant delays.
- There is a perception that DEC Boards provide a better recovery process, but there are insufficient data to support the hypothesis. DEC advocates feel their process advantage is face-to-face interaction with participants, Board and DEC members. It is an effective way to see changes in participants which is better than just reviewing hard data. Non-DEC advocates contend they can make more timely decisions that benefit participants without requiring Board approval. DEC DPMs claim the same decision-making advantage and can override a health care professional, but are reluctant to do so because they don't possess the same level of technical healthcare knowledge.
- Most DPMs claimed they lack formal drug training but would benefit from it.

As a result, many DPMs suggested the following Diversion Program improvements:

1. Hire more CCMs and increase the number of participants.
2. Identify ways to better manage or reduce participant costs.
3. Identify ways to better treat participants suffering from mental illness.
4. Provide DPMs with recovery training.

Recommendation

5. Maximus should consider and evaluate all of the DPM recommendations and, at a minimum, provide the DPMs with recovery training.

Treatment Provider Survey and Credential File Audit Results

As part of an outreach to key program stakeholders, CPS HR conducted a brief online survey directed to a sample of the following Diversion Program Treatment Providers:

- Clinical Assessors (30)
- Nurse Support Group leaders/facilitators (41)
- Health Support Group leaders/facilitators (19)
- Worksite Monitors (20)

The purpose of the survey was to both solicit general information on program stakeholder experience as well as identify ways to improve program effectiveness and efficiency. The following summarizes the survey findings and recommendations. The complete results are presented under separate cover.

Response Rates

A total of 60 of 110 invitees responded to the survey. With the exception of Worksite Monitors, the survey response rate exceeded the 50% target for the respondent sub-groups.

Stakeholder Group	# Responding	% Responding of those Invited
Clinical Assessors (CA)	20	66.7%
Nurse Support Group leaders/facilitators (NSG)	22	53.7%
Health Support Group leaders/facilitators (HSG)	12	63.2%
Worksite Monitors (WSM)	6	30.0%

Table 10 summarizes Treatment Provider respondent experience and their participation in the Diversion Program. Based on their collective experience, it appears the Boards and Maximus should pay attention to the results of this survey.

Table 10: Treatment Provider Experience and Program Participation

Experience and Program Participation	CA	NSG	HSG	WSM
Avg. years evaluating health care professionals?	21.6 yrs.	15.4 yrs.	21.0 yrs.	NA
Avg. years working with the Diversion Program?	12.3 yrs.	10.9 yrs.	15.6 yrs.	2.1 yrs.

Clinical Assessor Responses

Clinical Assessors indicated the following about key aspects of their practice:

- They assess up to three participants a month, but average one per month.
- An assessment appointment ranges from one to two hours, but averages one hour.
- All respondents indicated they were able to submit an assessment report within the required 10 days after the assessment is completed.

Clinical Assessors claim the following obstacles/challenges (not inclusive of all responses) hinder their role in the Diversion Program:

1. Participants miss appointments or cancel late.
2. Participants misunderstand the program requirements.
3. Untimely receipt of material for the assessment
4. There is a lack of treatment options in the area they work.
5. They are unable to complete the assessment on a computer.
6. Lost billings delay payment.

Many Clinical Assessors recommend the following improvements (not inclusive of all responses) to the Diversion Program:

1. Simplify and clarify the participant administrative requirements.
2. Provide for online transmission of program forms.
3. Update the clinical assessment tool.
4. Institute DECs for all professions.
5. Increase DEC training.
6. Pay for assessments cancelled with less than 48 hours' notice and for no show appointments.

Nurse Support Group Facilitator Responses

NSG facilitators indicated the following about key aspects of their practice:

- They facilitate up to three groups per week, but average about two per week.
- Participants range from 6 to 21 per session, but average about 12 per session.
- Session costs range from free to $40, but average $19 per session.
- On average, about 66% of group participants are in the Diversion Program; the balance are in the Probation Program.

NSG facilitators claim the following obstacles/challenges (not inclusive of all responses) hinder their role in the Diversion Program:

1. Lack of direct communication with Maximus about participants and changes in program policies and procedures, including untimely call backs and an inability to email case managers.
2. The implementation of SB 1441 has changed the program focus from rehabilitation to punitive discipline. The rules and regulations are often too rigid and inflexible, and there is an unreasonable, high frequency of drug testing.
3. Lack of adequate in-service training.
4. Access to the Maximus website can be frustrating and cumbersome.

5. When probationers exceed program participants, the group tends to become more negative.

NSG facilitators recommend the following improvements (not inclusive of all responses) to the Diversion Program:

1. Improve direct communication with Maximus case managers, including written notification of policy and procedure changes, and email notification of participant non-compliance, transition or completion.
2. Provide participants with more information about the Diversion Program and what to expect at their first Board or DEC meeting.
3. Maximus staff should observe more group sessions.
4. Provide more opportunities for facilitators to receive training, such as an annual, offsite conference.
5. Provide more mental health options.

Health Support Group Facilitator Responses

HSG facilitators indicated the following about key aspects of their practice:

- They facilitate up to eight groups per week, but average about three per week.
- Participants range from 2 to 14 per session, but average about 8 per session.
- Session costs range from $21 to $75, but average $47 per session.
- 92% of respondents indicated they are able to complete and submit the monthly attendance and participation report by the required 10th of the following month.

Many HSG facilitators claim the following obstacles/challenges (not inclusive of all responses) hinder their role in the Diversion Program:

1. The Maximus case manager caseload is too high to be effective, resulting in inadequate and untimely communication between all parties.
2. Maximus does not give enough consideration to HSG facilitator feedback.
3. The punitive manner in which participants are treated by their respective Boards.
4. Lack of program training.
5. Except for BRN, the participant census from the other Boards is low.

HSG facilitators recommend the following improvements (not inclusive of all responses) to the Diversion Program:

1. Reduce Maximus case manager caseloads.
2. Provide HSG facilitators with access to intake summary, evaluations and treatment reports.
3. Coordinate treatment decisions with HSG facilitators before implementation.

4. Maximus case managers should attend more HSG sessions.
5. Maximus should provide more diversion training through area meetings.
6. Maximus staff should observe more group sessions.
7. Improve marketing of services through more outreach.

Worksite Monitor Responses

WSMs indicated the following key aspect about their practice:

- They can monitor up to two participants at any time, but the average is one at a time.

WSMs claim the following obstacles/challenges (not inclusive of all responses) hinder their role in the Diversion Program:

1. They lack the ability to contact the Maximus CCM or CM by email.
2. Due to early diversion-related meetings, participants leave early from work.
3. Difficult to contact Board Diversion Program Managers.
4. They have limited time to observe in a clinical setting.
5. Often have to wait for mailed participant evaluations.

WSMs recommend the following improvements (not inclusive of all responses) to the Diversion Program:

1. Establish email communication with Maximus staff.
2. Provide the ability to either fax or submit online monthly and quarterly reports.
3. Provide improved access to Board Diversion Program Managers.
4. Provide participant evaluations by email.

Recommendation

6. Maximus should consider and evaluate all of the stated Treatment Provider obstacles/ challenges, then prioritize and implement the recommendations accordingly.
7. As evidenced by the success of this online survey, Maximus should periodically reach out to Treatment Providers and other stakeholders to identify ongoing issues and opportunities for continuous improvement.

Credential File Audit Results

CPS reviewed a 10% sample of Maximus and Board treatment provider credential files to ensure compliance with Uniform Standards 1, 5, 7 and 13. Except for WSMs with no files, all other credential files were found to partially comply with the Uniform Standards. Most files provided evidence of license/credential verification, experience and insurance. However, most lacked evidence of Board approval and a disclaimer to not accept licensees with whom they have had a personal, financial or business relationship within the last year.

Specifically, a review of four Clinical Assessor credential files revealed evidence of a valid license was independently verified through the state website (www.breeze.ca.gov) 100% of the time. However, evidence of three years' experience in providing evaluations of health professional with substance abuse disorders, and $1 million of malpractice and general liability insurance was present only half the time.

The review of four Health Support Group Facilitator credential files discovered that a valid license was independently verified through the state website or by hardcopy credential, and the three years' experience was documented 100% of the time. But, there was no evidence documenting whether there was a financial, personal or business relationship with the licensee within the last year.

The review of six Nurse Support Group Facilitator credential files exposed evidence of the three years' experience and a Board-signed document 100% of the time. However, in most cases there was no documentation of independent verification of the license or whether a financial, personal or business relationship existed with the licensee within the last year.

The review of WSMs disclosed almost a total absence of required documentation. CCMs report verifying WSM licenses, when applicable, but there aren't any WSM folders. Consequently, there is no evidence of license verification of licensed healthcare professionals, and a signed affirmation including a statement the WSM agrees to not accept licensees with whom they have had a financial, personal or business relationship within the last year.

Finally, PHCS noted the absence of two documents commonly found in healthcare credentials that are not covered under the Uniform Standards. These include an Office of the Inspector General (OIG) exclusion clearance and a HIPPA confidentiality statement.

Recommendations

8. Maximus and the Boards should ensure each credential review is completed in compliance with the Uniform Standards, including evidence of: a license, experience and insurance; do not accept licensees with whom they have had a personal, financial and business relationship within the last year; and Board approval.
9. Per healthcare standards, perform and document an OIG clearance for each Treatment Provider at https://exclusion.oig.hhs.gov
10. Per healthcare standards, require all Treatment Providers with access to records to sign HIPPA confidentiality statements.

Participant File Review Results

The following presents the participant file review methodology PHCS used and the audit findings and recommendations.

Participant File Review Methodology

The Maximus participant file review was based on the Uniform Standards Regarding Substance-Abusing Healing Arts Licensees dated April 2011, specific requirements of each Board, and the 2010 – 2014 Maximus contracts with the Department of Consumer Affairs.

PHCS selected and reviewed a random, statistically-valid sample of 103 Participant files spanning the audit period of 2010-2014. Files were reviewed for every Board, and for all 14 BRN DECs across the state. The files were reviewed by two PHCS registered nurses with master's degrees who have extensive experience reviewing patient charts.

Table 11 reveals most reviews were done on BRN participants (77.7%), followed by BOP (9.7%), PTB (4.9%), PAB (2.9%), DBC and OMB (1.9% each) and VMB (1%).

The cases reviewed contained 40 BRN participants who diverted drugs and four in the BOP. There were three participants in the BRN program who falsified prescriptions and one in the DBC program who self-prescribed.

Table 11
Summary of Program Closures of Participant Cases Reviewed

	SELF WITHDRAWALS			BOARD CLOSURES								
Board	Pre/Post DEC	Moved out-of-state	Financial hardship	Not clinically appropriate	Terminated: public risk	No longer eligible	Terminated: non-compliant	Continues in program	Continues in transition	Successful completion	Totals	% Total
BRN	7	2	0	1	8	0	4	22	18	18	**80**	***77.7%***
BOP	0	0	0	0	3	1	0	3	3	0	**10**	***9.7%***
PTB	0	0	1	1	0	0	0	1	2	0	**5**	***4.9%***
PAB	0	0	0	1	0	0	0	1	1	0	**3**	***2.9%***
DBC	0	0	0	1	0	0	0	0	1	0	**2**	***1.9%***
OMB	2	0	0	0	0	0	0	0	0	0	**2**	***1.9%***
VMB	0	0	0	0	0	0	0	0	1	0	**1**	***1.0%***
Totals	**9**	**2**	**1**	**4**	**11**	**1**	**4**	**27**	**26**	**18**	**103**	***100.0%***
% Total	***8.7%***	***1.9%***	***1.0%***	***3.9%***	***10.7%***	***1.0%***	***3.9%***	***26.2%***	***25.2%***	***17.5%***	***100.0%***	

Participant File Review Findings and Recommendations

PHCS found Maximus complied with all of the Uniform Standards and protocols for each participant file reviewed. In some cases, original supporting documents were not available for review, but the case logs summarized the document contents in compliance with the applicable Uniform Standards. Most participants had a history of drug and/or alcohol addiction. One BRN participant was in the psychiatric diversion program and two other participants had histories of mental illness with alcohol and chemical dependency. PHCS also identified opportunities for improvement.

Participant Contact

In compliance with Uniform Standard 14, because the participating Boards use a private-sector vendor to provide diversion services, they must and do publicly disclose their involvement in the Diversion Program and provide restricted licensee information on their websites.

According to the Maximus Annual Report, all test telephone calls made to the toll-free 24/7 telephone line were answered by Maximus within the five-minute standard. The auditor's tests confirmed this practice. However, it was not uncommon for participants to spend a prolonged amount of time trying to reach CCMs for routine calls.

Participant concerns documented in the case log and interviews with CCMs confirmed a problem with returning calls promptly. Until December 7, 2015, one CCM position had been vacant since June 2015. With all positions filled, the problem should improve and routine calls should be answered more promptly, but this should continue to be monitored.

For those employed participants, PHCS found evidence of written participant consent to communicate with employers in compliance with Uniform Standard 3.

Recommendation

11. Maximus should consider hiring a part-time CCM to cover vacations, illness and time away at DEC meetings, etc. This will improve the management of multiple calls.

Participant Orientation Documentation Lacking

In an isolated incident in 2011, one clinical case review did not show evidence of a licensee orientation. Maximus identified the problem and soon thereafter implemented an orientation template to ensure adequate documentation.

Clinical Assessments

PHCS found the summaries of the clinical assessment reports documented in the case logs revealed:

- The report contents meet the requirements of Uniform Standard 1;
- Uniform Standard 2, the temporary removal of the licensee from practice pending the results of the clinical assessment was met; and
- Treatment considered the clinical diagnostic evaluation recommendation required by Uniform Standard 6.

The auditor also found there was a slight delay occasionally in completing the clinical assessment within the standard 20 business days of the initial intake. In general, delays exceeding the standard were due to the participant being occupied in an inpatient treatment center or unable to keep the appointment. There was only one delay that was not explained in the case logs or participant's profile. Maximus staff should continue to work to diminish the obstacles and document reasons for delay.

Recommendation

12. Maximus program staff should continue to document reasons for assessment completion delays.

Participant File Maintenance Issues

PHCS found multiple instances of incorrect or unclear entries in case files, misspellings and incorrect use of pronouns.

A few participant entries were found in the wrong case logs. The errors were usually found several days later, but the wrong entry stayed in the case log. It is common practice for an error in an electronic record to be flagged to indicate it has been corrected.

Maximus currently lacks a written procedure for making deletions or retractions to case logs. The current informal practice is to correct the case log without marking the incorrect entry as an error.

There were also multiple misspelled words in the case logs which can lead to the wrong interpretation or meaning of the notes. The current Max-CMS version allows spell check capability for only a few employees. However, the upgraded version in 2016 will make spell check available to all employees and treatment providers and should correct much of this problem.

Some of the case log notes entered by one CCM were unclear due to fragmented sentence structure or imprecise documentation. This particular staff member is highly regarded for her ability to communicate with participants, but should use the improved spelling and grammar check feature in the upgraded Max-CMS. The Project Manager should also review and revise closing notes as necessary.

Finally, PHCS frequently found the incorrect use of 'he/she' pronouns. The wrong pronoun may cause the reader to question whether the entry in the case log is correct. Using the participant's first or last name rather than pronouns only will prevent misunderstandings concerning entries.

Recommendations

13. All program staff should take advantage of the improved spelling and grammar check feature in the upgraded Max-CMS.
14. The Project Manager should review and revise closing notes as necessary.
15. Use the participant's first or last name rather than pronouns only to prevent misunderstandings with case log entries.
16. Maximus should develop and implement a written policy for making deletions and retractions to case logs. The American Health Information Management Association website (http://www.ahima.org) has examples and sample policies Maximus could use.

Program Understanding and Obstacles to Compliance

Program participants face many obstacles on their road to recovery. Based on file reviews and interviews with Maximus program staff, applicants often have a difficult time comprehending all

the rules and expectations specified in Uniform Standard 10 early in the program due to high anxiety and/or their addiction/disease conditions.

PHCS identified obstacles including, but not limited to: financial hardships; temporary disability with less pay; loss of health insurance, car and/or driver's license, and home. Some participants ended up living in their car or in a sober living facility that was not always safe. Others suffered from guilt and anxiety, fear of failure, low self-esteem and relationship problems that made it difficult to comply with all aspects of the program. It was not clear how many participants withdrew due to these obstacles and others.

Some participants did not understand they needed to discard the drugs they were not allowed to use. Some participants gave their unused drugs to others and did not understand that this is a violation of the Nurse Practice Act.

CCMs and CMs continually reminded participants of their responsibilities and advised them that part of the recovery program is being accountable for their own actions and inactions.

Recommendations

17. Maximus program staff should track and trend the reasons for program withdrawal to determine the number of participants who withdrew for financial and other reasons.
18. Maximus program staff should improve the Program Handbook in the following ways:
    - Explain in the Handbook how to properly dispose of drugs according to the US Food and Drug Administration web site, and emphasize that participants may not give the drugs they are discarding to other persons for their use.
    - Attach a letter to the applicant's packet to encourage reading/re-reading the Handbook until they are familiar with the rules and expectations (participants are required to sign, date and return the Handbook Acknowledgment Signature Sheet), and consider giving applicants a pre-DEC test to validate their understanding.

Major Compliance Violations

The file reviews revealed the most common avoidable **MAJOR** violations were generated because participants failed to call the lab on a daily basis, missed a random drug test, or had a non-negative or positive drug test. It appears many participants have difficulty organizing their required daily and monthly tasks to comply with the program requirements. They reported posting notes all over the house so they would not forget to call the lab on a daily basis. However, they sometimes forgot and suffered the consequences.

Missed daily calls and/or missed tests result in immediate removal from work and at least an additional two urine drug screens. According to program policy, participants must pass two consecutive negative tests results before Maximus will allow them to return to work.

Recommendation

19. Maximus should modify the Program Handbook in the following ways:

- Add an index so applicants/participants can easily find needed information.
- Modify the drug testing information to include stronger language about the consequences of missing a call into the lab and missing a random drug test.
- Use **bold letters** or **highlight** the essential compliance information.
- Insert the Maximus Diversion Program Random Body Fluid letter into the Handbook and include additional information regarding caffeine and protein. For example: "Please be aware that any confirmed positive, dilute or out of range random body fluid testing (RBFT) may result in **immediate suspension of work privileges**.

  Tips to ensure test results fall within acceptable ranges include:

  - Do not use any mind-altering substances.
  - Test before 10:00 AM.
  - Avoid the use of caffeine before testing, including coffee and caffeinated drinks like energy drinks and sodas.
  - Limit fluid intake before the test.
  - Consume some protein in the morning before the test, such as an egg or protein bar, plain yogurt with fruit and nuts, breakfast burrito with black beans and cheese, whole wheat bread with 2 tablespoons of peanut butter, etc.
  - Avoid exercise before testing."
- Include information about how participants can prove they followed the protocol at the collection site, such as taking a photo of the specimen, and/or post test data.
- Many participants with an upper respiratory infection unknowingly took over-the-counter (OTC) medications without thinking of the consequences of taking a banned substance. CCM's suggest Mucinex **without** DM for coughs. Participants might also consider using home remedies such as hot tea and honey, saline gargles, humidifiers and 'Nedi" pots with saline water for nasal cleansing rather than other OTC drugs than contain prohibited ingredients.
- Include information on ways to remember to call the lab, such as setting alarms and/or always calling at the same time every day.
- Suggest possible call reminder tools, including but not limited to: paper calendars, check lists, Google calendar or similar smart phone applications.

Minor Compliance Violations

The most common non-compliance letters with **MINOR** violations were for receipt of late reports including:

- Monthly Self Report (MSR) and specifically the first page;
- 12-Step attendance cards;
- Health/Nurse Support Group Facilitator attendance reports; and
- Work Site Monitor reports.

Participants have control over the submission of MSR and 12-Step cards and should be able to submit them timely if they are organized. MSRs were often returned without the first page causing participants to be non-compliant with the required submission time lines. The first page of the MSR has a bar code but participants do not have to complete any information on this page. Therefore, participants often don't think they need to submit this page.

The Handbook does not currently include information about returning the first page. However, it would be beneficial if there was a note in the Handbook indicating "it is necessary to return the first page with the entire report." The updated Max-CMS system will allow participants to enter their MSR on-line which should improve timely submission of the completed report.

While sometimes submitted late, PHCS found the templates for reporting Health/Nurse Support Group attendance and the WSM monitor report comply with Uniform Standards 5 and 7. Maximus often received the initial WSM information and attestations late due to various reasons. This caused a delay in return to work for participants. PHCS also found some monthly WSM reports were received late because they were not mailed timely, resulting in late receipt and a non-compliance letter for the participant.

The upgraded Max-CMS system will allow WSMs to complete and submit pertinent forms and monthly reports online, which will have the potential to improve document timeliness, reduce non-compliance for participants, and delays to return participants to work.

However, to have any control over the submission of these other reports, participants must proactively request on a regular basis that WSMs, treatment providers and nurse/health support group facilitators submit the reports timely. PHCS noted some participants called their CCM or CM to find out if the forms had been submitted timely.

A review of the Handbook revealed there is little information regarding how to avoid non-compliance letters for these issues.

Recommendations

20. Maximus should modify the Program Handbook in the following ways:

- Remind participants that multiple minor violations hinder progress in the program and that 100% compliance is expected before being allowed to move to the transition phase.
- Revise the MSR information on page 8 to indicate the first page of the MSR must be submitted with the rest of the report and include a notation regarding the same on the first page.
- Revise the WSM information on page 9 to advise participants to check with their WSM by the first of the month to ensure their report is submitted timely.
- Revise the Treatment Provider Progress Report information on page 7 to advise participants to check with their treatment provider by the first of each month to ensure their reports are submitted timely.
- Revise the Support Group Facilitator information on pages 7-8 to advise participants to check with their group leader by the first of each month to ensure their reports are submitted timely.
- Include reminder tools such as, but not limited to: paper calendars, check lists, Google calendar or similar smart phone applications.
- Suggest participants call or email the Maximus CM or CCM monthly to verify that all reports have been received in a timely manner.

21. Maximus should include the following information from the USFDA website in the Handbook:
    - Mix medicines (do not crush tablets or capsules) with an unpalatable substance such as dirt, kitty litter, or used coffee grounds;
    - Place the mixture in a container such as a sealed plastic bag;
    - Throw the container in your household trash; and
    - Scratch out all personal information on the prescription label of the empty pill bottle or packaging to make it unreadable, then dispose of the container.

Participants with Mental Health Issues

Participants with mental health issues need groups for support. The usual groups, such as Alcoholics Anonymous (AA), Al-Anon and Narcotics Anonymous (NA) and are helpful but not specific to mental health participants. Emotions Anonymous (EA) groups are not as readily available as AA-type groups. A review of DEC notes indicated participants with a mental illness appear to take longer in recovery.

The options for participants with mental illness seem to be limited. The DPM survey includes a comment from the BRN representative that improved care for participants with mental health issues is needed. California county governments offer Adult System of Care services which

typically include Mental Health Support Services and authorization for Medi-Cal Mental Health Services.

Recommendation

22. Maximus should consider advising participants to seek out Mental Health Services from their local county government Adult System of Care, when appropriate.

Drug Testing

The file review revealed there were 40 BRN participants with a history of drug diversions who entered the program during the audit period. Most of the drug diversion was done by removing drugs from a Pyxis automated medication dispensing system and/or removing discarded medications from the hazardous waste container. The Pyxis MedStation or Omnicell systems were implemented to decrease medication error and improve inventory control. Currently, most hospital pharmacies run a monthly reconciliation report to identify narcotic users by determining if anyone has an unusual narcotic dispensing practice. If someone is identified as a high user, the management team will conduct an internal audit. In previous years, narcotics were counted by one nurse from the off-going shift and one nurse from the oncoming shift so it was more difficult to divert drugs.

PHCS found one positive test for morphine that was later rescinded after Maximus requested an investigation by the FirstLab Medical Review Officer (MRO). Fortunately, the participant was not working at the time. This incident proved to be an example of how the Maximus test results notification process identified the issue early and resolved the concern with the assistance of the MRO without effecting the participant's progress in the program.

Recommendation

23. Maximus should contact the California Chapter of the American Organization of Nurse Executives and California Hospital Association to speak at a regional or state-wide meeting regarding the prevention and detection of nurses diverting drugs.

Uniform Standards

The 2011 Uniform Standards are comprehensive, highly prescriptive, administratively-intense, and provide excellent criteria and procedures for managing the DCA Diversion Program. However, some of the drug testing standards appear to be overly prescriptive which limit the effectiveness and efficiency of random drug testing, resulting in increased participant time and cost which may be viewed as punitive.

Specifically, Uniform Standard 4 stipulates the following testing frequencies:

- Level 1 in year 1: 52 to 104 times for the year
- Level 2 in years 2 through 5: 36 to 104 times per year

According to the Board's DPMs, the implementation of the high testing frequency requirements contained in the Uniform Standard has reduced the benefits and flexibility of random testing and increased the cost. As a result, some DPMs claim self-referrals into the program have almost stopped and participant levels have dropped by 18% from approximately 690 in 2010 to 585 in 2015.

Recommendation

24. The Board's should collectively consider identifying an acceptable, but less frequent, random testing schedule that would accomplish the goal and reduce participant cost and loss, then modify Uniform Standard 4 accordingly.

Board Review and DEC Meetings

As previously mentioned, the BOP, PAB and PTB hold periodic review meetings to discuss participant progress, transition and completion without the individual being present, while participants are present at the BRN, DBC, OMB and VMB DEC meetings. Board and DEC actions concerning participant treatment, testing, and petitions for modification and reinstatement are compliant with Uniform Standards 4, 6, 8, 9, 10, 11 and 12.

The audit work plan included visiting several Board Review and DEC meetings. However, due to participant confidentiality reasons, the auditors were able to attend only one Board Review Meeting without any participants. The auditors did not attend a Board meeting or a DEC meeting. However, through reading the Board meeting minutes, PHCS was left with the following perceptions:

- The participants who did not attend a DEC meeting, or see the Diversion Program Manager during their meeting, appear to lack a connection to the program and are more negative in their comments about the program.
- DEC participants, however, expressed gratitude to the DEC, CCM's and CM's for their guidance throughout the program, their assistance in helping changing their life, teaching organization skills and feeling better about themselves. Following are a sample of participant quotes taken from the meeting minutes:
    - "I am so grateful for this program, it saved my life;"
    - "I am living and enjoying today;"
    - "I am so grateful for this program. I had lost my way spiritually and now I'm back in my life;"
    - "I am so proud and happy…you have given me a new life;"
    - "She reports doing well despite having her house burn down. She is working and doing well."

- The participant "is doing very well. She is back at work and loves it. She has come a long way from the first 6 months of her program. She turned the corner and never looked back. She is very happy and grateful to the DEC and the Diversion Program."

Additionally, Maximus program staff shared their feelings of satisfaction at hearing the participants tell their stories to the DEC meetings.

Recommendation

25. The non-DEC Board's should consider evaluating the effectiveness of the participants' non-attendance at Board review meetings, and consider ways to improve interpersonal interaction by Skype, Face Time or other forms of communication.

Health and Nurse Support Facilitated Groups

The audit work plan included visiting several health and nurse support facilitated groups. However, due to similar concerns about participant confidentiality, the auditors were unable to attend any groups. Instead, PHCS reviewed the CCM notes from their visits to the support groups.

During the file reviews, PHCS noted the support group facilitators helped participants understand the consequences of their failure to follow the program rules and how to deal with their addictions and other concerns. Only one participant asked for a different group leader and only one group leader asked to change a participant to another group.

The following table shows the evaluation ratings for six nurse and one health support group facilitators. The evaluation rating values are:

- Strongly disagree (1)
- Disagree (2)
- Neutral (3)
- Agree (4)
- Strongly agree (5)

As Table 12 indicates, attendees ranged from eight to 19 per session and evaluation ratings ranged from 3.9 to 5.0, with four of the facilitators earning perfect scores. The miscellaneous comments are generally positive, with two recommendations for a smaller group size.

Table 12: Nurse and Health Support Group Attendance and Facilitator Ratings

Group	NSGF #1	HSGF #2	NSGF #3	NSGF #4	NSGF #5	NSGF #6	NSGF #7
Location	Galt	Rancho Cucamonga	Folsom	Ranch Cucamonga	LA	Sacramento	Sacramento
Total Attendees	8	12	9	12	15 - 17	10	19
Diversion	2	NA	2	NA	NA	8	15
Probation	6	NA	8	NA	NA	2	3
	Rating	Rating	Rating	Rating	Rating	Rating	Rating
Location of group matches address on record	5	5	5	5	5	5	5
Location of group is easy to locate and access	5	5	5	5	4	4	4
Parking is available within 2 blocks	5	5	5	5	4	5	5
Location of group meets ADA standards	5	5	5	5	4	5	5
Location of group is clean and free from hazards	5	5	5	5	4	5	5
Group begins on time	5	5	5	5	4	5	5
New members are welcomed into group	5	5	5	5	3	5	5
Diversion Program standards are met	5	5	5	5	4	5	5
Sobriety and recovery are supported	5	5	5	5	4	5	5
Group members appear comfortable in speaking freely	5	5	5	5	4	5	5
Confidentiality is stressed	5	5	5	5	3	4	4
Group ends on time	5	5	5	5	4	5	5
Rating Average	**5**	**5**	**5**	**5**	**3.9**	**4.8**	**4.8**
Miscellaneous Comments							
HSGF group leader set appropriate boundaries.							
BOP applicant in HSGF was upset about diversion rules, but was re-directed.							
NSGF group leader set a supportive and approachable tone.							
NSGF was approachable warm and professional.							
A smaller group size is recommended for a NSGF. Disruptive activity happening in room with people							
A smaller group size is recommended for a NSGF. Need to consider another room for nurses who are working during the day.							

Source: Maximus

Policies and Procedures

PHCS also reviewed the Diversion Program policies and procedures. They are based on ISO principles and standards and provide detailed, step-by-step procedures. The policies and procedures are maintained in a current manner with frequent updates as changes occur.

As previously mentioned, PHCS discovered Maximus lacks a policy for deleting and retracting incorrect information from case logs and made recommendation 15 to correct this problem.

Maximus Educational and Outreach Presentations

	FY 2010-11	FY 2011-12	FY 2012-13	FY 2013-14	Total	Average
Educational & Outreach Presentations	9	9	12	12	**42**	**8.4**

Source: Maximus Diversion Program Annual Reports

Maximus is contractually required to conduct community education. Over the term of the audit period, Maximus has been increasing the number of educational programs they present each fiscal year.

Maximus has developed an excellent PowerPoint presentation entitled, "The Health Professional with Substance Abuse Disorders," and is giving the presentation to hospitals and other organizations.

Recommendation 22 specifies Maximus should contact appropriate California healthcare associations to make presentations concerning the prevention and detection of nurses diverting drugs.

Random Drug Testing Review

The following describes the Maximus contract with First Hospital Laboratories, Inc. (FirstLab), FirstLab subcontractors, FirstLab Quality Plan, customer satisfaction with FirstLab services, and the results of the random testing review.

Maximus Contract with FirstLab

FirstLab reports being in the drug and alcohol testing business for over a quarter century, serving approximately 2,500 clients, and averages over 800,000 medical services/tests per year. They also report having long term relationships with the majority of their clinics and collection sites.

Since 2010, Maximus has contracted with FirstLab as the third-party administrator for random body fluid testing and results reporting for the Diversion Program. Pursuant to the contract's Prime Contract Flow-Down provision, all work and/or deliverables produced and performed by the subcontractor (FirstLab) and its subcontractors (DrugScan and clinics/collection sites) shall be done in accordance with the Maximus prime contract.

Specifically, FirstLab is required to provide qualitative urine substance abuse testing for each participant. Specimen testing is to be performed by sub-contractor laboratories certified by the US Department of Health and Human Services (DHHS) and/or College of American Pathologists - Forensic Urine Drug Testing Program (CAPFUDT). All laboratories used to perform testing shall provide analytical services according to the protocols established by the US Department of Health and Human Services (DHHS) or to Maximus specifications on a per test fee basis.

The per test fees set forth in the 2010 contract escalates over time, covers the following services and allows for testing of additional drugs and panels upon client request for an extra cost:

- On-line Participant registration, Participant Tools and Case Manager Tools
- Create Random Testing Schedule Customized For Each Participant
- Web-Based Participant Login And Random Notification System and/or Toll Free Call-In Random Notification System
- Toll-Free Helpline
- Direct Participant Billing
- All Chain-of-Custody and Specimen Collection Supplies
- Collection Site Quality Assurance
- Overnight Delivery of Specimens to Lab
- Confirmation of All Positive Drug Screening Results
- Negative Results Available Within 24-48 Hours of Receipt of Specimens By Laboratory
- Positive Results Available Within 3-7 Business Days of Receipt of Specimens By Laboratory
- Internet Based Result Retrieval System

- Various Web-Based Program Management Reports
- Unlimited Telephone Consultation
- Administrative Services including Tracking of Test Results
- Dedicated Account Manager
- West Coast Customer Service Office

Required testing parameters include:

- FirstLab will provide for specimen collections within 50 miles of the participant's address or home of record, observed specimen collections performed by collectors of the same gender as the donor, and testing by alternative methods including expanded hair testing panels, oral fluid testing, blood and sweat.
- FirstLab will certify each collection site for use before permitting a participant to use it and will maintain an error correction log for each site.
- FirstLab subcontractors will test for drugs identified in, but not limited to "Description of Non-Regulated Testing Protocol" as directed by the Boards (see Appendix 4: FirstLab Drug Testing Panel). These panels are subject to change.
- The initial screen will be by immunoassay and gas chromatography/mass spectrometry (GC/MS).
- Presumptive positive results obtained on the initial screen will be confirmed by GC/MS or a more sensitive methodology with the exception of alcohol and Ethyl Glucuronide (EtG) positives. EtG testing is performed by liquid chromatography-tandem mass spectrometry/ mass spectrometry (LC-MS/MS).
- FirstLab will ensure all test results are legally defensible and will also have available a Medical Review Officer (MRO) to evaluate drug screen test results and to serve as an expert in this area upon the request of the participant or the DPM/DEC. In addition, FirstLab will provide access to industry experts and laboratory toxicologists to provide testimony at hearings or legal proceedings for an additional fee.

The contract includes the following drug testing critical service levels categories:

- **Drug Test Result Turnaround**: Negative screening results will be reported to Maximus within 2 business days of receipt of specimen by the lab 90% of the time. Non-negative results will be reported to Maximus within 4 business days of receipt of specimen by the lab 90% of the time. Compliance of this Service Level will be measured by reports generated by the FirstLab Account Manager and made available to Maximus after service is rendered.
- **New Participant Enrollment**: New participants in the program can be enrolled in the FirstLab program on-line immediately or receive start up package information by mail from FirstLab. FirstLab will have the participant enrolled (including the approval of their

chosen collection site) within 48 hours of receiving their enrollment and payment information via online communication or by return mail 95% of the time.

- **Collection site Selection and Approval**: When a participant needs a new collection site or requests the use of a collection site that does not already exist in FirstLab's data base, FirstLab will locate and approve a site within the State of California for usage within 24 hours 98% of the time.
- **Testing Accuracy:** Standard for accuracy in specimen testing is 100%.
- **Measurement and Evaluation:** The measurement of these Service Levels will be provided by FirstLab to Maximus based on the timely receipt of appropriate paperwork and documentation. The evaluation of these Service Levels will be done by the Maximus Vendor Manager in coordination with the Maximus Drug Program Manager.

FirstLab is also responsible for arranging, collecting directly from participants, processing, and accounting for all drug testing and all fees associated with drug testing. The BRN nor MAXIMUS will reimburse the FirstLab for any drug testing fees owed by participants.

Based on a review of the contract between Maximus and FirstLab and participants files, the program random drug testing process appears to meet the ASAM criteria and Uniform Standards 4, 8, 9 and 10.

FirstLab Subcontractors

FirstLab reports contracting with DrugScan, Inc. for over 20 years to provide analytical laboratory services for approximately 13,000 clinics and collection sites throughout the United States that are FirstLab subcontractors. There are about 900 sites in California and 689 for the Diversion Program.

Initially, FirstLab vets each collection site is through a phone interview which covers the Program collection policies and procedural requirements. Once the phone interview is completed and the site is willing to follow the requirements, FirstLab sends each clinic/collection site a client specific operating protocol/questionnaire. Once the protocol is satisfactorily completed and the site agrees to the terms, they are added to the client's approved collection site list in the FirstLab system.

FirstLab reports the collection site listing/directory is current, maintained and updated in real time. This is imperative because all FirstLab divisions use this information. Account Managers interface with the many clinics/collection sites and clients each day. During this interaction, data are validated and updated when required. The Provider Contracting Team, a dedicated unit that maintains, develops and negotiates with clinics and collectors, also provides oversight. In addition, as a condition of the Maximus contract, FirstLab conducts an annual audit of all assigned California clinics and collection sites.

FirstLab Quality Plan

The following briefly describes the FirstLab Quality Plan and explains how it monitors ongoing contractual compliance of DrugScan and the hundreds of clinics and collections sites used.

- FirstLab reports using only laboratories that are DHHS, SAMHSA (formerly NIDA) and/or CAP certified. This means the labs are physically inspected several times a year and their policies and procedures are subject to approval by those agencies. In addition, these labs receive blind proficiency specimens that are known negatives or non-negatives and they must perform with 100% accuracy or risk losing their certification. FirstLab reports being partially reliant on the clinic/collector's contractual obligations as well as state and federal certifications required to operate.
- FirstLab ensures specimen collection is observed by the same gender in the following manner: The FirstChoice provider database indicates those locations that do observed collections and for what gender, along with gender availability. When setting a participant up with a collection site, the participant is encouraged to call and verify availability of gender observation for when they anticipate being at the site. If there should be any issue when at the site either the participant or the collector will call FirstLab for instructions. FirstLab then takes appropriate steps to accommodate the Participant.

  In addition, the Account Manager receives automated alerts daily of any collections that were not marked as directly observed by the collector. The Account Manager conducts research on every result not marked as observed to determine whether the result was truly not observed or whether the collector simply neglected to check the "observed" box on the CCF. Then, the Account Manager updates the comments in the CaseNotes application to indicate the true observed status of the result, for the benefit of the Maximus Case Manager.
- FirstLab reports verifying the initial screen for all drugs is conducted by immunoassay technique in the following manner: All HealthCare Professional panels from Maximus are built into the LIS (Laboratory Information System) to create an initial screening aliquot (sample of a total amount of liquid). The order code directs the sample to the immunoassay screening instrument. This is an automated process that is followed, reviewed and certified by trained and experienced scientists. Part of the review and certification process is to ensure all testing protocols and quality assurance procedures are followed from initial accessioning through reporting.
- FirstLab reports verifying presumptive positive results are confirmed by gas chromatography/mass spectrometry (GC/MS) in the following manner: Every presumptive positive screen is automatically reflexed by the LIS to the corresponding mass spectrometry confirmation method for the respective presumptive positive analytes. This is an automated process that is followed and reviewed and certified by trained and

experienced scientists. Part of the review and certification process is to ensure all testing protocols and quality assurance procedures are followed from initial accessioning through reporting.

- FirstLab reports verifying EtG testing is based on Maximus requests built into the LIS to create an aliquot that is directed by the order code to an LC-MS/MS method. This is an automated process that is followed and reviewed and certified by trained and experienced scientists. Part of the review and certification process is to ensure all testing protocols and quality assurance procedures are followed from initial accessioning through reporting.
- FirstLab reports lab contractor staff are trained in each NIDA/US DOT standard operating procedure they are required to perform and a training record is maintained. Training in accordance with regulatory requirements including SAMHSA (formerly NIDA) which includes an initial, six-month and yearly recertification.

  In addition, the DrugScan Quality Assurance Department performs rotating monthly audits on all test systems which includes the "tracer" technique that follows samples from accessioning through reporting. This process involves observation of individual performance and review of training records to ensure all documentation and procedures within the scope of an individual's job description are up to date and compliant.
- FirstLab reports using the following the procedure to correct the actions of significant or repeated contractor violation of NIDA/DOT standards:
  1) Any critical errors identified at the lab are discussed with the Certifying Scientist and/or reported to the appropriate certifying organization for additional follow up, (SAMHSA etc.).
  2) Any ongoing critical errors identified at the collection site are handled in accordance with all applicable regulatory requirements (DOT SAMHSA, CA DOH etc.). The site would also be removed from the FirstLab FirstChoice network and replaced with a compliant organization. Due to the volume of testing conducted, FirstLab reports constantly monitoring the quality of collection services on behalf of all our clients to ensure a high quality product.
  3) In addition, FirstLab has quality review standards that couple both the lab and collection site output in the following manner:

     When FirstLab receives negative results and before reporting to the client, the Account Manager or Assistant Account Manager performs an administrative review on a sampling of negative results to ensure both the electronic result and the laboratory hard copy results are consistent with the test panels that have been signed off by the lab, the client and FirstLab. The results are also checked to make sure they are consistent with each other.

For positive results, the Account Manager or Assistant Account Manager again performs an administrative review on 100% of all positive results to ensure both the electronic result and the laboratory hard copy results are consistent with the test panels that have been signed off by the lab, the client and FirstLab. The results are also checked to make sure they are consistent with each other. If any discrepancies are found, the Account Manager will immediately notify the lab and begin corrective action.

FirstLab also reports that when it has chosen to discontinue the use of a clinic or collection site for quality or other issues that did not meet the expected level of services, it is important to note they were not in violation of applicable regulatory requirements. FirstLab indicated it has never reported a lab for not meeting standards.

Although the auditor was unable to field test the above FirstLab assertions, it is evident that between FirstLab and Maximus, there are sufficient controls in place to ensure the effectiveness and efficiency of program substance abuse testing.

Customer Satisfaction with FirstLab Services

In terms of this audit, customer satisfaction refers to the contentment of program participants and Maximus with FirstLab services.

For the most part, FirstLab does not interact with participants, so it must rely on collection site customer service to ensure program participants are treated courteously and respectfully by lab contractors. To monitor customer service practices, FirstLab reports that constant communication with customers is their key focus. This communication comes from the following sources:

- Participants who provide both positive and negative feedback.
- Day-to-day interaction with their Account Managers.
- Interaction with the Finance Department to facilitate payment for services.
- Interaction with the Provider Contracting Team.

FirstLab reports any issues are dealt with swiftly and definitively. Notes as to any issues are placed directly into the Provider database and the issue is reported to Provider Contracting. Any significant issue is reported to the Executive Vice President & CAO whose staff contacts the clinic/collection site. If the issue cannot be reasonably explained, the site will be deactivated for all FirstLab clients. If the issue can be reasonably explained, FirstLab notes the instance. If there is a second instance, the site will be deactivated.

From the perspective of Maximus, there is sufficient evidence the terms and conditions specified in the Maximus contract are being met. The monthly Maximus scorecard reports the results of critical services levels, service level requirements, monthly performance tracking and the

attainment of key performance indicators. The following table 13 summarizes the Maximus scorecard through December 2015.

Table 13: Maximus Scorecard Summary through December 2015

Critical Service Levels	Service Level Requirements	Monthly Performance Tracking	9-month Avg.
Drug Test Turnaround	Negative results reported within 2 business days of receipt by lab- 90% of the time	Negative results threshold achieved except for mass test days. For mass test days, FirstLab will work with lab to add staff	99.03%
	Non-negative results reported within 4 business days of receipt by lab – 90% of the time	Non-negative threshold achieved	98.97%
New Participant Enrollment	New participants enrolled within 2 business days of receiving information – 95% of the time	Thresholds achieved	100.00%
	FirstLab will locate and approve a travel site within 24 hours – 98% of the time	In-state travel collection sites within 24 hours	100.00%
		Out-of-state travel collections sites within 24 hours	100.00%
Testing Accuracy	Standard for specimen testing is 100%	DrugScan & FirstLab QA procedure ensures 100% accuracy	99.99%
		Incorrect Date	3.2
		Incorrect Substance	0
		Incorrect Participant	0.25
		Incorrect Value	0
		Other	0.11
FL Daily Result Reports		Low C results not reported	2.00
		Results reported late (10 mins or more)	1.10
		Result status not changed before reporting	0.38
Specimens Lost in Transit			0.38
Collection Site Errors		Cancelled at lab due to site error	0
		Urine	1.78
		Hair	0
		Phosphatidylethano (Peth)	0.38
Key Performance Indicators	**Service Level Requirements**	**Notes**	
Process Time	95% of time participants will be seen in less than 1 hour		
Participant/Maximus Satisfaction	Overall average rating of neutral or better		
Quality Adherence	100% adherence to Maximus quality standards	FirstLab policy is zero exceptions. Any exceptions are promptly reported to Maximus.	
Customer Service Inquiries	90% of time inquiries are responded to on same day	Agreed. Same day response subject to after business hours calls.	
Error Resolution	Resolution or plan for same to Maximus within 7 days	Agreed.	

Notification/Consultation Adherence	Respond to Maximus request with MRO within 24 hours	Agreed.	

Source: Maximus

Random Drug Testing Results

CPS reviewed a statistically-valid random sample of 114 participant drug testing files on the FirstLab website for compliance with applicable Uniform Standards. The drug test files include the participant name, license number, organization, test start and end dates, testing frequency, whether observed and current status. CPS found all but four participants in the files. After further review, it was determined the four omitted participants all withdrew or declined to join the program and did not register with FirstLab.

Recommendation

26. The Maximus Quality Analyst should periodically audit the FirstLab website files to ensure all program participants being drug tested are included in the database.

Program Effectiveness Reporting

Uniform Standard 16 concerns the use of measurable criteria and standards to determine whether each Board's method of dealing with substance-abusing licensees protects patients from harm and is effective in assisting them in recovering from substance abuse in the long term. Each Board is required to report specific information on a yearly basis to the DCA and the Legislature as it relates to licensees with substance abuse problems who are either in the Diversion Program or on Board probation. If the data indicates licensees in specific licensing categories or with specific substance abuse problems have either a higher or lower probability of success that information shall be taken into account when determining program success. The data may also be used to determine the risk factor when a board is determining whether a license should be revoked or placed on probation. The following indicates the PHSC observations, findings and recommendation for these specific reporting items.

Number of Intakes

Maximus tracks program intakes on a monthly basis and prepares an annual report for stakeholders. The information is tracked for all Boards by county and includes applicant interviews and acceptance into the program. The intake report is confusing because the monthly statistics are based on actual intakes but the year-to-date total is based on Maximus' July 1 - June 30 schedule.

Recommendation

27. Maximus should revise the intake report accordingly to eliminate the confusion between monthly and year-to-date reporting.

Number of Probationers

Maximus tracks the number of probation referrals whose conduct was related to a substance abuse problem on a monthly basis and prepares an annual report for stakeholders.

Number of Referrals to Treatment Programs

There was no evidence of Maximus tracking referrals to treatment programs but Maximus indicated the program will start tracking this indicator in 2016.

Number of Relapses (break in sobriety)

Maximus tracks relapse rates and relapse substance on a monthly basis. PHCS contractors found consistent documentation in the case logs when there was an identified relapse. The annual report summary shows the length of time from intake to relapse and indicates most relapses take place during the first year of enrollment.

Number of Cease Practice Orders/License In-activations

According to Maximus, this is a Board function and not the responsibility of Maximus.

Number of Suspensions

According to Maximus, this is a Board function and a formal process that is not the responsibility of Maximus.

Number Terminated for Noncompliance

Maximus tracks this data on a monthly basis and prepares an annual report for stakeholders.

Number of Successful Completions based on Uniform Standards

Maximus tracks this data on a monthly basis and prepares an annual report for stakeholders.

Number of Major Violations, Nature of Violation and Action Taken

For each participant, Maximus documents each violation and actions taken in the case logs but does not summarize them in the annual report.

Recommendation

28. Maximus should consider tracking and trending major violations and actions taken, and report this information in the annual report.

Number of Licensees Successfully Returned to Practice

Maximus documents each participant's return to practice and follows their progress on an ongoing basis until completion of the program. They do not include this information in the annual report.

Recommendation

29. Maximus should consider tracking and trending successful returns to work on a monthly and annual basis, and report this information in the annual report.

Number of Patients Harmed while in the Program

Maximus reports participants have not harmed any patients while in the program. In addition, the Boards are required to use the following criteria to determine if the program protects patients from harm and is effective in assisting its licensees in recovering from substance abuse in the long term.

- At least 100% of licensees who either entered the program or whose license was placed on probation as a result of a substance abuse problem successfully completed either the program or the probation, or had their license to practice revoked or surrendered on a timely basis based on noncompliance of those programs.
- At least 75% of licensees who successfully completed the program or probation did not have any substantiated complaints related to substance abuse for at least five (5) years after completion.

Regarding the first criterion, the PHCS review of 103 cases indicates 100% of the licensees/participants were all closed for the appropriate reasons and all documentation explained in detail the end status for each participant. Maximus tracks the information on a monthly basis and includes it in the annual report as well.

According to Maximus, the implementation of the second criterion is a Board responsibility and Maximus lacks access to this information after participants have completed the program. B&P code section 156.1 specifies a Board shall retain all participant records for treatment and rehabilitation services for three years from the date of the last treatment or services rendered, or until review for audit by the department. After that time period the documents may be purged. Purging the documents after three years eliminates the ability to measure long range participant outcomes.

Recommendation

30. Participating Boards should attempt to monitor long range participant outcomes after program completion.

Planned Technical Improvements

Hallmark technical features of the Maximus Diversion Program effectiveness and efficiency include, but are not limited to, implementation and application of ISO 9001:3015 standards and processes; use of a Client tracking matrix, Max-CMS and ITG Quality Assurance systems; and a mostly paperless environment.

During the course of the audit, the auditors learned Maximus plans to deploy in 2016 a variety of technical improvements that will address some Treatment Provider obstacles and a number of recommendations to improve program effectiveness and efficiency. All parties to the Diversion Program will benefit. These updated technical improvements include, but are not limited to, the following:

Improvements for Staff

- Increased efficiency for program staff through one login instead of multiple logins, improved navigation, and reduced data entry time.
- The licensee profile will be streamlined and will enable a participant image to be uploaded into the Max-CMS.
- The case log will be organized to include all notes instead of selective information.
- The applicant intake form will be consolidated into one long form with numbered questions that is auto saved instead of eight separate pages that needed to be saved individually. Users will also be able to add or change questions as needed.
- Staff will be able to add/change or delete recovery agreement terms on the fly and an electronic signature will be allowed.
- Scheduling for Maximus operations and administrative staff will be easier and faster. Staff will be able to drag and drop appointments instead of having to cancel old appointments before entering new appointments.

Improvements for Participants

- Participants will be able upload 12-step attendance cards and self-reports instead of faxing or mailing these documents.
- They will also be able to print the intake packet, reports, and the return to work packet. Once data are entered, the Max-CMS will notify the appropriate program staff electronically.
- These improvements should: eliminate paper and lost documents, and reduce mail handling, postage costs, and non-compliance-related tasks and consequences.

Improvements for Treatment Providers

- Treatment Providers will have their own portal.
- Clinical Assessors with be able to enter assessments online instead of submitting manual reports.
- HSG/NSG facilitators and WSMs will be able enter or upload monthly reports.

Improvements for Board staff and DEC Members

- Board staff and DEC members will have 24/7 access to all participant and program information. This will reduce time sorting and reviewing records, transit time waiting for hardcopy information, and printing time, materials and other related costs.

Appendix 1: Diversion Program Business & Professional Code Sections

The following is a partial listing of the enabling Diversion Program statutes within the California Business and Professions Code.

CHAPTER 4. Dentistry [1600 - 1976] (Chapter 4 added by Stats. 1937, Ch. 415.)

ARTICLE 4.7. Diversion Program [1695 - 1699] (Article 4.7 added by Stats. 1982, Ch. 1261, Sec. 1.)

1695.
It is the intent of the Legislature that the Board of Dental Examiners of California seek ways and means to identify and rehabilitate licentiates whose competency may be impaired due to abuse of dangerous drugs or alcohol, so that licentiates so afflicted may be treated and returned to the practice of dentistry in a manner which will not endanger the public health and safety. It is also the intent of the Legislature that the Board of Dental Examiners of California shall implement this legislation in part by establishing a diversion program as a voluntary alternative approach to traditional disciplinary actions. *(Added by Stats. 1982, Ch. 1261, Sec. 1.)*

1695.1.
As used in this article:
(a) "Board" means the Board of Dental Examiners of California.

(b) "Committee" means a diversion evaluation committee created by this article.

(c) "Program manager" means the staff manager of the diversion program, as designated by the executive officer of the board. The program manager shall have background experience in dealing with substance abuse issues.

(Amended by Stats. 2008, Ch. 548, Sec. 4. Effective January 1, 2009.)

1695.2.
One or more diversion evaluation committees is hereby created in the state to be established by the board. The board shall establish criteria for the selection of the committee. No board member shall serve on any committee.
(Added by Stats. 1982, Ch. 1261, Sec. 1.)

1695.3.
Each member of a committee shall receive per diem and expenses as provided in Section 103.
(Added by Stats. 1982, Ch. 1261, Sec. 1.)

ARTICLE 15. Osteopathic Physician and Surgeon Diversion Evaluation Committee [2360 - 2370] *(Article 15 added by Stats. 1988, Ch. 384, Sec. 1.)*
2360.
It is the intent of the Legislature that the Osteopathic Medical Board of California seek ways and means to identify and rehabilitate osteopathic physicians and surgeons whose competency may be impaired due to abuse of dangerous drugs and alcohol, so that osteopathic physicians and surgeons so afflicted may be treated and returned to the practice of medicine in a manner which will not endanger the public health and safety. It is also the intent of the Legislature that the Osteopathic Medical Board of California shall implement this legislation by establishing a diversion program as a voluntary alternative approach to traditional disciplinary actions.
(Amended by Stats. 1991, Ch. 359, Sec. 12.)

2361.
As used in this article:

(a) "Board" means the Osteopathic Medical Board of California.

(b) "Diversion program" means a treatment program created by this article for osteopathic physicians and surgeons whose competency may be threatened or diminished due to abuse of drugs or alcohol.

(c) "Committee" means a diversion evaluation committee created by this article.

(d) "Participant" means a California-licensed osteopathic physician and surgeon.

(e) "Program manager" means the staff manager of the diversion program, as designated by the executive officer of the board. The program manager shall have background experience in dealing with substance abuse issues.

(Amended by Stats. 2009, Ch. 140, Sec. 9. Effective January 1, 2010.)

2362.
One or more diversion evaluation committees are hereby created in the state to be established by the board. The board shall establish criteria and appoint the members of the committee pursuant thereto. *(Added by Stats. 1988, Ch. 384, Sec. 1.)*

2363.
Each member of the committee shall receive per diem and expenses as provided in Section 103. *(Added by Stats. 1988, Ch. 384, Sec. 1.)*

CHAPTER 5.7. Physical Therapy [2600 - 2696] (Chapter 5.7 added by Stats. 1953, Ch. 1826.)
ARTICLE 7. Substance Abuse Rehabilitation Program [2662 - 2669] *(Heading of Article 7 renumbered from Article 5.5 by Stats. 2013, Ch. 389, Sec. 62.)*
2662.
It is the intent of the Legislature that the board shall seek ways and means to identify and rehabilitate physical therapists and physical therapist assistants whose competency is impaired due to abuse of dangerous drugs or alcohol so that they may be treated and returned to the practice of physical therapy in a manner which will not endanger the public health and safety.
(Amended by Stats. 1996, Ch. 829, Sec. 52. Effective January 1, 1997.)

2663.
The board shall establish and administer a substance abuse rehabilitation program, hereafter referred to as the rehabilitation program, for the rehabilitation of physical therapists and physical therapist assistants whose competency is impaired due to the abuse of drugs or alcohol. The board may contract with any other state agency or a private organization to perform its duties under this article. The board may establish one or more rehabilitation evaluation committees to assist it in carrying out its duties under this article. Any rehabilitation evaluation committee established by the board shall operate under the direction of the rehabilitation program manager, as designated by the executive officer of the board. The program manager has the primary responsibility to review and evaluate recommendations of the committee. *(Amended by Stats. 2013, Ch. 389, Sec. 63. Effective January 1, 2014.)*

2664.
(a) Any rehabilitation evaluation committee established by the board shall have at least three members. In making appointments to a rehabilitation evaluation committee, the board shall consider the appointment of persons who are either recovering from substance abuse and have been free from substance abuse for at least three years immediately prior to their appointment or who are knowledgeable in the treatment and recovery of substance abuse. The board also shall consider the appointment of a physician and surgeon who is board certified in psychiatry.

(b) Appointments to a rehabilitation evaluation committee shall be by the affirmative vote of a majority of members appointed to the board. Each appointment shall be at the pleasure of the board for a term not to exceed four years. In its discretion, the board may stagger the terms of the initial members so appointed.

(c) A majority of the members of a rehabilitation evaluation committee shall constitute a quorum for the transaction of business. Any action requires an affirmative vote of a majority of those members present at a meeting constituting at least a quorum. Each rehabilitation evaluation committee shall elect from its membership a chairperson and a vice chairperson. Notwithstanding the Bagley-Keene Open Meeting Act (Article 9 (commencing with Section 11120) of Chapter 1 of Part 1 of Division 3 of Title 2 of the Government Code), relating to public meetings, a rehabilitation evaluation committee may convene in closed session to consider matters relating to any physical therapist or physical therapist assistant applying for or participating in a rehabilitation program, and a meeting which will be convened entirely in closed session need not comply with Section 11125 of the Government Code. A rehabilitation evaluation committee shall only convene in closed session to the extent it is necessary to protect the privacy of an applicant or participant. Each member of a rehabilitation evaluation committee shall receive a per diem and shall be reimbursed for expenses as provided in Section 103.

CHAPTER 6. Nursing [2700 - 2838.4] (Chapter 6 repealed and added by Stats. 1939, Ch. 807.)
ARTICLE 3.1. Diversion Program [2770 - 2770.14] (Article 3.1 added by Stats. 1984, Ch. 865, Sec. 1.)
2770.
It is the intent of the Legislature that the Board of Registered Nursing seek ways and means to identify and rehabilitate registered nurses whose competency may be impaired due to abuse of alcohol and other drugs, or due to mental illness so that registered nurses so afflicted may be rehabilitated and returned to the practice of nursing in a manner which will not endanger the public health and safety. It is also the intent of the Legislature that the Board of Registered Nursing shall implement this legislation by establishing a diversion program as a voluntary alternative to traditional disciplinary actions. *(Added by Stats. 1984, Ch. 865, Sec. 1.)*

2770.1.
As used in this article:

(a) “Board” means the Board of Registered Nursing.

(b) “Committee” means a diversion evaluation committee created by this article.

(c) “Program manager” means the staff manager of the diversion program, as designated by the executive officer of the board. The program manager shall have background experience in dealing with substance abuse issues.

(Amended by Stats. 2008, Ch. 548, Sec. 17. Effective January 1, 2009.)

2770.2.
One or more diversion evaluation committees is hereby created in the state to be established by the board. Each committee shall be composed of five persons appointed by the board. No board member shall serve on any committee.

Each committee shall have the following composition:

(a) Three registered nurses, holding active California licenses, who have demonstrated expertise in the field of chemical dependency or psychiatric nursing.

(b) One physician, holding an active California license, who specializes in the diagnosis and treatment of addictive diseases or mental illness.

(c) One public member who is knowledgeable in the field of chemical dependency or mental illness.

It shall require a majority vote of the board to appoint a person to a committee. Each appointment shall be at the pleasure of the board for a term not to exceed four years. In its discretion the board may stagger the terms of the initial members appointed. *(Amended by Stats. 1999, Ch. 655, Sec. 36. Effective January 1, 2000.)*

2770.3.
Each member of a committee shall receive per diem and expenses as provided in Section 103.
(Added by Stats. 1984, Ch. 865, Sec. 1.)

2770.4.
Three members of a committee shall constitute a quorum for the transaction of business at any meeting. Any action requires a majority vote of the committee.

CHAPTER 7.7. Physician Assistants [3500 - 3546] (Heading of Chapter 7.7 amended by Stats. 1992, Ch. 427, Sec. 5.)
ARTICLE 6.5. Diversion of Impaired Physician Assistants [3534 - 3534.10] (Article 6.5 added by Stats. 1988, Ch. 385, Sec. 2.)
3534.
It is the intent of the Legislature that the board shall seek ways and means to identify and rehabilitate physician assistants whose competency is impaired due to abuse of dangerous drugs or alcohol so that they may be treated and returned to the practice of medicine in a manner which will not endanger the public health and safety.
(Amended by Stats. 2012, Ch. 332, Sec. 66. Effective January 1, 2013.)

3534.1.
The board shall establish and administer a diversion program for the rehabilitation of physician assistants whose competency is impaired due to the abuse of drugs or alcohol. The board may contract with any other state agency or a private organization to perform its duties under this article. The board may establish one or more diversion evaluation committees to assist it in carrying out its duties under this article. As used in this article, "committee" means a diversion evaluation committee. A committee created under this article operates under the direction of the diversion program manager, as designated by the executive officer of the board. The program manager has the primary responsibility to review and evaluate recommendations of the committee.
(Amended by Stats. 2012, Ch. 332, Sec. 67. Effective January 1, 2013.)

3534.2.
(a) Any committee established by the board shall have at least three members. In making appointments to a committee the board shall consider the appointments of persons who are either recovering of substance abuse and have been free from abuse for at least three years immediately prior to their appointment or who are knowledgeable in the treatment and recovery of substance abuse. The board also shall consider the appointment of a physician and surgeon who is board certified in psychiatry.

(b) Appointments to a committee shall be by the affirmative vote of a majority of members appointed to the board. Each appointment shall be at the pleasure of the board for a term not to exceed four years. In its discretion, the board may stagger the terms of the initial members so appointed.

(c) A majority of the members of a committee shall constitute a quorum for the transaction of business. Any action requires an affirmative vote of a majority of those members present at a meeting constituting at least a quorum. Each committee shall elect from its membership a chairperson and a vice chairperson. Notwithstanding Article 9 (commencing with Section 11120) of Chapter 1 of Part 1 of

Division 3 of Title 2 of the Government Code, relating to public meetings, a committee may convene in closed session to consider matters relating to any physician assistant applying for or participating in a diversion program, and a meeting which will be convened entirely in closed session need not comply with Section 11125 of the Government Code. A committee shall only convene in closed session to the extent it is necessary to protect the privacy of an applicant or participant. Each member of a committee shall receive a per diem and shall be reimbursed for expenses as provided in Section 103.

(Amended by Stats. 2012, Ch. 332, Sec. 68. Effective January 1, 2013.)

CHAPTER 9. Pharmacy [4000 - 4426] (Chapter 9 repealed and added by Stats. 1996, Ch. 890, Sec. 3.)
ARTICLE 21. Pharmacists Recovery Program [4360 - 4373] (Article 21 added by Stats. 1996, Ch. 890, Sec. 3.)

4360.

The board shall operate a pharmacist's recovery program to rehabilitate pharmacists and intern pharmacists whose competency may be impaired due to abuse of alcohol, drug use, or mental illness. The intent of the pharmacists' recovery program is to return these pharmacists and intern pharmacists to the practice of pharmacy in a manner that will not endanger the public health and safety. *(Amended by Stats. 2005, Ch. 621, Sec. 63. Effective January 1, 2006.)*

4361.

(a) "Participant" means a pharmacist or intern pharmacist who has entered the pharmacists' recovery program.

(b) "Pharmacists recovery program" means the rehabilitation program created by this article for pharmacists and intern pharmacists. *(Repealed and added by Stats. 2005, Ch. 621, Sec. 65. Effective January 1, 2006.)*

4362.

(a) A pharmacist or intern pharmacist may enter the pharmacists recovery program if:

(1) The pharmacist or intern pharmacist is referred by the board instead of, or in addition to, other means of disciplinary action.

(2) The pharmacist or intern pharmacist voluntarily elects to enter the pharmacists' recovery program.

(b) A pharmacist or intern pharmacist who enters the pharmacists recovery program pursuant to paragraph (2) of subdivision (a) shall not be subject to discipline or other enforcement action by the board solely on his or her entry into the pharmacists recovery program or on information obtained from the pharmacist or intern pharmacist while participating in the program unless the pharmacist or intern pharmacist would pose a threat to the health and safety of the public. However, if the board receives information regarding the conduct of the pharmacist or intern pharmacist, that information may serve as a basis for discipline or other enforcement by the board.

(Repealed and added by Stats. 2005, Ch. 621, Sec. 67. Effective January 1, 2006.)

4364.

(a) The board shall establish criteria for the participation of pharmacists and intern pharmacists in the pharmacists' recovery program.

(b) The board may deny a pharmacist or intern pharmacist who fails to meet the criteria for participation entry into the pharmacists' recovery program.

(c) The establishment of criteria for participation in the pharmacists recovery program shall not be subject to the requirements of Chapter 3.5 (commencing with Section 11340) of Part 1 of Division 3 of Title 2 of the Government Code. *(Amended by Stats. 2005, Ch. 621, Sec. 69. Effective January 1, 2006.)*

4365.
The board shall contract with one or more qualified contractors to administer the pharmacists' recovery program.
(Amended by Stats. 2005, Ch. 621, Sec. 70. Effective January 1, 2006.)

CHAPTER 11. Veterinary Medicine [4800 - 4917] (Chapter 11 repealed and added by Stats. 1937, Ch. 933.)
ARTICLE 3.5. Diversion Evaluation Committees [4860 - 4873] (Article 3.5 added by Stats. 1982, Ch. 870, Sec. 1.)
4860.
It is the intent of the Legislature that the Veterinary Medical Board seek ways and means to identify and rehabilitate veterinarians and registered veterinary technicians with impairment due to abuse of dangerous drugs or alcohol, affecting competency so that veterinarians and registered veterinary technicians so afflicted may be treated and returned to the practice of veterinary medicine in a manner that will not endanger the public health and safety. *(Amended by Stats. 1995, Ch. 60, Sec. 35. Effective July 6, 1995.)*

4861.
One or more diversion evaluation committees is hereby authorized to be established by the board. Each diversion evaluation committee shall be composed of five persons appointed by the board.

Each diversion evaluation committee shall have the following composition:

(a) Three veterinarians licensed under this chapter. The board in making its appointments shall give consideration to recommendations of veterinary associations and local veterinary societies and shall consider, among others, where appropriate, the appointment of veterinarians who have recovered from impairment or who have knowledge and expertise in the management of impairment.

(b) Two public members.

Each person appointed to a diversion evaluation committee shall have experience or knowledge in the evaluation or management of persons who are impaired due to alcohol or drug abuse.

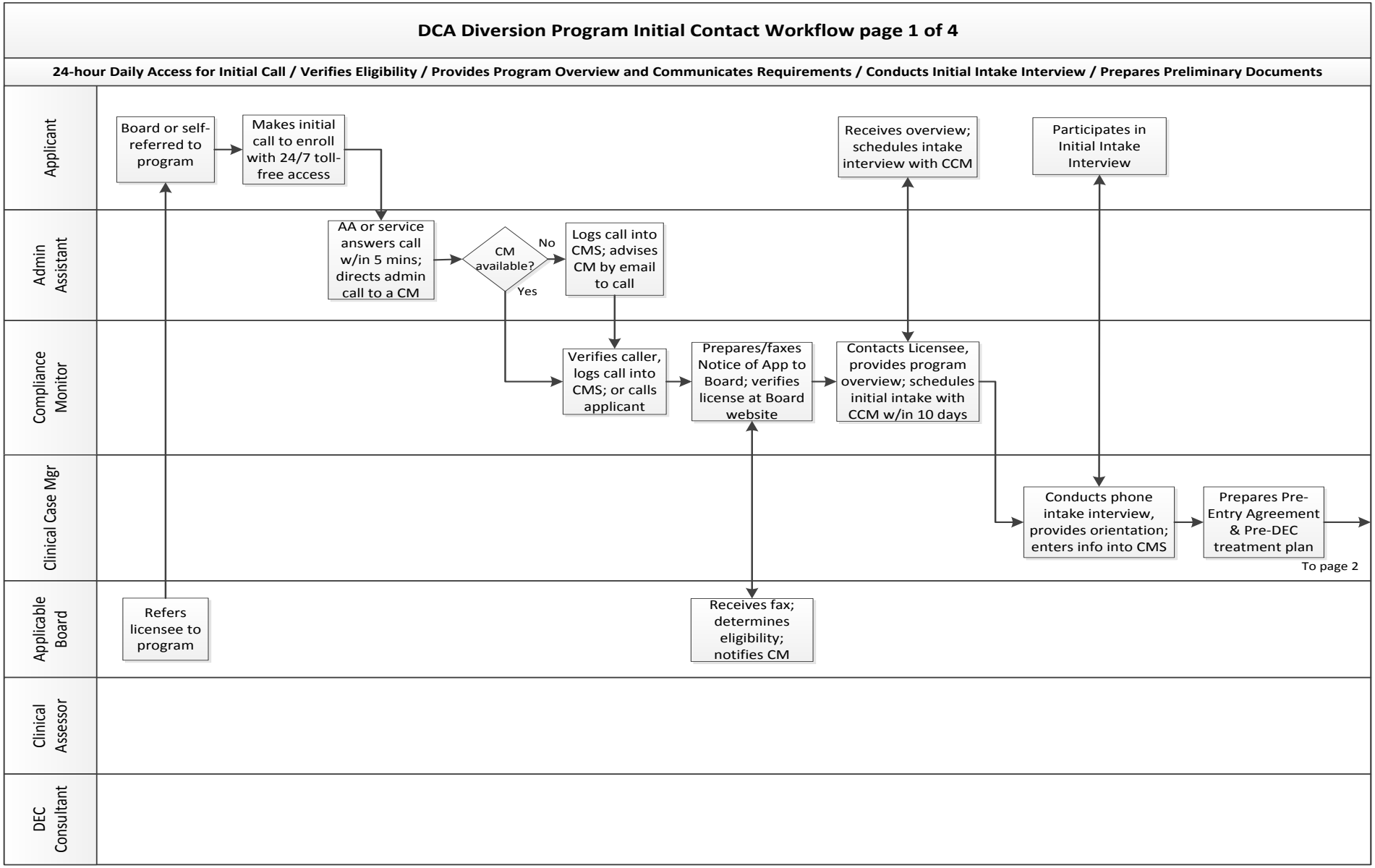
It shall require the majority vote of the board to appoint a person to a diversion evaluation committee. Each appointment shall be at the pleasure of the board for a term not to exceed four years. In its discretion the board may stagger the terms of the initial members appointed.

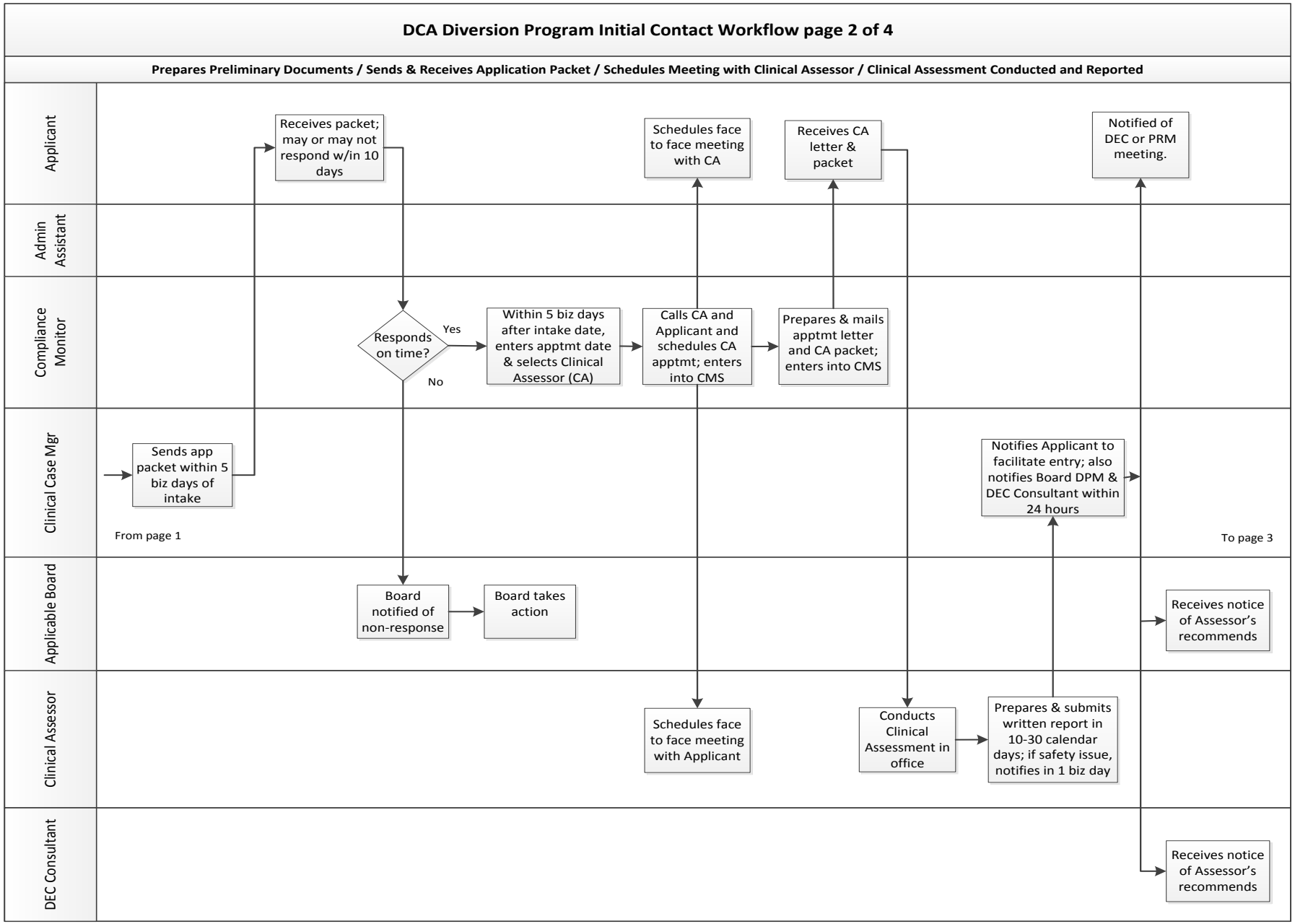
The board may appoint a program director and other personnel as necessary to carry out provisions of this article.
(Added by Stats. 1982, Ch. 870, Sec. 1.)

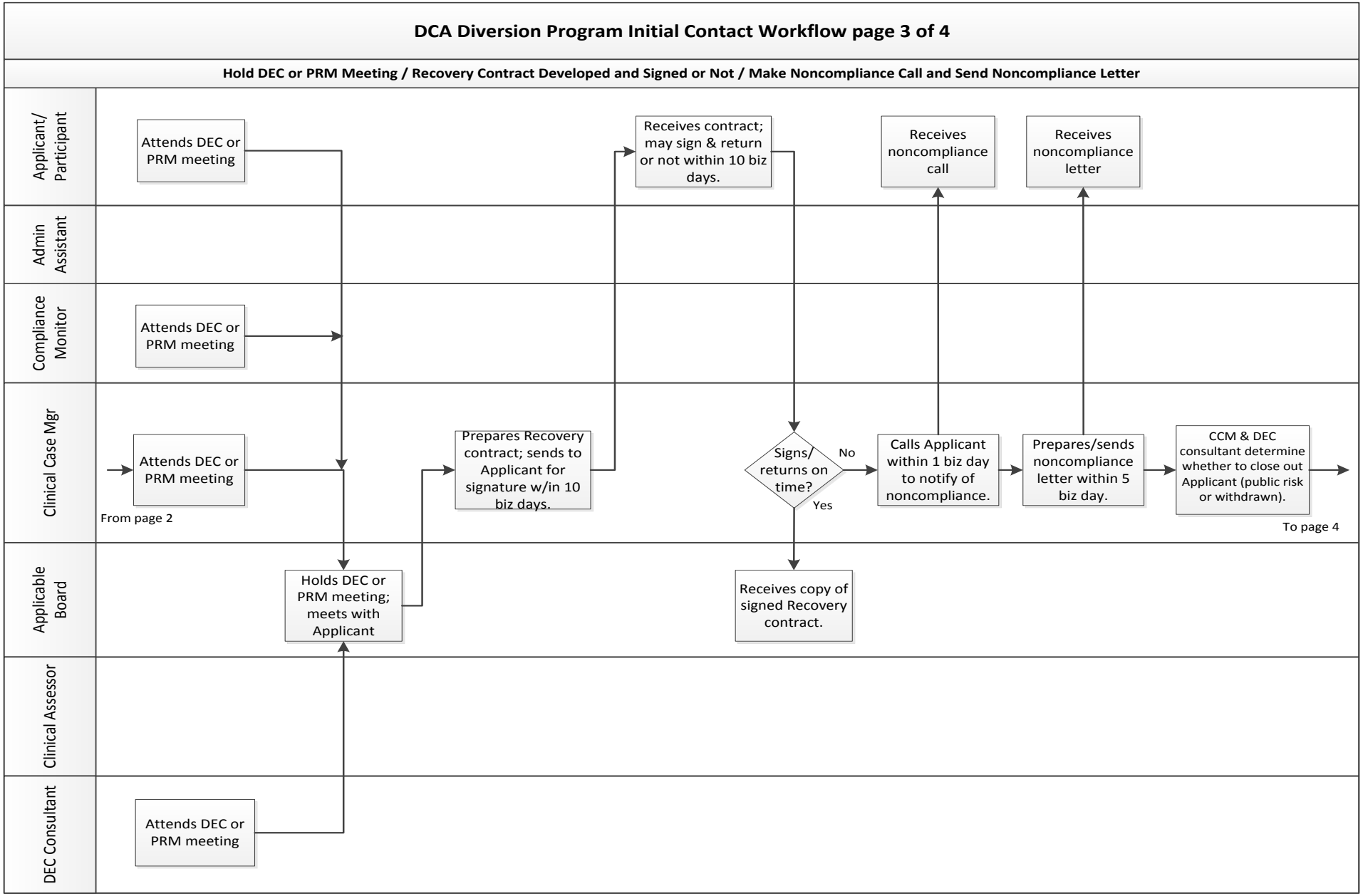
4862.
Each member of a diversion evaluation committee shall receive per diem and expenses as provided in Section 103.
(Added by Stats. 1982, Ch. 870, Sec. 1.)

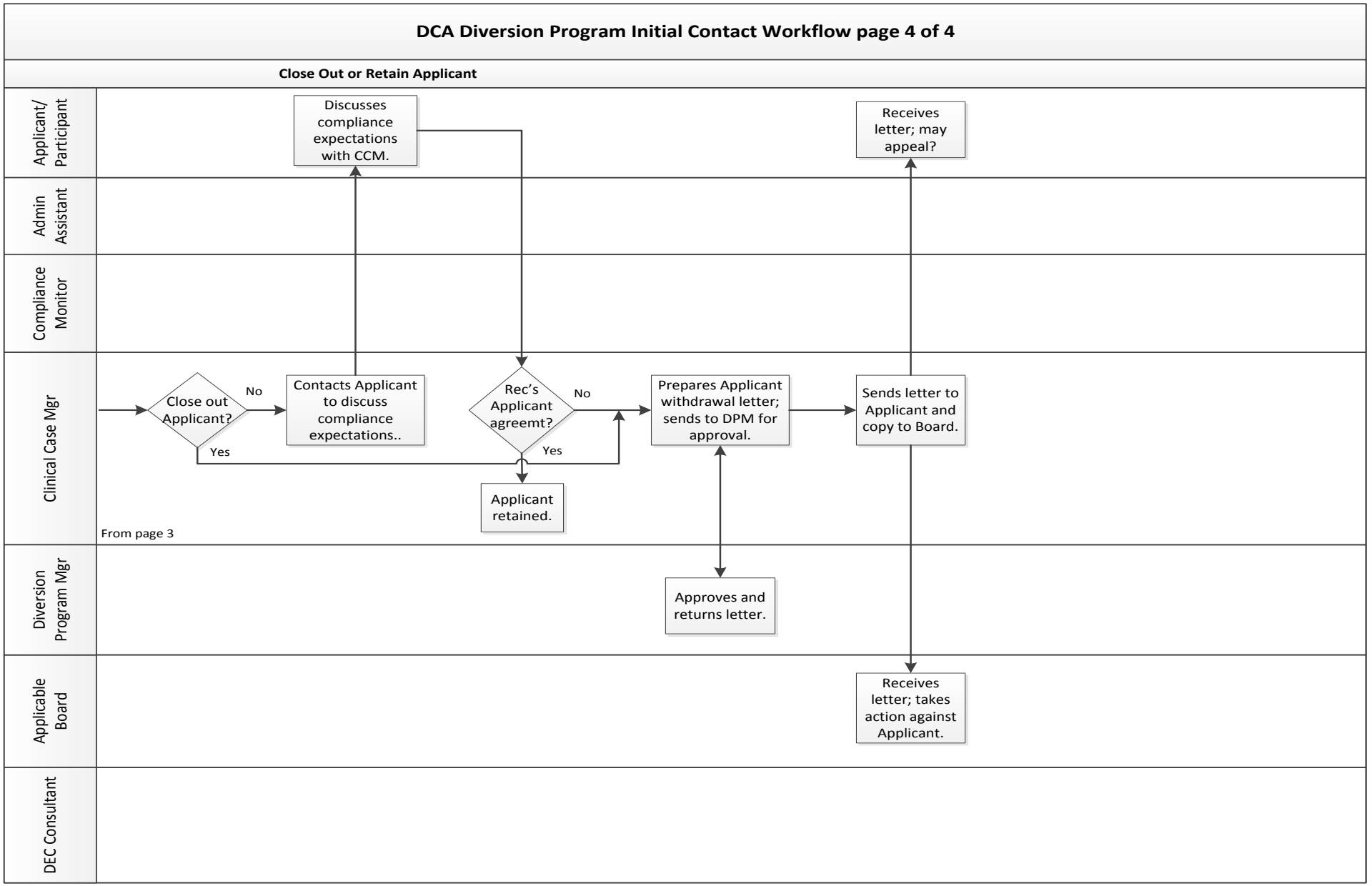
4863.
Three members of a diversion evaluation committee shall constitute a quorum for the transaction of business at any meeting. Any action requires the majority vote of the diversion evaluation committee.
(Added by Stats. 1982, Ch. 870, Sec. 1.)

Appendix 2: High Level Flowchart of Initial Participant Contact

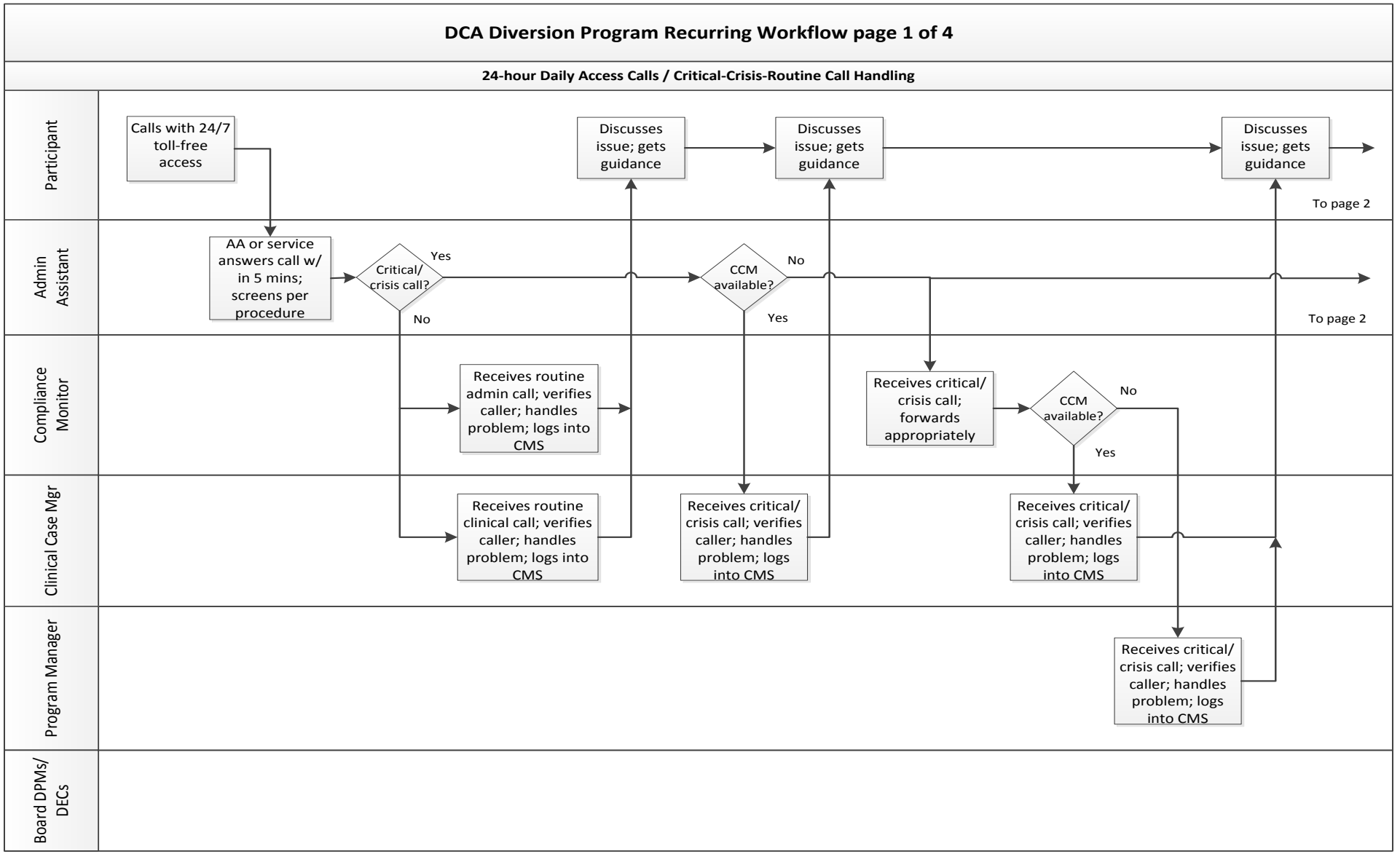


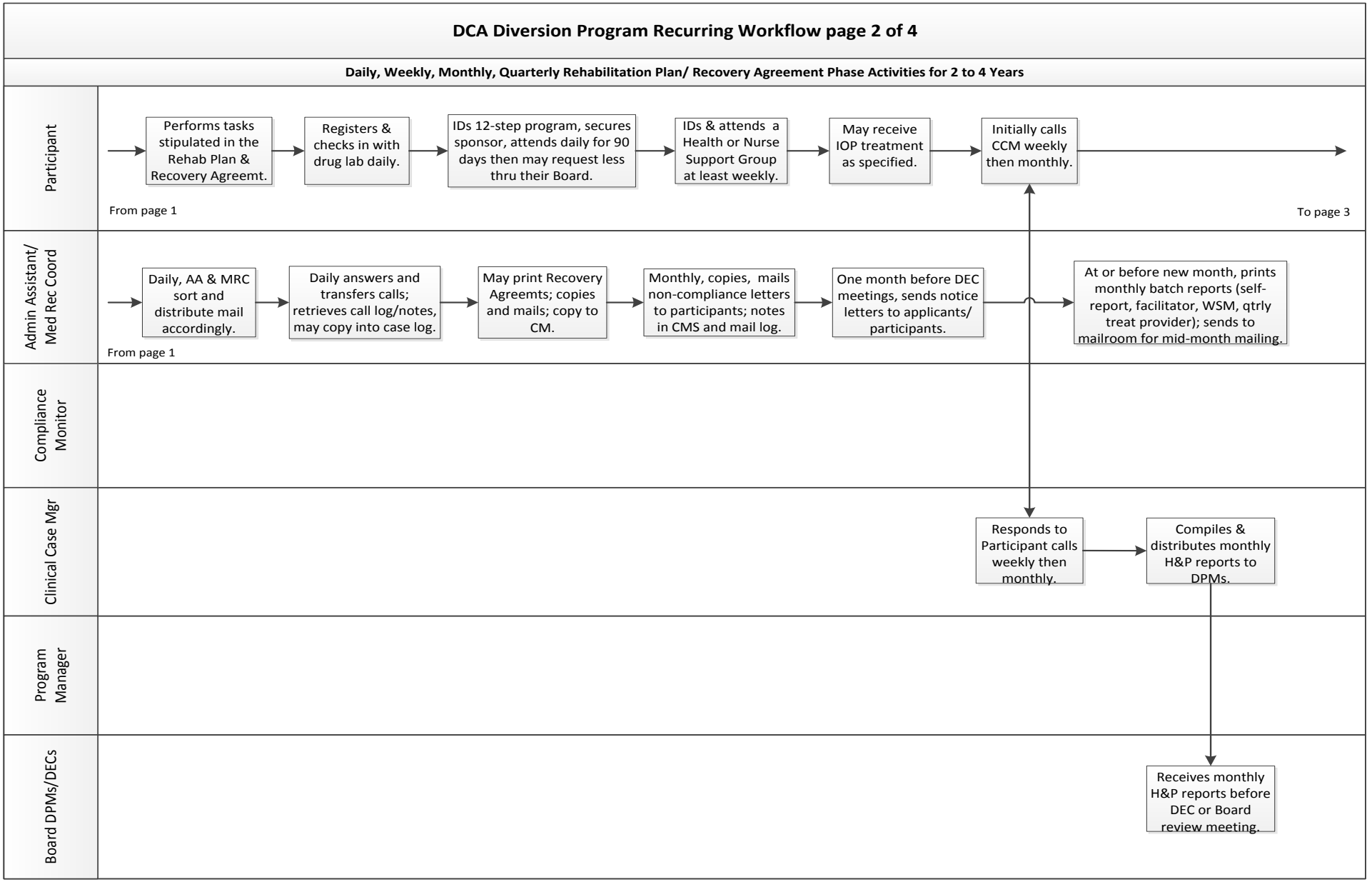

DCA Diversion Program Initial Contact Workflow page 2 of 4
Prepares Preliminary Documents / Sends & Receives Application Packet / Schedules Meeting with Clinical Assessor / Clinical Assessment Conducted and Reported
Applicant
Admin Assistant
Compliance Monitor
Clinical Case Mgr
Applicable Board
Clinical Assessor
DEC Consultant
Receives packet; may or may not respond w/in 10 days
Schedules face to face meeting with CA
Receives CA letter & packet
Notified of DEC or PRM meeting.
Responds on time?
Yes
No
Within 5 biz days after intake date, enters apptmt date & selects Clinical Assessor (CA)
Calls CA and Applicant and schedules CA apptmt; enters into CMS
Prepares & mails apptmt letter and CA packet; enters into CMS
Sends app packet within 5 biz days of intake
From page 1
Notifies Applicant to facilitate entry; also notifies Board DPM & DEC Consultant within 24 hours
To page 3
Board notified of non-response
Board takes action
Receives notice of Assessor's recommends
Schedules face to face meeting with Applicant
Conducts Clinical Assessment in office
Prepares & submits written report in 10-30 calendar days; if safety issue, notifies in 1 biz day
Receives notice of Assessor's recommends

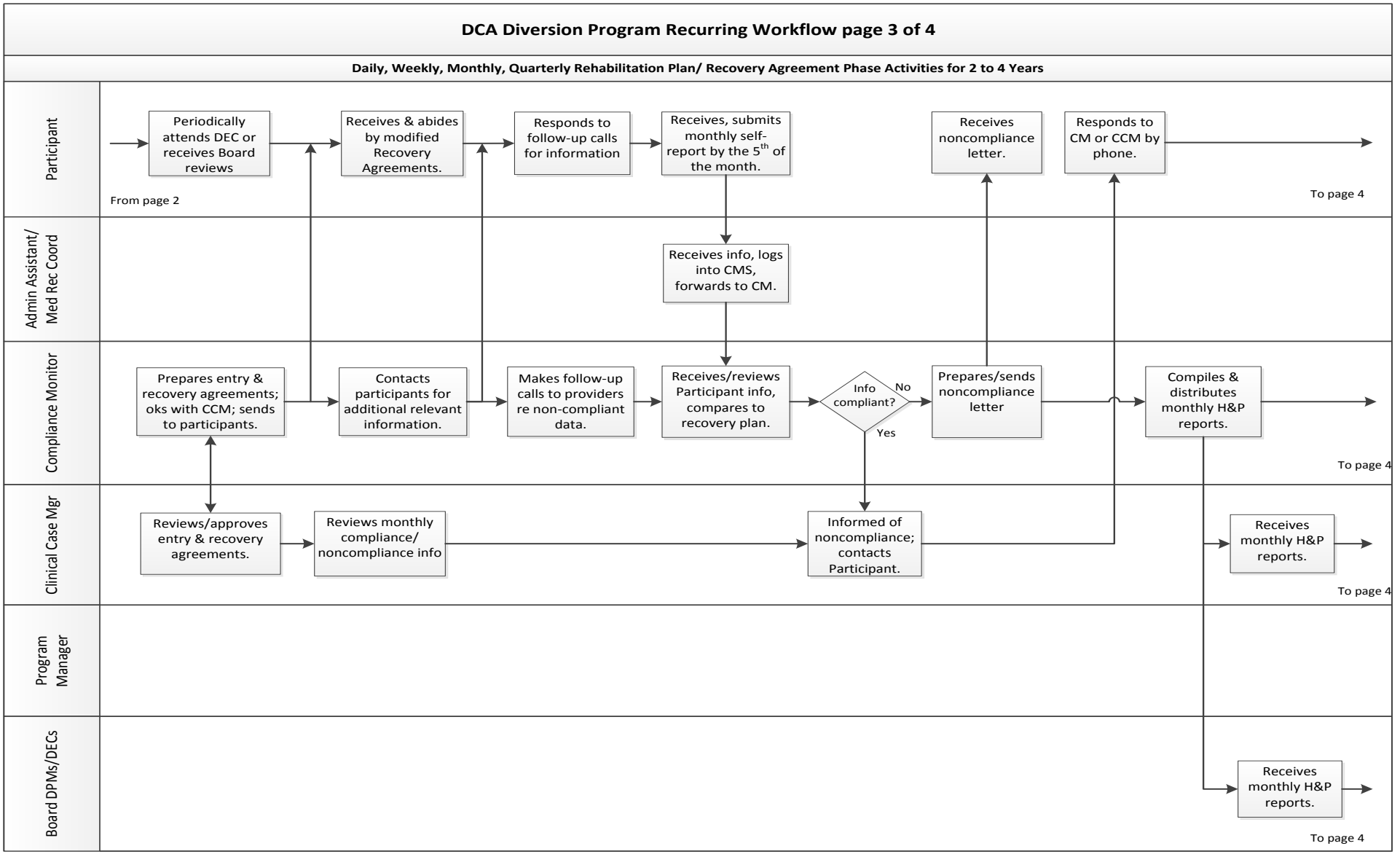

DCA Diversion Program Initial Contact Workflow page 3 of 4
Hold DEC or PRM Meeting / Recovery Contract Developed and Signed or Not / Make Noncompliance Call and Send Noncompliance Letter
Applicant/ Participant
Admin Assistant
Compliance Monitor
Clinical Case Mgr
Applicable Board
Clinical Assessor
DEC Consultant
Attends DEC or PRM meeting
Attends DEC or PRM meeting
Attends DEC or PRM meeting
From page 2
Attends DEC or PRM meeting
Holds DEC or PRM meeting; meets with Applicant
Prepares Recovery contract; sends to Applicant for signature w/in 10 biz days.
Receives contract; may sign & return or not within 10 biz days.
Signs/ returns on time?
No
Yes
Receives copy of signed Recovery contract.
Calls Applicant within 1 biz day to notify of noncompliance.
Receives noncompliance call
Prepares/sends noncompliance letter within 5 biz day.
Receives noncompliance letter
CCM & DEC consultant determine whether to close out Applicant (public risk or withdrawn).
To page 4

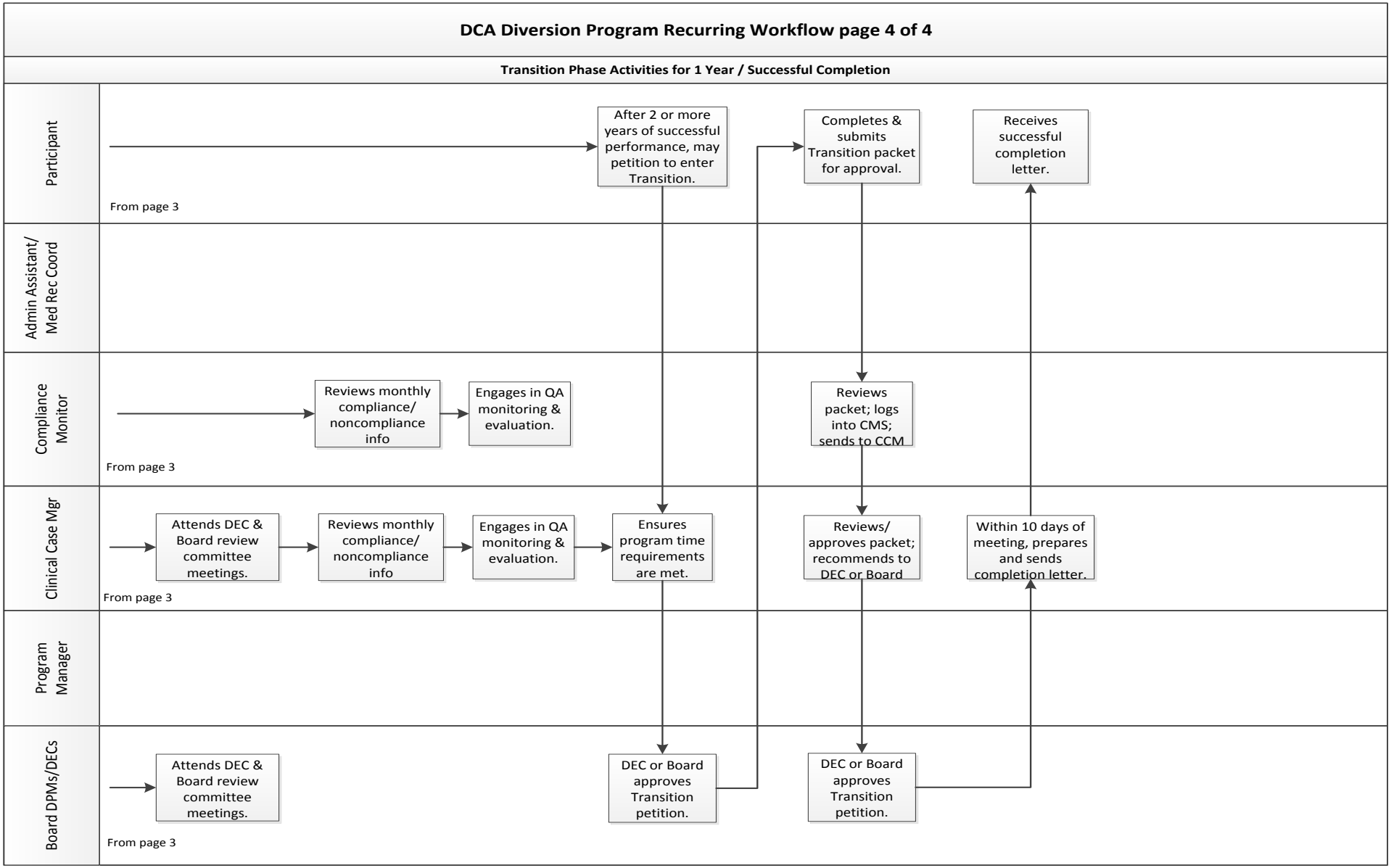

DCA Diversion Program Initial Contact Workflow page 4 of 4
Close Out or Retain Applicant
Applicant/ Participant
Admin Assistant
Compliance Monitor
Clinical Case Mgr
Diversion Program Mgr
Applicable Board
DEC Consultant
Discusses compliance expectations with CCM.
Receives letter; may appeal?
Close out Applicant?
No
Yes
Contacts Applicant to discuss compliance expectations..
Rec's Applicant agreemt?
No
Yes
Applicant retained.
Prepares Applicant withdrawal letter; sends to DPM for approval.
Sends letter to Applicant and copy to Board.
From page 3
Approves and returns letter.
Receives letter; takes action against Applicant.

Appendix 3: High Level Flowchart of Recurring Program Tasks




DCA Diversion Program Recurring Workflow page 2 of 4
Daily, Weekly, Monthly, Quarterly Rehabilitation Plan/ Recovery Agreement Phase Activities for 2 to 4 Years
Participant
Performs tasks stipulated in the Rehab Plan & Recovery Agreemt.
Registers & checks in with drug lab daily.
IDs 12-step program, secures sponsor, attends daily for 90 days then may request less thru their Board.
IDs & attends a Health or Nurse Support Group at least weekly.
May receive IOP treatment as specified.
Initially calls CCM weekly then monthly.
From page 1
To page 3
Admin Assistant/ Med Rec Coord
Daily, AA & MRC sort and distribute mail accordingly.
Daily answers and transfers calls; retrieves call log/notes, may copy into case log.
May print Recovery Agreemts; copies and mails; copy to CM.
Monthly, copies, mails non-compliance letters to participants; notes in CMS and mail log.
One month before DEC meetings, sends notice letters to applicants/ participants.
At or before new month, prints monthly batch reports (self-report, facilitator, WSM, qtrly treat provider); sends to mailroom for mid-month mailing.
From page 1
Compliance Monitor
Clinical Case Mgr
Responds to Participant calls weekly then monthly.
Compiles & distributes monthly H&P reports to DPMs.
Program Manager
Board DPMs/DECs
Receives monthly H&P reports before DEC or Board review meeting.


DCA Diversion Program Recurring Workflow page 3 of 4
Daily, Weekly, Monthly, Quarterly Rehabilitation Plan/ Recovery Agreement Phase Activities for 2 to 4 Years
Participant
Admin Assistant/ Med Rec Coord
Compliance Monitor
Clinical Case Mgr
Program Manager
Board DPMs/DECs
From page 2
Periodically attends DEC or receives Board reviews
Receives & abides by modified Recovery Agreements.
Responds to follow-up calls for information
Receives, submits monthly self-report by the 5th of the month.
Receives noncompliance letter.
Responds to CM or CCM by phone.
To page 4
Receives info, logs into CMS, forwards to CM.
Prepares entry & recovery agreements; oks with CCM; sends to participants.
Contacts participants for additional relevant information.
Makes follow-up calls to providers re non-compliant data.
Receives/reviews Participant info, compares to recovery plan.
Info compliant?
No
Yes
Prepares/sends noncompliance letter
Compiles & distributes monthly H&P reports.
To page 4
Reviews/approves entry & recovery agreements.
Reviews monthly compliance/ noncompliance info
Informed of noncompliance; contacts Participant.
Receives monthly H&P reports.
To page 4
Receives monthly H&P reports.
To page 4


DCA Diversion Program Recurring Workflow page 4 of 4
Transition Phase Activities for 1 Year / Successful Completion
Participant
From page 3
After 2 or more years of successful performance, may petition to enter Transition.
Completes & submits Transition packet for approval.
Receives successful completion letter.
Admin Assistant/ Med Rec Coord
Compliance Monitor
From page 3
Reviews monthly compliance/ noncompliance info
Engages in QA monitoring & evaluation.
Reviews packet; logs into CMS; sends to CCM
Clinical Case Mgr
From page 3
Attends DEC & Board review committee meetings.
Reviews monthly compliance/ noncompliance info
Engages in QA monitoring & evaluation.
Ensures program time requirements are met.
Reviews/ approves packet; recommends to DEC or Board
Within 10 days of meeting, prepares and sends completion letter.
Program Manager
Board DPMs/DECs
From page 3
Attends DEC & Board review committee meetings.
DEC or Board approves Transition petition.
DEC or Board approves Transition petition.

Appendix 4: FirstLab Drug Testing Panel

The following is the drug testing panel used during the audit period.

DRUG GROUP.	SCREEN DETECTION LEVEL* ng/inl**	MASS SPECTROMETRY CONFIRMATION DETECTION I EV ET * na/tnl*
Ethanol (Alcohol)	0.02%	0.02%
Ethyl Glucuronide (ETG/ETS)	250	250
Amphetamines (EMIT)	1000	500
Barbiturates (EMIT)	300	200
Benzodiazepines (EMIT)	300	300
Cocaine Metabolites (EMIT)	300	150
Marijuana Metabolites (EMIT)	20	15
Methadone (EMIT)	300	200
Methaqualone (EMIT)	300	200
Opiates/metabolites (EMIT)	300	300
Phencyclidine (EMIT)	25	25
Propoxyphene (EMIT)	300	200

BENZODIAZEPINES (MASS SPECTROMETRY)		
Alprazolam (Xanax)	50	50
Bromazepam CLectopam)	***LOD	***LOD
Clorazepate (Tranxene)	100	100
Chlordiazepoxide (Librium)	100	100
Clonazepam (Klonopin)	100	100
Diazepam (Valium)	100	100
Flunitrazepam (Rohypnol)	50	50
Flurazepam (Dalmane)	100	100
Halazepam (Paxipam)	100	100
Lorazepam (Ativan)	100	100
Lormetazepam (Noctamid)	100	100
Medazepam (Nobrium)	100	100
Midazolam (Versed)	50	50
Nitrazepam (Somnibel)	100	100
Oxazepam (Serax)	100	100
Prazepam (Centrax)	100	100
Temazepam (Restoril)	100	100
Triazolam (Halcion)	50	50

NARCOTICS (MASS SPECTROMETRY)		
Buprenorphine (Buprenex)	10	10
Butorphanol (Stadol)	***LOD	***LOD
Dextromethorphan (Rornilar)	100	100
Fentanyl	50	50
Hydrocodone (Vicodin)	100	100
Hydromorphone (Dilaudid)	100	100
Ketamine (Ketalar)	***LOD	***LOD
Meperedine (Demerol)	100	100

Meprobamate/Carisoprodol (Miltown/Soma)	100	100
Nalbuphine (Nubain)	100	100
Naltrexone (Trexan)	***LOD	***LOD
Oxycodone (Percocet)	100	100
Oxymorphone (Numorphan)	100	100
Pentazocine (Talwin)	100	100
Tramadol (Ultram)	***LOD	***LOD

Appendix 5: Contract Performance Standards Measured

#	
1	The Contractor must prepare a yearly calendar of upcoming DEC and PRM meetings. The calendar must be approved by the DPM for that Board and once approved the Contractor will distribute the calendar to all DEC members and the DPM by November 1st preceding each year. (§4.A.17; page 57) (LD's $500.00/day)
2	Contractor shall prepare and provide a History and Profile Report, and a current list relevant to the applicant/participant(s) monitored by their respective DECs and/or DPM who have had a Positive Drug Screen, Relapse and/or Public Threat Report(s) on each applicant/participant for their respective DEC and DPM no less than five (5) business days prior to the DEC or PRM. (§4.A.17; page 58)(§4.A.15; page 50) (LD's $500/day)
3	If a positive drug screen is determined to be a relapse by the CCM or DEC Case Consultant, a copy of the drug screen and a Relapse Report must be mailed or faxed to the DPM and DEC consultant within five (5) business days. (§4.A.13. B; page 43) (LD's $200/day
4	Contractor shall prepare and provide a written Board specific Monthly Participant Statistical Profile Report on the applicant/participant(s) in the Diversion Program and distribute the report to each DPM for their respective participant(s) within five (5) business days of the end of each month. (§4.A.12; page 41) (LD $250/day
5	Contractor shall prepare and provide to the DPM a Monthly Status Report for their respective Board by the tenth of each month. (§4.F.2; page 127) (LD $250/day
6	Contractor shall prepare and provide to the DPM a Quarterly Report for their respective Board by the twentieth day of the month following each quarter. (RFP §4.F.3; page 128) (LD $250/day)
7	Contractor shall prepare and provide to the DPM an Annual Diversion Program Report within 45 days following the end of the state fiscal year, June 30.(§4.F.4; page 131) (LD $250/day
8	If terminated, the Contractor shall provide a Termination Report to the DPM and/or DEC Case Consultant within five (5) calendar days from the termination date.(§4.A.10; page 33
9	BRN: Contractor shall include a Compliance Report with the Monthly Participant Statistical Profile Report detailing the areas for non-compliance for each applicant/participant that must be distributed to the DPM, DEC Chairperson, and assigned DEC Case Consultant monthly and within five (5) business days of the following month.(§5.A. 12; page 133
10	BRN: A supplemental report shall be provided to each DEC regarding that particular DECs applicant/participant cases. This report along with the History and Profile Report (H&Ps) shall be mailed and received by the DEC and DPM. (§5.A. 15; page 141) (per contract, provided at DEC
11	Contractor shall verify a self-referral participant's license online with the Board's website prior to accepting him or her into the Diversion Program and quarterly to ensure the licensee has a current and valid license. (§6. A. 2; page 149 and §8.A.2; page 165) DBC and PTBC; (§9.A.2.; page 175)
12	DBC: The CCM shall consult with the DPM and DEC Chair to determine if the licensee needs to be removed from practice no more than seven (7) business days after completing the initial intake interview. (§6. A. 5; page 149)
13	A written breakdown of the Diversion Program requirements, the applicant/participant's financial obligation, and the required consent forms shall be mailed to the applicant/participant within five (5) business days of the initial intake interview. The CCM shall inform the applicant/participant to return the consent forms within 10 days of receipt. (§4.A.4; page 19
14	The CCM… assigned to the applicant/participant's Board shall conduct an applicant/participant initial intake interview within 10 business days of application to the Diversion Program. (§4.A.5; page 20)
15	The clinical in-person assessment(s) shall take place within 10 days from the date of the CCM's initial clinical intake assessment interview. (§4.A.6; page 22)
16	The clinical assessor shall submit his or her written assessment of the applicant/participant to the Contractor within 30 days of the clinical in-person assessment. (§4.A.6; page 22)

17	If the clinical assessor recommends the applicant/participant requires immediate in-patient treatment, the clinical assessor shall notify the Contractor within one (1) business day. Upon notification from the clinical assessor, the CCM shall notify the DPM or DEC Case Consultant within 24 hours of the clinical assessor's recommendation. (§4.A.6; page 22)
18	The DPM must be notified within one (1) business day that the Intake has been completed along with the date and location of the applicant's first DEC meeting. (§5.A. 5; page 133)
19	BRN: The DPM must be notified of the scheduled date of the Intake within one (1) business day of scheduling. (§5.A. 5; page 133)
20	All Pre-Entry and Recovery Contracts shall be prepared and mailed to the applicant/participant and the DPM within 10 business days of approval by DEC or DPM. (§4.A.8; page 24)
21	All applicant/participants must have a designated worksite monitor. The Contractor shall validate that the approved worksite monitor is in place. (§4.A.9; page 29)
22	The CCM assigned to the applicant/participant shall contact the applicant/participant's worksite monitor within 10 business days from receipt of worksite monitor notification to communicate the responsibilities of being a worksite monitor and to review how to identify and detect certain indicators of relapse or threat to themselves or the public and how to report such instances to the CCM. (§4.A.9; page 29)
23	The Contractor shall provide… Successful Completion… Letter to the participant within 10 business days from the date of the DEC or PRM meeting or if terminated, from the date of termination (§4.A.10; page 31)
24	The Contractor shall provide a Termination Letter to the participant within 10 business days from the date of the DEC or PRM meeting or if terminated, from the date of termination (§4.A.10; page 31)
25	If the applicant/participant fails to return a signed copy of the contract as required, the Contractor shall… mail a Non-Compliance Letter within five (5) business days to the DPM and applicant/participant. (§4.A.10; page 31)
26	If the applicant/participant fails to return a signed copy of the contract as required, the Contractor shall verbally notify the applicant/participant within one (1) business day... (§4.A.10; page 31)
27	The Non-Compliance Letter must be prepared and mailed to the applicant/participant within five (5) business days of discovery of non-compliance. (§4.A.11; page 38)
28	The Non-Compliance Letter must be prepared and mailed to the DPM and/or Board's designee within five (5) business days of discovery of non-compliance. (§4.A.11; page 38)
29	For any termination resulting from non-compliance that is not deemed a public risk, the CCM shall provide to the DPM and/or Board's designee within five (5) business days of the termination a Termination Letter. (§4.A.11; page 22)
30	BOP: If the confirmed positive drug screen is positive for any unauthorized substance, the CCM shall verbally notify the Board's DPM within one (1) hour of notification by the drug testing provider either via telephone or email that pursuant to the participant's recovery contract they are prohibited from practicing. (§7.A.13.A; page 158)
31	Non-negative drug screens are reported to the DPM or DEC Case Consultant on a Non-negative Drug Screen Report within one business day (§4.A.13; Page 46)
32	If the confirmed positive drug screen is positive for any unauthorized substance, the CCM shall verbally notify the applicant/participant within one (1) hour of notification by the drug testing provider that he or she has tested positive for an unauthorized substance and they are immediately removed from practicing until further notice. (§4.A.13; page 43)

33	If a confirmed positive drug screen is positive for any unauthorized substance, The CCM shall notify the worksite monitor within one (1) hour of notification by the drug testing provider that pursuant to the applicant/participant's recovery contract they are prohibited from practicing until further notice. (RFP §4.A.13; page 43)
34	If a confirmed positive drug screen is positive for any unauthorized substance, The CCM shall notify and confer with the Board's DPM or DEC Case Consultant within one (1) business day and provide remediation plans. (§4.A.13; page 43)
35	If a confirmed positive drug screen is positive for any unauthorized substance, The CCM must notify the applicant/participant's support group facilitator within one (1) business day. (§4.A.13; page 43)
36	Any treatment contract modifications resulting from a positive or non-negative drug screen or relapse shall be provided to the applicant/participant via telephone within (1) business day (§4.A.13; page 43)
37	A modified Recovery Contract shall be mailed within five (5) business days after consulting with the Board's DEC Case Consultant and/or DPM regarding any treatment contract modifications resulting from a positive or non-negative drug screen or relapse. (§4.A.13; page 43)
38	If the applicant/participant fails to return a signed copy of the modified Recovery contract resulting from a positive or non-negative drug screen or relapse as required, the Contractor shall verbally notify the applicant/participant within one (1) business day and shall mail a Non-Compliance Letter within five (5) business days to the DPM and applicant/participant. (§4.A.13; page 43)
39	In the event that an applicant/participant has been determined by the appropriate authority as designated in the Board Specific Requirements to be a threat to themselves or others, the CCM assigned as the designated consistent team for that applicant/participant must notify the DPM and/or DEC Case Consultant within one (1) business day by sending a Public Threat Report. (§4.A.14; page 48)
40	If the applicant/participant is terminated from the Diversion Program, the CCM shall submit a Termination Letter to the applicant/participant and the DPM within five (5) business days (§4.A.14; page 48)
41	All closure documents, files, and a written in-depth Public Threat Report describing the justification as to why the applicant/participant is being terminated must be mailed only to the DPM, DEC Consultant & Participant within five (5) business days of the closure.(§4.A.14; page 48,§ 5.A.14; Page 140)
42	Contractor shall have a CCM attend HSG/NSG support group meetings at a minimum once per year to ensure that the groups are functioning properly and that the facilitator is supporting the goals and objectives of the Diversion Program unless otherwise indicated in Board Specific Requirements. (§4.B.4; page 81)
43	Contractor shall survey the participant who successfully completed or was terminated from the program within thirty (30) days of exiting the program. (§4.F.1; page 120)
44	Contractor shall meet quarterly with the DPMs for a Quality Review Meeting to report verbally and in writing on the quality of the program. (RFP §4.F.1.1; page 122)
45	Contractor shall investigate and resolve complaints made about services provided by Contractor's staff or subcontractors. The Contractor shall provide written documentation to the DPM detailing the initial complaint(s) and corrective action(s) taken within ten (10) days of receiving the complaint. Contractor will develop a standardized complaint resolution process that will be approved by the DPMs. (§4.B.3, page 80)

Appendix 6: Auditee Responses

The following includes audit responses prepared by Maximus and the seven participating Boards. Inaccuracies identified by the auditees in the draft report have been corrected in this final report.

MAXIMUS Response to the DCA audit of the California Health Professionals Diversion Program Conducted by CPS-HR Consulting February 10, 2016

EXECUTIVE SUMMARY

MAXIMUS appreciates the opportunity to participate in this audit and respects the decision of the Department of Consumer Affairs (DCA) to conduct such an audit. We understand the importance of an agency to audit and confirm that an Administrative Vendor is in compliance with contract requirements and the program is operated as designed.

We applaud the DCA for the incorporation of key elements contained in SB1441 Uniform Standards into the program before the legislation was enacted. As noted in our responses, the 2015 contract has resulted in several improvements to processes and procedures that further strengthen the program. Quality and continuous improvement are core tenets of the services MAXIMUS provides to its clients and stakeholders.

We recognize that there were no audit findings, and are responding to the recommendations of the Audit Team. All actions that are described in the responses are the responsibility of the Project Manager to implement.

We continue to work closely with the DCA to continue to improve the processes which protect the safety of the healthcare consumers of California.

RECOMMENDATION #1:

If applicable and warranted, other DCA healing arts Boards should consider participating in the Diversion Program, and in particular, the Medical Board of California and Board of Vocational Nursing and Psychiatric Technicians.

MAXIMUS RESPONSE:

Thank you for the recommendation for standardization of services to add the DCA healing arts boards who do not currently participate in the Diversion Program. Although MAXIMUS is not required to respond to this specific recommendation, we do believe in the mission of the Diversion program and support this recommendation for the Boards that are not currently served by the Program. MAXIMUS stands at the ready to assist the Boards in drafting the appropriate legislation to allow for implementation of this recommendation.

RECOMMENDATION #2:

The BRN should consider making probationers attend the Diversion Program as a condition of probation.

MAXIMUS RESPONSE:

Thank you for the recommendation for standardization of services to Probationers managed by the BRN Enforcement unit. MAXIMUS is not required to respond to this recommendation, however, wishes to state that several other Boards currently enroll the Probation Participants in the Diversion Program to assist with management of their Substance Use Disorders. This is a very effective partnership for these Boards, assists them to interpret and manage the clinical aspects of Addiction, and allows the Probation Monitors to conduct their enforcement duties without distraction.

RECOMMENDATION #3:

Maximus should identify a program staff member whose sole responsibility is to become knowledgeable about health insurance coverage benefits and referral sources, and periodically update the Clinical Case Managers and Compliance Monitors.

MAXIMUS RESPONSE:

MAXIMUS recognizes the value of employing an individual whose sole responsibility it is to become knowledgeable about health insurance coverage benefits and referral sources, and periodically update the Clinical Case Managers and Compliance Monitors; however such a position is not contractually required and is beyond what the program can support financially at this point in time.

RECOMMENDATION #4:

Program participants should assume personal responsibility to contact and research coverage options and costs with the health insurance companies listed on the Covered California website.

MAXIMUS RESPONSE:

MAXIMUS concurs with the recommendation to place personal responsibility for insurance coverage options and costs onto the program participants, however, participants are often overwhelmed and fragile when entering the program, and they need the program's assistance to sort through the many options available to them. In response to this recommendation, and although not contractually required, MAXIMUS will investigate the feasibility of creating a tool to assist participants with referral sources and coverage options.

RECOMMENDATION #5:

Maximus should consider and evaluate all of the Diversion Program Manager (DPM) recommendations and, at a minimum, provide the DPMs with recovery training.

1. Hire more CCMs and increase the number of participants.
2. Identify ways to better manage or reduce participant costs.
3. Identify ways to better treat participants suffering from mental illness.
4. Provide DPMs with recovery training.

MAXIMUS RESPONSE:

1. MAXIMUS staffing meets or exceeds the contractual requirement of a maximum of 130 participants per Clinical Case Manager/Compliance Monitor Team.
2. MAXIMUS is sensitive to the program costs, and concurs that the frequency of Random Drug Testing that is required by the Uniform Standards has increased the costs participants must bear. We encourage participants to work together to identify collection sites with lower fees, and the CCMs and Boards/DECs evaluate testing frequencies often in order to reduce them if possible. Due to the extensive nature of the test panel, the per-test fee is the lowest MAXIMUS was able to negotiate among possible vendors. MAXIMUS will continue to work to identify ways to manage or reduce participant costs.
3. The Board of Registered Nursing has called together a subcommittee of Intervention Program Committee Chairs who have volunteered to review the guidelines currently in use to manage Mental Health Participants. MAXIMUS will be involved in this process and will actively participate in developing the improved guidelines.
4. Although not contractually required, MAXIMUS has provided multiple sessions of training in conjunction with the Laboratory Subcontractor which have been made available to all DPMs. In the past, training has been provided at no charge to the DPMs in a variety of formats, including all-day workshops, via interactive

web conference, and in one-hour webinars. The Diversion Project Manager makes relevant articles and publications available to the DPMs as they become available. The MAXIMUS Project Manager has also provided small group or one-on-one training as requested.

RECOMMENDATION #6:

Maximus should consider and evaluate all of the stated Treatment Provider obstacles/ challenges, then prioritize and implement the recommendations accordingly.

MAXIMUS RESPONSE:

MAXIMUS appreciates the opportunity to review the challenges faced by the Clinical Assessors, Support Group Facilitators, and Worksite Monitors, and commits to reviewing the suggestions for improvements. It is noted that Clinical Assessor recommendations # 4 and 5 are at the discretion of the Boards if the enabling statutes permit, and if not, would require legislative changes to implement. In response to a recurring request to provide online reporting access, MAXIMUS is developing an enhanced version of the online case management system, which will allow for online transmission of forms and an update to the clinical assessment tool by July, 2016.

RECOMMENDATION #7:

As evidenced by the success of the auditor's online survey, Maximus should periodically reach out to Treatment Providers and other stakeholders to identify ongoing issues and opportunities for continuous improvement.

MAXIMUS RESPONSE:
Thank you for the recommendation. MAXIMUS values the input from stakeholders. It appears that direct email invitations are very effective in generating a response to surveys, and this method will be considered in the future.

RECOMMENDATION #8:

Maximus and the Boards should ensure each credential review is completed in compliance with the Uniform Standards, including evidence of: a license, experience and insurance; do not accept licensees with whom they have had a personal, financial and business relationship within the last year; and Board approval.

MAXIMUS RESPONSE:

Thank you for the recommendation. MAXIMUS will implement the credentialing changes that have been suggested.

RECOMMENDATION #9:

Per healthcare standards, perform and document an OIG clearance for each Treatment Provider at https://exclusion.oig.hhs.gov

MAXIMUS RESPONSE:

Thank you for the recommendation. Although not contractually required, MAXIMUS will consider implementing an OIG clearance for Support Group Facilitators and Clinical Assessors.

RECOMMENDATION #10:

Per healthcare standards, require all Treatment Providers with access to records to sign HIPPA confidentiality statements.

MAXIMUS RESPONSE:

Thank you for the recommendation. MAXIMUS will implement the use of a confidentiality statement for the treatment providers who access the participant records.

RECOMMENDATION #11:

Maximus should consider hiring a part-time CCM to cover vacations, illness and time away at DEC meetings, etc. This will improve the management of multiple calls.

MAXIMUS RESPONSE:

Thank you for this recommendation. MAXIMUS is currently in the process of filling a part-time Clinical Case Manager position to assist with coverage of Case Manager duties.

RECOMMENDATION #12:

Maximus program staff should continue to document reasons for delay.

MAXIMUS RESPONSE:

Thank you for the recommendation. The Audit Team reports that "There was only one delay that was not explained in the case logs or participant's profile." MAXIMUS agrees that it is good practice to document the reasons for the delays, and the Diversion staff will be reminded to do so.

RECOMMENDATION #13:

All program staff should take advantage of the improved spelling and grammar check feature in the upgraded Max-CMS.

MAXIMUS RESPONSE:

Thank you for the recommendation. As noted in the audit report, the upgraded version in 2016 will make spell check available to all employees and treatment providers and should correct much of this problem.

RECOMMENDATION #14:

The Project Manager should review and revise closing notes as necessary.

MAXIMUS RESPONSE:

Thank you for the recommendation. The Project Manager currently reviews the majority of closure notes written by the Clinical Case Managers, and will continue to do so.

RECOMMENDATION #15:

Use the participant's first or last name rather than pronouns only to prevent misunderstandings with case log entries.

MAXIMUS RESPONSE:

Thank you for the recommendation. MAXIMUS will review options for improving clarity of documentation.

RECOMMENDATION #16:

Maximus should develop and implement a written policy for making deletions and retractions to case logs. The American Health Information Management Association website (http://www.ahima.org) has examples and sample policies Maximus could use.

MAXIMUS RESPONSE:

Thank you for the recommendation. Permission to delete and edit case log notes is limited to the Project Manager, the Operations Manager, and the Information Systems Administrator. This access will continue to be restricted, and a written policy will be developed to manage this process.

RECOMMENDATION #17:

Maximus program staff should track and trend the reasons for program withdrawal to determine the number of participants who withdrew for financial and other reasons.

MAXIMUS RESPONSE:

Thank you for the recommendation. MAXIMUS will begin tracking this data, beginning January 1, 2016.

RECOMMENDATION #18:

Maximus program staff should improve or modify the Program Handbook in a variety of ways.

1. Explain in the Handbook how to properly dispose of drugs according to the US Food and Drug Administration web site, and emphasize that participants may not give the drugs they are discarding to other persons for their use.
2. Attach a letter to the applicant's packet to encourage reading/re-reading the Handbook until they are familiar with the rules and expectations (participants are required to sign, date and return the Handbook Acknowledgment Signature Sheet), and consider giving applicants a pre-DEC test to validate their understanding.

MAXIMUS RESPONSE:

Thank you for the recommendation. These recommendations will be taken into consideration and will be discussed with the Diversion Program Managers. The information on how to properly and safely dispose of medications will be added to the Handbook.

RECOMMENDATION #19:

Maximus program staff should improve or modify the Program Handbook in a variety of ways

- Add an index so applicants/participants can easily find needed information.
- Modify the drug testing information to include stronger language about the consequences of missing a call into the lab and missing a random drug test.
- Use bold letters or highlight the essential compliance information.
- Insert the Maximus Diversion Program Random Body Fluid letter into the Handbook and include additional information regarding caffeine and protein. For example: "Please be aware that any confirmed positive, dilute or out of range random body fluid testing (RBFT) may result in immediate suspension of work privileges.
- Tips to ensure test results fall within acceptable ranges include:
    - Do not use any mind-altering substances.
    - Test before 10:00 AM.
    - Avoid the use of caffeine before testing, including coffee and caffeinated drinks like energy drinks and sodas.
    - Limit fluid intake before the test.
    - Consume some protein in the morning before the test, such as an egg or protein bar, plain yogurt with fruit and nuts, breakfast burrito with black beans and cheese, whole wheat bread with 2 tablespoons of peanut butter, etc.
- Avoid exercise before testing."
- Include information about how participants can prove they followed the protocol at the collection site, such as taking a photo of the specimen, and/or post test data.

- Many participants with an upper respiratory infection unknowingly took over-the-counter (OTC) medications without thinking of the consequences of taking a banned substance. CCM's suggest Mucinex without DM for coughs. Participants might also consider using home remedies such as hot tea and honey, saline gargles, humidifiers and 'Nedi" pots with saline water for nasal cleansing rather than other OTC drugs than contain prohibited ingredients.
- Include information on ways to remember to call the lab, such as setting alarms and/or always calling at the same time every day.
- Suggest possible call reminder tools, including but not limited to: paper calendars, check lists, Google calendar or similar smart phone applications.

MAXIMUS RESPONSE:

Thank you for the multiple recommendations for improvement of the Program Handbook. These suggestions will be reviewed and implemented as appropriate.

RECOMMENDATION #20:

Maximus program staff should improve or modify the Program Handbook in a variety of ways.

- Remind participants that multiple minor violations hinder progress in the program and that 100% compliance is expected before being allowed to move to the transition phase.
- Revise the MSR information on page 8 to indicate the first page of the MSR must be submitted with the rest of the report and include a notation regarding the same on the first page.
- Revise the WSM information on page 9 to advise participants to check with their WSM by the first of the month to ensure their report is submitted timely.
- Revise the Treatment Provider Progress Report information on page 7 to advise participants to check with their treatment provider by the first of each month to ensure their reports are submitted timely.
- Revise the Support Group Facilitator information on pages 7-8 to advise participants to check with their group leader by the first of each month to ensure their reports are submitted timely.
- Include reminder tools such as, but not limited to: paper calendars, check lists, Google calendar or similar smart phone applications.
- Suggest participants call or email the Maximus CM or CCM monthly to verify that all reports have been received in a timely manner.

MAXIMUS RESPONSE:

Thank you for the multiple recommendations for improvement of the Program Handbook. These suggestions will be reviewed and implemented as appropriate.

RECOMMENDATION #21:

Maximus should include medicine disposal information from the USFDA website in the Program Handbook.

MAXIMUS RESPONSE:

Thank you for the recommendation. This recommendation appears to be a duplicate of #18, and is addressed above.

RECOMMENDATION #22:

Maximus should consider advising participants to seek out Mental Health Services from their local county government Adult System of Care, when appropriate.

MAXIMUS RESPONSE:

Thank you for the recommendation. The MAXIMUS Clinical Case Mangers offer a variety of referrals to treatment, and this resource will be made available to participants.

RECOMMENDATION #23:

Maximus should contact the California Chapter of the American Organization of Nurse Executives and California Hospital Association to speak at a regional or state-wide meeting regarding the prevention and detection of nurses diverting drugs.

MAXIMUS RESPONSE:

Thank you for the recommendation. The MAXIMUS Project Manager and a representative of the BRN provided a presentation to the Southern California chapter of the California Hospital Association and more recently to the Kern County Chapter of the California Association of Nurse Leaders. MAXIMUS and the BRN are scheduled to present to the San Diego chapter of the California Association of Nurse Leaders in March, 2016. MAXIMUS will continue to reach out to these organizations to expand awareness of the Diversion Programs.

RECOMMENDATION #24:

The Board's should collectively consider identifying an acceptable, but less frequent, random testing schedule that would accomplish the goal and reduce participant cost and loss, then modify Uniform Standard 4 accordingly.

MAXIMUS RESPONSE:

MAXIMUS is not required to respond to this recommendation.

RECOMMENDATION #25:

The non-DEC Board's should consider evaluating the effectiveness of the participants' non-attendance at Board review meetings, and consider ways to improve interpersonal interaction by Skype, Face Time or other forms of communication.

MAXIMUS RESPONSE:

MAXIMUS is not required to respond to this recommendation.

RECOMMENDATION #26:

The Maximus Quality Analyst should periodically audit the FirstLab website files to ensure all program participants being drug tested are included in the database.

MAXIMUS RESPONSE:

Thank you for the recommendation. The Laboratory Vendor has recently implemented a process to notify MAXIMUS when a new applicant establishes an account with the Lab. This will ensure that any delays are identified. In addition, the MAXIMUS QA Coordinator will implement a periodic comparison of MAXIMUS and FirstLab participant enrollment information.

RECOMMENDATION #27:

Maximus should revise the intake report accordingly to eliminate the confusion between monthly and year-to-date reporting.

MAXIMUS RESPONSE:

Thank you for the recommendation. MAXIMUS will review the report for accuracy and clarity.

RECOMMENDATION #28:

Maximus should consider tracking and trending major violations and actions taken, and report this information in the annual report.

MAXIMUS RESPONSE:

Thank you for the recommendation. This data will be tracked beginning January 1, 2016.

RECOMMENDATION #29:

Maximus should consider tracking and trending successful returns to work on a monthly and annual basis, and report this information in the annual report.

MAXIMUS RESPONSE:

Thank you for the recommendation. This data will be tracked beginning January 1, 2016.

RECOMMENDATION #30:

Participating Boards should attempt to monitor long range participant outcomes after program completion.

MAXIMUS RESPONSE:

MAXIMUS is not required to respond to this recommendation.

STATE OF CALIFORNIA
DEPARTMENT OF CONSUMER AFFAIRS

BUSINESS, CONSUMER SERVICES, AND HOUSING AGENCY • GOVERNOR EDMUND G. BROWN JR.
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February 10, 2016

CPS HR Consulting
241 Lathrop Way
Sacramento, CA 95815

Dear Auditor,

Enclosed is the Board of Registered Nursing's (BRN) response to the CPS HR Consulting draft report, "Department of Consumer Affairs — Contract and Performance Audit of the DCA Diversion Program provided by Maximus Health Services" dated January 28, 2016.

Thank you for the opportunity to respond to the draft audit report. Please contact Don Henry Walker, Intervention Program Manager, at (916) 574-7619 if you have any questions.

Stacie Berumen
Assistant Executive Officer
Board of Registered Nursing

Board of Registered Nursing (BRN) Response to CPS HR Consulting's Draft Report: "Department of Consumer Affairs — Contract and Performance Audit of the DCA Diversion Program provided by Maximus Health Services"
January 28, 2016

Recommendations

1) If applicable and warranted, other DCA healing arts Boards should consider participating in the Diversion Program, and in particular, the Medical Board of Vocational Nursing and Psychiatric Technicians.

The BRN agrees with this recommendation.
No action plan needed.

2) The BRN should consider making probationers attend the Intervention Program as a condition of probation.

The BRN will consider this recommendation.

Action Plan: The BRN will review the probation program to determine if opportunities exist to require probationers with substance use disorder to attend the Intervention Program as a condition of certain probation orders.

Contact Person: Elizabeth Elias, Probation Program Manager

4) Program participants should assume personal responsibility to contact and research coverage options and costs with the health insurance companies listed on the covered California website.

The BRN agrees with this recommendation.

Action Plan: The BRN will add language to the BRN website FAQ section that refers individuals without health insurance coverage questions to the Covered California website.

Contact Person: Don Henry Walker, Intervention Program Manager

8) MAXIMUS and the Boards should ensure each credential review is completed in compliance with the Uniform Standards, including evidence of a license, experience and insurance; do not accept licensees with whom they have had a personal, financial and business relationship within the last year, and Board approval.

The BRN agrees with this recommendation.

Board of Registered Nursing (BRN) Response to CPS HR Consulting's Draft Report: "Department of Consumer Affairs — Contract and Performance Audit of the DCA Diversion Program provided by Maximus Health Services"
January 28, 2016

Action Plan: The BRN is in compliance with this recommendation. The BRN has a policy document NSG P-10 that addresses this recommendation.

Contact Person: Don Henry Walker, Intervention Program Manager

24) The Boards should collectively consider identifying an acceptable, but less frequent, random testing schedule that would accomplish the goal and reduce participant cost and loss, then modify Uniform Standard 4 accordingly.

The BRN agrees with this recommendation.

Action Plan: This would require the Department of Consumer Affairs to reconvene the Substance Abuse Coordination Committee who created the document, "Uniform Standards Regarding Substance-Abuse Healing Arts Licensees" that specifies the testing requirements in Uniform Standard 4.

The BRN is willing to participate in the process to develop acceptable random testing requirements.

Contact Person: Don Henry Walker, Intervention Program Manager

30) Participating Boards should attempt to monitor long range participant outcomes after program completion.

The BRN will consider this recommendation. The BRN requests clarification of the definition of "long range."

Action Plan: Business and Professions Code (B&PC) section 2770.12(b) states in pertinent part that all board and committee records pertaining to participation in the Intervention Program shall be kept confidential and not subject to discovery or subpoena, except as specified. B&PC section 2770.12(a) states in pertinent part that all records for a registered nurse who has successfully completed the intervention program shall be purged. B&PC section 156.1 specifies that a board shall retain all records for treatment and rehabilitation services for three years from the date of the last treatment or service rendered or until reviewed for audit by the department. After that time period the documents may be purged.

Based on the current laws stated above the information requested may only be available for three years yet participation in the program is deemed confidential. The BRN would need to seek guidance from DCA legal counsel as to what information is available to monitor outcomes.

Contact Person: Don Henry Walker, Intervention Program Manager

STATE OF CALIFORNIA
DEPARTMENT OF CONSUMER AFFAIRS

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February 10, 2016

CPS HR Consulting
241 Lathrop Way
Sacramento, CA 95815

Attention: Jeff Mikles

Dear Mr. Mikles:

I have reviewed the draft report "Contract and Performance Audit of the DCA Diversion Program provided by Maximus Health Services", dated January 28, 2016. The report is comprehensive and well written. I do have a few comments.

On page 13 in the last paragraph you refer to entry into the Diversion program via "in lieu of discipline" and go on to reference the Board of Pharmacy (BOP) and the Dental Board (DBC). I recommend that last sentence be revised to reference the dental law as well as the pharmacy law....."if there has been no significant violation of pharmacy or dental laws, respectively".

Also, on page 16 in the last paragraph that starts "In 2011, Senate Bill 1441..." The second sentence implies that the DCA Substance Abuse Coordination Committee still exists. It does not. Therefore the sentence should indicate that the committee was comprised of 20 Executive Officers.....

Your recommendations for all boards have been noted. Once the report is final, I will take these recommendations to the Board for consideration.

Please feel free to contact me if you have any questions. I can be reached at Karen.fischer@dca.ca.gov or (916) 263-2188.

Sincerely,

Karen M. Fischer

Karen M. Fischer, MPA
Executive Officer

PHYSICIAN ASSISTANT BOARD

RESPONSE TO THE JANUARY 2016 CONTRACT AND PERFORMANCE AUDIT OF THE DCA DIVERSION PROGRAM PROVIDED BY MAXIMUS HEALTH SERVICES

Recommendation	PAB Response
1	Agree. The PAB believes that the Diversion Program provides an additional level of consumer protection with regard to licensees who have drug and alcohol issues. Other Boards could benefit from such a program. Board staff and probation monitors do not possess the knowledge to appropriately manage these types of licensees and probationers. Maximus does. At the PAB the probation monitors and Maximus staff work cooperatively to ensure that probationers are in compliance with all terms of their probation, including abstinence from drugs and alcohol.
4	Generally agree. While we agree that participants should assume responsibility to contact and research coverage options, they are often not in a condition to do so. The PAB believes that Maximus should have the ability to assist or direct participants to appropriate resources.
8	Agree. Maximus should take the lead on this due to their knowledge and experience in this area.
24	Disagree. While the PAB is sympathetic to drug testing costs incurred by participants, as a consumer protection agency we are more concerned with ensuring consumer protection. The PAB needs the flexibility to test as often as appropriate. Additionally, the PAB must comply with the Uniform Standards. Drug testing is the most effective tool to ensure that participants/probationers are not using drugs and/or alcohol. The PAB utilizes alternative tests such as blood and hair. DCA boards review the test panels to ensure that they are up-to-date and at the lowest cost as available.
25	Agree. Alternative methods of communication would be beneficial to participants. The PAB also encourages the CCM to meet with PAB participants when attending DEC meetings for other boards.
30	Disagree. While these statistics would be valuable, we might have difficulty in following up with prior participants due to the fact that these are medical issues and would be confidential. To the best of my knowledge, the PAB does not have legal authority to randomly inquiry as to a prior participant's health issues with regard to drug and alcohol concerns once the probation is completed. The PAB has the authority react to new complaints or criminal convictions and those involving prior discipline history would be taken into consideration when investigating the new compliant.

Veterinary Medical Board Audit Response

From: Mathes, Ethan@DCA
Sent: Friday, February 12, 2016 12:23 PM
To: Wallace, Annecia@DCA
Cc: DelMugnaio, Annemarie@DCA
Subject: RE: Maximus audit responses

Greetings Annecia,

Here are my comments, some are duplicative/similar to CPS's comments:

-Maximus should consider new DPM training, but at the minimum yearly refresher training covering all facets of the program, contract, recovery, etc. (and including an orientation manual?)

-Maximus should audit its program costs and costs paid by participants generally and provide suggestions on reducing costs to participants

-Maximus should audit the effectiveness of the program, including the effectiveness of a 3-year minimum mandatory participation

-Maximus should study/evaluate in cooperation with boards how to increase program participation, especially in light of diminishing participation in the last 3 years

-Maximus should study different means for participants to subsidize their recovery via insurance, and pass that information along during intake

One note on the audit for accuracy, the Board's participant co-pay in Table 7 is incorrectly identified and yearly; it is a one-time fee.

That's about it!

Regards,

Ethan Mathes
Operations Manager
Veterinary Medical Board
1747 N. Market Blvd., Suite 230
Sacramento, California 95834-2934
Phone: (916) 515-5227
Fax: (916) 928-6849

February 16, 2016

To: Annecia Wallace

From: Board of Pharmacy

Comments on Draft Audit as Conducted and Prepared by CPS

In general the board is concerned with the "semantic allness" used in portions of this report. We have provided some instances below in the specific comments, but feel compelled to note that portions of the report appear to indicate that it was the consensus of all DPMS when making some statements. This is not true. Further, the board is not clear how some of the conclusions were reached and as such question some of the conclusions as applicable to the Board of Pharmacy program. In the hopes it is helpful the Board of Pharmacy has referenced specific page numbers as well as the Board of Pharmacy's comment.

Board of Pharmacy Specific Comments

Page 6 Drug Test File Audit Results
The Board of Pharmacy understands the four drug test files that are identified in the audit were applicants that declined to join. Therefore, these participants would not have signed up with First Lab.

Page 8 Second sentence
The year needs to be fixed to 2016 not 2106.

Page 12 Board of Pharmacy section codes needs a dash between 4360-4373.

Page 13 The definition provided in the audit of referral types is inaccurate. For instance the In Lieu of Referral specifies in the audit this definition pertains to BOP and DBC, which is inaccurate. The definition for In Lieu of Referral in the contract only pertains to BOP and the definition itself in the contract is different than what is defined in the audit.

The definitions provided below is the exact language provided in contact. The statistical information that is provided within the definitions in the audit report may need to be revisited to ensure the data is based on the accurate definition. This could present a problem in the future if the data does not match the statistical information reported by Maximus vs. the audit. The appropriate definitions included in the contract are provided below.

Definitions of Referral Types per Contract

Board Referrals
1) Investigative/Informal Referral (BOP, DBC, and DHCC) A licensee who may have a Board investigation pending, and upon recommendation of a Board inspector/investigator, may seek admission into the Diversion Program. The participant signs a release authorizing the Contractor to discuss his or her progress with the Board's DPM.

2) Non-Disciplinary Referral (BRN) A licensee referred to the Diversion Program by the Board, based on information or complaint received by the Board, indicating that the licensee may be impaired due to substance abuse disorder or mental illness.
3) Probation/Disciplinary Referral A licensee referred to the Diversion Program by the Board as a condition of a Board-imposed disciplinary action.
4) In Lieu of (BOP) A licensee who the Board investigated and referred into the program to be assessed in order to determine if the licensee has a substance use disorder.
Self-Referral
1) A licensee who voluntarily seeks admission into the Diversion Program.

Page 14 Top paragraph after bullets
The language should reflect recovery plan not rehabilitation plan in the second sentence.

The statement in the last sentence of the first paragraph is inaccurate.
"However, if a participant does not successfully complete the program, the original complaint, would be sent to enforcement." This statement is inaccurate for the Board of Pharmacy Program because the board never diverts a licensee from the investigation process. Although it may be true for some board programs, there is no qualifier applied to the sentence if that is the case.

Under Program Intake and Clinical Assessment
The last sentence in the first paragraph should reflect recovery plan not treatment plan.

Page 19 Under the heading Worksite monitors.
Should read - WSM observe participants up to a maximum of 100% and not just one day a week as appears in the audit. The worksite monitoring percentage can be reduced to zero percent in the transition phase. The worksite monitor percentage that is established for the participant depends on what stage the participant is at in his/her recovery.

Page 24 The last sentence in the paragraph.- One closure type that is conspicuously absent is financial hardship.
This is not a closure type.

Page 40 Under As a result of the DPM meeting, CPS learned the following:
The bullet that pertains to speaking on behalf of "All DPMs" leads the reader to believe this statement is agreed upon by all DPMs. The Board of Pharmacy did make such a claim regarding formal training.

The bullet that pertains to DPMs stating "some DECs have gotten away with poor practices", the Board of Pharmacy is concerned this leads a reader to believe all DPMs agree with this statement. The Board of Pharmacy does not have DECs and is not in a position to make such a statement.

As a result, the DPMs suggested the following Diversion Program improvements.

The bullets in this section lead the reader to believe this is agreed upon by all DPMs.

Page 42 Under Clinical Assessors recommend - Institute DECs for all professions
The Board of Pharmacy is concerned with this overall statement and questions if all the clinical assessors truly recommend this.

Page 43 Under HSG Facilitators claim the following obstacles/challenges in bullet number 2 - Maximus does not give enough consideration to HSG facilitator feedback.
The Board of Pharmacy takes exception to this comment. The Board of Pharmacy routinely requests feedback from the HSG facilitators and considers such feedback as part of the overall clinical picture of the participant. The Board of Pharmacy questions if all health support group facilitators made this statement and applied it to all board programs.

Under HSG Facilitators recommend in bullet number 2 - Provide HSG facilitators with access to intake summary, evaluations, and treatment reports.
The clinical assessors are required to independently assess the licensee.

Page 44 Under Worksite Monitor Responses in the section WSMs recommend in bulet number 3 - Provide improved access to Board Diversion Program Managers.
The Board of Pharmacy suggests that clarification should be sought in regards to this statement as the WSMs communicate directly with the clinical case managers. Further, worksite monitors are interviewed by the Board of Pharmacy staff, generally on a quarterly basis to gain understanding of how a participant is performing at work. This is in addition to the worksite monitor reports provided.

Page 50 Under Recommendations
In the bullet pertaining to the handbook the bold section – remove the term "**suspension"** and replace with "**removed from practice."** The Board of Pharmacy does not delegate the authority to the vendor to suspend a license, rather the board does this.

Page 54 The first paragraph at the top of the page
In the sentence, "As a result, the DPMs claim self-referrals into the program have almost stopped and participant levels have dropped", the use of the word "claims" attributes this statement to all DPMs. The Board of Pharmacy does not believe this is an accurate statement.

Board Review and DEC Meetings
In the second paragraph, last sentence, in stating "through reading meeting minutes", what type of meeting minutes contain statements by participants? The DEC and Review Meetings have summary notes from the meetings that contain changes to a participants recovery plan. For example: participant is approved to reduce attending five 12-step meetings to four 12-step meetings per week.

With respect to the first bullet, the Board of Pharmacy is curious to know if the auditors surveyed board participants. If not, we are unclear how the statement can be made. The Board of Pharmacy is concerned with the overall

representation of non-DEC boards. Furthermore, the Board of Pharmacy is not aware of any board meeting minutes that would reflect comments made by participants and is unaware of any discussion at a board meeting or review meeting when a board participant has made these assumptions.

Second Bullet – DECs
The Board of Pharmacy is not aware of any board meeting minutes that would reflect comments made by participants and recommends that additional information be sought to clarify if minutes from DEC meetings are maintained that include specific quotes from participants.

Page 55 <u>Recommendation to use SKYPE for non-Dec boards to improve interpersonal interaction.</u>
The Board of Pharmacy takes exception to this comment as all probation referred participants meet with Board of Pharmacy inspectors on a quarterly basis to ensure compliance not only with his/her probation but with the Pharmacist Recovery Program. In addition, the Board of Pharmacy inspectors also meet with the worksite monitors in person.

Audit Grid
Recommendation Respondents

1. The Board of Pharmacy does not have a position on whether other boards participate in the Diversion Program.

4. The contracted vendor is there to assist participants with locating services. However, the Board of Pharmacy also thinks it is the responsibility of the participant.

8. As part of the scope of work, the credential review is included in the contract.

24. The drug testing was established by the Uniform Standards Committee as implementation of SB 1441.

25. As stated above, the Board of Pharmacy has concerns with this recommendation. Refer to the board's comment from page 55 of the report.

30. The Board of Pharmacy has in the contract in its Board Specifics section 7.F.1 to conduct an annual longitudinal study of former BOP participants who have successfully completed the Pharmacist Recovery Program within the past three years. This recommendation appears to apply to all programs. The board requests clarification on the specific recommendation, i.e. should it be done every three years, standard questions to assess, etc.

Physical Therapy Board Audit Response

From: Kaiser, Jason@DCA
Sent: Tuesday, February 16, 2016 4:29 PM
To: Wallace, Annecia@DCA
Subject: RE: Any more Board responses?

Hi Annecia,

After looking at the Matrix of responses you provided, I assuming we fit under the categories of "All Boards" and Non-DEC Boards".

Here is PTBC's take on the audit report.

For findings for "All-Boards",

1) The PTBC concurs with recommendation 1.

4) The PTBC concurs with recommendation 4.

8) The PTBC concurs with recommendation 8

24) The PTBC concurs with recommendation 24.

30) The PTBC does not concur with recommendation 30. Once a probationer has completed the Maximus program, they typically have 1 more year of probation compliance. Subsequent to that, should the Board have to have to monitor the licensee outside of the Disciplinary Order, we would be doing so without authority or ability to collect costs, which would be an additional draw on the Boards resources that could not be absorbed.

For findings for "Non-DEC Boards",

25) The PTBC concurs with recommendation 25.

Let me know if you need anything else for the response.

Thanks.

Jason Kaiser
Executive Officer
Physical Therapy Board of California
2005 Evergreen St. Suite 1350
Sacramento CA. 95815
916-561-8278

Attachment 4

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

FDA News Release

FDA announces enhanced warnings for immediate-release opioid pain medications related to risks of misuse, abuse, addiction, overdose and death

New safety warnings also added to all prescription opioid medications to inform prescribers and patients of additional risks related to opioid use

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For Immediate Release

March 22, 2016

Release

Español (/NewsEvents/Newsroom/ComunicadosdePrensa/ucm491811.htm)

In a continuing effort to educate prescribers and patients about the potential risks related to opioid use, the U.S. Food and Drug Administration today announced required class-wide safety labeling changes for immediate-release (IR) opioid pain medications. Among the changes, the FDA is requiring a new boxed warning about the serious risks of misuse, abuse, addiction, overdose and death. Today's actions are among a number of steps the agency recently outlined in a plan to reassess its approach to opioid medications. The plan is focused on policies aimed at reversing the epidemic, while still providing patients in pain access to effective relief.

The FDA is also requiring several additional safety labeling changes across all prescription opioid products to include additional information on the risk of these medications. This is part of the agency's overall effort to help inform prescribers about the importance of balancing the serious risks of opioids with their role in managing pain.

"Opioid addiction and overdose have reached epidemic levels over the past decade, and the FDA remains steadfast in our commitment to do our part to help reverse the devastating impact of the misuse and abuse of prescription opioids," said Robert Califf, M.D., FDA commissioner. "Today's

actions are one of the largest undertakings for informing prescribers of risks across opioid products, and one of many steps the FDA intends to take this year as part of our comprehensive action plan to reverse this epidemic."

Opioid analgesics are powerful pain-reducing medications that include prescription oxycodone, hydrocodone and morphine, among others. Prescription opioids are divided into two main categories – IR products, usually intended for use every four to six hours; and extended-release/long-acting (ER/LA) products, which are primarily intended to be taken once or twice a day, depending on the individual product and patient. Certain opioids, such as methadone and buprenorphine, are also used as a form of treatment for opioid addiction, and in combination with behavioral therapy and counseling, are known as medication-assisted treatment, or MAT.

The updated indication clarifies that because of these risks, IR opioids should be reserved for pain severe enough to require opioid treatment and for which alternative treatment options (e.g., non-opioid analgesics or opioid combination products, as appropriate) are inadequate or not tolerated. The dosing information also provides clearer instructions regarding patient monitoring and drug administration, including initial dosage, dosage changes during therapy and a warning not to abruptly stop treatment in a physically dependent patient.

As part of the boxed warning on IR opioid analgesics, the FDA now requires a precaution that chronic maternal use of opioids during pregnancy can result in neonatal opioid withdrawal syndrome (NOWS), which may be life-threatening if not recognized and treated using protocols developed by neonatology experts. NOWS may occur in a newborn exposed to opioid drugs for a prolonged period while in utero.

In 2013, the FDA **required class-wide labeling changes for ER/LA opioid analgesics (/NewsEvents/Newsroom/PressAnnouncements/ucm367726.htm)** that included modifications to the products' indications, limitations of use, and warnings, including boxed warnings to more effectively communicate to prescribers the serious risks associated with these drugs. Today, the FDA is requiring similar changes to the labeling of IR opioid analgesics.

"We know that there is persistent abuse, addiction, overdose mortality and risk of NOWS associated with IR opioid products," said Douglas Throckmorton, M.D., deputy center director of regulatory programs, FDA's Center for Drug Evaluation and Research. "Today, we have taken an important next step in clarifying and making more prominent the known risks of IR opioid medications."

Additionally, the FDA is requiring updated labeling for all opioids (both ER/LA and IR products) to include safety information about potentially harmful drug interactions with other medicines that can result in a serious central nervous system condition called serotonin syndrome. Updated labeling will also include information about opioid effects on the endocrine system, including a rare but serious disorder of the adrenal glands (called adrenal insufficiency) and decreased sex hormone levels (androgen deficiency). These labeling changes will also make it clear that these negative outcomes can occur whether a patient is taking an opioid to treat pain or if the product is being used for MAT. Today, the FDA issued a **Drug Safety Communication (/Drugs/DrugSafety/ucm489676.htm)** outlining these risks.

"The broad set of actions announced today is reflective of the FDA's efforts to improve informed prescribing of opioids across the board," said Janet Woodcock, M.D., director of the FDA's Center for Drug Evaluation and Research. "We have been and will continue to evaluate all new data to ensure that labels of opioid drugs contain appropriate prescribing information about the benefits and risks of prescription opioids."

The FDA is also aware of, and carefully reviewing, available scientific information about potentially serious outcomes related to interactions between benzodiazepines and opioids. Once a review of all available scientific information is completed, the FDA will take necessary actions to ensure prescribers and the public are informed of the risks involved with the use of these medications.

These actions are the latest examples of the agency's commitment to combat this public health crisis and its profound impact on individuals, families and communities across our country. Health and Human Services Secretary Sylvia M. Burwell has made addressing opioid misuse, addiction and overdose a priority. Other work on this important issue is underway within HHS. **The evidence-based HHS-wide opioid initiative (http://www.hhs.gov/news/press/2015pres/03/20150326a.html)** focuses on three priority areas: informing opioid prescribing practices, increasing the use of naloxone (a rescue medication that can prevent death from overdose) and expanding access to and the use of MAT to treat opioid use disorder.

The FDA, an agency within the U.S. Department of Health and Human Services, protects the public health by assuring the safety, effectiveness, and security of human and veterinary drugs, vaccines and other biological products for human use, and medical devices. The agency also is responsible for the safety and security of our nation's food supply, cosmetics, dietary supplements, products that give off electronic radiation, and for regulating tobacco products.

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Consumers

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Related Information

- **FDA: Opioid Medications (/Drugs/DrugSafety/InformationbyDrugClass/ucm337066.htm)**
- **FDA: Fact Sheet – FDA Opioids Action Plan (/NewsEvents/Newsroom/FactSheets/ucm484714.htm)**
- **FDA: Approved Drugs: Questions and Answers (/Drugs/ResourcesForYou/Consumers/ucm054420.htm)**

- **CDC: Prescription Painkiller Overdoses in the US (http://www.cdc.gov/vitalsigns/PainkillerOverdoses/index.html)**

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U.S. Food and Drug Administration
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Drug Safety Communications

FDA Drug Safety Communication: FDA warns about several safety issues with opioid pain medicines; requires label changes

Safety Announcement

[3-22-2016] The U.S. Food and Drug Administration (FDA) is warning about several safety issues with the entire class of opioid pain medicines. These safety risks are potentially harmful interactions with numerous other medications, problems with the adrenal glands, and decreased sex hormone levels. We are requiring changes to the labels of all opioid drugs to warn about these risks.

More specifically, the labels will warn about the following:

- Opioids can interact with antidepressants and migraine medicines to cause a serious central nervous system reaction called serotonin syndrome, in which high levels of the chemical serotonin build up in the brain and cause toxicity (see List of Serotonergic Medicines).
- Taking opioids may lead to a rare, but serious condition in which the adrenal glands do not produce adequate amounts of the hormone cortisol. Cortisol helps the body respond to stress.
- Long-term use of opioids may be associated with decreased sex hormone levels and symptoms such as reduced interest in sex, impotence, or infertility.

Opioids are a class of powerful narcotic pain medicines that are used to treat moderate to severe pain that may not respond well to other pain medicines (see List of Opioids). They can help manage pain when other treatments and medicines are not able to provide enough pain relief, but they also have serious risks including misuse and abuse, addiction, overdose, and death.

Recommendations and information for patients and health care professionals

Serotonin syndrome:
Patients taking an opioid along with a serotonergic medicine (see List of Serotonergic Medicines) should seek medical attention immediately if they develop symptoms such as agitation; hallucinations; rapid heart rate; fever; excessive sweating; shivering or shaking; muscle twitching or stiffness; trouble with coordination; and/or nausea, vomiting, or diarrhea. Symptoms generally start within several hours to a few days of taking an opioid with another medicine that increases the effects of serotonin in the brain, but symptoms may occur later, particularly after a dose increase.

Health care professionals should discontinue opioid treatment and/or use of the other medicine if serotonin syndrome is suspected.

Cases of serotonin syndrome in the FDA Adverse Event Reporting System (FAERS) database were reported more frequently with the opioids fentanyl and methadone used at the recommended doses. Therefore, we are requiring a new statement in the *Warnings and Precautions* section to be added to these drug labels. Some opioids, including tramadol, tapentadol, and meperidine, already have warnings about serotonin syndrome. Cases were also reported with other opioids, so the labels of all these drugs will be updated to include information about serotonin syndrome in the *Drug Interactions* and *Adverse Reactions* sections.

Adrenal insufficiency:
Patients should seek medical attention if they experience symptoms of adrenal insufficiency such as nausea, vomiting, loss of appetite, fatigue, weakness, dizziness, or low blood pressure. **Health care professionals** should perform diagnostic testing if adrenal insufficiency is suspected. If diagnosed, treat with corticosteroids and wean the patient off of the opioid, if appropriate. If the opioid can be discontinued, follow-up assessment of adrenal function should be performed to determine if treatment with corticosteroids can be discontinued.

We are requiring a new statement about adrenal insufficiency to be added to the *Warnings and Precautions* section of all opioid labels.

Decreased sex hormone levels:
Patients should inform their health care professionals if they experience symptoms of low libido, impotence, erectile dysfunction, lack of menstruation, or infertility.
Health care professionals should conduct laboratory evaluation in patients presenting with such signs or symptoms.

We reviewed published studies that assessed levels of sex hormones in patients taking opioids chronically;[1-21] however, all had limitations that make it difficult to determine whether the symptoms were caused by the opioids or other factors. The labels of some opioids already describe this possible risk, and we are now adding consistent information to the *Adverse Reactions* section of all opioid labels.

We urge patients and health care professionals to report side effects involving opioids or other medicines to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of the page.

List of Opioids

Generic Name	Found in Brand Name(s)
alfentanil	Alfenta
buprenorphine	Belbuca, Bunavail, Buprenex, Butrans, Suboxone, Zubsolv
butorphanol	No brand name currently marketed
codeine	Fioricet w/ codeine, Fiorinal w/ codeine, Tylenol w/ codeine
dihydrocodeine	Synalgos-DC
fentanyl	Abstral, Actiq, Duragesic, Fentora, Ionsys, Lazanda, Sublimaze, Subsys
hydrocodone	Anexsia, Hysingla ER, Lortab, Norco, Reprexain, Vicodin, Vicoprofen, Zohydro ER
hydromorphone	Dilaudid, Dilaudid-HP, Exalgo
meperidine	Demerol
methadone	Dolophine, Methadose
morphine	Astramorph PF, Duramorph PF, Embeda, Infumorph, Kadian, Morphabond, MS Contin
oxycodone	Oxaydo, Oxycet, Oxycontin, Percocet, Percodan, Roxicet, Roxicodone, Xartemis XR
oxymorphone	Opana, Opana ER
pentazocine	Talwin
remifentanil	Ultiva
sufentanil	Sufenta
tapentadol	Nucynta, Nucynta ER
tramadol	Conzip, Ultracet, Ultram, Ultram ER

List of Serotonergic Medicines

Generic Name	Found in Brand Name(s)
Selective Serotonin Reuptake Inhibitors (SSRIs)	
paroxetine	Paxil, Paxil CR, Pexeva, Brisdelle
fluvoxamine	Luvox, Luvox CR
fluoxetine	Prozac, Prozac Weekly, Sarafem, Selfemra, Symbyax
sertraline	Zoloft
citalopram	Celexa
escitalopram	Lexapro
Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)	
venlafaxine	Effexor XR
desvenlafaxine	Pristiq, Khedezla
duloxetine	Cymbalta
milnacipran	Savella
Tricyclic Antidepressants (TCAs)	
amitriptyline	No brand name currently marketed
desipramine	Norpramin
clomipramine	Anafranil
imipramine	Tofranil, Tofranil PM
nortriptyline	Pamelor, Aventyl
protriptyline	Vivactil
doxepin	Zonalon, Silenor
trimipramine	Surmontil
Monoamine Oxidase Inhibitors (MAOIs)	
isocarboxazid	Marplan
phenelzine	Nardil
selegiline	Emsam, Eldepryl, Zelapar
tranylcypromine	Parnate
Other Psychiatric Medicines	
amoxapine	No brand name currently marketed
maprotiline	No brand name currently marketed
nefazodone	No brand name currently marketed
trazodone	Oleptro
buspirone	No brand name currently marketed
vilazodone	Viibryd
mirtazapine	Remeron, Remeron Soltab
lithium	Lithobid
Migraine Medicines	
almotriptan	Axert
frovatriptan	Frova
naratriptan	Amerge

rizatriptan	Maxalt, Maxalt-MLT
sumatriptan	Imitrex, Imitrex Statdose, Alsuma, Sumavel Dosepro, Zecuity, Treximet
zolmitriptan	Zomig, Zomig-ZMT
Antiemetics	
ondansetron	Zofran, Zofran ODT, Zuplenz
granisetron	Kytril, Sancuso
dolasetron	Anzemet
palonosetron	Aloxi
Other Serotonergic Medicines	
dextromethorphan	Bromfed-DM, Delsym, Mucinex DM, Nuedexta
linezolid	Zyvox
cyclobenzaprine	Amrix
methylene blue	
St. John's wort	
tryptophan	

Facts about Opioids

- Opioids are powerful prescription medicines that can help manage pain when other treatments and medicines are not able to provide enough pain relief (see List of Opioid Medicines). However, opioids also carry serious risks, including of misuse and abuse, addiction, overdose, and death.
- Prescription opioids are divided into two main categories – immediate-release (IR) products, usually intended for use every 4 to 6 hours; and extended release/long acting (ER/LA) products, intended to be taken once or twice a day, depending on the individual product and patient.
- Certain opioids, such as methadone and buprenorphine, can also be prescribed as a form of treatment for opioid addiction.
- Opioids are available in many different formulations, including tablets, capsules, lozenges, sublingual tablets, transdermal patches, nasal sprays, and injections.
- Common side effects of opioids include drowsiness, dizziness, nausea, vomiting, constipation, physical dependence, and slowed or difficult breathing.
- The risk of opioid addiction, abuse or misuse is increased in patients with a personal or family history of substance abuse, or mental illness.
- It is important to lock up opioids and to dispose of them properly to keep them from falling into the wrong hands.

Additional Information for Patients

- FDA is warning about several safety issues with the class of powerful narcotic opioid pain medicines:

    - Opioids can interact with certain medicines that increase the effects of serotonin, which is a chemical in the brain. The interacting medicines include antidepressants and migraine medicines, and the interaction causes a serious central nervous system reaction called serotonin syndrome (see List of Serotonergic Medicines).
    - Taking opioids may lead to a rare, but serious condition called adrenal insufficiency in which the adrenal glands do not produce adequate amounts of the steroid hormone, cortisol, particularly during stressful conditions.
    - Long-term use of opioids may be associated with decreased sex hormone levels.
- Inform your health care professional about all the drugs you are taking, including prescription and over-the-counter medicines. It is helpful to keep a list of all your current medicines in your wallet or another location where it can be easily retrieved. You can fill out and print a copy of My Medicine Record.
- If you are taking an opioid pain reliever and don't know if you are also receiving serotonergic medicines or other medicines that interact with opioids, contact your health care professional.
- Opioids are powerful narcotic pain medicines that can help manage pain when other treatments and medicines are not able to provide enough pain relief. However, even when used properly, opioids also carry serious risks, and they can be misused and abused, causing addiction, overdose, and death.
- Seek medical attention immediately if you develop any symptoms of serotonin syndrome such as:
    - Agitation
    - Hallucinations
    - Rapid heart rate
    - Fever
    - Excessive sweating
    - Shivering or shaking
    - Muscle twitching or stiffness
    - Trouble with coordination
    - Nausea, vomiting, or diarrhea
- Also seek medical attention if you experience symptoms of adrenal insufficiency such as:
    - Nausea or vomiting
    - Loss of appetite
    - Fatigue
    - Weakness
    - Dizziness
    - Low blood pressure.
- Inform your health care professional if you experience signs or symptoms of decreased sex hormone levels such as low libido, impotence, erectile dysfunction, lack of menstruation, or infertility.

- Talk to your health care professional if you have any questions or concerns about opioids or other medicines you are taking.
- Read the patient information leaflet or Medication Guide that comes with your filled prescription(s).
- Report side effects from opioids or other medicines to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

Additional Information for Health Care Professionals

- FDA is warning about several safety issues with the class of opioid pain medicines. These include serotonin syndrome, adrenal insufficiency, and androgen deficiency.

Serotonin syndrome

- Serotonin syndrome can occur during concomitant use of opioids with serotonergic drugs. This may occur within the recommended dosage range.
- If concomitant use of an opioid with a serotonergic drug is warranted, carefully observe the patient, particularly during treatment initiation and dose increases.
- Symptoms of serotonin syndrome may include mental status changes such as agitation, hallucinations, or coma; autonomic instability such as tachycardia, labile blood pressure, or hyperthermia; and neurologic abnormalities such as hyperreflexia, incoordination, or rigidity.
- The onset of symptoms generally occurs within several hours to a few days of concomitant use but may occur later, particularly after dose increases.
- Discontinue opioid treatment and/or use of the concomitant serotonergic drug if serotonin syndrome is suspected.
- Counsel patients about the symptoms of serotonin syndrome and advise them to seek medical attention immediately if symptoms develop.
- Instruct patients to inform their health care professionals if they are taking or plan to take serotonergic drugs.

Adrenal insufficiency

- Cases of adrenal insufficiency have been reported with opioid use.
- Presentation of adrenal insufficiency may include nonspecific symptoms and signs, including nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure.
- If adrenal insufficiency is suspected, confirm with diagnostic testing as soon as possible. The patient should be treated with physiologic replacement doses of corticosteroids and weaned off of the opioid to allow adrenal function to recover.
- If the opioid can be discontinued, follow-up assessment of adrenal function should be performed to determine if treatment with corticosteroids can be discontinued.
- Other opioids may be tried as some cases reported use of a different opioid without recurrence of adrenal insufficiency.
- The information available does not identify any particular opioids as being more likely to be associated with adrenal insufficiency.

Androgen deficiency

- Chronic use of opioids may influence the hypothalamic-pituitary-gonadal axis, leading to androgen deficiency that may manifest as low libido, impotence, erectile dysfunction, amenorrhea, or infertility.
- The causal role of opioids in the clinical syndrome of hypogonadism is unknown because the various medical, physical, lifestyle, and psychological stressors that may influence gonadal hormone levels have not been adequately controlled in studies conducted to date.
- Patients presenting with symptoms or signs of androgen deficiency should undergo laboratory evaluation.

General information

- Encourage patients to read the information leaflets or Medication Guides that come with their filled prescription(s).
- Report adverse events involving opioids or other medicines to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

Data Summary

FDA investigated several safety issues associated with the class of opioid pain medicines:

- Serotonin syndrome
- Adrenal insufficiency
- Androgen deficiency

Serotonin syndrome

A search of the FDA Adverse Event Reporting System (FAERS) database for the period January 1, 1969, to June 12, 2013, identified 43 cases of serotonin syndrome in which opioids were used concomitantly with other serotonergic drugs. The review excluded meperidine, tramadol, and tapentadol, which were already labeled for the risk of serotonin syndrome at the time of the review. The most commonly reported opioids associated with serotonin syndrome were fentanyl (n=28), oxycodone (n=7), and methadone (n=5). Other reported opioids included hydromorphone, morphine, alfentanil/remifentanil/sufentanil, hydrocodone, naltrexone, and pentazocine. Although there were no reports of serotonin syndrome with an opioid used alone, five cases reported that serotonin syndrome occurred with the use of two or more opioids concurrently. All of these five cases reported use of fentanyl along with at least one other opioid [oxycodone (n=4), morphine (n=1), hydromorphone (n=1), and hydrocodone (n=1)].

Adrenal insufficiency

A search of FAERS for the period January 1, 1969, to February 5, 2014, identified 37 cases of adrenal insufficiency reported with the use of opioids. Twenty-seven cases reported opioid monotherapy, and 10 reported use of more than one opioid at the same time. The most commonly reported opioids associated with adrenal insufficiency were fentanyl (n=10) and oxycodone (n=10), followed by buprenorphine or

buprenorphine/naloxone (n=7), hydromorphone (n=6), and tramadol (n=4). When reported, the time to onset of adrenal insufficiency after the start of opioid therapy ranged from within 1 day to more than 1 year; however, many of the cases reported adrenal insufficiency after at least 1 month of use. Many of the patients were hospitalized. Of the 37 cases, 21 described that the patients received corticosteroid treatment. Sixteen cases reported discontinuing or reducing the dose of the opioid. Of the 16, nine of these patients improved, three had ongoing symptoms, and four did not report an outcome. Some patients experienced a relief in symptoms when they were switched from one opioid to another.

Androgen deficiency

We reviewed the medical literature to evaluate the association between opioids and androgen deficiency. [1-21] A range of studies in a variety of settings demonstrated decreased gonadal hormones in men and women taking long-term opioids. However, most of the studies were descriptive prevalence studies that did not include baseline values for the hormone levels, and there was a lack of comparability between the opioid-treated groups and control groups regarding medical, physical, lifestyle, and psychological factors that may influence gonadal hormone levels. Due to limitations of the studies, it is unclear whether the low gonadal hormone levels and associated symptoms and signs in men and women could be attributed to long-term opioid use or to other factors such as the patient's underlying medical condition warranting opioid treatment; physical, mental, or life stressors; weight changes; or concomitant medication or supplement use.

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Attachment 5

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CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CONTENTS

Disclosure of Relationship

The Core Expert Group (CEG) members disclose that they have no financial conflicts of interest. Experts disclose the following activities related to the content of this guideline: Pam Archer discloses authorship of the Oklahoma Emergency Department and Urgent Care Clinic Opioid Prescribing Guidelines and the Opioid Prescribing Guidelines for Oklahoma Health Care Providers in the Office Based Setting; Bonnie Burman discloses authorship of the Ohio Guidelines for Prescribing Opioids for the Treatment of Chronic, Non-Terminal Pain; Jane Ballantyne discloses that she has served as a paid consultant to Cohen Milstein Sellers & Toll, PLLC, and has special advisory committee responsibilities on the Food and Drug Administration (FDA) Risk Evaluation and Mitigation Strategies committee; Phillip Coffin discloses that in 2012 he provided expert testimony to the California State Assembly regarding a bill to expand naloxone access and reports that he is the principal investigator on a research study of methamphetamine dependence that receives donated injectable naltrexone from Alkermes, Inc.; Gary Franklin discloses authorship of the AMDG Interagency Guideline on Prescribing Opioids for Pain; Erin Krebs discloses that she represented the American College of Physicians at a 2014 Food and Drug Administration meeting on Abuse Deterrent Opioid Formulations; Lewis Nelson discloses his ad-hoc membership on the FDA Drug Safety and Risk Management Advisory Committee; Trupti Patel discloses authorship of the Arizona Opioid Prescribing Guidelines; Robert "Chuck" Rich discloses that he was an author of the 2013 American Academy of Family Physicians position paper on opioids and pain management; Joanna Starrels discloses that she received honoraria from the Betty Ford Institute; Thomas Tape discloses that he was an author of the 2013 American College of Physicians policy position paper on prescription drug abuse. CDC provided 100% of the funding for the supplemental evidence review tasks and meeting support. No foundation or industry support was accepted.

The Opioid Guideline Workgroup (OGW) members disclose that they have no financial conflicts of interest. Experts disclose the following activities related to the content of this guideline: Anne Burns discloses that she participated in a congressional briefing sponsored by Reps. Carter and DeSaulnier on the pharmacist's role of furnishing Naloxone and that she participates on the National Advisory Board for the Prescription Drug Abuse and Heroin Summit. Chinazo Cunningham discloses that her husband is employed by Quest Diagnostics and Dr. Cunningham was recused from any discussion related to urine drug testing. Traci Green discloses that she was previously employed by Inflexxion, a small business that conducts Small Business Innovation Research on behavioral interventions for behavioral health and chronic pain and created several psychometric tools for conducting risk assessment for prescription opioid abuse potential. Dr. Green also discloses that while at the hospital where she is employed, she provided consultation to Purdue Pharma Ltd to design overdose prevention brochures for persons who use diverted prescription opioids non-medically with an emphasis on persons who inject prescription drugs, and not for patients using opioid therapy for pain. Dr. Green was recused from any discussion related to risk assessment tools and patient education materials. Erin Krebs discloses that she served on the CDC Opioid Prescribing Guideline CEG. Christina Porucznik discloses that she served on the CDC Opioid Prescribing Guideline CEG. Greg Terman discloses that he serves as the President of the American Pain Society. Mark Wallace discloses that he served on a Kempharma advisory panel for an abuse-deterrent hydrocodone formulation to treat acute postoperative pain and Dr. Wallace was recused form any discussion related to abuse-deterrent drugs.

The NCIPC Board of Scientific Counselors (BSC) members disclose that they have no financial conflicts of interest. Two BSC members, Traci Green and Christina Porucznik, served on the Opioid Guideline Workgroup. Traci Green discloses that she was previously employed by Inflexxion, a small business that conducts Small Business Innovation Research on behavioral interventions for behavioral health and chronic pain and created several psychometric tools for conducting risk assessment for prescription opioid abuse potential. Dr. Green also discloses that while at the hospital where she is employed, she provided consultation to Purdue Pharma Ltd to design overdose prevention brochures for persons who use diverted prescription opioids non-medically with an emphasis on persons who inject prescription drugs, and not for patients using opioid therapy for pain. Dr. Green was recused from any discussion related to risk assessment tools and patient education materials. Christina Porucznik discloses that she served on the CDC Opioid Prescribing Guideline CEG.

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CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

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Summary

This guideline provides recommendations for primary care clinicians who are prescribing opioids for chronic pain outside of active cancer treatment, palliative care, and end-of-life care. The guideline addresses 1) when to initiate or continue opioids for chronic pain; 2) opioid selection, dosage, duration, follow-up, and discontinuation; and 3) assessing risk and addressing harms of opioid use. CDC developed the guideline using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework, and recommendations are made on the basis of a systematic review of the scientific evidence while considering benefits and harms, values and preferences, and resource allocation. CDC obtained input from experts, stakeholders, the public, peer reviewers, and a federally chartered advisory committee. It is important that patients receive appropriate pain treatment with careful consideration of the benefits and risks of treatment options. This guideline is intended to improve communication between clinicians and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death. CDC has provided a checklist for prescribing opioids for chronic pain (http://stacks.cdc.gov/view/cdc/38025) as well as a website (http://www.cdc.gov/drugoverdose/prescribingresources.html) with additional tools to guide clinicians in implementing the recommendations.

Introduction

Background

Opioids are commonly prescribed for pain. An estimated 20% of patients presenting to physician offices with noncancer pain symptoms or pain-related diagnoses (including acute and chronic pain) receive an opioid prescription (*1*). In 2012, health care providers wrote 259 million prescriptions for opioid pain medication, enough for every adult in the United States to have a bottle of pills (*2*). Opioid prescriptions per capita increased 7.3% from 2007 to 2012, with opioid prescribing rates increasing more for family practice, general practice, and internal medicine compared with other specialties (*3*). Rates of opioid prescribing vary greatly across states in ways that cannot be explained by the underlying health status of the population, highlighting the lack of consensus among clinicians on how to use opioid pain medication (*2*).

Prevention, assessment, and treatment of chronic pain are challenges for health providers and systems. Pain might go unrecognized, and patients, particularly members of racial and ethnic minority groups, women, the elderly, persons with cognitive impairment, and those with cancer and at the end of life, can be at risk for inadequate pain treatment (*4*). Patients can experience persistent pain that is not well controlled. There are clinical, psychological, and social consequences associated with chronic pain including limitations in complex activities, lost work productivity, reduced quality of life, and stigma, emphasizing the importance of appropriate and compassionate patient care (*4*). Patients should receive appropriate pain treatment based on a careful consideration of the benefits and risks of treatment options.

Chronic pain has been variably defined but is defined within this guideline as pain that typically lasts >3 months or past the time of normal tissue healing (*5*). Chronic pain can be the result of an underlying medical disease or condition, injury, medical treatment, inflammation, or an unknown cause (*4*). Estimates of the prevalence of chronic pain vary, but it is clear that the number of persons experiencing chronic pain in the United States is substantial. The 1999–2002 National Health and Nutrition Examination Survey estimated that 14.6% of adults have current widespread or localized pain lasting at least 3 months (*6*). Based on a survey conducted during 2001–2003 (*7*), the overall prevalence of common, predominantly musculoskeletal pain conditions (e.g., arthritis, rheumatism, chronic back or neck problems, and frequent severe headaches) was estimated at 43% among adults in the

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United States, although minimum duration of symptoms was not specified. Most recently, analysis of data from the 2012 National Health Interview Study showed that 11.2% of adults report having daily pain (*8*). Clinicians should consider the full range of therapeutic options for the treatment of chronic pain. However, it is hard to estimate the number of persons who could potentially benefit from opioid pain medication long term. Evidence supports short-term efficacy of opioids for reducing pain and improving function in noncancer nociceptive and neuropathic pain in randomized clinical trials lasting primarily ≤12 weeks (*9*,*10*), and patients receiving opioid therapy for chronic pain report some pain relief when surveyed (*11*–*13*). However, few studies have been conducted to rigorously assess the long-term benefits of opioids for chronic pain (pain lasting >3 months) with outcomes examined at least 1 year later (*14*). On the basis of data available from health systems, researchers estimate that 9.6–11.5 million adults, or approximately 3%–4% of the adult U.S. population, were prescribed long-term opioid therapy in 2005 (*15*).

Opioid pain medication use presents serious risks, including overdose and opioid use disorder. From 1999 to 2014, more than 165,000 persons died from overdose related to opioid pain medication in the United States (*16*). In the past decade, while the death rates for the top leading causes of death such as heart disease and cancer have decreased substantially, the death rate associated with opioid pain medication has increased markedly (*17*). Sales of opioid pain medication have increased in parallel with opioid-related overdose deaths (*18*). The Drug Abuse Warning Network estimated that >420,000 emergency department visits were related to the misuse or abuse of narcotic pain relievers in 2011, the most recent year for which data are available (*19*). Although clinical criteria have varied over time, opioid use disorder is a problematic pattern of opioid use leading to clinically significant impairment or distress. This disorder is manifested by specific criteria such as unsuccessful efforts to cut down or control use and use resulting in social problems and a failure to fulfill major role obligations at work, school, or home (*20*). This diagnosis has also been referred to as "abuse or dependence" and "addiction" in the literature, and is different from tolerance (diminished response to a drug with repeated use) and physical dependence (adaptation to a drug that produces symptoms of withdrawal when the drug is stopped), both of which can exist without a diagnosed disorder. In 2013, on the basis of DSM-IV diagnosis criteria, an estimated 1.9 million persons abused or were dependent on prescription opioid pain medication (*21*). Having a history of a prescription for an opioid pain medication increases the risk for overdose and opioid use disorder (*22*–*24*), highlighting the value of guidance on safer prescribing practices for clinicians. For example, a recent study of patients aged 15–64 years receiving opioids for chronic noncancer pain and followed for up to 13 years revealed that one in 550 patients died from opioid-related overdose at a median of 2.6 years from their first opioid prescription, and one in 32 patients who escalated to opioid dosages >200 morphine milligram equivalents (MME) died from opioid-related overdose (*25*).

This guideline provides recommendations for the prescribing of opioid pain medication by primary care clinicians for chronic pain (i.e., pain conditions that typically last >3 months or past the time of normal tissue healing) in outpatient settings outside of active cancer treatment, palliative care, and end-of-life care. Although the guideline does not focus broadly on pain management, appropriate use of long-term opioid therapy must be considered within the context of all pain management strategies (including nonopioid pain medications and nonpharmacologic treatments). CDC's recommendations are made on the basis of a systematic review of the best available evidence, along with input from experts, and further review and deliberation by a federally chartered advisory committee. The guideline is intended to ensure that clinicians and patients consider safer and more effective treatment, improve patient outcomes such as reduced pain and improved function, and reduce the number of persons who develop opioid use disorder, overdose, or experience other adverse events related to these drugs. Clinical decision making should be based on a relationship between the clinician and patient, and an understanding of the patient's clinical situation, functioning, and life context. The recommendations in the guideline are voluntary, rather than prescriptive standards. They are based on emerging evidence, including observational studies or randomized clinical trials with notable limitations. Clinicians should consider the circumstances and unique needs of each patient when providing care.

Rationale

Primary care clinicians report having concerns about opioid pain medication misuse, find managing patients with chronic pain stressful, express concern about patient addiction, and report insufficient training in prescribing opioids (*26*). Across specialties, physicians believe that opioid pain medication can be effective in controlling pain, that addiction is a common consequence of prolonged use, and that long-term opioid therapy often is overprescribed for patients with chronic noncancer pain (*27*). These attitudes and beliefs, combined with increasing trends in opioid-related overdose, underscore the need for better clinician guidance on opioid prescribing. Clinical practice guidelines focused on prescribing can improve clinician knowledge, change prescribing practices (*28*), and ultimately benefit patient health.

Professional organizations, states, and federal agencies (e.g., the American Pain Society/American Academy of Pain Medicine, 2009; the Washington Agency Medical Directors Group, 2015; and the U.S. Department of Veterans Affairs/Department of Defense, 2010) have developed guidelines for opioid prescribing (*29–31*). Existing guidelines share some common elements, including dosing thresholds, cautious titration, and risk mitigation strategies such as using risk assessment tools, treatment agreements, and urine drug testing. However, there is considerable variability in the specific recommendations (e.g., range of dosing thresholds of 90 MME/day to 200 MME/day), audience (e.g., primary care clinicians versus specialists), use of evidence (e.g., systematic review, grading of evidence and recommendations, and role of expert opinion), and rigor of methods for addressing conflict of interest (*32*). Most guidelines, especially those that are not based on evidence from scientific studies published in 2010 or later, also do not reflect the most recent scientific evidence about risks related to opioid dosage.

This CDC guideline offers clarity on recommendations based on the most recent scientific evidence, informed by expert opinion and stakeholder and public input. Scientific research has identified high-risk prescribing practices that have contributed to the overdose epidemic (e.g., high-dose prescribing, overlapping opioid and benzodiazepine prescriptions, and extended-release/long-acting [ER/LA] opioids for acute pain) (*24*,*33*,*34*). Using guidelines to address problematic prescribing has the potential to optimize care and improve patient safety based on evidence-based practice (*28*), as well as reverse the cycle of opioid pain medication misuse that contributes to the opioid overdose epidemic.

Scope and Audience

This guideline is intended for primary care clinicians (e.g., family physicians and internists) who are treating patients with chronic pain (i.e., pain lasting >3 months or past the time of normal tissue healing) in outpatient settings. Prescriptions by primary care clinicians account for nearly half of all dispensed opioid prescriptions, and the growth in prescribing rates among these clinicians has been above average (*3*). Primary care clinicians include physicians as well as nurse practitioners and physician assistants. Although the focus is on primary care clinicians, because clinicians work within team-based care, the recommendations refer to and promote integrated pain management and collaborative working relationships with other providers (e.g., behavioral health providers, pharmacists, and pain management specialists). Although the transition from use of opioid therapy for acute pain to use for chronic pain is hard to predict and identify, the guideline is intended to inform clinicians who are considering prescribing opioid pain medication for painful conditions that can or have become chronic.

This guideline is intended to apply to patients aged ≥18 years with chronic pain outside of palliative and end-of-life care. For this guideline, palliative care is defined in a manner consistent with that of the Institute of Medicine as care that provides relief from pain and other symptoms, supports quality of life, and is focused on patients with serious advanced illness. Palliative care can begin early in the course of treatment for any serious illness that requires excellent management of pain or other distressing symptoms (*35*). End-of-life care is defined as care for persons with a terminal illness or at high risk for dying in the near future in hospice care, hospitals, long-term care settings, or at home. Patients within the scope of this guideline include cancer survivors with chronic pain who have completed cancer treatment, are in clinical remission, and are under cancer surveillance only. The guideline is not intended for patients undergoing active cancer treatment, palliative care, or end-of-life care because of the unique therapeutic goals, ethical considerations, opportunities for medical supervision, and balance of risks and benefits with opioid therapy in such care.

The recommendations address the use of opioid pain medication in certain special populations (e.g., older adults and pregnant women) and in populations with conditions posing special risks (e.g., a history of substance use disorder). The recommendations do not address the use of opioid pain medication in children or adolescents aged <18 years. The available evidence concerning the benefits and harms of long-term opioid therapy in children and adolescents is limited, and few opioid medications provide information on the label regarding safety and effectiveness in pediatric patients. However, observational research shows significant increases in opioid prescriptions for pediatric populations from 2001 to 2010 (*36*), and a large proportion of adolescents are commonly prescribed opioid pain medications for conditions such as headache and sports injuries (e.g., in one study, 50% of adolescents presenting with headache received a prescription for an opioid pain medication [*37*,*38*]). Adolescents who misuse opioid pain medication often misuse medications from their own previous prescriptions (*39*), with an estimated 20% of adolescents with currently prescribed opioid medications reporting using them intentionally to get high or increase the effects of alcohol or other drugs (*40*). Use of prescribed opioid pain medication before high school graduation is associated with a 33% increase in the risk of later opioid misuse (*41*). Misuse of opioid pain medications in adolescence strongly predicts later onset of heroin use (*42*). Thus, risk of opioid medication use in pediatric populations is of great concern. Additional clinical trial and observational research is needed,

and encouraged, to inform development of future guidelines for this critical population.

The recommendations are not intended to provide guidance on use of opioids as part of medication-assisted treatment for opioid use disorder. Some of the recommendations might be relevant for acute care settings or other specialists, such as emergency physicians or dentists, but use in these settings or by other specialists is not the focus of this guideline. Readers are referred to other sources for prescribing recommendations within acute care settings and in dental practice, such as the American College of Emergency Physicians' guideline for prescribing of opioids in the emergency department (*43*); the American Society of Anesthesiologists' guideline for acute pain management in the perioperative setting (*44*); the Washington Agency Medical Directors' Group Interagency Guideline on Prescribing Opioids for Pain, Part II: Prescribing Opioids in the Acute and Subacute Phase (*30*); and the Pennsylvania Guidelines on the Use of Opioids in Dental Practice (*45*). In addition, given the challenges of managing the painful complications of sickle cell disease, readers are referred to the NIH National Heart, Lung, and Blood Institute's Evidence Based Management of Sickle Cell Disease Expert Panel Report for management of sickle cell disease (*46*).

Guideline Development Methods

Guideline Development Using the Grading of Recommendations Assessment, Development, and Evaluation Method

CDC developed this guideline using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method (http://www.gradeworkinggroup.org). This method specifies the systematic review of scientific evidence and offers a transparent approach to grading quality of evidence and strength of recommendations. The method has been adapted by the CDC Advisory Committee on Immunization Practices (ACIP) (*47*). CDC has applied the ACIP translation of the GRADE framework in this guideline. Within the ACIP GRADE framework, the body of evidence is categorized in a hierarchy. This hierarchy reflects degree of confidence in the effect of a clinical action on health outcomes. The categories include type 1 evidence (randomized clinical trials or overwhelming evidence from observational studies), type 2 evidence (randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies), type 3 evidence (observational studies or randomized clinical trials with notable limitations), and type 4 evidence (clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations). Type of evidence is categorized by study design as well as limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and a constellation of plausible biases that could change observations of effects. Type 1 evidence indicates that one can be very confident that the true effect lies close to that of the estimate of the effect; type 2 evidence means that the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; type 3 evidence means that confidence in the effect estimate is limited and the true effect might be substantially different from the estimate of the effect; and type 4 evidence indicates that one has very little confidence in the effect estimate, and the true effect is likely to be substantially different from the estimate of the effect (*47*,*48*). When no studies are present, evidence is considered to be insufficient. The ACIP GRADE framework places recommendations in two categories, Category A and Category B. Four major factors determine the category of the recommendation: the quality of evidence, the balance between desirable and undesirable effects, values and preferences, and resource allocation (cost). Category A recommendations apply to all persons in a specified group and indicate that most patients should receive the recommended course of action. Category B recommendations indicate that there should be individual decision making; different choices will be appropriate for different patients, so clinicians must help patients arrive at a decision consistent with patient values and preferences, and specific clinical situations (*47*). According to the GRADE methodology, a particular quality of evidence does not necessarily imply a particular strength of recommendation (*48*–*50*). Category A recommendations can be made based on type 3 or type 4 evidence when the advantages of a clinical action greatly outweigh the disadvantages based on a consideration of benefits and harms, values and preferences, and costs. Category B recommendations are made when the advantages and disadvantages of a clinical action are more balanced. GRADE methodology is discussed extensively elsewhere (*47*,*51*). The U.S. Preventive Services Task Force (USPSTF) follows different methods for developing and categorizing recommendations (http://www.uspreventiveservicestaskforce.org). USPSTF recommendations focus on preventive services and are categorized as A, B, C, D, and I. Under the Affordable Care Act, all "nongrandfathered" health plans (that is, those health plans not in existence prior to March 23, 2010 or those with significant changes to their coverage) and expanded Medicaid plans are required to cover

preventive services recommended by USPSTF with a category A or B rating with no cost sharing. The coverage requirements went into effect September 23, 2010. Similar requirements are in place for vaccinations recommended by ACIP, but do not exist for other recommendations made by CDC, including recommendations within this guideline.

A previously published systematic review sponsored by the Agency for Healthcare Research and Quality (AHRQ) on the effectiveness and risks of long-term opioid treatment of chronic pain (*14*,*52*) initially served to directly inform the recommendation statements. This systematic clinical evidence review addressed the effectiveness of long-term opioid therapy for outcomes related to pain, function, and quality of life; the comparative effectiveness of different methods for initiating and titrating opioids; the harms and adverse events associated with opioids; and the accuracy of risk-prediction instruments and effectiveness of risk mitigation strategies on outcomes related to overdose, addiction, abuse, or misuse. For the current guideline development, CDC conducted additional literature searches to update the evidence review to include more recently available publications and to answer an additional clinical question about the effect of opioid therapy for acute pain on long-term use. More details about the literature search strategies and GRADE methods applied are provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026). CDC developed GRADE evidence tables to illustrate the quality of the evidence for each clinical question.

As identified in the AHRQ-sponsored clinical evidence review, the overall evidence base for the effectiveness and risks of long-term opioid therapy is low in quality per the GRADE criteria. Thus, contextual evidence is needed to provide information about the benefits and harms of nonpharmacologic and nonopioid pharmacologic therapy and the epidemiology of opioid pain medication overdose and inform the recommendations. Further, as elucidated by the GRADE Working Group, supplemental information on clinician and patient values and preferences and resource allocation can inform judgments of benefits and harms and be helpful for translating the evidence into recommendations. CDC conducted a contextual evidence review to supplement the clinical evidence review based on systematic searches of the literature. The review focused on the following four areas: effectiveness of nonpharmacologic and nonopioid pharmacologic treatments; benefits and harms related to opioid therapy (including additional studies not included in the clinical evidence review such as studies that evaluated outcomes at any duration or used observational study designs related to specific opioid pain medications, high-dose opioid therapy, co-prescription of opioids with other controlled substances, duration of opioid use, special populations, risk stratification/mitigation approaches, and effectiveness of treatments for addressing potential harms of opioid therapy); clinician and patient values and preferences; and resource allocation. CDC constructed narrative summaries of this contextual evidence and used the information to support the clinical recommendations. More details on methods for the contextual evidence review are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027).

On the basis of a review of the clinical and contextual evidence (review methods are described in more detail in subsequent sections of this report), CDC drafted recommendation statements focused on determining when to initiate or continue opioids for chronic pain; opioid selection, dosage, duration, follow-up, and discontinuation; and assessing risk and addressing harms of opioid use. To help assure the draft guideline's integrity and credibility, CDC then began a multistep review process to obtain input from experts, stakeholders, and the public to help refine the recommendations.

Solicitation of Expert Opinion

CDC sought the input of experts to assist in reviewing the evidence and providing perspective on how CDC used the evidence to develop the draft recommendations. These experts, referred to as the "Core Expert Group" (CEG) included subject matter experts, representatives of primary care professional societies and state agencies, and an expert in guideline development methodology.* CDC identified subject matter experts with high scientific standing; appropriate academic and clinical training and relevant clinical experience; and proven scientific excellence in opioid prescribing, substance use disorder treatment, and pain management. CDC identified representatives from leading primary care professional organizations to represent the audience for this guideline. Finally, CDC identified state agency officials and representatives based on their experience with state guidelines for opioid prescribing that were developed with multiple agency stakeholders and informed by scientific literature and existing evidence-based guidelines.

Prior to their participation, CDC asked potential experts to reveal possible conflicts of interest such as financial relationships with industry, intellectual preconceptions, or previously stated public positions. Experts could not serve if they had conflicts that might have a direct and predictable effect on the recommendations. CDC excluded experts who had a financial or promotional relationship with a company

* A list of the members appears at the end of this report. The recommendations and all statements included in this guideline are those of CDC and do not necessarily represent the official position of any persons or organizations providing comments on the draft guideline.

that makes a product that might be affected by the guideline. CDC reviewed potential nonfinancial conflicts carefully (e.g., intellectual property, travel, public statements or positions such as congressional testimony) to determine if the activities would have a direct and predictable effect on the recommendations. CDC determined the risk of these types of activities to be minimal for the identified experts. All experts completed a statement certifying that there was no potential or actual conflict of interest. Activities that did not pose a conflict (e.g., participation in Food and Drug Administration [FDA] activities or other guideline efforts) are disclosed.

CDC provided to each expert written summaries of the scientific evidence (both the clinical and contextual evidence reviews conducted for this guideline) and CDC's draft recommendation statements. Experts provided individual ratings for each draft recommendation statement based on the balance of benefits and harms, evidence strength, certainty of values and preferences, cost, recommendation strength, rationale, importance, clarity, and ease of implementation. CDC hosted an in-person meeting of the experts that was held on June 23–24, 2015, in Atlanta, Georgia, to seek their views on the evidence and draft recommendations and to better understand their premeeting ratings. CDC sought the experts' individual opinions at the meeting. Although there was widespread agreement on some of the recommendations, there was disagreement on others. Experts did not vote on the recommendations or seek to come to a consensus. Decisions about recommendations to be included in the guideline, and their rationale, were made by CDC. After revising the guideline, CDC sent written copies of it to each of the experts for review and asked for any additional comments; CDC reviewed these written comments and considered them when making further revisions to the draft guideline. The experts have not reviewed the final version of the guideline.

Federal Partner Engagement

Given the scope of this guideline and the interest of agencies across the federal government in appropriate pain management, opioid prescribing, and related outcomes, CDC invited its National Institute of Occupational Safety and Health and CDC's federal partners to observe the expert meeting, provide written comments on the full draft guideline after the meeting, and review the guideline through an agency clearance process; CDC reviewed comments and incorporated changes. Interagency collaboration will be critical for translating these recommendations into clinical practice. Federal partners included representatives from the Substance Abuse and Mental Health Services Administration, the National Institute on Drug Abuse, FDA, the U.S. Department of Veterans Affairs, the U.S. Department of Defense, the Office of the National Coordinator for Health Information Technology, the Centers for Medicare and Medicaid Services, the Health Resources and Services Administration, AHRQ, and the Office of National Drug Control Policy.

Stakeholder Comment

Given the importance of the guideline for a wide variety of stakeholders, CDC also invited review from a Stakeholder Review Group (SRG) to provide comment so that CDC could consider modifications that would improve the recommendations' specificity, applicability, and ease of implementation. The SRG included representatives from professional organizations that represent specialties that commonly prescribe opioids (e.g., pain medicine, physical medicine and rehabilitation), delivery systems within which opioid prescribing occurs (e.g., hospitals), and representation from community organizations with interests in pain management and opioid prescribing.* Representatives from each of the SRG organizations were provided a copy of the guideline for comment. Each of these representatives provided written comments. Once input was received from the full SRG, CDC reviewed all comments and carefully considered them when revising the draft guideline.

Constituent Engagement

To obtain initial perspectives from constituents on the recommendation statements, including clinicians and prospective patients, CDC convened a constituent engagement webinar and circulated information about the webinar in advance through announcements to partners. CDC hosted the webinar on September 16 and 17, 2015, provided information about the methodology for developing the guideline, and presented the key recommendations. A fact sheet was posted on the CDC Injury Center website (http://www.cdc.gov/injury) summarizing the guideline development process and clinical practice areas addressed in the guideline; instructions were included on how to submit comments via email. CDC received comments during and for 2 days following the first webinar. Over 1,200 constituent comments were received. Comments were reviewed and carefully considered when revising the draft guideline.

Peer Review

Per the final information quality bulletin for peer review (https://www.whitehouse.gov/sites/default/files/omb/memoranda/fy2005/m05-03.pdf), peer review requirements applied to this guideline because it provides influential

scientific information that could have a clear and substantial impact on public- and private-sector decisions. Three experts independently reviewed the guideline to determine the reasonableness and strength of recommendations; the clarity with which scientific uncertainties were clearly identified; and the rationale, importance, clarity, and ease of implementation of the recommendations.* CDC selected peer reviewers based on expertise, diversity of scientific viewpoints, and independence from the guideline development process. CDC assessed and managed potential conflicts of interest using a process similar to the one as described for solicitation of expert opinion. No financial interests were identified in the disclosure and review process, and nonfinancial activities were determined to be of minimal risk; thus, no significant conflict of interest concerns were identified. CDC placed the names of peer reviewers on the CDC and the National Center for Injury Prevention and Control Peer Review Agenda websites that are used to provide information about the peer review of influential documents. CDC reviewed peer review comments and revised the draft guideline accordingly.

Public Comment

To obtain comments from the public on the full guideline, CDC published a notice in the *Federal Register* (80 FR 77351) announcing the availability of the guideline and the supporting clinical and contextual evidence reviews for public comment. The comment period closed January 13, 2016. CDC received more than 4,350 comments from the general public, including patients with chronic pain, clinicians, families who have lost loved ones to overdose, medical associations, professional organizations, academic institutions, state and local governments, and industry. CDC reviewed each of the comments and carefully considered them when revising the draft guideline.

Federal Advisory Committee Review and Recommendation

The National Center for Injury Prevention and Control (NCIPC) Board of Scientific Counselors (BSC) is a federal advisory committee that advises and makes recommendations to the Secretary of the Department of Health and Human Services, the Director of CDC, and the Director of NCIPC.* The BSC makes recommendations regarding policies, strategies, objectives, and priorities, and reviews progress toward injury and violence prevention. CDC sought the BSC's advice on the draft guideline. BSC members are special government employees appointed as CDC advisory committee members; as such, all members completed an OGE Form 450 to disclose relevant interests. BSC members also reported on their disclosures during meetings. Disclosures for the BSC are reported in the guideline.

To assist in guideline review, on December 14, 2015, via Federal Register notice, CDC announced the intent to form an Opioid Guideline Workgroup (OGW) to provide observations on the draft guideline to the BSC. CDC provided the BSC with the draft guideline as well as summaries of comments provided to CDC by stakeholders, constituents, and peer reviewers, and edits made to the draft guideline in response. During an open meeting held on January 7, 2016, the BSC recommended the formation of the OGW. The OGW included a balance of perspectives from audiences directly affected by the guideline, audiences that would be directly involved with implementing the recommendations, and audiences qualified to provide representation. The OGW comprised clinicians, subject matter experts, and a patient representative, with the following perspectives represented: primary care, pain medicine, public health, behavioral health, substance abuse treatment, pharmacy, patients, and research.* Additional sought-after attributes were appropriate academic and clinical training and relevant clinical experience; high scientific standing; and knowledge of the patient, clinician, and caregiver perspectives. In accordance with CDC policy, two BSC committee members also served as OGW members, with one serving as the OGW Chair. The professional credentials and interests of OGW members were carefully reviewed to identify possible conflicts of interest such as financial relationships with industry, intellectual preconceptions, or previously stated public positions. Only OGW members whose interests were determined to be minimal were selected. When an activity was perceived as having the potential to affect a specific aspect of the recommendations, the activity was disclosed, and the OGW member was recused from discussions related to that specific aspect of the recommendations (e.g., urine drug testing and abuse-deterrent formulations). Disclosures for the OGW are reported. CDC and the OGW identified ad-hoc consultants to supplement the workgroup expertise, when needed, in the areas of pediatrics, occupational medicine, obstetrics and gynecology, medical ethics, addiction psychiatry, physical medicine and rehabilitation, guideline development methodology, and the perspective of a family member who lost a loved one to opioid use disorder or overdose.

The BSC charged the OGW with reviewing the quality of the clinical and contextual evidence reviews and reviewing each of the recommendation statements and accompanying rationales. For each recommendation statement, the OGW considered the quality of the evidence, the balance of benefits and risks, the values and preferences of clinicians and patients, the cost feasibility, and the category designation

of the recommendation (A or B). The OGW also reviewed supplementary documents, including input provided by the CEG, SRG, peer reviewers, and the public. OGW members discussed the guideline accordingly during virtual meetings and drafted a summary report of members' observations, including points of agreement and disagreement, and delivered the report to the BSC.

NCIPC announced an open meeting of the NCIPC BSC in the Federal Register on January 11, 2015. The BSC met on January 28, 2016, to discuss the OGW report and deliberate on the draft guideline itself. Members of the public provided comments at this meeting. After discussing the OGW report, deliberating on specific issues about the draft guideline identified at the meeting, and hearing public comment, the BSC voted unanimously: to support the observations made by the OGW; that CDC adopt the guideline recommendations that, according to the workgroup's report, had unanimous or majority support; and that CDC further consider the guideline recommendations for which the group had mixed opinions. CDC carefully considered the OGW observations, public comments, and BSC recommendations, and revised the guideline in response.

Summary of the Clinical Evidence Review

Primary Clinical Questions

CDC conducted a clinical systematic review of the scientific evidence to identify the effectiveness, benefits, and harms of long-term opioid therapy for chronic pain, consistent with the GRADE approach (*47*,*48*). Long-term opioid therapy is defined as use of opioids on most days for >3 months. A previously published AHRQ-funded systematic review on the effectiveness and risks of long-term opioid therapy for chronic pain comprehensively addressed four clinical questions (*14*,*52*). CDC, with the assistance of a methodology expert, searched the literature to identify newly published studies on these four original questions. Because long-term opioid use might be affected by use of opioids for acute pain, CDC subsequently developed a fifth clinical question (last in the series below), and in collaboration with a methodologist conducted a systematic review of the scientific evidence to address it. In brief, five clinical questions were addressed:

- The effectiveness of long-term opioid therapy versus placebo, no opioid therapy, or nonopioid therapy for long term (≥1 year) outcomes related to pain, function, and quality of life, and how effectiveness varies according to the type/cause of pain, patient demographics, and patient comorbidities (Key Question [KQ] 1).
- The risks of opioids versus placebo or no opioids on abuse, addiction, overdose, and other harms, and how harms vary according to the type/cause of pain, patient demographics, patient comorbidities, and dose (KQ2).
- The comparative effectiveness of opioid dosing strategies (different methods for initiating and titrating opioids; immediate-release versus ER/LA opioids; different ER/LA opioids; immediate-release plus ER/LA opioids versus ER/LA opioids alone; scheduled, continuous versus as-needed dosing; dose escalation versus dose maintenance; opioid rotation versus maintenance; different strategies for treating acute exacerbations of chronic pain; decreasing opioid doses or tapering off versus continuation; and different tapering protocols and strategies) (KQ3).
- The accuracy of instruments for predicting risk for opioid overdose, addiction, abuse, or misuse; the effectiveness of risk mitigation strategies (use of risk prediction instruments); effectiveness of risk mitigation strategies including opioid management plans, patient education, urine drug testing, prescription drug monitoring program (PDMP) data, monitoring instruments, monitoring intervals, pill counts, and abuse-deterrent formulations for reducing risk for opioid overdose, addiction, abuse, or misuse; and the comparative effectiveness of treatment strategies for managing patients with addiction (KQ4).
- The effects of prescribing opioid therapy versus not prescribing opioid therapy for acute pain on long-term use (KQ5).

The review was focused on the effectiveness of long-term opioid therapy on long-term (>1 year) outcomes related to pain, function, and quality of life to ensure that findings are relevant to patients with chronic pain and long-term opioid prescribing. The effectiveness of short-term opioid therapy has already been established (*10*). However, opioids have unique effects such as tolerance and physical dependence that might influence assessments of benefit over time. These effects raise questions about whether findings on short-term effectiveness of opioid therapy can be extrapolated to estimate benefits of long-term therapy for chronic pain. Thus, it is important to consider studies that provide data on long-term benefit. For certain opioid-related harms (overdose, fractures, falls, motor vehicle crashes), observational studies were included with outcomes measured at shorter intervals because such outcomes can occur early during opioid therapy, and such harms are not captured well in short-term clinical trials. A detailed listing of the key questions is provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026).

Clinical Evidence Systematic Review Methods

Complete methods and data for the 2014 AHRQ report, upon which this updated systematic review is based, have been published previously (*14*,*52*). Study authors developed the protocol using a standardized process (*53*) with input from experts and the public and registered the protocol in the PROSPERO database (*54*). For the 2014 AHRQ report, a research librarian searched MEDLINE, the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, PsycINFO, and CINAHL for English-language articles published January 2008 through August 2014, using search terms for opioid therapy, specific opioids, chronic pain, and comparative study designs. Also included were relevant studies from an earlier review (*10*) in which searches were conducted without a date restriction, reference lists were reviewed, and ClinicalTrials.gov was searched. CDC updated the AHRQ literature search using the same search strategies as in the original review including studies published before April, 2015. Seven additional studies met inclusion criteria and were added to the review. CDC used the GRADE approach outlined in the ACIP Handbook for Developing Evidence-Based Recommendations (*47*) to rate the quality of evidence for the full body of evidence (evidence from the 2014 AHRQ review plus the update) for each clinical question. Evidence was categorized into the following types: type 1 (randomized clinical trials or overwhelming evidence from observational studies), type 2 (randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies), type 3 (observational studies, or randomized clinical trials with notable limitations), or type 4 (clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations). When no studies were present, evidence was considered to be insufficient. Per GRADE methods, type of evidence was categorized by study design as well as a function of limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and constellation of plausible biases that could change effects. Results were synthesized qualitatively, highlighting new evidence identified during the update process. Meta-analysis was not attempted due to the small numbers of studies, variability in study designs and clinical heterogeneity, and methodological shortcomings of the studies. More detailed information about data sources and searches, study selection, data extraction and quality assessment, data synthesis, and update search yield and new evidence for the current review is provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026).

Summary of Findings for Clinical Questions

The main findings of this updated review are consistent with the findings of the 2014 AHRQ report (*14*). In summary, evidence on long-term opioid therapy for chronic pain outside of end-of-life care remains limited, with insufficient evidence to determine long-term benefits versus no opioid therapy, though evidence suggests risk for serious harms that appears to be dose-dependent. These findings supplement findings from a previous review of the effectiveness of opioids for adults with chronic noncancer pain. In this previous review, based on randomized trials predominantly ≤12 weeks in duration, opioids were found to be moderately effective for pain relief, with small benefits for functional outcomes; although estimates vary, based on uncontrolled studies, a high percentage of patients discontinued long-term opioid use because of lack of efficacy and because of adverse events (*10*).

The GRADE evidence summary with type of evidence ratings for the five clinical questions for the current evidence review are outlined (Table 1). This summary is based on studies included in the AHRQ 2014 review (35 studies) plus additional studies identified in the updated search (seven studies). Additional details on findings from the original review are provided in the full 2014 AHRQ report (*14*,*52*). Full details on the clinical evidence review findings supporting this guideline are provided in the Clinical Evidence Review (http://stacks.cdc.gov/view/cdc/38026).

Effectiveness

For KQ1, no study of opioid therapy versus placebo, no opioid therapy, or nonopioid therapy for chronic pain evaluated long-term (≥1 year) outcomes related to pain, function, or quality of life. Most placebo-controlled randomized clinical trials were ≤6 weeks in duration. Thus, the body of evidence for KQ1 is rated as insufficient (0 studies contributing) (*14*).

Harms

For KQ2, the body of evidence is rated as type 3 (12 studies contributing; 11 from the original review plus one new study). One fair-quality cohort study found that long-term opioid therapy is associated with increased risk for an opioid abuse or dependence diagnosis (as defined by ICD-9-CM codes) versus no opioid prescription (*22*). Rates of opioid abuse or dependence diagnosis ranged from 0.7% with lower-dose (≤36 MME) chronic therapy to 6.1% with higher-dose (≥120 MME) chronic therapy, versus 0.004% with no opioids prescribed. Ten fair-quality uncontrolled studies reported estimates of opioid abuse, addiction, and related outcomes (*55*–*65*). In primary care settings, prevalence of opioid dependence

(using DSM-IV criteria) ranged from 3% to 26% (*55*,*56*,*59*). In pain clinic settings, prevalence of addiction ranged from 2% to 14% (*57*,*58*,*60*,*61*,*63–65*).

Factors associated with increased risk for misuse included history of substance use disorder, younger age, major depression, and use of psychotropic medications (*55*,*62*). Two studies reported on the association between opioid use and risk for overdose (*66*,*67*). One large fair-quality retrospective cohort study found that recent opioid use was associated with increased risk for any overdose events and serious overdose events versus nonuse (*66*). It also found higher doses associated with increased risk. Relative to 1–19 MME/day, the adjusted hazard ratio (HR) for any overdose event (consisting of mostly nonfatal overdose) was 1.44 for 20 to 49 MME/day, 3.73 for 50–99 MME/day, and 8.87 for ≥100 MME/day. A similar pattern was observed for serious overdose. A good-quality population-based, nested case-control study also found a dose-dependent association with risk for overdose death (*67*). Relative to 1–19 MME/day, the adjusted odds ratio (OR) was 1.32 for 20–49 MME/day, 1.92 for 50–99 MME/day, 2.04 for 100–199 MME/day, and 2.88 for ≥200 MME/day.

Findings of increased fracture risk for current opioid use, versus nonuse, were mixed in two studies (*68*,*69*). Two studies found an association between opioid use and increased risk for cardiovascular events (*70*,*71*). Indirect evidence was found for endocrinologic harms (increased use of medications for erectile dysfunction or testosterone from one previously included study; laboratory-defined androgen deficiency from one newly reviewed study) (*72*,*73*). One study found that opioid dosages ≥20 MME/day were associated with increased odds of road trauma among drivers (*74*).

Opioid Dosing Strategies

For KQ3, the body of evidence is rated as type 4 (14 studies contributing; 12 from the original review plus two new studies). For initiation and titration of opioids, the 2014 AHRQ report found insufficient evidence from three fair-quality, open-label trials to determine comparative effectiveness of ER/LA versus immediate-release opioids for titrating patients to stable pain control (*75*,*76*). One new fair-quality cohort study of Veterans Affairs patients found initiation of therapy with an ER/LA opioid associated with greater risk for nonfatal overdose than initiation with an immediate-release opioid, with risk greatest in the first 2 weeks after initiation of treatment (*77*).

For comparative effectiveness and harms of ER/LA opioids, the 2014 AHRQ report included three randomized, head-to-head trials of various ER/LA opioids that found no clear differences in 1-year outcomes related to pain or function (*78–80*) but had methodological shortcomings. A fair-quality retrospective cohort study based on national Veterans Health Administration system pharmacy data found that methadone was associated with lower overall risk for all-cause mortality versus morphine (*81*), and a fair-quality retrospective cohort study based on Oregon Medicaid data found no statistically significant differences between methadone and long-acting morphine in risk for death or overdose symptoms (*82*). However, a new observational study (*83*) found methadone associated with increased risk for overdose versus sustained-release morphine among Tennessee Medicaid patients. The observed inconsistency in study findings suggests that risks of methadone might vary in different settings as a function of different monitoring and management protocols, though more research is needed to understand factors associated with safer methadone prescribing.

For dose escalation, the 2014 AHRQ report included one fair-quality randomized trial that found no differences between more liberal dose escalation and maintenance of current doses after 12 months in pain, function, all-cause withdrawals, or withdrawals due to opioid misuse (*84*). However, the difference in opioid dosages prescribed at the end of the trial was relatively small (mean 52 MME/day with more liberal dosing versus 40 MME/day). Evidence on other comparisons related to opioid dosing strategies (ER/LA versus immediate-release opioids; immediate-release plus ER/LA opioids versus ER/LA opioids alone; scheduled continuous dosing versus as-needed dosing; or opioid rotation versus maintenance of current therapy; long-term effects of strategies for treating acute exacerbations of chronic pain) was not available or too limited to determine effects on long-term clinical outcomes. For example, evidence on the comparative effectiveness of opioid tapering or discontinuation versus maintenance, and of different opioid tapering strategies, was limited to small, poor-quality studies (*85–87*).

Risk Assessment and Mitigation

For KQ4, the body of evidence is rated as type 3 for the accuracy of risk assessment tools and insufficient for the effectiveness of use of risk assessment tools and mitigation strategies in reducing harms (six studies contributing; four from the original review plus two new studies). The 2014 AHRQ report included four studies (*88–91*) on the accuracy of risk assessment instruments, administered prior to opioid therapy initiation, for predicting opioid abuse or misuse. Results for the Opioid Risk Tool (ORT) (*89–91*) were extremely inconsistent; evidence for other risk assessment instruments was very sparse, and studies had serious methodological shortcomings. One additional fair-quality (*92*) and one poor-quality (*93*) study identified for this update compared the predictive accuracy of the ORT, the Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R), and the Brief Risk Interview.

For the ORT, sensitivity was 0.58 and 0.75 and specificity 0.54 and 0.86; for the SOAPP-R, sensitivity was 0.53 and 0.25 and specificity 0.62 and 0.73; and for the Brief Risk Interview, sensitivity was 0.73 and 0.83 and specificity 0.43 and 0.88. For the ORT, positive likelihood ratios ranged from noninformative (positive likelihood ratio close to 1) to moderately useful (positive likelihood ratio >5). The SOAPP-R was associated with noninformative likelihood ratios (estimates close to 1) in both studies.

No study evaluated the effectiveness of risk mitigation strategies (use of risk assessment instruments, opioid management plans, patient education, urine drug testing, use of PDMP data, use of monitoring instruments, more frequent monitoring intervals, pill counts, or use of abuse-deterrent formulations) for improving outcomes related to overdose, addiction, abuse, or misuse.

Effects of Opioid Therapy for Acute Pain on Long-Term Use

For KQ5, the body of evidence is rated as type 3 (two new studies contributing). Two fair-quality retrospective cohort studies found opioid therapy prescribed for acute pain associated with greater likelihood of long-term use. One study evaluated opioid-naïve patients who had undergone low-risk surgery, such as cataract surgery and varicose vein stripping (*94*). Use of opioids within 7 days of surgery was associated with increased risk for use at 1 year. The other study found that among patients with a workers' compensation claim for acute low back pain, compared to patients who did not receive opioids early after injury (defined as use within 15 days following onset of pain), patients who did receive early opioids had an increased likelihood of receiving five or more opioid prescriptions 30–730 days following onset that increased with greater early exposure. Versus no early opioid use, the adjusted OR was 2.08 (95% CI = 1.55–2.78) for 1–140 MME/day and increased to 6.14 (95% confidence interval [CI] = 4.92–7.66) for ≥450 MME/day (*95*).

Summary of the Contextual Evidence Review

Primary Areas of Focus

Contextual evidence is complementary information that assists in translating the clinical research findings into recommendations. CDC conducted contextual evidence reviews on four topics to supplement the clinical evidence review findings:

- Effectiveness of nonpharmacologic (e.g., cognitive behavioral therapy [CBT], exercise therapy, interventional treatments, and multimodal pain treatment) and nonopioid pharmacologic treatments (e.g., acetaminophen, nonsteroidal anti-inflammatory drugs [NSAIDs], antidepressants, and anticonvulsants), including studies of any duration.
- Benefits and harms of opioid therapy (including additional studies not included in the clinical evidence review, such as studies that were not restricted to patients with chronic pain, evaluated outcomes at any duration, performed ecological analyses, or used observational study designs other than cohort and case-cohort control studies) related to specific opioids, high-dose therapy, co-prescription with other controlled substances, duration of use, special populations, and potential usefulness of risk stratification/mitigation approaches, in addition to effectiveness of treatments associated with addressing potential harms of opioid therapy (opioid use disorder).
- Clinician and patient values and preferences related to opioids and medication risks, benefits, and use.
- Resource allocation including costs and economic efficiency of opioid therapy and risk mitigation strategies.

CDC also reviewed clinical guidelines that were relevant to opioid prescribing and could inform or complement the CDC recommendations under development (e.g., guidelines on nonpharmacologic and nonopioid pharmacologic treatments and guidelines with recommendations related to specific clinician actions such as urine drug testing or opioid tapering protocols).

Contextual Evidence Review Methods

CDC conducted a contextual evidence review to assist in developing the recommendations by providing an assessment of the balance of benefits and harms, values and preferences, and cost, consistent with the GRADE approach. Given the public health urgency for developing opioid prescribing recommendations, a rapid review was required for the contextual evidence review for the current guideline. Rapid reviews are used when there is a need to streamline the systematic review process to obtain evidence quickly (*96*). Methods used to streamline the process include limiting searches by databases, years, and languages considered, and truncating quality assessment and data abstraction protocols. CDC conducted "rapid reviews" of the contextual evidence on nonpharmacologic and nonopioid pharmacologic treatments, benefits and harms, values and preferences, and resource allocation.

Detailed information about contextual evidence data sources and searches, inclusion criteria, study selection, and

data extraction and synthesis are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027). In brief, CDC conducted systematic literature searches to identify original studies, systematic reviews, and clinical guidelines, depending on the topic being searched. CDC also solicited publication referrals from subject matter experts. Given the need for a rapid review process, grey literature (e.g., literature by academia, organizations, or government in the forms of reports, documents, or proceedings not published by commercial publishers) was not systematically searched. Database sources, including MEDLINE, PsycINFO, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews, varied by topic. Multiple reviewers scanned study abstracts identified through the database searches and extracted relevant studies for review. CDC constructed narrative summaries and tables based on relevant articles that met inclusion criteria, which are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027).

Findings from the contextual reviews provide indirect evidence and should be interpreted accordingly. CDC did not formally rate the quality of evidence for the studies included in the contextual evidence review using the GRADE method. The studies that addressed benefits and harms, values and preferences, and resource allocation most often employed observational methods, used short follow-up periods, and evaluated selected samples. Therefore the strength of the evidence from these contextual review areas was considered to be low, comparable to type 3 or type 4 evidence. The quality of evidence for nonopioid pharmacologic and nonpharmacologic pain treatments was generally rated as moderate, comparable to type 2 evidence, in systematic reviews and clinical guidelines (e.g., for treatment of chronic neuropathic pain, low back pain, osteoarthritis, and fibromyalgia). Similarly, the quality of evidence on pharmacologic and psychosocial opioid use disorder treatment was generally rated as moderate, comparable to type 2 evidence, in systematic reviews and clinical guidelines.

Summary of Findings for Contextual Areas

Full narrative reviews and tables that summarize key findings from the contextual evidence review are provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027).

Effectiveness of Nonpharmacologic and Nonopioid Pharmacologic Treatments

Several nonpharmacologic and nonopioid pharmacologic treatments have been shown to be effective in managing chronic pain in studies ranging in duration from 2 weeks to 6 months. For example, CBT that trains patients in behavioral techniques and helps patients modify situational factors and cognitive processes that exacerbate pain has small positive effects on disability and catastrophic thinking (*97*). Exercise therapy can help reduce pain and improve function in chronic low back pain (*98*), improve function and reduce pain in osteoarthritis of the knee (*99*) and hip (*100*), and improve well-being, fibromyalgia symptoms, and physical function in fibromyalgia (*101*). Multimodal and multidisciplinary therapies (e.g., therapies that combine exercise and related therapies with psychologically based approaches) can help reduce pain and improve function more effectively than single modalities (*102*,*103*). Nonopioid pharmacologic approaches used for pain include analgesics such as acetaminophen, NSAIDs, and cyclooxygenase 2 (COX-2) inhibitors; selected anticonvulsants; and selected antidepressants (particularly tricyclics and serotonin and norepinephrine reuptake inhibitors [SNRIs]). Multiple guidelines recommend acetaminophen as first-line pharmacotherapy for osteoarthritis (*104*–*109*) or for low back pain (*110*) but note that it should be avoided in liver failure and that dosage should be reduced in patients with hepatic insufficiency or a history of alcohol abuse (*109*). Although guidelines also recommend NSAIDs as first-line treatment for osteoarthritis or low back pain (*106*,*110*), NSAIDs and COX-2 inhibitors do have risks, including gastrointestinal bleeding or perforation as well as renal and cardiovascular risks (*111*). FDA has recently strengthened existing label warnings that NSAIDs increase risks for heart attack and stroke, including that these risks might increase with longer use or at higher doses (*112*). Several guidelines agree that first- and second-line drugs for neuropathic pain include anticonvulsants (gabapentin or pregabalin), tricyclic antidepressants, and SNRIs (*113*–*116*). Interventional approaches such as epidural injection for certain conditions (e.g., lumbar radiculopathy) can provide short-term improvement in pain (*117*–*119*). Epidural injection has been associated with rare but serious adverse events, including loss of vision, stroke, paralysis, and death (*120*).

Benefits and Harms of Opioid Therapy

Balance between benefits and harms is a critical factor influencing the strength of clinical recommendations. In particular, CDC considered what is known from the epidemiology research about benefits and harms related to specific opioids and formulations, high dose therapy, co-prescription with other controlled substances, duration of use, special populations, and risk stratification and mitigation approaches. Additional information on benefits and harms of long-term opioid therapy from studies meeting rigorous selection criteria is provided in the clinical evidence review (e.g., see KQ2). CDC also considered the number of persons experiencing chronic pain, numbers potentially benefiting

from opioids, and numbers affected by opioid-related harms. A review of these data is presented in the background section of this document, with detailed information provided in the Contextual Evidence Review (http://stacks.cdc.gov/view/cdc/38027). Finally, CDC considered the effectiveness of treatments that addressed potential harms of opioid therapy (opioid use disorder).

Regarding specific opioids and formulations, as noted by FDA, there are serious risks of ER/LA opioids, and the indication for this class of medications is for management of pain severe enough to require daily, around-the-clock, long-term opioid treatment in patients for whom other treatment options (e.g., nonopioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain (*121*). Time-scheduled opioid use was associated with substantially higher average daily opioid dosage than as-needed opioid use in one study (*122*). Methadone has been associated with disproportionate numbers of overdose deaths relative to the frequency with which it is prescribed for pain. Methadone has been found to account for as much as a third of opioid-related overdose deaths involving single or multiple drugs in states that participated in the Drug Abuse Warning Network, which was more than any opioid other than oxycodone, despite representing <2% of opioid prescriptions outside of opioid treatment programs in the United States; further, methadone was involved in twice as many single-drug deaths as any other prescription opioid (*123*).

Regarding high-dose therapy, several epidemiologic studies that were excluded from the clinical evidence review because patient samples were not restricted to patients with chronic pain also examined the association between opioid dosage and overdose risk (*23*,*24*,*124*–*126*). Consistent with the clinical evidence review, the contextual review found that opioid-related overdose risk is dose-dependent, with higher opioid dosages associated with increased overdose risk. Two of these studies (*23*,*24*), as well as the two studies in the clinical evidence review (*66*,*67*), evaluated similar MME/day dose ranges for association with overdose risk. In these four studies, compared with opioids prescribed at <20 MME/day, the odds of overdose among patients prescribed opioids for chronic nonmalignant pain were between 1.3 (*67*) and 1.9 (*24*) for dosages of 20 to <50 MME/day, between 1.9 (*67*) and 4.6 (*24*) for dosages of 50 to <100 MME/day, and between 2.0 (*67*) and 8.9 (*66*) for dosages of ≥100 MME/day. Compared with dosages of 1–<20 MME/day, absolute risk difference approximation for 50–<100 MME/day was 0.15% for fatal overdose (*24*) and 1.40% for any overdose (*66*), and for ≥100 MME/day was 0.25% for fatal overdose (*24*) and 4.04% for any overdose (*66*). A recent study of Veterans Health Administration patients with chronic pain found that patients who died of overdoses related to opioids were prescribed higher opioid dosages (mean: 98 MME/day; median: 60 MME/day) than controls (mean: 48 MME/day, median: 25 MME/day) (*127*). Finally, another recent study of overdose deaths among state residents with and without opioid prescriptions revealed that prescription opioid-related overdose mortality rates rose rapidly up to prescribed doses of 200 MME/day, after which the mortality rates continued to increase but grew more gradually (*128*). A listing of common opioid medications and their MME equivalents is provided (Table 2).

Regarding coprescription of opioids with benzodiazepines, epidemiologic studies suggest that concurrent use of benzodiazepines and opioids might put patients at greater risk for potentially fatal overdose. Three studies of fatal overdose deaths found evidence of concurrent benzodiazepine use in 31%–61% of decedents (*67*,*128*,*129*). In one of these studies (*67*), among decedents who received an opioid prescription, those whose deaths were related to opioids were more likely to have obtained opioids from multiple physicians and pharmacies than decedents whose deaths were not related to opioids.

Regarding duration of use, patients can experience tolerance and loss of effectiveness of opioids over time (*130*). Patients who do not experience clinically meaningful pain relief early in treatment (i.e., within 1 month) are unlikely to experience pain relief with longer-term use (*131*).

Regarding populations potentially at greater risk for harm, risk is greater for patients with sleep apnea or other causes of sleep-disordered breathing, patients with renal or hepatic insufficiency, older adults, pregnant women, patients with depression or other mental health conditions, and patients with alcohol or other substance use disorders. Interpretation of clinical data on the effects of opioids on sleep-disordered breathing is difficult because of the types of study designs and methods employed, and there is no clear consensus regarding association with risk for developing obstructive sleep apnea syndrome (*132*). However, opioid therapy can decrease respiratory drive, a high percentage of patients on long-term opioid therapy have been reported to have an abnormal apnea-hypopnea index (*133*), opioid therapy can worsen central sleep apnea in obstructive sleep apnea patients, and it can cause further desaturation in obstructive sleep apnea patients not on continuous positive airway pressure (CPAP) (*31*). Reduced renal or hepatic function can result in greater peak effect and longer duration of action and reduce the dose at which respiratory depression and overdose occurs (*134*). Age-related changes in patients aged ≥65 years, such as reduced renal function and medication clearance, even in the absence of renal disease (*135*), result in a smaller therapeutic window between safe dosages and dosages associated with respiratory depression and overdose. Older adults might also be at increased risk for falls and fractures related to opioids (*136*–*138*). Opioids used

in pregnancy can be associated with additional risks to both mother and fetus. Some studies have shown an association of opioid use in pregnancy with birth defects, including neural tube defects (*139*,*140*), congenital heart defects (*140*), and gastroschisis (*140*); preterm delivery (*141*), poor fetal growth (*141*), and stillbirth (*141*). Importantly, in some cases, opioid use during pregnancy leads to neonatal opioid withdrawal syndrome (*142*). Patients with mental health comorbidities and patients with histories of substance use disorders might be at higher risk than other patients for opioid use disorder (*62*,*143*,*144*). Recent analyses found that depressed patients were at higher risk for drug overdose than patients without depression, particularly at higher opioid dosages, although investigators were unable to distinguish unintentional overdose from suicide attempts (*145*). In case-control and case-cohort studies, substance abuse/dependence was more prevalent among patients experiencing overdose than among patients not experiencing overdose (12% versus 6% [*66*], 40% versus 10% [*24*], and 26% versus 9% [*23*]).

Regarding risk stratification approaches, limited evidence was found regarding benefits and harms. Potential benefits of PDMPs and urine drug testing include the ability to identify patients who might be at higher risk for opioid overdose or opioid use disorder, and help determine which patients will benefit from greater caution and increased monitoring or interventions when risk factors are present. For example, one study found that most fatal overdoses could be identified retrospectively on the basis of two pieces of information, multiple prescribers and high total daily opioid dosage, both important risk factors for overdose (*124*,*146*) that are available to prescribers in the PDMP (*124*). However, limited evaluation of PDMPs at the state level has revealed mixed effects on changes in prescribing and mortality outcomes (*28*). Potential harms of risk stratification include underestimation of risks of opioid therapy when screening tools are not adequately sensitive, as well as potential overestimation of risk, which could lead to inappropriate clinical decisions.

Regarding risk mitigation approaches, limited evidence was found regarding benefits and harms. Although no studies were found to examine prescribing of naloxone with opioid pain medication in primary care settings, naloxone distribution through community-based programs providing prevention services for substance users has been demonstrated to be associated with decreased risk for opioid overdose death at the community level (*147*).

Concerns have been raised that prescribing changes such as dose reduction might be associated with unintended negative consequences, such as patients seeking heroin or other illicitly obtained opioids (*148*) or interference with appropriate pain treatment (*149*). With the exception of a study noting an association between an abuse-deterrent formulation of OxyContin and heroin use, showing that some patients in qualitative interviews reported switching to another opioid, including heroin, for many reasons, including cost and availability as well as ease of use (*150*), CDC did not identify studies evaluating these potential outcomes.

Finally, regarding the effectiveness of opioid use disorder treatments, methadone and buprenorphine for opioid use disorder have been found to increase retention in treatment and to decrease illicit opioid use among patients with opioid use disorder involving heroin (*151*–*153*). Although findings are mixed, some studies suggest that effectiveness is enhanced when psychosocial treatments (e.g., contingency management, community reinforcement, psychotherapeutic counseling, and family therapy) are used in conjunction with medication-assisted therapy; for example, by reducing opioid misuse and increasing retention during maintenance therapy, and improving compliance after detoxification (*154*,*155*).

Clinician and Patient Values and Preferences

Clinician and patient values and preferences can inform how benefits and harms of long-term opioid therapy are weighted and estimate the effort and resources required to effectively provide implementation support. Many physicians lack confidence in their ability to prescribe opioids safely (*156*), to predict (*157*) or detect (*158*) prescription drug abuse, and to discuss abuse with their patients (*158*). Although clinicians have reported favorable beliefs and attitudes about improvements in pain and quality of life attributed to opioids (*159*), most consider prescription drug abuse to be a "moderate" or "big" problem in their community, and large proportions are "very" concerned about opioid addiction (55%) and death (48%) (*160*). Clinicians do not consistently use practices intended to decrease the risk for misuse, such as PDMPs (*161*,*162*), urine drug testing (*163*), and opioid treatment agreements (*164*). This is likely due in part to challenges related to registering for PDMP access and logging into the PDMP (which can interrupt normal clinical workflow if data are not integrated into electronic health record systems) (*165*), competing clinical demands, perceived inadequate time to discuss the rationale for urine drug testing and to order confirmatory testing, and feeling unprepared to interpret and address results (*166*).

Many patients do not have an opinion about "opioids" or know what this term means (*167*). Most are familiar with the term "narcotics." About a third associated "narcotics" with addiction or abuse, and about half feared "addiction" from long-term "narcotic" use (*168*). Most patients taking opioids experience side effects (73% of patients taking hydrocodone for noncancer pain [*11*], 96% of patients taking opioids for chronic pain [*12*]), and side effects, rather than pain relief,

have been found to explain most of the variation in patients' preferences related to taking opioids (*12*). For example, patients taking hydrocodone for noncancer pain commonly reported side effects including dizziness, headache, fatigue, drowsiness, nausea, vomiting, and constipation (*11*). Patients with chronic pain in focus groups emphasized effectiveness of goal setting for increasing motivation and functioning (*168*). Patients taking high dosages report reliance on opioids despite ambivalence about their benefits (*169*) and regardless of pain reduction, reported problems, concerns, side effects, or perceived helpfulness (*13*).

Resource Allocation

Resource allocation (cost) is an important consideration in understanding the feasibility of clinical recommendations. CDC searched for evidence on opioid therapy compared with other treatments; costs of misuse, abuse, and overdose from prescription opioids; and costs of specific risk mitigation strategies (e.g., urine drug testing). Yearly direct and indirect costs related to prescription opioids have been estimated (based on studies published since 2010) to be $53.4 billion for nonmedical use of prescription opioids (*170*); $55.7 billion for abuse, dependence (i.e., opioid use disorder), and misuse of prescription opioids (*171*); and $20.4 billion for direct and indirect costs related to opioid-related overdose alone (*172*). In 2012, total expenses for outpatient prescription opioids were estimated at $9.0 billion, an increase of 120% from 2002 (*173*). Although there are perceptions that opioid therapy for chronic pain is less expensive than more time-intensive nonpharmacologic management approaches, many pain treatments, including acetaminophen, NSAIDs, tricyclic antidepressants, and massage therapy, are associated with lower mean and median annual costs compared with opioid therapy (*174*). COX-2 inhibitors, SNRIs, anticonvulsants, topical analgesics, physical therapy, and CBT are also associated with lower median annual costs compared with opioid therapy (*174*). Limited information was found on costs of strategies to decrease risks associated with opioid therapy; however, urine drug testing, including screening and confirmatory tests, has been estimated to cost $211–$363 per test (*175*).

Recommendations

The recommendations are grouped into three areas for consideration:

- Determining when to initiate or continue opioids for chronic pain.
- Opioid selection, dosage, duration, follow-up, and discontinuation.
- Assessing risk and addressing harms of opioid use.

There are 12 recommendations (Box 1). Each recommendation is followed by a rationale for the recommendation, with considerations for implementation noted. In accordance with the ACIP GRADE process, CDC based the recommendations on consideration of the clinical evidence, contextual evidence (including benefits and harms, values and preferences, resource allocation), and expert opinion. For each recommendation statement, CDC notes the recommendation category (A or B) and the type of the evidence (1, 2, 3, or 4) supporting the statement (Box 2). Expert opinion is reflected within each of the recommendation rationales. While there was not an attempt to reach consensus among experts, experts from the Core Expert Group and from the Opioid Guideline Workgroup ("experts") expressed overall, general support for all recommendations. Where differences in expert opinion emerged for detailed actions within the clinical recommendations or for implementation considerations, CDC notes the differences of opinion in the supporting rationale statements.

Category A recommendations indicate that most patients should receive the recommended course of action; category B recommendations indicate that different choices will be appropriate for different patients, requiring clinicians to help patients arrive at a decision consistent with patient values and preferences and specific clinical situations. Consistent with the ACIP (*47*) and GRADE process (*48*), category A recommendations were made, even with type 3 and 4 evidence, when there was broad agreement that the advantages of a clinical action greatly outweighed the disadvantages based on a consideration of benefits and harms, values and preferences, and resource allocation. Category B recommendations were made when there was broad agreement that the advantages and disadvantages of a clinical action were more balanced, but advantages were significant enough to warrant a recommendation. All recommendations are category A recommendations, with the exception of recommendation 10, which is rated as category B. Recommendations were associated with a range of evidence types, from type 2 to type 4.

In summary, the categorization of recommendations was based on the following assessment:

- No evidence shows a long-term benefit of opioids in pain and function versus no opioids for chronic pain with outcomes examined at least 1 year later (with most placebo-controlled randomized trials ≤6 weeks in duration).
- Extensive evidence shows the possible harms of opioids (including opioid use disorder, overdose, and motor vehicle injury).
- Extensive evidence suggests some benefits of nonpharmacologic and nonopioid pharmacologic treatments compared with long-term opioid therapy, with less harm.

BOX 1. CDC recommendations for prescribing opioids for chronic pain outside of active cancer, palliative, and end-of-life care

Determining When to Initiate or Continue Opioids for Chronic Pain

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.
7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

Assessing Risk and Addressing Harms of Opioid Use

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.
9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.
10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.
11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

* All recommendations are category A (apply to all patients outside of active cancer treatment, palliative care, and end-of-life care) except recommendation 10 (designated category B, with individual decision making required); see full guideline for evidence ratings.

BOX 2. Interpretation of recommendation categories and evidence type

Recommendation Categories

Based on evidence type, balance between desirable and undesirable effects, values and preferences, and resource allocation (cost).

Category A recommendation: Applies to all persons; most patients should receive the recommended course of action.

Category B recommendation: Individual decision making needed; different choices will be appropriate for different patients. Clinicians help patients arrive at a decision consistent with patient values and preferences and specific clinical situations.

Evidence Type

Based on study design as well as a function of limitations in study design or implementation, imprecision of estimates, variability in findings, indirectness of evidence, publication bias, magnitude of treatment effects, dose-response gradient, and constellation of plausible biases that could change effects.

Type 1 evidence: Randomized clinical trials or overwhelming evidence from observational studies.

Type 2 evidence: Randomized clinical trials with important limitations, or exceptionally strong evidence from observational studies.

Type 3 evidence: Observational studies or randomized clinical trials with notable limitations.

Type 4 evidence: Clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations.

Determining When to Initiate or Continue Opioids for Chronic Pain

1. **Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate (recommendation category: A, evidence type: 3).**

Patients with pain should receive treatment that provides the greatest benefits relative to risks. The contextual evidence review found that many nonpharmacologic therapies, including physical therapy, weight loss for knee osteoarthritis, psychological therapies such as CBT, and certain interventional procedures can ameliorate chronic pain. There is high-quality evidence that exercise therapy (a prominent modality in physical therapy) for hip (*100*) or knee (*99*) osteoarthritis reduces pain and improves function immediately after treatment and that the improvements are sustained for at least 2–6 months. Previous guidelines have strongly recommended aerobic, aquatic, and/or resistance exercises for patients with osteoarthritis of the knee or hip (*176*). Exercise therapy also can help reduce pain and improve function in low back pain and can improve global well-being and physical function in fibromyalgia (*98*,*101*). Multimodal therapies and multidisciplinary biopsychosocial rehabilitation-combining approaches (e.g., psychological therapies with exercise) can reduce long-term pain and disability compared with usual care and compared with physical treatments (e.g., exercise) alone. Multimodal therapies are not always available or reimbursed by insurance and can be time-consuming and costly for patients. Interventional approaches such as arthrocentesis and intraarticular glucocorticoid injection for pain associated with rheumatoid arthritis (*117*) or osteoarthritis (*118*) and subacromial corticosteroid injection for rotator cuff disease (*119*) can provide short-term improvement in pain and function. Evidence is insufficient to determine the extent to which repeated glucocorticoid injection increases potential risks such as articular cartilage changes (in osteoarthritis) and sepsis (*118*). Serious adverse events are rare but have been reported with epidural injection (*120*).

Several nonopioid pharmacologic therapies (including acetaminophen, NSAIDs, and selected antidepressants and anticonvulsants) are effective for chronic pain. In particular, acetaminophen and NSAIDs can be useful for arthritis and low back pain. Selected anticonvulsants such as pregabalin and gabapentin can improve pain in diabetic neuropathy and post-herpetic neuralgia (contextual evidence review). Pregabalin, gabapentin, and carbamazepine are FDA-approved for treatment of certain neuropathic pain conditions, and pregabalin is FDA approved for fibromyalgia management. In patients with or without depression, tricyclic antidepressants and SNRIs provide effective analgesia for neuropathic pain conditions including diabetic neuropathy and post-herpetic neuralgia, often at lower dosages and with a shorter time to onset of effect than for treatment of depression (see contextual evidence review). Tricyclics and SNRIs can also relieve fibromyalgia symptoms. The SNRI duloxetine is FDA-approved for the treatment of diabetic neuropathy and fibromyalgia. Because patients with chronic pain often suffer from concurrent depression (*144*), and depression can exacerbate physical symptoms including pain (*177*), patients with co-occurring pain and depression are especially likely to benefit from antidepressant medication (see Recommendation 8). Nonopioid pharmacologic therapies

are not generally associated with substance use disorder, and the numbers of fatal overdoses associated with nonopioid medications are a fraction of those associated with opioid medications (contextual evidence review). For example, acetaminophen, NSAIDs, and opioid pain medication were involved in 881, 228, and 16,651 pharmaceutical overdose deaths in the United States in 2010 (*178*). However, nonopioid pharmacologic therapies are associated with certain risks, particularly in older patients, pregnant patients, and patients with certain co-morbidities such as cardiovascular, renal, gastrointestinal, and liver disease (see contextual evidence review). For example, acetaminophen can be hepatotoxic at dosages of >3–4 grams/day and at lower dosages in patients with chronic alcohol use or liver disease (*109*). NSAID use has been associated with gastritis, peptic ulcer disease, cardiovascular events (*111*,*112*), and fluid retention, and most NSAIDs (choline magnesium trilisate and selective COX-2 inhibitors are exceptions) interfere with platelet aggregation (*179*). Clinicians should review FDA-approved labeling including boxed warnings before initiating treatment with any pharmacologic therapy.

Although opioids can reduce pain during short-term use, the clinical evidence review found insufficient evidence to determine whether pain relief is sustained and whether function or quality of life improves with long-term opioid therapy (KQ1). While benefits for pain relief, function, and quality of life with long-term opioid use for chronic pain are uncertain, risks associated with long-term opioid use are clearer and significant. Based on the clinical evidence review, long-term opioid use for chronic pain is associated with serious risks including increased risk for opioid use disorder, overdose, myocardial infarction, and motor vehicle injury (KQ2). At a population level, more than 165,000 persons in the United States have died from opioid pain-medication-related overdoses since 1999 (see Contextual Evidence Review).

Integrated pain management requires coordination of medical, psychological, and social aspects of health care and includes primary care, mental health care, and specialist services when needed (*180*). Nonpharmacologic physical and psychological treatments such as exercise and CBT are approaches that encourage active patient participation in the care plan, address the effects of pain in the patient's life, and can result in sustained improvements in pain and function without apparent risks. Despite this, these therapies are not always or fully covered by insurance, and access and cost can be barriers for patients. For many patients, aspects of these approaches can be used even when there is limited access to specialty care. For example, previous guidelines have strongly recommended aerobic, aquatic, and/or resistance exercises for patients with osteoarthritis of the knee or hip (*176*) and maintenance of activity for patients with low back pain (*110*). A randomized trial found no difference in reduced chronic low back pain intensity, frequency or disability between patients assigned to relatively low-cost group aerobics and individual physiotherapy or muscle reconditioning sessions (*181*). Low-cost options to integrate exercise include brisk walking in public spaces or use of public recreation facilities for group exercise. CBT addresses psychosocial contributors to pain and improves function (*97*). Primary care clinicians can integrate elements of a cognitive behavioral approach into their practice by encouraging patients to take an active role in the care plan, by supporting patients in engaging in beneficial but potentially anxiety-provoking activities, such as exercise (*179*), or by providing education in relaxation techniques and coping strategies. In many locations, there are free or low-cost patient support, self-help, and educational community-based programs that can provide stress reduction and other mental health benefits. Patients with more entrenched anxiety or fear related to pain, or other significant psychological distress, can be referred for formal therapy with a mental health specialist (e.g., psychologist, psychiatrist, clinical social worker). Multimodal therapies should be considered for patients not responding to single-modality therapy, and combinations should be tailored depending on patient needs, cost, and convenience.

To guide patient-specific selection of therapy, clinicians should evaluate patients and establish or confirm the diagnosis. Detailed recommendations on diagnosis are provided in other guidelines (*110*,*179*), but evaluation should generally include a focused history, including history and characteristics of pain and potentially contributing factors (e.g., function, psychosocial stressors, sleep) and physical exam, with imaging or other diagnostic testing only if indicated (e.g., if severe or progressive neurologic deficits are present or if serious underlying conditions are suspected) (*110*,*179*). For complex pain syndromes, pain specialty consultation can be considered to assist with diagnosis as well as management. Diagnosis can help identify disease-specific interventions to reverse or ameliorate pain; for example, improving glucose control to prevent progression of diabetic neuropathy; immune-modulating agents for rheumatoid arthritis; physical or occupational therapy to address posture, muscle weakness, or repetitive occupational motions that contribute to musculoskeletal pain; or surgical intervention to relieve mechanical/compressive pain (*179*). The underlying mechanism for most pain syndromes can be categorized as neuropathic (e.g., diabetic neuropathy, postherpetic neuralgia, fibromyalgia), or nociceptive (e.g., osteoarthritis, muscular back pain). The diagnosis and pathophysiologic mechanism of pain have implications for symptomatic pain treatment with medication. For example, evidence is limited or insufficient

for improved pain or function with long-term use of opioids for several chronic pain conditions for which opioids are commonly prescribed, such as low back pain (*182*), headache (*183*), and fibromyalgia (*184*). Although NSAIDs can be used for exacerbations of nociceptive pain, other medications (e.g., tricyclics, selected anticonvulsants, or transdermal lidocaine) generally are recommended for neuropathic pain. In addition, improvement of neuropathic pain can begin weeks or longer after symptomatic treatment is initiated (*179*). Medications should be used only after assessment and determination that expected benefits outweigh risks given patient-specific factors. For example, clinicians should consider falls risk when selecting and dosing potentially sedating medications such as tricyclics, anticonvulsants, or opioids, and should weigh risks and benefits of use, dose, and duration of NSAIDs when treating older adults as well as patients with hypertension, renal insufficiency, or heart failure, or those with risk for peptic ulcer disease or cardiovascular disease. Some guidelines recommend topical NSAIDs for localized osteoarthritis (e.g., knee osteoarthritis) over oral NSAIDs in patients aged ≥75 years to minimize systemic effects (*176*).

Experts agreed that opioids should not be considered first-line or routine therapy for chronic pain (i.e., pain continuing or expected to continue >3 months or past the time of normal tissue healing) outside of active cancer, palliative, and end-of-life care, given small to moderate short-term benefits, uncertain long-term benefits, and potential for serious harms; although evidence on long-term benefits of nonopioid therapies is also limited, these therapies are also associated with short-term benefits, and risks are much lower. This does not mean that patients should be required to sequentially "fail" nonpharmacologic and nonopioid pharmacologic therapy before proceeding to opioid therapy. Rather, expected benefits specific to the clinical context should be weighed against risks before initiating therapy. In some clinical contexts (e.g., headache or fibromyalgia), expected benefits of initiating opioids are unlikely to outweigh risks regardless of previous nonpharmacologic and nonopioid pharmacologic therapies used. In other situations (e.g., serious illness in a patient with poor prognosis for return to previous level of function, contraindications to other therapies, and clinician and patient agreement that the overriding goal is patient comfort), opioids might be appropriate regardless of previous therapies used. In addition, when opioid pain medication is used, it is more likely to be effective if integrated with nonpharmacologic therapy. Nonpharmacologic approaches such as exercise and CBT should be used to reduce pain and improve function in patients with chronic pain. Nonopioid pharmacologic therapy should be used when benefits outweigh risks and should be combined with nonpharmacologic therapy to reduce pain and improve function. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate, to provide greater benefits to patients in improving pain and function.

2. **Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety (recommendation category: A, evidence type: 4).**

The clinical evidence review found insufficient evidence to determine long-term benefits of opioid therapy for chronic pain and found an increased risk for serious harms related to long-term opioid therapy that appears to be dose-dependent. In addition, studies on currently available risk assessment instruments were sparse and showed inconsistent results (KQ4). The clinical evidence review for the current guideline considered studies with outcomes examined at ≥1 year that compared opioid use versus nonuse or placebo. Studies of opioid therapy for chronic pain that did not have a nonopioid control group have found that although many patients discontinue opioid therapy for chronic noncancer pain due to adverse effects or insufficient pain relief, there is weak evidence that patients who are able to continue opioid therapy for at least 6 months can experience clinically significant pain relief and insufficient evidence that function or quality of life improves (*185*). These findings suggest that it is very difficult for clinicians to predict whether benefits of opioids for chronic pain will outweigh risks of ongoing treatment for individual patients. Opioid therapy should not be initiated without consideration of an "exit strategy" to be used if the therapy is unsuccessful.

Experts agreed that before opioid therapy is initiated for chronic pain outside of active cancer, palliative, and end-of-life care, clinicians should determine how effectiveness will be evaluated and should establish treatment goals with patients. Because the line between acute pain and initial chronic pain is not always clear, it might be difficult for clinicians to determine when they are initiating opioids for chronic pain rather than treating acute pain. Pain lasting longer than 3 months or past the time of normal tissue healing (which could be substantially shorter than 3 months, depending on the condition) is generally no longer considered acute. However, establishing treatment goals with a patient who has already received opioid therapy for 3 months would defer this discussion well past the point of

initiation of opioid therapy for chronic pain. Clinicians often write prescriptions for long-term use in 30-day increments, and opioid prescriptions written for ≥30 days are likely to represent initiation or continuation of long-term opioid therapy. Before writing an opioid prescription for ≥30 days, clinicians should establish treatment goals with patients. Clinicians seeing new patients already receiving opioids should establish treatment goals for continued opioid therapy. Although the clinical evidence review did not find studies evaluating the effectiveness of written agreements or treatment plans (KQ4), clinicians and patients who set a plan in advance will clarify expectations regarding how opioids will be prescribed and monitored, as well as situations in which opioids will be discontinued or doses tapered (e.g., if treatment goals are not met, opioids are no longer needed, or adverse events put the patient at risk) to improve patient safety.

Experts thought that goals should include improvement in both pain relief and function (and therefore in quality of life). However, there are some clinical circumstances under which reductions in pain without improvement in physical function might be a more realistic goal (e.g., diseases typically associated with progressive functional impairment or catastrophic injuries such as spinal cord trauma). Experts noted that function can include emotional and social as well as physical dimensions. In addition, experts emphasized that mood has important interactions with pain and function. Experts agreed that clinicians may use validated instruments such as the three-item "Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale (*186*) to track patient outcomes. Clinically meaningful improvement has been defined as a 30% improvement in scores for both pain and function (*187*). Monitoring progress toward patient-centered functional goals (e.g., walking the dog or walking around the block, returning to part-time work, attending family sports or recreational activities) can also contribute to the assessment of functional improvement. Clinicians should use these goals in assessing benefits of opioid therapy for individual patients and in weighing benefits against risks of continued opioid therapy (see Recommendation 7, including recommended intervals for follow-up). Because depression, anxiety, and other psychological co-morbidities often coexist with and can interfere with resolution of pain, clinicians should use validated instruments to assess for these conditions (see Recommendation 8) and ensure that treatment for these conditions is optimized. If patients receiving opioid therapy for chronic pain do not experience meaningful improvements in both pain and function compared with prior to initiation of opioid therapy, clinicians should consider working with patients to taper and discontinue opioids (see Recommendation 7) and should use nonpharmacologic and nonopioid pharmacologic approaches to pain management (see Recommendation 1).

3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy (recommendation category: A, evidence type: 3).

The clinical evidence review did not find studies evaluating effectiveness of patient education or opioid treatment plans as risk-mitigation strategies (KQ4). However, the contextual evidence review found that many patients lack information about opioids and identified concerns that some clinicians miss opportunities to effectively communicate about safety. Given the substantial evidence gaps on opioids, uncertain benefits of long-term use, and potential for serious harms, patient education and discussion before starting opioid therapy are critical so that patient preferences and values can be understood and used to inform clinical decisions. Experts agreed that essential elements to communicate to patients before starting and periodically during opioid therapy include realistic expected benefits, common and serious harms, and expectations for clinician and patient responsibilities to mitigate risks of opioid therapy.

Clinicians should involve patients in decisions about whether to start or continue opioid therapy. Given potentially serious risks of long-term opioid therapy, clinicians should ensure that patients are aware of potential benefits of, harms of, and alternatives to opioids before starting or continuing opioid therapy. Clinicians are encouraged to have open and honest discussions with patients to inform mutual decisions about whether to start or continue opioid therapy. Important considerations include the following:

- Be explicit and realistic about expected benefits of opioids, explaining that while opioids can reduce pain during short-term use, there is no good evidence that opioids improve pain or function with long-term use, and that complete relief of pain is unlikely (clinical evidence review, KQ1).
- Emphasize improvement in function as a primary goal and that function can improve even when pain is still present.
- Advise patients about serious adverse effects of opioids, including potentially fatal respiratory depression and development of a potentially serious lifelong opioid use disorder that can cause distress and inability to fulfill major role obligations.
- Advise patients about common effects of opioids, such as constipation, dry mouth, nausea, vomiting, drowsiness, confusion, tolerance, physical dependence, and withdrawal symptoms when stopping opioids. To prevent constipation associated with opioid use, advise patients to increase

hydration and fiber intake and to maintain or increase physical activity. Stool softeners or laxatives might be needed.
- Discuss effects that opioids might have on ability to safely operate a vehicle, particularly when opioids are initiated, when dosages are increased, or when other central nervous system depressants, such as benzodiazepines or alcohol, are used concurrently.
- Discuss increased risks for opioid use disorder, respiratory depression, and death at higher dosages, along with the importance of taking only the amount of opioids prescribed, i.e., not taking more opioids or taking them more often.
- Review increased risks for respiratory depression when opioids are taken with benzodiazepines, other sedatives, alcohol, illicit drugs such as heroin, or other opioids.
- Discuss risks to household members and other individuals if opioids are intentionally or unintentionally shared with others for whom they are not prescribed, including the possibility that others might experience overdose at the same or at lower dosage than prescribed for the patient, and that young children are susceptible to unintentional ingestion. Discuss storage of opioids in a secure, preferably locked location and options for safe disposal of unused opioids (*188*).
- Discuss the importance of periodic reassessment to ensure that opioids are helping to meet patient goals and to allow opportunities for opioid discontinuation and consideration of additional nonpharmacologic or nonopioid pharmacologic treatment options if opioids are not effective or are harmful.
- Discuss planned use of precautions to reduce risks, including use of prescription drug monitoring program information (see Recommendation 9) and urine drug testing (see Recommendation 10). Consider including discussion of naloxone use for overdose reversal (see Recommendation 8).
- Consider whether cognitive limitations might interfere with management of opioid therapy (for older adults in particular) and, if so, determine whether a caregiver can responsibly co-manage medication therapy. Discuss the importance of reassessing safer medication use with both the patient and caregiver.

Given the possibility that benefits of opioid therapy might diminish or that risks might become more prominent over time, it is important that clinicians review expected benefits and risks of continued opioid therapy with patients periodically, at least every 3 months (see Recommendation 7).

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids (recommendation category: A, evidence type: 4).

ER/LA opioids include methadone, transdermal fentanyl, and extended-release versions of opioids such as oxycodone, oxymorphone, hydrocodone, and morphine. The clinical evidence review found a fair-quality study showing a higher risk for overdose among patients initiating treatment with ER/LA opioids than among those initiating treatment with immediate-release opioids (*77*). The clinical evidence review did not find evidence that continuous, time-scheduled use of ER/LA opioids is more effective or safer than intermittent use of immediate-release opioids or that time-scheduled use of ER/LA opioids reduces risks for opioid misuse or addiction (KQ3).

In 2014, the FDA modified the labeling for ER/LA opioid pain medications, noting serious risks and recommending that ER/LA opioids be reserved for "management of pain severe enough to require daily, around-the-clock, long-term opioid treatment" when "alternative treatment options (e.g., nonopioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain" and not used as "as needed" pain relievers (*121*). FDA has also noted that some ER/LA opioids are only appropriate for opioid-tolerant patients, defined as patients who have received certain dosages of opioids (e.g., 60 mg daily of oral morphine, 30 mg daily of oral oxycodone, or equianalgesic dosages of other opioids) for at least 1 week (*189*). Time-scheduled opioid use can be associated with greater total average daily opioid dosage compared with intermittent, as-needed opioid use (contextual evidence review). In addition, experts indicated that there was not enough evidence to determine the safety of using immediate-release opioids for breakthrough pain when ER/LA opioids are used for chronic pain outside of active cancer pain, palliative care, or end-of-life care, and that this practice might be associated with dose escalation.

Abuse-deterrent technologies have been employed to prevent manipulation intended to defeat extended-release properties of ER/LA opioids and to prevent opioid use by unintended routes of administration, such as injection of oral opioids. As indicated in FDA guidance for industry on evaluation and labeling of abuse-deterrent opioids (*190*), although abuse-deterrent technologies are expected to make manipulation of opioids more difficult or less rewarding, they do not prevent

opioid abuse through oral intake, the most common route of opioid abuse, and can still be abused by nonoral routes. The "abuse-deterrent" label does not indicate that there is no risk for abuse. No studies were found in the clinical evidence review assessing the effectiveness of abuse-deterrent technologies as a risk mitigation strategy for deterring or preventing abuse. In addition, abuse-deterrent technologies do not prevent unintentional overdose through oral intake. Experts agreed that recommendations could not be offered at this time related to use of abuse-deterrent formulations.

In comparing different ER/LA formulations, the clinical evidence review found inconsistent results for overdose risk with methadone versus other ER/LA opioids used for chronic pain (KQ3). The contextual evidence review found that methadone has been associated with disproportionate numbers of overdose deaths relative to the frequency with which it is prescribed for chronic pain. In addition, methadone is associated with cardiac arrhythmias along with QT prolongation on the electrocardiogram, and it has complicated pharmacokinetics and pharmacodynamics, including a long and variable half-life and peak respiratory depressant effect occurring later and lasting longer than peak analgesic effect. Experts noted that the pharmacodynamics of methadone are subject to more inter-individual variability than other opioids. In regard to other ER/LA opioid formulations, experts noted that the absorption and pharmacodynamics of transdermal fentanyl are complex, with gradually increasing serum concentration during the first part of the 72-hour dosing interval, as well as variable absorption based on factors such as external heat. In addition, the dosing of transdermal fentanyl in mcg/hour, which is not typical for a drug used by outpatients, can be confusing. Experts thought that these complexities might increase the risk for fatal overdose when methadone or transdermal fentanyl is prescribed to a patient who has not used it previously or by clinicians who are not familiar with its effects.

Experts agreed that for patients not already receiving opioids, clinicians should not initiate opioid treatment with ER/LA opioids and should not prescribe ER/LA opioids for intermittent use. ER/LA opioids should be reserved for severe, continuous pain and should be considered only for patients who have received immediate-release opioids daily for at least 1 week. When changing to an ER/LA opioid for a patient previously receiving a different immediate-release opioid, clinicians should consult product labeling and reduce total daily dosage to account for incomplete opioid cross-tolerance. Clinicians should use additional caution with ER/LA opioids and consider a longer dosing interval when prescribing to patients with renal or hepatic dysfunction because decreased clearance of drugs among these patients can lead to accumulation of drugs to toxic levels and persistence in the body for longer durations. Although there might be situations in which clinicians need to prescribe immediate-release and ER/LA opioids together (e.g., transitioning patients from ER/LA opioids to immediate-release opioids by temporarily using lower dosages of both), in general, avoiding the use of immediate-release opioids in combination with ER/LA opioids is preferable, given potentially increased risk and diminishing returns of such an approach for chronic pain.

When an ER/LA opioid is prescribed, using one with predictable pharmacokinetics and pharmacodynamics is preferred to minimize unintentional overdose risk. In particular, unusual characteristics of methadone and of transdermal fentanyl make safe prescribing of these medications for pain especially challenging.

- Methadone should not be the first choice for an ER/LA opioid. Only clinicians who are familiar with methadone's unique risk profile and who are prepared to educate and closely monitor their patients, including risk assessment for QT prolongation and consideration of electrocardiographic monitoring, should consider prescribing methadone for pain. A clinical practice guideline that contains further guidance regarding methadone prescribing for pain has been published previously (*191*).
- Because dosing effects of transdermal fentanyl are often misunderstood by both clinicians and patients, only clinicians who are familiar with the dosing and absorption properties of transdermal fentanyl and are prepared to educate their patients about its use should consider prescribing it.

5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day (recommendation category: A, evidence type: 3).

Benefits of high-dose opioids for chronic pain are not established. The clinical evidence review found only one study (*84*) addressing effectiveness of dose titration for outcomes related to pain control, function, and quality of life (KQ3). This randomized trial found no difference in pain or function between a more liberal opioid dose escalation strategy and maintenance of current dosage. (These groups were prescribed average dosages of 52 and 40 MME/day, respectively, at the end of the trial.) At the same time, risks for serious harms

related to opioid therapy increase at higher opioid dosage. The clinical evidence review found that higher opioid dosages are associated with increased risks for motor vehicle injury, opioid use disorder, and overdose (KQ2). The clinical and contextual evidence reviews found that opioid overdose risk increases in a dose-response manner, that dosages of 50–<100 MME/day have been found to increase risks for opioid overdose by factors of 1.9 to 4.6 compared with dosages of 1–<20 MME/day, and that dosages ≥100 MME/day are associated with increased risks of overdose 2.0–8.9 times the risk at 1–<20 MME/day. In a national sample of Veterans Health Administration patients with chronic pain who were prescribed opioids, mean prescribed opioid dosage among patients who died from opioid overdose was 98 MME (median 60 MME) compared with mean prescribed opioid dosage of 48 MME (median 25 MME) among patients not experiencing fatal overdose (*127*).

The contextual evidence review found that although there is not a single dosage threshold below which overdose risk is eliminated, holding dosages <50 MME/day would likely reduce risk among a large proportion of patients who would experience fatal overdose at higher prescribed dosages. Experts agreed that lower dosages of opioids reduce the risk for overdose, but that a single dosage threshold for safe opioid use could not be identified. Experts noted that daily opioid dosages close to or greater than 100 MME/day are associated with significant risks, that dosages <50 MME/day are safer than dosages of 50–100 MME/day, and that dosages <20 MME/day are safer than dosages of 20–50 MME/day. One expert thought that a specific dosage at which the benefit/risk ratio of opioid therapy decreases could not be identified. Most experts agreed that, in general, increasing dosages to 50 or more MME/day increases overdose risk without necessarily adding benefits for pain control or function and that clinicians should carefully reassess evidence of individual benefits and risks when considering increasing opioid dosages to ≥50 MME/day. Most experts also agreed that opioid dosages should not be increased to ≥90 MME/day without careful justification based on diagnosis and on individualized assessment of benefits and risks.

When opioids are used for chronic pain outside of active cancer, palliative, and end-of-life care, clinicians should start opioids at the lowest possible effective dosage (the lowest starting dosage on product labeling for patients not already taking opioids and according to product labeling guidance regarding tolerance for patients already taking opioids). Clinicians should use additional caution when initiating opioids for patients aged ≥65 years and for patients with renal or hepatic insufficiency because decreased clearance of drugs in these patients can result in accumulation of drugs to toxic levels. Clinicians should use caution when increasing opioid dosages and increase dosage by the smallest practical amount because overdose risk increases with increases in opioid dosage. Although there is limited evidence to recommend specific intervals for dosage titration, a previous guideline recommended waiting at least five half-lives before increasing dosage and waiting at least a week before increasing dosage of methadone to make sure that full effects of the previous dosage are evident (*31*). Clinicians should re-evaluate patients after increasing dosage for changes in pain, function, and risk for harm (see Recommendation 7). Before increasing total opioid dosage to ≥50 MME/day, clinicians should reassess whether opioid treatment is meeting the patient's treatment goals (see Recommendation 2). If a patient's opioid dosage for all sources of opioids combined reaches or exceeds 50 MME/day, clinicians should implement additional precautions, including increased frequency of follow-up (see Recommendation 7) and considering offering naloxone and overdose prevention education to both patients and the patients' household members (see Recommendation 8). Clinicians should avoid increasing opioid dosages to ≥90 MME/day or should carefully justify a decision to increase dosage to ≥90 MME/day based on individualized assessment of benefits and risks and weighing factors such as diagnosis, incremental benefits for pain and function relative to harms as dosages approach 90 MME/day, other treatments and effectiveness, and recommendations based on consultation with pain specialists. If patients do not experience improvement in pain and function at ≥90 MME/day, or if there are escalating dosage requirements, clinicians should discuss other approaches to pain management with the patient, consider working with patients to taper opioids to a lower dosage or to taper and discontinue opioids (see Recommendation 7), and consider consulting a pain specialist. Some states require clinicians to implement clinical protocols at specific dosage levels. For example, before increasing long-term opioid therapy dosage to >120 MME/day, clinicians in Washington state must obtain consultation from a pain specialist who agrees that this is indicated and appropriate (*30*). Clinicians should be aware of rules related to MME thresholds and associated clinical protocols established by their states.

Established patients already taking high dosages of opioids, as well as patients transferring from other clinicians, might consider the possibility of opioid dosage reduction to be anxiety-provoking, and tapering opioids can be especially challenging after years on high dosages because of physical and psychological dependence. However, these patients should be offered the opportunity to re-evaluate their continued use of opioids at high dosages in light of recent evidence regarding the association of opioid dosage and overdose risk. Clinicians should explain in a nonjudgmental manner to patients already taking high opioid dosages (≥90 MME/day) that there is

now an established body of scientific evidence showing that overdose risk is increased at higher opioid dosages. Clinicians should empathically review benefits and risks of continued high-dosage opioid therapy and should offer to work with the patient to taper opioids to safer dosages. For patients who agree to taper opioids to lower dosages, clinicians should collaborate with the patient on a tapering plan (see Recommendation 7). Experts noted that patients tapering opioids after taking them for years might require very slow opioid tapers as well as pauses in the taper to allow gradual accommodation to lower opioid dosages. Clinicians should remain alert to signs of anxiety, depression, and opioid use disorder (see Recommendations 8 and 12) that might be unmasked by an opioid taper and arrange for management of these co-morbidities. For patients agreeing to taper to lower opioid dosages as well as for those remaining on high opioid dosages, clinicians should establish goals with the patient for continued opioid therapy (see Recommendation 2), maximize pain treatment with nonpharmacologic and nonopioid pharmacologic treatments as appropriate (see Recommendation 1), and consider consulting a pain specialist as needed to assist with pain management.

6. **Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed (recommendation category: A, evidence type: 4).**

The clinical evidence review found that opioid use for acute pain (i.e., pain with abrupt onset and caused by an injury or other process that is not ongoing) is associated with long-term opioid use, and that a greater amount of early opioid exposure is associated with greater risk for long-term use (KQ5). Several guidelines on opioid prescribing for acute pain from emergency departments (*192*–*194*) and other settings (*195*,*196*) have recommended prescribing ≤3 days of opioids in most cases, whereas others have recommended ≤7 days (*197*) or <14 days (*30*). Because physical dependence on opioids is an expected physiologic response in patients exposed to opioids for more than a few days (contextual evidence review), limiting days of opioids prescribed also should minimize the need to taper opioids to prevent distressing or unpleasant withdrawal symptoms. Experts noted that more than a few days of exposure to opioids significantly increases hazards, that each day of unnecessary opioid use increases likelihood of physical dependence without adding benefit, and that prescriptions with fewer days' supply will minimize the number of pills available for unintentional or intentional diversion.

Experts agreed that when opioids are needed for acute pain, clinicians should prescribe opioids at the lowest effective dose and for no longer than the expected duration of pain severe enough to require opioids to minimize unintentional initiation of long-term opioid use. The lowest effective dose can be determined using product labeling as a starting point with calibration as needed based on the severity of pain and on other clinical factors such as renal or hepatic insufficiency (see Recommendation 8). Experts thought, based on clinical experience regarding anticipated duration of pain severe enough to require an opioid, that in most cases of acute pain not related to surgery or trauma, a ≤3 days' supply of opioids will be sufficient. For example, in one study of the course of acute low back pain (not associated with malignancies, infections, spondylarthropathies, fractures, or neurological signs) in a primary care setting, there was a large decrease in pain until the fourth day after treatment with paracetamol, with smaller decreases thereafter (*198*). Some experts thought that because some types of acute pain might require more than 3 days of opioid treatment, it would be appropriate to recommend a range of ≤3–5 days or ≤3–7 days when opioids are needed. Some experts thought that a range including 7 days was too long given the expected course of severe acute pain for most acute pain syndromes seen in primary care.

Acute pain can often be managed without opioids. It is important to evaluate the patient for reversible causes of pain, for underlying etiologies with potentially serious sequelae, and to determine appropriate treatment. When the diagnosis and severity of nontraumatic, nonsurgical acute pain are reasonably assumed to warrant the use of opioids, clinicians should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids, often 3 days or less, unless circumstances clearly warrant additional opioid therapy. More than 7 days will rarely be needed. Opioid treatment for post-surgical pain is outside the scope of this guideline but has been addressed elsewhere (*30*). Clinicians should not prescribe additional opioids to patients "just in case" pain continues longer than expected. Clinicians should re-evaluate the subset of patients who experience severe acute pain that continues longer than the expected duration to confirm or revise the initial diagnosis and to adjust management accordingly. Given longer half-lives and longer duration of effects (e.g., respiratory depression) with ER/LA opioids such as methadone, fentanyl patches, or extended release versions of opioids such as oxycodone, oxymorphone, or morphine, clinicians should not prescribe ER/LA opioids for the treatment of acute pain.

7. **Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids (recommendation category: A, evidence type: 4).**

Although the clinical evidence review did not find studies evaluating the effectiveness of more frequent monitoring intervals (KQ4), it did find that continuing opioid therapy for 3 months substantially increases risk for opioid use disorder (KQ2); therefore, follow-up earlier than 3 months might be necessary to provide the greatest opportunity to prevent the development of opioid use disorder. In addition, risk for overdose associated with ER/LA opioids might be particularly high during the first 2 weeks of treatment (KQ3). The contextual evidence review found that patients who do not have pain relief with opioids at 1 month are unlikely to experience pain relief with opioids at 6 months. Although evidence is insufficient to determine at what point within the first 3 months of opioid therapy the risks for opioid use disorder increase, reassessment of pain and function within 1 month of initiating opioids provides an opportunity to minimize risks of long-term opioid use by discontinuing opioids among patients not receiving a clear benefit from these medications. Experts noted that risks for opioid overdose are greatest during the first 3–7 days after opioid initiation or increase in dosage, particularly when methadone or transdermal fentanyl are prescribed; that follow-up within 3 days is appropriate when initiating or increasing the dosage of methadone; and that follow-up within 1 week might be appropriate when initiating or increasing the dosage of other ER/LA opioids.

Clinicians should evaluate patients to assess benefits and harms of opioids within 1 to 4 weeks of starting long-term opioid therapy or of dose escalation. Clinicians should consider follow-up intervals within the lower end of this range when ER/LA opioids are started or increased or when total daily opioid dosage is ≥50 MME/day. Shorter follow-up intervals (within 3 days) should be strongly considered when starting or increasing the dosage of methadone. At follow up, clinicians should assess benefits in function, pain control, and quality of life using tools such as the three-item "Pain average, interference with Enjoyment of life, and interference with General activity" (PEG) Assessment Scale (*186*) and/or asking patients about progress toward functional goals that have meaning for them (see Recommendation 2). Clinicians should also ask patients about common adverse effects such as constipation and drowsiness (see Recommendation 3), as well as asking about and assessing for effects that might be early warning signs for more serious problems such as overdose (e.g., sedation or slurred speech) or opioid use disorder (e.g., craving, wanting to take opioids in greater quantities or more frequently than prescribed, or difficulty controlling use). Clinicians should ask patients about their preferences for continuing opioids, given their effects on pain and function relative to any adverse effects experienced.

Because of potential changes in the balance of benefits and risks of opioid therapy over time, clinicians should regularly reassess all patients receiving long-term opioid therapy, including patients who are new to the clinician but on long-term opioid therapy, at least every 3 months. At reassessment, clinicians should determine whether opioids continue to meet treatment goals, including sustained improvement in pain and function, whether the patient has experienced common or serious adverse events or early warning signs of serious adverse events, signs of opioid use disorder (e.g., difficulty controlling use, work or family problems related to opioid use), whether benefits of opioids continue to outweigh risks, and whether opioid dosage can be reduced or opioids can be discontinued. Ideally, these reassessments would take place in person and be conducted by the prescribing clinician. In practice contexts where virtual visits are part of standard care (e.g., in remote areas where distance or other issues make follow-up visits challenging), follow-up assessments that allow the clinician to communicate with and observe the patient through video and audio could be conducted, with in-person visits occurring at least once per year. Clinicians should re-evaluate patients who are exposed to greater risk of opioid use disorder or overdose (e.g., patients with depression or other mental health conditions, a history of substance use disorder, a history of overdose, taking ≥50 MME/day, or taking other central nervous system depressants with opioids) more frequently than every 3 months. If clinically meaningful improvements in pain and function are not sustained, if patients are taking high-risk regimens (e.g., dosages ≥50 MME/day or opioids combined with benzodiazepines) without evidence of benefit, if patients believe benefits no longer outweigh risks or if they request dosage reduction or discontinuation, or if patients experience overdose or other serious adverse events (e.g., an event leading to hospitalization or disability) or warning signs of serious adverse events, clinicians should work with patients to reduce opioid dosage or to discontinue opioids when possible. Clinicians should maximize pain treatment with nonpharmacologic and nonopioid pharmacologic treatments as appropriate (see Recommendation 1) and consider consulting a pain specialist as needed to assist with pain management.

Considerations for Tapering Opioids

Although the clinical evidence review did not find high-quality studies comparing the effectiveness of different tapering protocols for use when opioid dosage is reduced or opioids are discontinued (KQ3), tapers reducing weekly dosage by 10%–50% of the original dosage have been recommended by other clinical guidelines (*199*), and a rapid taper over 2–3 weeks has been recommended in the case of a severe adverse event such as overdose (*30*). Experts noted that tapers slower than 10% per week (e.g., 10% per month) also might be appropriate and better tolerated than more rapid tapers, particularly when patients have been taking opioids for longer durations (e.g., for years). Opioid withdrawal during pregnancy has been associated with spontaneous abortion and premature labor.

When opioids are reduced or discontinued, a taper slow enough to minimize symptoms and signs of opioid withdrawal (e.g., drug craving, anxiety, insomnia, abdominal pain, vomiting, diarrhea, diaphoresis, mydriasis, tremor, tachycardia, or piloerection) should be used. A decrease of 10% of the original dose per week is a reasonable starting point; experts agreed that tapering plans may be individualized based on patient goals and concerns. Experts noted that at times, tapers might have to be paused and restarted again when the patient is ready and might have to be slowed once patients reach low dosages. Tapers may be considered successful as long as the patient is making progress. Once the smallest available dose is reached, the interval between doses can be extended. Opioids may be stopped when taken less frequently than once a day. More rapid tapers might be needed for patient safety under certain circumstances (e.g., for patients who have experienced overdose on their current dosage). Ultrarapid detoxification under anesthesia is associated with substantial risks, including death, and should not be used (*200*). Clinicians should access appropriate expertise if considering tapering opioids during pregnancy because of possible risk to the pregnant patient and to the fetus if the patient goes into withdrawal. Patients who are not taking opioids (including patients who are diverting all opioids they obtain) do not require tapers. Clinicians should discuss with patients undergoing tapering the increased risk for overdose on abrupt return to a previously prescribed higher dose. Primary care clinicians should collaborate with mental health providers and with other specialists as needed to optimize nonopioid pain management (see Recommendation 1), as well as psychosocial support for anxiety related to the taper. More detailed guidance on tapering, including management of withdrawal symptoms has been published previously (*30*,*201*). If a patient exhibits signs of opioid use disorder, clinicians should offer or arrange for treatment of opioid use disorder (see Recommendation 12) and consider offering naloxone for overdose prevention (see Recommendation 8).

Assessing Risk and Addressing Harms of Opioid Use

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present (recommendation category: A, evidence type: 4).

The clinical evidence review found insufficient evidence to determine how harms of opioids differ depending on patient demographics or patient comorbidities (KQ2). However, based on the contextual evidence review and expert opinion, certain risk factors are likely to increase susceptibility to opioid-associated harms and warrant incorporation of additional strategies into the management plan to mitigate risk. Clinicians should assess these risk factors periodically, with frequency varying by risk factor and patient characteristics. For example, factors that vary more frequently over time, such as alcohol use, require more frequent follow up. In addition, clinicians should consider offering naloxone, re-evaluating patients more frequently (see Recommendation 7), and referring to pain and/or behavioral health specialists when factors that increase risk for harm, such as history of overdose, history of substance use disorder, higher dosages of opioids (≥50 MME/day), and concurrent use of benzodiazepines with opioids, are present.

Patients with Sleep-Disordered Breathing, Including Sleep Apnea

Risk factors for sleep-disordered breathing include congestive heart failure, and obesity. Experts noted that careful monitoring and cautious dose titration should be used if opioids are prescribed for patients with mild sleep-disordered breathing. Clinicians should avoid prescribing opioids to patients with moderate or severe sleep-disordered breathing whenever possible to minimize risks for opioid overdose (contextual evidence review).

Pregnant Women

Opioids used in pregnancy might be associated with additional risks to both mother and fetus. Some studies have shown an association of opioid use in pregnancy with stillbirth, poor fetal growth, pre-term delivery, and birth defects (contextual evidence review). Importantly, in some cases, opioid use during pregnancy leads to neonatal opioid withdrawal syndrome. Clinicians and patients together should carefully weigh risks and benefits when making decisions

about whether to initiate opioid therapy for chronic pain during pregnancy. In addition, before initiating opioid therapy for chronic pain for reproductive-age women, clinicians should discuss family planning and how long-term opioid use might affect any future pregnancy. For pregnant women already receiving opioids, clinicians should access appropriate expertise if considering tapering opioids because of possible risk to the pregnant patient and to the fetus if the patient goes into withdrawal (see Recommendation 7). For pregnant women with opioid use disorder, medication-assisted therapy with buprenorphine or methadone has been associated with improved maternal outcomes and should be offered (*202*) (see Recommendation 12). Clinicians caring for pregnant women receiving opioids for pain or receiving buprenorphine or methadone for opioid use disorder should arrange for delivery at a facility prepared to monitor, evaluate for, and treat neonatal opioid withdrawal syndrome. In instances when travel to such a facility would present an undue burden on the pregnant woman, it is appropriate to deliver locally, monitor and evaluate the newborn for neonatal opioid withdrawal syndrome, and transfer the newborn for additional treatment if needed. Neonatal toxicity and death have been reported in breast-feeding infants whose mothers are taking codeine (contextual evidence review); previous guidelines have recommended that codeine be avoided whenever possible among mothers who are breast feeding and, if used, should be limited to the lowest possible dose and to a 4-day supply (*203*).

Patients with Renal or Hepatic Insufficiency

Clinicians should use additional caution and increased monitoring (see Recommendation 7) to minimize risks of opioids prescribed for patients with renal or hepatic insufficiency, given their decreased ability to process and excrete drugs, susceptibility to accumulation of opioids, and reduced therapeutic window between safe dosages and dosages associated with respiratory depression and overdose (contextual evidence review; see Recommendations 4, 5, and 7).

Patients Aged ≥65 Years

Inadequate pain treatment among persons aged ≥65 years has been documented (*204*). Pain management for older patients can be challenging given increased risks of both nonopioid pharmacologic therapies (see Recommendation 1) and opioid therapy in this population. Given reduced renal function and medication clearance even in the absence of renal disease, patients aged ≥65 years might have increased susceptibility to accumulation of opioids and a smaller therapeutic window between safe dosages and dosages associated with respiratory depression and overdose (contextual evidence review). Some older adults suffer from cognitive impairment, which can increase risk for medication errors and make opioid-related confusion more dangerous. In addition, older adults are more likely than younger adults to experience co-morbid medical conditions and more likely to receive multiple medications, some of which might interact with opioids (such as benzodiazepines). Clinicians should use additional caution and increased monitoring (see Recommendations 4, 5, and 7) to minimize risks of opioids prescribed for patients aged ≥65 years. Experts suggested that clinicians educate older adults receiving opioids to avoid risky medication-related behaviors such as obtaining controlled medications from multiple prescribers and saving unused medications. Clinicians should also implement interventions to mitigate common risks of opioid therapy among older adults, such as exercise or bowel regimens to prevent constipation, risk assessment for falls, and patient monitoring for cognitive impairment.

Patients with Mental Health Conditions

Because psychological distress frequently interferes with improvement of pain and function in patients with chronic pain, using validated instruments such as the Generalized Anxiety Disorder (GAD)-7 and the Patient Health Questionnaire (PHQ)-9 or the PHQ-4 to assess for anxiety, post-traumatic stress disorder, and/or depression (*205*), might help clinicians improve overall pain treatment outcomes. Experts noted that clinicians should use additional caution and increased monitoring (see Recommendation 7) to lessen the increased risk for opioid use disorder among patients with mental health conditions (including depression, anxiety disorders, and PTSD), as well as increased risk for drug overdose among patients with depression. Previous guidelines have noted that opioid therapy should not be initiated during acute psychiatric instability or uncontrolled suicide risk, and that clinicians should consider behavioral health specialist consultation for any patient with a history of suicide attempt or psychiatric disorder (*31*). In addition, patients with anxiety disorders and other mental health conditions are more likely to receive benzodiazepines, which can exacerbate opioid-induced respiratory depression and increase risk for overdose (see Recommendation 11). Clinicians should ensure that treatment for depression and other mental health conditions is optimized, consulting with behavioral health specialists when needed. Treatment for depression can improve pain symptoms as well as depression and might decrease overdose risk (contextual evidence review). For treatment of chronic pain in patients with depression, clinicians should strongly consider using tricyclic or SNRI antidepressants for analgesic as well as antidepressant effects if these medications are not otherwise contraindicated (see Recommendation 1).

Patients with Substance Use Disorder

Illicit drugs and alcohol are listed as contributory factors on a substantial proportion of death certificates for opioid-related overdose deaths (contextual evidence review). Previous guidelines have recommended screening or risk assessment tools to identify patients at higher risk for misuse or abuse of opioids. However, the clinical evidence review found that currently available risk-stratification tools (e.g., Opioid Risk Tool, Screener and Opioid Assessment for Patients with Pain Version 1, SOAPP-R, and Brief Risk Interview) show insufficient accuracy for classification of patients as at low or high risk for abuse or misuse (KQ4). Clinicians should always exercise caution when considering or prescribing opioids for any patient with chronic pain outside of active cancer, palliative, and end-of-life care and should not overestimate the ability of these tools to rule out risks from long-term opioid therapy.

Clinicians should ask patients about their drug and alcohol use. Single screening questions can be used (*206*). For example, the question "How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?" (with an answer of one or more considered positive) was found in a primary care setting to be 100% sensitive and 73.5% specific for the detection of a drug use disorder compared with a standardized diagnostic interview (*207*). Validated screening tools such as the Drug Abuse Screening Test (DAST) (*208*) and the Alcohol Use Disorders Identification Test (AUDIT) (*209*) can also be used. Clinicians should use PDMP data (see Recommendation 9) and drug testing (see Recommendation 10) as appropriate to assess for concurrent substance use that might place patients at higher risk for opioid use disorder and overdose. Clinicians should also provide specific counseling on increased risks for overdose when opioids are combined with other drugs or alcohol (see Recommendation 3) and ensure that patients receive effective treatment for substance use disorders when needed (see Recommendation 12).

The clinical evidence review found insufficient evidence to determine how harms of opioids differ depending on past or current substance use disorder (KQ2), although a history of substance use disorder was associated with misuse. Similarly, based on contextual evidence, patients with drug or alcohol use disorders are likely to experience greater risks for opioid use disorder and overdose than persons without these conditions. If clinicians consider opioid therapy for chronic pain outside of active cancer, palliative, and end-of-life care for patients with drug or alcohol use disorders, they should discuss increased risks for opioid use disorder and overdose with patients, carefully consider whether benefits of opioids outweigh increased risks, and incorporate strategies to mitigate risk into the management plan, such as considering offering naloxone (see Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present) and increasing frequency of monitoring (see Recommendation 7) when opioids are prescribed. Because pain management in patients with substance use disorder can be complex, clinicians should consider consulting substance use disorder specialists and pain specialists regarding pain management for persons with active or recent past history of substance abuse. Experts also noted that clinicians should communicate with patients' substance use disorder treatment providers if opioids are prescribed.

Patients with Prior Nonfatal Overdose

Although studies were not identified that directly addressed the risk for overdose among patients with prior nonfatal overdose who are prescribed opioids, based on clinical experience, experts thought that prior nonfatal overdose would substantially increase risk for future nonfatal or fatal opioid overdose. If patients experience nonfatal opioid overdose, clinicians should work with them to reduce opioid dosage and to discontinue opioids when possible (see Recommendation 7). If clinicians continue opioid therapy for chronic pain outside of active cancer, palliative, and end-of-life care in patients with prior opioid overdose, they should discuss increased risks for overdose with patients, carefully consider whether benefits of opioids outweigh substantial risks, and incorporate strategies to mitigate risk into the management plan, such as considering offering naloxone (see Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present) and increasing frequency of monitoring (see Recommendation 7) when opioids are prescribed.

Offering Naloxone to Patients When Factors That Increase Risk for Opioid-Related Harms Are Present

Naloxone is an opioid antagonist that can reverse severe respiratory depression; its administration by lay persons, such as friends and family of persons who experience opioid overdose, can save lives. Naloxone precipitates acute withdrawal among patients physically dependent on opioids. Serious adverse effects, such as pulmonary edema, cardiovascular instability, and seizures, have been reported but are rare at doses consistent with labeled use for opioid overdose (*210*). The contextual evidence review did not find any studies on effectiveness of prescribing naloxone for overdose prevention among patients prescribed opioids for chronic pain. However, there is evidence for effectiveness of naloxone provision in preventing opioid-related overdose death at the community level through community-based distribution (e.g., through overdose education and naloxone distribution programs in community service agencies) to persons at risk for overdose

(mostly due to illicit opiate use), and it is plausible that effectiveness would be observed when naloxone is provided in the clinical setting as well. Experts agreed that it is preferable not to initiate opioid treatment when factors that increase risk for opioid-related harms are present. Opinions diverged about the likelihood of naloxone being useful to patients and the circumstances under which it should be offered. However, most experts agreed that clinicians should consider offering naloxone when prescribing opioids to patients at increased risk for overdose, including patients with a history of overdose, patients with a history of substance use disorder, patients taking benzodiazepines with opioids (see Recommendation 11), patients at risk for returning to a high dose to which they are no longer tolerant (e.g., patients recently released from prison), and patients taking higher dosages of opioids (≥50 MME/day). Practices should provide education on overdose prevention and naloxone use to patients receiving naloxone prescriptions and to members of their households. Experts noted that naloxone co-prescribing can be facilitated by clinics or practices with resources to provide naloxone training and by collaborative practice models with pharmacists. Resources for prescribing naloxone in primary care settings can be found through Prescribe to Prevent at http://prescribetoprevent.org.

9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months (recommendation category: A, evidence type: 4).

PDMPs are state-based databases that collect information on controlled prescription drugs dispensed by pharmacies in most states and, in select states, by dispensing physicians as well. In addition, some clinicians employed by the federal government, including some clinicians in the Indian Health Care Delivery System, are not licensed in the states where they practice, and do not have access to PDMP data. Certain states require clinicians to review PDMP data prior to writing each opioid prescription (see state-level PDMP-related policies on the National Alliance for Model State Drug Laws website at http://www.namsdl.org/prescription-monitoring-programs.cfm). The clinical evidence review did not find studies evaluating the effectiveness of PDMPs on outcomes related to overdose, addiction, abuse, or misuse (KQ4). However, even though evidence is limited on the effectiveness of PDMP implementation at the state level on prescribing and mortality outcomes (*28*), the contextual evidence review found that most fatal overdoses were associated with patients receiving opioids from multiple prescribers and/or with patients receiving high total daily opioid dosages; information on both of these risk factors for overdose are available to prescribers in the PDMP. PDMP data also can be helpful when patient medication history is not otherwise available (e.g., for patients from other locales) and when patients transition care to a new clinician. The contextual evidence review also found that PDMP information could be used in a way that is harmful to patients. For example, it has been used to dismiss patients from clinician practices (*211*), which might adversely affect patient safety.

The contextual review found variation in state policies that affect timeliness of PDMP data (and therefore benefits of reviewing PDMP data) as well as time and workload for clinicians in accessing PDMP data. In states that permit delegating access to other members of the health care team, workload for prescribers can be reduced. These differences might result in a different balance of benefits to clinician workload in different states. Experts agreed that PDMPs are useful tools that should be consulted when starting a patient on opioid therapy and periodically during long-term opioid therapy. However, experts disagreed on how frequently clinicians should check the PDMP during long-term opioid therapy, given PDMP access issues and the lag time in reporting in some states. Most experts agreed that PDMP data should be reviewed every 3 months or more frequently during long-term opioid therapy. A minority of experts noted that, given the current burden of accessing PDMP data in some states and the lack of evidence surrounding the most effective interval for PDMP review to improve patient outcomes, annual review of PDMP data during long-term opioid therapy would be reasonable when factors that increase risk for opioid-related harms are not present.

Clinicians should review PDMP data for opioids and other controlled medications patients might have received from additional prescribers to determine whether a patient is receiving high total opioid dosages or dangerous combinations (e.g., opioids combined with benzodiazepines) that put him or her at high risk for overdose. Ideally, PDMP data should be reviewed before every opioid prescription. This is recommended in all states with well-functioning PDMPs and where PDMP access policies make this practicable (e.g., clinician and delegate access permitted), but it is not currently possible in states without functional PDMPs or in those that do not permit certain prescribers to access them. As vendors and practices facilitate integration of PDMP information into regular clinical workflow (e.g., data made available in electronic health records), clinicians' ease of access in reviewing PDMP data is expected to improve.

In addition, improved timeliness of PDMP data will improve their value in identifying patient risks.

If patients are found to have high opioid dosages, dangerous combinations of medications, or multiple controlled substance prescriptions written by different clinicians, several actions can be taken to augment clinicians' abilities to improve patient safety:

- Clinicians should discuss information from the PDMP with their patient and confirm that the patient is aware of the additional prescriptions. Occasionally, PDMP information can be incorrect (e.g., if the wrong name or birthdate has been entered, the patient uses a nickname or maiden name, or another person has used the patient's identity to obtain prescriptions).
- Clinicians should discuss safety concerns, including increased risk for respiratory depression and overdose, with patients found to be receiving opioids from more than one prescriber or receiving medications that increase risk when combined with opioids (e.g., benzodiazepines) and consider offering naloxone (see Recommendation 8).
- Clinicians should avoid prescribing opioids and benzodiazepines concurrently whenever possible. Clinicians should communicate with others managing the patient to discuss the patient's needs, prioritize patient goals, weigh risks of concurrent benzodiazepine and opioid exposure, and coordinate care (see Recommendation 11).
- Clinicians should calculate the total MME/day for concurrent opioid prescriptions to help assess the patient's overdose risk (see Recommendation 5). If patients are found to be receiving high total daily dosages of opioids, clinicians should discuss their safety concerns with the patient, consider tapering to a safer dosage (see Recommendations 5 and 7), and consider offering naloxone (see Recommendation 8).
- Clinicians should discuss safety concerns with other clinicians who are prescribing controlled substances for their patient. Ideally clinicians should first discuss concerns with their patient and inform him or her that they plan to coordinate care with the patient's other prescribers to improve the patient's safety.
- Clinicians should consider the possibility of a substance use disorder and discuss concerns with their patient (see Recommendation 12).
- If clinicians suspect their patient might be sharing or selling opioids and not taking them, clinicians should consider urine drug testing to assist in determining whether opioids can be discontinued without causing withdrawal (see Recommendations 7 and 10). A negative drug test for prescribed opioids might indicate the patient is not taking prescribed opioids, although clinicians should consider other possible reasons for this test result (see Recommendation 10).

Experts agreed that clinicians should not dismiss patients from their practice on the basis of PDMP information. Doing so can adversely affect patient safety, could represent patient abandonment, and could result in missed opportunities to provide potentially lifesaving information (e.g., about risks of opioids and overdose prevention) and interventions (e.g., safer prescriptions, nonopioid pain treatment [see Recommendation 1], naloxone [see Recommendation 8], and effective treatment for substance use disorder [see Recommendation 12]).

10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs (recommendation category: B, evidence type: 4).

Concurrent use of opioid pain medications with other opioid pain medications, benzodiazepines, or heroin can increase patients' risk for overdose. Urine drug tests can provide information about drug use that is not reported by the patient. In addition, urine drug tests can assist clinicians in identifying when patients are not taking opioids prescribed for them, which might in some cases indicate diversion or other clinically important issues such as difficulties with adverse effects. Urine drug tests do not provide accurate information about how much or what dose of opioids or other drugs a patient took. The clinical evidence review did not find studies evaluating the effectiveness of urine drug screening for risk mitigation during opioid prescribing for pain (KQ4). The contextual evidence review found that urine drug testing can provide useful information about patients assumed not to be using unreported drugs. Urine drug testing results can be subject to misinterpretation and might sometimes be associated with practices that might harm patients (e.g., stigmatization, inappropriate termination from care). Routine use of urine drug tests with standardized policies at the practice or clinic level might destigmatize their use. Although random drug testing also might destigmatize urine drug testing, experts thought that truly random testing was not feasible in clinical practice. Some clinics obtain a urine specimen at every visit, but only send it for testing on a random schedule. Experts noted that in addition to direct costs of urine drug testing, which often are not covered fully by insurance and can be a burden for patients, clinician time is needed to interpret, confirm, and communicate results.

Experts agreed that prior to starting opioids for chronic pain and periodically during opioid therapy, clinicians should

use urine drug testing to assess for prescribed opioids as well as other controlled substances and illicit drugs that increase risk for overdose when combined with opioids, including nonprescribed opioids, benzodiazepines, and heroin. There was some difference of opinion among experts as to whether this recommendation should apply to all patients, or whether this recommendation should entail individual decision making with different choices for different patients based on values, preferences, and clinical situations. While experts agreed that clinicians should use urine drug testing before initiating opioid therapy for chronic pain, they disagreed on how frequently urine drug testing should be conducted during long-term opioid therapy. Most experts agreed that urine drug testing at least annually for all patients was reasonable. Some experts noted that this interval might be too long in some cases and too short in others, and that the follow-up interval should be left to the discretion of the clinician. Previous guidelines have recommended more frequent urine drug testing in patients thought to be at higher risk for substance use disorder (*30*). However, experts thought that predicting risk prior to urine drug testing is challenging and that currently available tools do not allow clinicians to reliably identify patients who are at low risk for substance use disorder.

In most situations, initial urine drug testing can be performed with a relatively inexpensive immunoassay panel for commonly prescribed opioids and illicit drugs. Patients prescribed less commonly used opioids might require specific testing for those agents. The use of confirmatory testing adds substantial costs and should be based on the need to detect specific opioids that cannot be identified on standard immunoassays or on the presence of unexpected urine drug test results. Clinicians should be familiar with the drugs included in urine drug testing panels used in their practice and should understand how to interpret results for these drugs. For example, a positive "opiates" immunoassay detects morphine, which might reflect patient use of morphine, codeine, or heroin, but this immunoassay does not detect synthetic opioids (e.g., fentanyl or methadone) and might not detect semisynthetic opioids (e.g., oxycodone). However, many laboratories use an oxycodone immunoassay that detects oxycodone and oxymorphone. In some cases, positive results for specific opioids might reflect metabolites from opioids the patient is taking and might not mean the patient is taking the specific opioid for which the test was positive. For example, hydromorphone is a metabolite of hydrocodone, and oxymorphone is a metabolite of oxycodone. Detailed guidance on interpretation of urine drug test results, including which tests to order and expected results, drug detection time in urine, drug metabolism, and other considerations has been published previously (*30*). Clinicians should not test for substances for which results would not affect patient management or for which implications for patient management are unclear. For example, experts noted that there might be uncertainty about the clinical implications of a positive urine drug test for tetrahyrdocannabinol (THC). In addition, restricting confirmatory testing to situations and substances for which results can reasonably be expected to affect patient management can reduce costs of urine drug testing, given the substantial costs associated with confirmatory testing methods. Before ordering urine drug testing, clinicians should have a plan for responding to unexpected results. Clinicians should explain to patients that urine drug testing is intended to improve their safety and should also explain expected results (e.g., presence of prescribed medication and absence of drugs, including illicit drugs, not reported by the patient). Clinicians should ask patients about use of prescribed and other drugs and ask whether there might be unexpected results. This will provide an opportunity for patients to provide information about changes in their use of prescribed opioids or other drugs. Clinicians should discuss unexpected results with the local laboratory or toxicologist and with the patient. Discussion with patients prior to specific confirmatory testing can sometimes yield a candid explanation of why a particular substance is present or absent and obviate the need for expensive confirmatory testing on that visit. For example, a patient might explain that the test is negative for prescribed opioids because she felt opioids were no longer helping and discontinued them. If unexpected results are not explained, a confirmatory test using a method selective enough to differentiate specific opioids and metabolites (e.g., gas or liquid chromatography/mass spectrometry) might be warranted to clarify the situation.

Clinicians should use unexpected results to improve patient safety (e.g., change in pain management strategy [see Recommendation 1], tapering or discontinuation of opioids [see Recommendation 7], more frequent re-evaluation [see Recommendation 7], offering naloxone [see Recommendation 8], or referral for treatment for substance use disorder [see Recommendation 12], all as appropriate). If tests for prescribed opioids are repeatedly negative, confirming that the patient is not taking the prescribed opioid, clinicians can discontinue the prescription without a taper. Clinicians should not dismiss patients from care based on a urine drug test result because this could constitute patient abandonment and could have adverse consequences for patient safety, potentially including the patient obtaining opioids from alternative sources and the clinician missing opportunities to facilitate treatment for substance use disorder.

11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently

whenever possible (recommendation category: A, evidence type: 3).

Benzodiazepines and opioids both cause central nervous system depression and can decrease respiratory drive. Concurrent use is likely to put patients at greater risk for potentially fatal overdose. The clinical evidence review did not address risks of benzodiazepine co-prescription among patients prescribed opioids. However, the contextual evidence review found evidence in epidemiologic series of concurrent benzodiazepine use in large proportions of opioid-related overdose deaths, and a case-cohort study found concurrent benzodiazepine prescription with opioid prescription to be associated with a near quadrupling of risk for overdose death compared with opioid prescription alone (*212*). Experts agreed that although there are circumstances when it might be appropriate to prescribe opioids to a patient receiving benzodiazepines (e.g., severe acute pain in a patient taking long-term, stable low-dose benzodiazepine therapy), clinicians should avoid prescribing opioids and benzodiazepines concurrently whenever possible. In addition, given that other central nervous system depressants (e.g., muscle relaxants, hypnotics) can potentiate central nervous system depression associated with opioids, clinicians should consider whether benefits outweigh risks of concurrent use of these drugs. Clinicians should check the PDMP for concurrent controlled medications prescribed by other clinicians (see Recommendation 9) and should consider involving pharmacists and pain specialists as part of the management team when opioids are co-prescribed with other central nervous system depressants. Because of greater risks of benzodiazepine withdrawal relative to opioid withdrawal, and because tapering opioids can be associated with anxiety, when patients receiving both benzodiazepines and opioids require tapering to reduce risk for fatal respiratory depression, it might be safer and more practical to taper opioids first (see Recommendation 7). Clinicians should taper benzodiazepines gradually if discontinued because abrupt withdrawal can be associated with rebound anxiety, hallucinations, seizures, delirium tremens, and, in rare cases, death (contextual evidence review). A commonly used tapering schedule that has been used safely and with moderate success is a reduction of the benzodiazepine dose by 25% every 1–2 weeks (*213*,*214*). CBT increases tapering success rates and might be particularly helpful for patients struggling with a benzodiazepine taper (*213*). If benzodiazepines prescribed for anxiety are tapered or discontinued, or if patients receiving opioids require treatment for anxiety, evidence-based psychotherapies (e.g., CBT) and/or specific anti-depressants or other nonbenzodiazepine medications approved for anxiety should be offered. Experts emphasized that clinicians should communicate with mental health professionals managing the patient to discuss the patient's needs, prioritize patient goals, weigh risks of concurrent benzodiazepine and opioid exposure, and coordinate care.

12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder (recommendation category: A, evidence type: 2).

Opioid use disorder (previously classified as opioid abuse or opioid dependence) is defined in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) as a problematic pattern of opioid use leading to clinically significant impairment or distress, manifested by at least two defined criteria occurring within a year (http://pcssmat.org/wp-content/uploads/2014/02/5B-DSM-5-Opioid-Use-Disorder-Diagnostic-Criteria.pdf) (*20*).

The clinical evidence review found prevalence of opioid dependence (using DSM-IV diagnosis criteria) in primary care settings among patients with chronic pain on opioid therapy to be 3%–26% (KQ2). As found in the contextual evidence review and supported by moderate quality evidence, opioid agonist or partial agonist treatment with methadone maintenance therapy or buprenorphine has been shown to be more effective in preventing relapse among patients with opioid use disorder (*151–153*). Some studies suggest that using behavioral therapies in combination with these treatments can reduce opioid misuse and increase retention during maintenance therapy and improve compliance after detoxification (*154*,*155*); behavioral therapies are also recommended by clinical practice guidelines (*215*). The cited studies primarily evaluated patients with a history of illicit opioid use, rather than prescription opioid use for chronic pain. Recent studies among patients with prescription opioid dependence (based on DSM-IV criteria) have found maintenance therapy with buprenorphine and buprenorphine-naloxone effective in preventing relapse (*216*,*217*). Treatment need in a community is often not met by capacity to provide buprenorphine or methadone maintenance therapy (*218*), and patient cost can be a barrier to buprenorphine treatment because insurance coverage of buprenorphine for opioid use disorder is often limited (*219*). Oral or long-acting injectable formulations of naltrexone can also be used as medication-assisted treatment for opioid use disorder in nonpregnant adults, particularly for highly motivated persons (*220*,*221*). Experts agreed that clinicians prescribing opioids should identify treatment resources for opioid use disorder in the community and should work together to ensure sufficient treatment capacity for opioid use disorder at the practice level.

If clinicians suspect opioid use disorder based on patient concerns or behaviors or on findings in prescription drug monitoring program data (see Recommendation 9) or from urine drug testing (see Recommendation 10), they should discuss their concern with their patient and provide an opportunity for the patient to disclose related concerns or problems. Clinicians should assess for the presence of opioid use disorder using DSM-5 criteria (*20*). Alternatively, clinicians can arrange for a substance use disorder treatment specialist to assess for the presence of opioid use disorder. For patients meeting criteria for opioid use disorder, clinicians should offer or arrange for patients to receive evidence-based treatment, usually medication-assisted treatment with buprenorphine or methadone maintenance therapy in combination with behavioral therapies. Oral or long-acting injectable naltrexone, a long-acting opioid antagonist, can also be used in non-pregnant adults. Naltrexone blocks the effects of opioids if they are used but requires adherence to daily oral therapy or monthly injections. For pregnant women with opioid use disorder, medication-assisted therapy with buprenorphine (without naloxone) or methadone has been associated with improved maternal outcomes and should be offered (see Recommendation 8). Clinicians should also consider offering naloxone for overdose prevention to patients with opioid use disorder (see Recommendation 8). For patients with problematic opioid use that does not meet criteria for opioid use disorder, experts noted that clinicians can offer to taper and discontinue opioids (see Recommendation 7). For patients who choose to but are unable to taper, clinicians may reassess for opioid use disorder and offer opioid agonist therapy if criteria are met.

Physicians not already certified to provide buprenorphine in an office-based setting can undergo training to receive a waiver from the Substance Abuse and Mental Health Services Administration (SAMHSA) that allows them to prescribe buprenorphine to treat patients with opioid use disorder. Physicians prescribing opioids in communities without sufficient treatment capacity for opioid use disorder should strongly consider obtaining this waiver. Information about qualifications and the process to obtain a waiver are available from SAMHSA (*222*). Clinicians do not need a waiver to offer naltrexone for opioid use disorder as part of their practice.

Additional guidance has been published previously (*215*) on induction, use, and monitoring of buprenorphine treatment (see Part 5) and naltrexone treatment (see Part 6) for opioid use disorder and on goals, components of, and types of effective psychosocial treatment that are recommended in conjunction with pharmacological treatment of opioid use disorder (see Part 7). Clinicians unable to provide treatment themselves should arrange for patients with opioid use disorder to receive care from a substance use disorder treatment specialist, such as an office-based buprenorphine or naltrexone treatment provider, or from an opioid treatment program certified by SAMHSA to provide supervised medication-assisted treatment for patients with opioid use disorder. Clinicians should assist patients in finding qualified treatment providers and should arrange for patients to follow up with these providers, as well as arranging for ongoing coordination of care. Clinicians should not dismiss patients from their practice because of a substance use disorder because this can adversely affect patient safety and could represent patient abandonment. Identification of substance use disorder represents an opportunity for a clinician to initiate potentially life-saving interventions, and it is important for the clinician to collaborate with the patient regarding their safety to increase the likelihood of successful treatment. In addition, although identification of an opioid use disorder can alter the expected benefits and risks of opioid therapy for pain, patients with co-occurring pain and substance use disorder require ongoing pain management that maximizes benefits relative to risks. Clinicians should continue to use nonpharmacologic and nonopioid pharmacologic pain treatments as appropriate (see Recommendation 1) and consider consulting a pain specialist as needed to provide optimal pain management.

Resources to help with arranging for treatment include SAMHSA's buprenorphine physician locator (http://buprenorphine.samhsa.gov/bwns_locator); SAMHSA's Opioid Treatment Program Directory (http://dpt2.samhsa.gov/treatment/directory.aspx); SAMHSA's Provider Clinical Support System for Opioid Therapies (http://pcss-o.org), which offers extensive experience in the treatment of substance use disorders and specifically of opioid use disorder, as well as expertise on the interface of pain and opioid misuse; and SAMHSA's Provider's Clinical Support System for Medication-Assisted Treatment (http://pcssmat.org), which offers expert physician mentors to answer questions about assessment for and treatment of substance use disorders.

Conclusions and Future Directions

Clinical guidelines represent one strategy for improving prescribing practices and health outcomes. Efforts are required to disseminate the guideline and achieve widespread adoption and implementation of the recommendations in clinical settings. CDC will translate this guideline into user-friendly materials for distribution and use by health systems, medical professional societies, insurers, public health departments, health information technology developers, and clinicians and engage in dissemination efforts. CDC has provided a

checklist for prescribing opioids for chronic pain (http://stacks.cdc.gov/view/cdc/38025), additional resources such as fact sheets (http://www.cdc.gov/drugoverdose/prescribing/resources.html), and will provide a mobile application to guide clinicians in implementing the recommendations. CDC will also work with partners to support clinician education on pain management options, opioid therapy, and risk mitigation strategies (e.g., urine drug testing). Activities such as development of clinical decision support in electronic health records to assist clinicians' treatment decisions at the point of care; identification of mechanisms that insurers and pharmacy benefit plan managers can use to promote safer prescribing within plans; and development of clinical quality improvement measures and initiatives to improve prescribing and patient care within health systems have promise for increasing guideline adoption and improving practice. In addition, policy initiatives that address barriers to implementation of the guidelines, such as increasing accessibility of PDMP data within and across states, e-prescribing, and availability of clinicians who can offer medication-assisted treatment for opioid use disorder, are strategies to consider to enhance implementation of the recommended practices. CDC will work with federal partners and payers to evaluate strategies such as payment reform and health care delivery models that could improve patient health and safety. For example, strategies might include strengthened coverage for nonpharmacologic treatments, appropriate urine drug testing, and medication-assisted treatment; reimbursable time for patient counseling; and payment models that improve access to interdisciplinary, coordinated care.

As highlighted in the forthcoming report on the National Pain Strategy, an overarching federal effort that outlines a comprehensive population-level health strategy for addressing pain as a public health problem, clinical guidelines complement other strategies aimed at preventing illnesses and injuries that lead to pain. A draft of the National Pain Strategy has been published previously (*180*). These strategies include strengthening the evidence base for pain prevention and treatment strategies, reducing disparities in pain treatment, improving service delivery and reimbursement, supporting professional education and training, and providing public education. It is important that overall improvements be made in developing the workforce to address pain management in general, in addition to opioid prescribing specifically. This guideline also complements other federal efforts focused on addressing the opioid overdose epidemic including prescriber training and education, improving access to treatment for opioid use disorder, safe storage and disposal programs, utilization management mechanisms, naloxone distribution programs, law enforcement and supply reduction efforts, prescription drug monitoring program improvements, and support for community coalitions and state prevention programs.

This guideline provides recommendations that are based on the best available evidence that was interpreted and informed by expert opinion. The clinical scientific evidence informing the recommendations is low in quality. To inform future guideline development, more research is necessary to fill in critical evidence gaps. The evidence reviews forming the basis of this guideline clearly illustrate that there is much yet to be learned about the effectiveness, safety, and economic efficiency of long-term opioid therapy. As highlighted by an expert panel in a recent workshop sponsored by the National Institutes of Health on the role of opioid pain medications in the treatment of chronic pain, "evidence is insufficient for every clinical decision that a provider needs to make about the use of opioids for chronic pain" (*223*). The National Institutes of Health panel recommended that research is needed to improve our understanding of which types of pain, specific diseases, and patients are most likely to be associated with benefit and harm from opioid pain medications; evaluate multidisciplinary pain interventions; estimate cost-benefit; develop and validate tools for identification of patient risk and outcomes; assess the effectiveness and harms of opioid pain medications with alternative study designs; and investigate risk identification and mitigation strategies and their effects on patient and public health outcomes. It is also important to obtain data to inform the cost feasibility and cost-effectiveness of recommended actions, such as use of nonpharmacologic therapy and urine drug testing. Research that contributes to safer and more effective pain treatment can be implemented across public health entities and federal agencies (*4*). Additional research can inform the development of future guidelines for special populations that could not be adequately addressed in this guideline, such as children and adolescents, where evidence and guidance is needed but currently lacking. CDC is committed to working with partners to identify the highest priority research areas to build the evidence base. Yet, given that chronic pain is recognized as a significant public health problem, the risks associated with long-term opioid therapy, the availability of effective nonpharmacological and nonopioid pharmacologic treatment options for pain, and the potential for improvement in the quality of health care with the implementation of recommended practices, a guideline for prescribing is warranted with the evidence that is currently available. The balance between the benefits and the risks of long-term opioid therapy for chronic pain based on both clinical and contextual evidence is strong enough to support the issuance of category A recommendations in most cases.

CDC will revisit this guideline as new evidence becomes available to determine when evidence gaps have been sufficiently closed to warrant an update of the guideline. Until this research is conducted, clinical practice guidelines will have to be based on the best available evidence and expert opinion. This guideline is intended to improve communication between clinicians and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death. CDC is committed to evaluating the guideline to identify the impact of the recommendations on clinician and patient outcomes, both intended and unintended, and revising the recommendations in future updates when warranted.

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TABLE 1. Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Effectiveness and comparative effectiveness (KQ1)							
Effectiveness of long-term opioid therapy versus placebo or no opioid therapy for long-term (≥1 year) outcomes							
Pain, function, and quality of life	None	—[†]	—	—	Insufficient	—	No evidence
Harms and adverse events (KQ2)							
Risks of opioids versus placebo or no opioids on opioid abuse, addiction, and related outcomes; overdose; and other harms							
Abuse or addiction	1 cohort study (n = 568,640)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	One retrospective cohort study found long-term use of prescribed opioids associated with an increased risk of abuse or dependence diagnosis versus no opioid use (adjusted OR ranged from 14.9 to 122.5, depending on dose).
Abuse or addiction	10 uncontrolled studies (n = 3,780)	Very serious limitations	Very serious inconsistency	No imprecision	4	None identified	In primary care settings, prevalence of opioid abuse ranged from 0.6% to 8% and prevalence of dependence from 3% to 26%. In pain clinic settings, prevalence of misuse ranged from 8% to 16% and addiction from 2% to 14%. Prevalence of aberrant drug-related behaviors ranged from 6% to 37%.
Overdose	1 cohort study (n = 9,940)	Serious limitations	Unknown (1 study)	Serious imprecision	3	None identified	Current opioid use associated with increased risk of any overdose events (adjusted HR 5.2, 95% CI = 2.1–12) and serious overdose events (adjusted HR 8.4, 95% CI = 2.5–28) versus current nonuse.
Fractures	1 cohort study (n = 2,341) and 1 case–control study (n = 21,739 case patients)	Serious limitations	No inconsistency	No imprecision	3	None identified	Opioid use associated with increased risk of fracture in 1 cohort study (adjusted HR 1.28, 95% CI = 0.99–1.64) and 1 case-control study (adjusted OR 1.27, 95% CI = 1.21–1.33).
Myocardial infarction	1 cohort study (n = 426,124) and 1 case–control study (n = 11,693 case patients)	No limitations	No inconsistency	No imprecision	3	None identified	Current opioid use associated with increased risk of myocardial infarction versus nonuse (adjusted OR 1.28, 95% CI = 1.19–1.37 and incidence rate ratio 2.66, 95% CI = 2.30–3.08).
Endocrinologic harms	1 cross-sectional study (n = 11,327)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	Long-term opioid use associated with increased risk for use of medications for erectile dysfunction or testosterone replacement versus nonuse (adjusted OR 1.5, 95% CI = 1.1–1.9).
How do harms vary depending on the opioid dose used?							
Abuse or addiction	1 cohort study (n = 568,640)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	One retrospective cohort study found higher doses of long-term opioid therapy associated with increased risk of opioid abuse or dependence than lower doses. Compared to no opioid prescription, the adjusted odds ratios were 15 (95% CI = 10–21) for 1 to 36 MME/day, 29 (95 % CI = 20–41) for 36 to120 MME/day, and 122 (95 % CI = 73–205) for ≥120 MME/day.
Overdose	1 cohort study (n = 9,940) and 1 case–control study (n = 593 case patients in primary analysis)	Serious limitations	No inconsistency	No imprecision	3	Magnitude of effect, dose response relationship	Versus 1 to <20 MME/day, one cohort study found an adjusted HR for an overdose event of 1.44 (95% CI = 0.57–3.62) for 20 to <50 MME/day that increased to 8.87 (95% CI = 3.99–19.72) at ≥100 MME/day; one case-control study found an adjusted OR for an opioid-related death of 1.32 (95% CI = 0.94–1.84) for 20 to 49 MME/day that increased to 2.88 (95% CI = 1.79–4.63) at ≥200 MME/day.
Fractures	1 cohort study (n = 2,341)	Serious limitations	Unknown (1 study)	Serious imprecision	3	None identified	Risk of fracture increased from an adjusted HR of 1.20 (95% CI = 0.92–1.56) at 1 to <20 MME/day to 2.00 (95% CI = 1.24–3.24) at ≥50 MME/day; the trend was of borderline statistical significance.

See table footnotes on page 47.

TABLE 1. (*Continued*) Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Myocardial infarction	1 cohort study (n = 426,124)	Serious limitations	Unknown (1 study)	No imprecision	3	None identified	Relative to a cumulative dose of 0 to 1,350 MME during a 90-day period, the incidence rate ratio for myocardial infarction for 1350 to <2700 MME was 1.21 (95% CI = 1.02–1.45), for 2,700 to <8,100 MME was 1.42 (95% CI = 1.21–1.67), for 8,100 to <18,000 MME was 1.89 (95% CI = 1.54–2.33), and for ≥18,000 MME was 1.73 (95% CI = 1.32–2.26).
Motor vehicle crash injuries	1 case–control study (n = 5,300 case patients)	No limitations	Unknown (1 study)	No imprecision	3	None identified	No association between opioid dose and risk of motor vehicle crash injuries even though opioid doses >20 MME/day were associated with increased odds of road trauma among drivers.
Endocrinologic harms	1 cross-sectional study (n = 11,327) New for update: 1 additional cross-sectional study (n=1,585)	Serious limitations	Consistent	No imprecision	3	None identified	Relative to 0 to <20 MME/day, the adjusted OR for ≥120 MME/day for use of medications for erectile dysfunction or testosterone replacement was 1.6 (95% CI = 1.0–2.4). One new cross-sectional study found higher-dose long-term opioid therapy associated with increased risk of androgen deficiency among men receiving immediate-release opioids (adjusted OR per 10 MME/day 1.16, 95% CI = 1.09–1.23), but the dose response was very weak among men receiving ER/LA opioids.
Dosing strategies (KQ3)							
Comparative effectiveness of different methods for initiating opioid therapy and titrating doses							
Pain	3 randomized trials (n = 93)	Serious limitations	Serious inconsistency	Very serious imprecision	4	None identified	Trials on effects of titration with immediate-release versus ER/LA opioids reported inconsistent results and had additional differences between treatment arms in dosing protocols (titrated versus fixed dosing) and doses of opioids used.
Overdose	New for update: 1 cohort study (n = 840,606)	Serious limitations	Unknown (1 study)	No imprecision	4	None identified	One new cross-sectional study found initiation of therapy with an ER/LA opioid associated with increased risk of overdose versus initiation with an immediate-release opioid (adjusted HR 2.33, 95% CI = 1.26–4.32).
Comparative effectiveness of different ER/LA opioids							
Pain and function	3 randomized trials (n = 1,850)	Serious limitations	No inconsistency	No imprecision	3	None identified	No differences
All-cause mortality	1 cohort study (n = 108,492) New for update: 1 cohort study (n = 38,756)	Serious limitations	Serious inconsistency	No imprecision	4	None identified	One cohort study found methadone to be associated with lower all-cause mortality risk than sustained-release morphine in a propensity-adjusted analysis (adjusted HR 0.56, 95% CI = 0.51–0.62) and one cohort study among Tennessee Medicaid patients found methadone to be associated with higher risk of all-cause mortality than sustained-release morphine (adjusted HR 1.46, 95% CI = 1.17–1.73).
Abuse and related outcomes	1 cohort study (n = 5,684)	Serious limitations	Unknown (1 study)	Serious imprecision	4	None identified	One cohort study found some differences between ER/LA opioids in rates of adverse outcomes related to abuse, but outcomes were nonspecific for opioid-related adverse events, precluding reliable conclusions.
ER/LA versus immediate-release opioids							
Endocrinologic harms	New for update: 1 cross-sectional study (n = 1,585)	Serious limitations	Unknown (1 study)	No imprecision	4	None identified	One cross-sectional study found ER/LA opioids associated with increased risk of androgen deficiency versus immediate-release opioids (adjusted OR 3.39, 95% CI = 2.39–4.77).

See table footnotes on page 47.

TABLE 1. (*Continued*) Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Dose escalation versus dose maintenance or use of dose thresholds							
Pain, function, or withdrawal due to opioid misuse	1 randomized trial (n = 140)	Serious limitations	Unknown (1 study)	Very serious imprecision	3	None identified	No difference between more liberal dose escalation versus maintenance of current doses in pain, function, or risk of withdrawal due to opioid misuse, but there was limited separation in opioid doses between groups (52 versus 40 MME/day at the end of the trial).
Immediate-release versus ER/LA opioids; immediate-release plus ER/LA opioids versus ER/LA opioids alone; scheduled and continuous versus as-needed dosing of opioids; or opioid rotation versus maintenance of current therapy							
Pain, function, quality of life, and outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effects of decreasing or tapering opioid doses versus continuation of opioid therapy							
Pain and function	1 randomized trial (n = 10)	Very serious limitations	Unknown (1 study)	Very serious imprecision	4	None identified	Abrupt cessation of morphine was associated with increased pain and decreased function compared with continuation of morphine.
Comparative effectiveness of different tapering protocols and strategies							
Opioid abstinence	2 nonrandomized trials (n = 150)	Very serious limitations	No inconsistency	Very serious imprecision	4	None identified	No clear differences between different methods for opioid discontinuation or tapering in likelihood of opioid abstinence after 3–6 months
Risk assessment and risk mitigation strategies (KQ4)							
Diagnostic accuracy of instruments for predicting risk for opioid overdose, addiction, abuse, or misuse among patients with chronic pain being considered for long-term opioid therapy							
Opioid risk tool	3 studies of diagnostic accuracy (n = 496) New for update: 2 studies of diagnostic accuracy (n = 320)	Serious limitations	Very serious inconsistency	Serious imprecision	4	None identified	Based on a cutoff score of >4 (or unspecified), five studies (two fair-quality, three poor-quality) reported sensitivity that ranged from 0.20 to 0.99 and specificity that ranged from 0.16 to 0.88.
Screener and Opioid Assessment for Patients with Pain, Version 1	2 studies of diagnostic accuracy (n = 203)	Very serious limitations	No inconsistency	Serious imprecision	3	None identified	Based on a cutoff score of ≥8, sensitivity was 0.68 and specificity was 0.38 in one study, for a positive likelihood ratio of 1.11 and a negative likelihood ratio of 0.83. Based on a cutoff score of >6, sensitivity was 0.73 in one study.
Screener and Opioid Assessment for Patients with Pain-Revised	New for update: 2 studies of diagnostic accuracy (n = 320)	Very serious limitations	No inconsistency	Serious imprecision	3	None identified	Based on a cutoff score of >3 or unspecified, sensitivity was 0.25 and 0.53 and specificity was 0.62 and 0.73 in two studies, for likelihood ratios close to 1.
Brief Risk Interview	New for update: 2 studies of diagnostic accuracy (n = 320)	Very serious limitations	No inconsistency	Serious imprecision	3	None identified	Based on a "high risk" assessment, sensitivity was 0.73 and 0.83 and specificity was 0.43 and 0.88 in two studies, for positive likelihood ratios of 1.28 and 7.18 and negative likelihood ratios of 0.63 and 0.19.

See table footnotes on page 47.

TABLE 1. (*Continued*) Grading of Recommendations Assessment, Development and Evaluation (GRADE) clinical evidence review ratings of the evidence for the key clinical questions regarding effectiveness and risks of long-term opioid therapy for chronic pain

Outcome	Studies	Limitations	Inconsistency	Imprecision	Type of evidence	Other factors	Estimates of effect/findings
Effectiveness of risk prediction instruments on outcomes related to overdose, addiction, abuse, or misuse in patients with chronic pain							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effectiveness of risk mitigation strategies, including opioid management plans, patient education, urine drug screening, use of prescription drug monitoring program data, use of monitoring instruments, more frequent monitoring intervals, pill counts, and use of abuse-deterrent formulations, on outcomes related to overdose, addiction, abuse, or misuse							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effectiveness of risk prediction instruments on outcomes related to overdose, addiction, abuse, or misuse in patients with chronic pain							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effectiveness of risk mitigation strategies, including opioid management plans, patient education, urine drug screening, use of prescription drug monitoring program data, use of monitoring instruments, more frequent monitoring intervals, pill counts, and use of abuse-deterrent formulations, on outcomes related to overdose, addiction, abuse, or misuse							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Comparative effectiveness of treatment strategies for managing patients with addiction to prescription opioids							
Outcomes related to abuse	None	—	—	—	Insufficient	—	No evidence
Effects of opioid therapy for acute pain on long-term use (KQ5)							
Long-term opioid use	New for update: 2 cohort studies (n = 399,852)	Serious limitations	No inconsistency	No imprecision	3	None identified	One study found use of opioids within 7 days of low-risk surgery associated with increased likelihood of opioid use at 1 year (adjusted OR 1.44, 95% CI = 1.39–1.50), and one study found use of opioids within 15 days of onset of low back pain among workers with a compensation claim associated with increased risk of late opioid use (adjusted OR 2.08, 95% CI = 1.55–2.78 for 1 to 140 MME/day and OR 6.14, 95% CI = 4.92–7.66 for ≥450 MME/day).

Abbreviations: CI = confidence interval; ER/LA = extended release/long-acting; HR = hazard ratio; MME = morphine milligram equivalents; OR = odds ratio.
* Ratings were made per GRADE quality assessment criteria; "no limitations" indicates that limitations assessed through the GRADE method were not identified.
† Not applicable as no evidence was available for rating.

TABLE 2. Morphine milligram equivalent (MME) doses for commonly prescribed opioids

Opioid	Conversion factor*
Codeine	0.15
Fentanyl transdermal (in mcg/hr)	2.4
Hydrocodone	1
Hydromorphone	4
Methadone	
1–20 mg/day	4
21–40 mg/day	8
41–60 mg/day	10
≥61–80 mg/day	12
Morphine	1
Oxycodone	1.5
Oxymorphone	3
Tapentadol†	0.4

Source: Adapted from Von Korff M, Saunders K, Ray GT, et al. Clin J Pain 2008;24:521–7 and Washington State Interagency Guideline on Prescribing Opioids for Pain (http://www.agencymeddirectors.wa.gov/Files/2015AMDGOpioidGuideline.pdf).

* Multiply the dose for each opioid by the conversion factor to determine the dose in MMEs. For example, tablets containing hydrocodone 5 mg and acetaminophen 300 mg taken four times a day would contain a total of 20 mg of hydrocodone daily, equivalent to 20 MME daily; extended-release tablets containing oxycodone 10mg and taken twice a day would contain a total of 20mg of oxycodone daily, equivalent to 30 MME daily. The following cautions should be noted: 1) All doses are in mg/day except for fentanyl, which is mcg/hr. 2) Equianalgesic dose conversions are only estimates and cannot account for individual variability in genetics and pharmacokinetics. 3) Do not use the calculated dose in MMEs to determine the doses to use when converting opioid to another; when converting opioids the new opioid is typically dosed at substantially lower than the calculated MME dose to avoid accidental overdose due to incomplete cross-tolerance and individual variability in opioid pharmacokinetics. 4) Use particular caution with methadone dose conversions because the conversion factor increases at higher doses. 5) Use particular caution with fentanyl since it is dosed in mcg/hr instead of mg/day, and its absorption is affected by heat and other factors.

† Tapentadol is a mu receptor agonist and norepinephrine reuptake inhibitor. MMEs are based on degree of mu-receptor agonist activity, but it is unknown if this drug is associated with overdose in the same dose-dependent manner as observed with medications that are solely mu receptor agonists.

Steering Committee and Core Expert Group Members

Steering Committee: *Deborah Dowell, MD, Tamara M. Haegerich, PhD; Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, CDC; Roger Chou, MD; on detail to CDC under contract.*

Core Expert Group Members: *Pam Archer, MPH, Oklahoma State Department of Health; Jane Ballantyne, MD; University of Washington (retired); Amy Bohnert, PhD; University of Michigan; Bonnie Burman, ScD; Ohio Department on Aging; Roger Chou, MD; on detail to CDC under contract; Phillip Coffin, MD, San Francisco Department of Public Health; Gary Franklin, MD, MPH; Washington State Department of Labor and Industries/University of Washington; Erin Krebs, MDH; Minneapolis VA Health Care System/University of Minnesota; Mitchel Mutter, MD, Tennessee Department of Health; Lewis Nelson, MD; New York University School of Medicine; Trupti Patel, MD, Arizona Department of Health Services; Christina A. Porucznik, PhD, University of Utah; Robert "Chuck" Rich, MD, FAAFP, American Academy of Family Physicians; Joanna Starrels, MD, Albert Einstein College of Medicine of Yeshiva University; Michael Steinman, MD, Society of General Internal Medicine; Thomas Tape, MD, American College of Physicians; Judith Turner, PhD, University of Washington.*

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Opioid Guideline Workgroup

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Workgroup Members: *Anne Burns, RPh; Penney Cowan; Chinazo Cunningham, MD, MS; Katherine Galluzzi, DO; Traci Green, PhD, MSC; Mitchell Katz, MD; Erin Krebs, MD, MPH; Gregory Terman, MD, PhD; Mark Wallace, MD. Workgroup Consultants: Roger Chou, MD; Edward Covington, MD; Diana Eppolito; Michael Greene, MD; Steven Stanos, DO.*

Peer Reviewers

Jeanmarie Perrone, MD, University of Pennsylvania; Matthew Bair, MD, Indiana University School of Medicine;, David Tauben, MD, University of Washington.

NCIPC Board of Scientific Counselors

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BUSINESS, CONSUMER SERVICES AND HOUSING AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
GOVERNOR EDMUND G. BROWN JR.

January 13, 2016

Submitted via: https://www.federalregister.gov/articles/2015/12/14/2015-31375/proposed-2016-guideline-for-prescribing-opioids-for-chronic-pain#open-comment

Re: Centers for Disease Control and Prevention, Docket No. CDC-2015-0112

The California State Board of Pharmacy writes this letter in support of the Center for Disease Control and Prevention's draft guidelines for Prescribing Opioids for Chronic Pain. We recognize and acknowledge the substantial effort which the CDC committed to producing these guidelines. We believe they provide meaningful direction and guidance to prescribers and dispensers, and will greatly benefit public health.

The California State Board of Pharmacy is the nation's largest board of pharmacy. We regulate over 140,000 businesses and individuals that dispense, compound, store, ship and transport prescription drugs and prescription devices to patients, practitioners and health care facilities within and outside California. This includes pharmacies, sterile compounding pharmacies, pharmacists, drug wholesalers. The board is mandated to address public safety needs first, a mandate the board takes seriously.

The board has been a strong advocate of addressing prescription drug abuse, an area we recognize that the CDC has declared an epidemic in the US. We have been aggressive in identifying and removing practitioners who failed to exercise their required corresponding responsibility to ensure medication dispensed, even when prescribed, is appropriate for the patient. We have conducted educational sessions and conferences, and developed materials to educate licensees about this topic. The board has also worked with a number of agencies to produce and share consumer and licensee materials on the topic.

As the nation transitions away from the widespread prescribing and dispensing of opioids, prescribers and dispensers look for guidance. In California, the California Medical Board revised *Guidelines for Prescribing Controlled Substances for Pain* in late 2014. Your guidance document will provide additional, much needed, guidance to pharmacists as they exercise their corresponding responsibility to ensure that medication dispensed by pharmacies, and patient care provided by pharmacists is appropriate. It will also enable pharmacists to work with prescribers in developing and supporting strong patient care.

Once finalized, the board will aid in the dissemination of this information to our licensees and to the public. The succinct presentation provided in Box 1 Recommendations for Prescribing Opioids for Chronic Pain Outside of Active Cancer, Palliative and End-of-Life Care is well-designed for such education.

We congratulate the CDC on the development of this guideline. Thank you.

Sincerely,

Virginia Herold
Executive Officer
California State Board of Pharmacy

Attachment 6

Excerpt of the February 2016 Board Meeting Minutes

Registration of Automated Delivery Devices in Use

President Gutierrez explained that pharmacies are able to operate automated dispensing machines or devices in various settings away from the licensed pharmacy. This includes in:

- Skilled nursing homes and other health care facilities licensed under Health and Safety Code section 1250 (c), (d) or (k) (the devices are authorized under section 1261.6 of the Health and Safety Code, authority for pharmacies to do this in specific locations is specified in Business and Professions Code section 4119.1)
- Clinics licensed under section 4180 of the Business and Professions Code (the devices are authorized under section 4186) – these include licensed, nonprofit community or free clinics defined under Health and Safety Code 1204(a)(1), a clinic operated by a federally recognized Indian tribe or tribal organization referred to in Health and Safety Code section 1206(b), a clinic operated by a primary care community or free clinic operated on a separate premises from a licensed clinic and that is open no more than 20 hours per week as referred to in Health and Safety Code section 1206(h), a student health center clinic operated by a public institution of higher education such as college health center as referred to in Health and Safety Code section 1206(j).
- Hospitals may use Pyxis or Pyxis-type machines throughout a hospital to store medication under application of provisions in Title 22 that allow drugs to be stored in nursing stations. The Pyxis and like devices are considered secured storage units for drugs.

President Gutierrez explained that the board has no idea how many of these machines are in use, where they are in use, or which pharmacy is responsible for any machine.

President Gutierrez reported that the demand for additional use of devices is growing. As scheduled earlier at this meeting, a pilot study is underway that if proven valuable, would allow patients to pick up medication from machines not specifically located in a pharmacy.

President Gutierrez stated that at the September 9, 2015, committee meeting, staff suggested that a simple registration be established for pharmacies that operate each of these machines that identifies their locations, as a beneficial step in board oversight and enforcement. The list could be updated as needed via form submission to the board by a pharmacy adding, moving or removing a machine. This registration could operate much like the off-site storage waivers for records waivers. Then at annual renewal of the pharmacy, the pharmacy would update or confirm the list of machines it operates and where each is located. President Gutierrez noted that a regulation or statutory amendment is likely needed to establish this requirement.

The board reviewed the draft language provided by board staff.

Note: the draft language is provided immediately following these minutes.

President Gutierrez asked board staff to clearly define the term “devices” as there are many different types of devices that store medication. Ms. Sodergren explained that the language references the health and safety code that defines devices. President Gutierrez agreed that the definition of device in the health and safety code was appropriate and did not need augmentation.

Ms. Veale asked the board to consider requiring inventory of the automated dispensing machines be taken a specific number of times per year.

Dr. Steve Gray, representing Kaiser, asked the board to consider creating separate requirements for automated dispensing devices that are being used in hospitals as they are more likely to be moved to different areas in within the hospital. President Gutierrez stated that the board may consider exempting the reporting of location changes for devices that are being used under a consolidated hospital license.

Dr. Gray stated that small hospitals that do not have a pharmacy (hospitals with less than 100 beds) may need different requirements than larger hospitals.

Dr. Gray noted that any machine that contains controlled substances would require DEA registration; he recommended that board address this requirement in the language.

Dr. Gray asked if unused medication in the machines could be transferred back to the hospital pharmacy. Ms. Herold confirmed that the drugs in the machine are part of the pharmacy inventory and could be transferred from the machine back to the pharmacy.

Stan Goldenberg, pharmacist, stated that most machines have an automated inventory program that sends inventory reports to the pharmacy. He recommended that the board consider this automated inventory feature when drafting the language.

Dr. Robert Stein, representing KGI School of Pharmacy, recommended that the board require hospitals to report the location dispensing devices that are being used in sites outside of the physical address of the main hospital.

The board asked staff to modify the draft language based on the discussion and bring it to the Enforcement Committee for further review and discussion.

Attachment 7

Excerpt of the February 2016 Board Meeting Minutes

Proposal for Routine Inspections of Pharmacies Every Four Years

Note: Mr. Brooks returned to the meeting at 2:07 p.m.

President Gutierrez explained that the board's charge is to regulate the pharmacy profession necessitates routine inspections of licensed facilities to confirm adherence to or identify failures in adherence to the requirements of pharmacy law. Failure to perform such inspections means that the board's enforcement program is reactive rather than proactive and relies solely on being advised of a potential violation of pharmacy law via a complaint or other information that would trigger an investigation.

President Gutierrez reported that for a number of years the board has wanted to inspect all facilities every three or four years. The board has been unable to complete these routine inspections of all facilities with any regularity, and in recent years has had to substantially reduce such inspections. She noted that while inspections are completed, inspections occur generally as part of the investigative process, prior to issuance or renewal of a sterile compounding license or as part of probation monitoring.

President Gutierrez stated that mandatory inspections on a routine but random basis would enable the board to perform compliance inspections to educate licensees about pharmacy law as well as identify problems early to prevent more serious consumer issues from developing. Like all inspections, such inspections would be unannounced.

President Gutierrez explained that compliance inspections provide an opportunity for board staff to answer questions about pharmacy law and to complete follow up inspections of facilities previously issued either citations or letters of admonishment to confirm compliance.

President Gutierrez reported that mandatory inspections once every four years would be an alternative to our current practice of conducting inspections principally to investigate problems (or inspect sterile compounders).

President Gutierrez explained that the board currently has 6,572 community pharmacies licensed in California. Some of these pharmacies have never been inspected by the board. The creation of a statutory mandate directing the board to perform inspections of all pharmacies every four years would require approximately 1,650 routine inspections annually. She added that over the last two years, the board completed an average of 1,215 inspections annually (routine plus investigation inspections).

President Gutierrez reported that after discussion, the Enforcement Committee made a motion to create a statutory mandate to complete random, unannounced routine inspections of resident pharmacies once every four years.

Ms. Herold explained that currently most pharmacies (with the exception of sterile

compounding pharmacies) are only inspected if they are under investigation for a complaint.

Dr. Castellblanch expressed concern with the ability of the board to complete routine inspections with existing funding and staffing levels. The board discussed how many inspections each inspector would have to complete each year to meet the goal of visiting each pharmacy every four years.

The board asked staff to provide statistics on the types of violations and citations that inspectors find in pharmacies.

Dr. Dang, Supervising Inspector, explained the process that inspectors use to schedule inspections. She also noted that when inspectors are in locations the pharmacy staff uses it as an opportunity to ask law questions. The board encouraged the inspectors to look for ways to improve time their time management so that they can complete more routine inspections.

Brian Warren with CPhA supported the board using routine inspections to educate licensees and promote compliance.

Mr. Law stated that he agreed with the need for routine inspections; however he was unsure of the need to create a statutory mandate. Ms. Herold explained that she recommended creating the mandate to ensure that the board staff redirects resources as needed to meet the requirement.

Note: Mr. Weisser left the meeting at 2:16 p.m.

Dr. Castellblanch stated that he would support creating a statutory mandate.
Mr. Brooks asked if the board would need to increase funding. Ms. Herold responded that board staff believes that the inspections can be completed using existing funding and staffing levels.

The board discussed the need to consider ways to use technology and other recourses to increase productivity.

Board members expressed their support of conducting routine inspections, but questioned the need to make it a statutory mandate.

Megan Harwood, pharmacist, stated her support of increasing routine inspections.

President Gutierrez called for a vote on the committee's recommendation mandate routine inspections every four years.

Committee Recommendation (motion): create a statutory mandate to complete random, unannounced routine inspections of resident pharmacies once every four years.

Support: 5 Oppose: 4 Abstain: 0

Name	Support	Oppose	Abstain	Not Present
Brooks	x			
Butler	x			
Castellblanch	x			
Gutierrez	x			
Law		x		
Lippe		x		
Murphy				x
Sanchez				x
Schaad		x		
Veale	x			
Weisser				x
Wong		x		

The board recessed for a break at 2:45 p.m. and resumed at 3:00 p.m.

When the board returned from the break the members asked to conduct a vote to reconsider the prior motion.

Ms. Freedman recommended that the board members discuss the reason that they would like the vote to be reconsidered to avoid any issues with the Open Meetings Act and to ensure that the board's actions are transparent. Mr. Brooks and President Gutierrez explained that they had discussed their desire to have the board complete the routine inspections without creating a statutory mandate and therefor would like the board to reconsider the issue.

Motion: Reconsider the prior motion.

M/S: Books/Veale

Support: 8 Oppose: 1 Abstain: 1

Name	Support	Oppose	Abstain	Not Present
Brooks	x			
Butler	x			
Castellblanch		x		
Gutierrez	x			
Law	x			
Lippe	x			
Murphy				x
Sanchez				x
Schaad	x			
Veale	x			
Weisser				x
Wong	x			

Ms. Freedman explained that the board could now revote on the motion to create a statutory mandate to complete random, unannounced routine inspections of resident pharmacies once every four years.

Dr. Castellblanch stated that he supports the board creating a statutory mandate to complete routine inspections every four years as it increases public protection.

President Gutierrez and Mr. Law stated that they support routine inspections; however they would like it to be completed via board policy rather than a statutory mandate. Mr. Brooks recommended that when creating the policy the board consider consequences for not completing the inspections.

Ms. Veale stated that this item should be sent back to the Enforcement Committee for further discussion.

Committee Recommendation (motion): create a statutory mandate to complete random, unannounced routine inspections of resident pharmacies once every four years.

Support: 1 Oppose: 8 Abstain: 0

Name	Support	Oppose	Abstain	Not Present
Brooks		x		
Butler		x		
Castellblanch	x			
Gutierrez		x		
Law		x		
Lippe		x		
Murphy				x
Sanchez				x
Schaad		x		
Veale		x		
Weisser				x
Wong		x		

Motion: Instruct the Enforcement Committee discuss the issue further and provide recommendations on how routine inspections could be completed every four years with existing funding and inspector staff.

M/S: Veale/Lippe

Support: 9 Oppose: 0 Abstain: 0

Name	Support	Oppose	Abstain	Not Present
Brooks	x			
Butler	x			
Castellblanch	x			
Gutierrez	x			
Law	x			
Lippe	x			
Murphy				x
Sanchez				x
Schaad	x			
Veale	x			
Weisser				x
Wong	x			

Attachment 8

Board of Pharmacy

Order of Adoption

To Amend § 1735 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735. Compounding in Licensed Pharmacies.

(a) "Compounding" means any of the following activities occurring in a licensed pharmacy, by or under the supervision of a licensed pharmacist, pursuant to a prescription:

(1) Altering the dosage form or delivery system of a drug

(2) Altering the strength of a drug

(3) Combining components or active ingredients

(4) Preparing a compounded drug ~~product~~ preparation from chemicals or bulk drug substances

(b) "Compounding" does not include reconstitution of a drug pursuant to a manufacturer's direction(s) ~~for oral, rectal, topical, or injectable administration~~, nor does it include the sole act of tablet splitting or crushing, capsule opening, or the addition of flavoring agent(s) to enhance palatability.

~~(c) "Compounding" does not include, except in small quantities under limited circumstances as justified by a specific, documented, medical need, preparation of a compounded drug product that is commercially available in the marketplace or that is essentially a copy of a drug product that is commercially available in the marketplace~~

~~(d)~~(c) The parameters and requirements stated by ~~this~~ Article 4.5 (Section 1735 et seq.) apply to all compounding practices. Additional parameters and requirements applicable solely to sterile ~~injectable~~ compounding are stated by Article 7 (Section 1751 et seq.).

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

To Amend § 1735.1 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735.1. Compounding Definitions.

(a) "Ante-area" means an area with ISO Class 8 or better air quality where personnel hand hygiene and garbing procedures, staging of components, and other high-particulate-generating activities are performed, that is adjacent to the area designated for sterile compounding. It is a transition area that begins the systematic reduction of particles, prevents large fluctuations in air temperature and pressures in the cleanroom, and maintains air flows from clean to dirty areas. ISO Class 7 or better air quality is required for ante-areas providing air to a negative pressure room.

(b) "Beyond use date" means the date, or date and time, after which administration of a compounded drug preparation shall not begin, the preparation shall not be dispensed, and the preparation shall not be stored (other than for quarantine purposes).

(c) "Biological Safety Cabinet (BSC)" means a ventilated cabinet for compounding sterile drug preparations, having an open front with inward airflow for personnel protection, downward HEPA-filtered laminar airflow for product protection, and HEPA-filtered exhausted air for environmental protection. Where hazardous drugs are prepared, the exhaust air from the biological safety cabinet shall be appropriately removed by properly designed external building ventilation. This external venting should be dedicated to one BSC or CACI.

(d) "Bulk drug substance" means any substance that, when used in the preparation of a compounded drug preparation, processing, or packaging of a drug, is an active ingredient or a finished dosage form of the drug, but the term does not include any intermediate used in the synthesis of such substances.

(e) "Cleanroom or clean area or buffer area" means a room or area with HEPA-filtered air that provides ISO Class 7 or better air quality where the primary engineering control (PEC) is physically located.

(1) For nonhazardous compounding a positive pressure differential of 0.02- to 0.05-inch water column relative to all adjacent spaces is required.

(2) For hazardous compounding at least 30 air changes per hour of HEPA-filtered supply air and a negative pressure of between 0.01 to 0.03 inches of water column relative to all adjacent spaces is required.

(f) "Compounding Aseptic Containment Isolator (CACI)" means a unidirectional HEPA-filtered airflow compounding aseptic isolator (CAI) designed to provide worker protection from exposure to undesirable levels of airborne drug throughout the compounding and material transfer processes and to provide an aseptic environment for compounding sterile preparations. Air exchange with the surrounding environment should not occur unless the air is first passed through a microbial retentive filter (HEPA minimum) system capable of containing airborne concentrations of the physical size and state of the drug being compounded. Where hazardous drugs are prepared, the exhaust air from the isolator shall be appropriately removed by properly designed external building ventilation. This external venting should be dedicated to one BSC or CACI. Air within the CACI shall not be recirculated nor turbulent.

(g) "Compounding Aseptic Isolator (CAI)" means a form of isolator specifically designed for non-hazardous compounding of pharmaceutical ingredients or preparations while bathed with unidirectional HEPA-filtered air. It is designed to maintain an aseptic compounding environment within the isolator throughout the compounding and material transfer processes. Air exchange into the isolator from the surrounding environment should not occur unless the air has first passed through a microbial retentive filter (HEPA minimum) system capable of containing airborne concentrations of the physical size and state of the drug being compounded. Air within the CAI shall not be recirculated nor turbulent.

(h) "Controlled cold temperature" means 2 degrees to 8 degrees C (35 degrees to 46 degrees F).

(i) "Controlled freezer temperature" means -25 degrees to -10 degrees C (-13 degrees to 14 degrees F) or at a range otherwise specified by the pharmaceutical manufacturer(s) for that product.

(j) "Controlled room temperature" means 20 degrees to 25 degrees C (68 degrees to 77 degrees F).

(k) "Copy or essentially a copy" of a commercially available drug product includes all preparations that are comparable in active ingredients to commercially available drug

products, except that it does not include any preparations in which there has been a change, made for an identified individual patient, which produces for that patient a clinically significant difference, as determined by a prescribing practitioner, between that compounded preparation and the comparable commercially available drug product.

(l) "Daily" means occurring every day the pharmacy is operating, except when daily monitoring of refrigerator and freezer temperature are required, then daily means every 24 hours.

(m) "Displacement airflow method" means a concept which utilizes a low pressure differential, high airflow principle to maintain segregation from the adjacent ante-area by means of specific pressure differentials. This principle of displacement airflow shall require an air velocity of 40 ft per minute or more, from floor to ceiling and wall to wall, from the clean area across the line of demarcation into the ante-area. The displacement concept may not be used to maintain clean area requirements for sterile compounds which originate from any ingredient that was at any time non-sterile, regardless of intervening sterilization of the ingredient, or for hazardous compounds.

(n) "Dosage unit" means a quantity sufficient for one administration to one patient.

(o) "Equipment" means items that must be calibrated, maintained or periodically certified.

(p) "First air" means the air exiting the HEPA filter in a unidirectional air stream that is essentially particle free.

(q) "Gloved fingertip sampling" means a process whereby compounding personnel lightly press each fingertip and thumb of each hand onto appropriate growth media, which are then incubated at a temperature and for a time period conducive to multiplication of microorganisms, and then examined for growth of microorganisms.

(r) "Hazardous" means all anti-neoplastic agents identified by the National Institute for Occupational Safety and Health (NIOSH) as meeting the criteria for a hazardous drug and any other drugs, compounds, or materials identified as hazardous by the pharmacist-in-charge.

(s) "Integrity" means retention of potency until the ~~expiration~~ beyond use date ~~noted~~ provided on the label, so long as the preparation is stored and handled according to the label directions.

(t) "Lot" means one or more compounded drug preparation(s) prepared during one uninterrupted continuous cycle of compounding from one or more common active

ingredient(s).

(u) “Media-fill test” means a test used to measure the efficacy of compounding personnel in aseptic techniques whereby compounding procedures are mimicked using a growth-based media and then the resulting preparation is evaluated for sterility. The media-fill test must mimic the most complex compounding procedures performed by the pharmacy.

(v) “Non-sterile-to-sterile batch” means any compounded drug preparation containing two (2) or more dosage units with any ingredient that was at any time non-sterile, regardless of intervening sterilization of that ingredient.

(w) “Parenteral” means a preparation of drugs administered in a manner other than through the digestive tract. It does not include topical, sublingual, rectal or buccal routes of administration.

(x) “Personal protective equipment” means clothing or devices that protect the employee from exposure to compounding ingredients and/or potential toxins and minimize the contamination of compounded preparations. These include shoe covers, head and facial hair covers, face masks, gowns, and gloves.

(y) “Potency” means active ingredient strength within +/- 10% (or the range specified in USP37-NF32, 37th Revision, Through 2nd Supplement Effective December 1, 2014) of the labeled amount. Sterile injectable products compounded solely from commercially manufactured sterile pharmaceutical products in a health care facility licensed under section 1250 of the Health and Safety Code are exempt from this definition. For those exempt, the range shall be calculated and defined in the master formula.

(z) “Preparation” means a drug or nutrient compounded in a licensed pharmacy; the preparation may or may not be sterile.

(aa) "Prescriber's office" or "prescriber office" means an office or suite of offices in which a prescriber regularly sees patients for outpatient diagnosis and treatment. This definition does not include any hospital, pharmacy, or other facility, whether or not separately licensed, that may be affiliated with, adjacent to, or co-owned by, the prescriber’s practice environment.

(ab) “Primary Engineering Control (PEC)” means a device that provides an ISO Class 5 or better environment through the use of non-turbulent, unidirectional HEPA-filtered first air for

compounding sterile preparations. Examples of PEC devices include, but are not limited to, laminar airflow workbenches, biological safety cabinets, sterile compounding automated robots, compounding aseptic isolators, and compounding aseptic containment isolators.

(ac) "Process validation" means demonstrating that when a process is repeated within specified limits, the process will consistently produce preparations complying with predetermined requirements. If any aspect of the process is changed, the process would need to be revalidated.

(ad) "Product" means a commercially manufactured drug or nutrient evaluated for safety and efficacy by the FDA.

(ae) "Quality" means the absence of harmful levels of contaminants, including filth, putrid, or decomposed substances, ~~and~~ the absence of active ingredients other than those listed on the label, and the absence of inactive ingredients other than those listed on the master formula document.

(af) "Segregated sterile compounding area" means a designated space for sterile-to-sterile compounding where a PEC is located within either a demarcated area (at least three foot perimeter) or in a separate room. Such area or room shall not contain and shall be void of activities and materials that are extraneous to sterile compounding. The segregated sterile compounding area shall not be in a location that has unsealed windows or doors that connect to the outdoors, in a location with high traffic flow, or in a location that is adjacent to construction sites, warehouses, or food preparation. The segregated sterile compounding area shall not have a sink, other than an emergency eye-washing station, located within three feet of a PEC. The segregated sterile compounding area shall be restricted to preparation of sterile-to-sterile compounded preparations.

(1) The BUD of a sterile drug preparation made in a segregated sterile compounding area is limited to 12 hours or less as defined by section 1751.8(d).

(2) When the PEC in the segregated sterile compounding area is a CAI or a CACI and the documentation provided by the manufacturer shows it meets the requirements listed in section 1751.4(f)(1)-(3), the assigned BUD shall comply with section 1751.8(a-b) or (d).

(ag) "Strength" means amount of active ingredient per unit of a compounded drug ~~product~~

preparation.

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

To Amend § 1735.2 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735.2. Compounding Limitations and Requirements; Self-Assessment.

(a) Except as specified in (b) and (c), no drug ~~product~~ preparation shall be compounded prior to receipt by a pharmacy of a valid prescription for an individual patient where the prescriber has approved use of a compounded drug ~~product~~ preparation either orally or in writing. Where approval is given orally, that approval shall be noted on the prescription prior to compounding.

(b) A pharmacy may prepare and store a limited quantity of a compounded drug ~~product~~ preparation in advance of receipt of a patient-specific prescription where and solely in such quantity as is necessary to ensure continuity of care for an identified population of patients of the pharmacy based on a documented history of prescriptions for that patient population.

(c) A "reasonable quantity" ~~as used in~~ that may be furnished to a prescriber for office use by the prescriber as authorized by Business and Professions Code section 4052, subdivision (a)(1), means that amount of compounded drug ~~product~~ preparation that:

(1) ~~i~~Is ordered by the prescriber or the prescriber's agent using a purchase order or other documentation received by the pharmacy prior to furnishing that lists the number of patients seen or to be seen in the prescriber's office for whom the drug is needed or anticipated, and the quantity for each patient that is sufficient for office administration ~~or application to patients in the prescriber's office, or for distribution of not more than a 72-hour supply to the prescriber's patients, as estimated by the prescriber~~; and

(2) Is delivered to the prescriber's office and signed for by the prescriber or the prescriber's agent; and

(3) Is sufficient for administration or application to patients solely in the prescriber's office, or

for furnishing of not more than a 120-hour supply for veterinary medical practices, solely to the prescriber's own veterinary patients seen as part of regular treatment in the prescriber's office, as fairly estimated by the prescriber and documented on the purchase order or other documentation submitted to the pharmacy prior to furnishing; and

~~(2)~~(4) That the pharmacist has a credible basis for concluding it is a reasonable quantity for office use ~~is reasonable~~ considering the intended use of the compounded medication and the nature of the prescriber's practice; and

~~(3)~~ (5) ~~for~~ With regard to any individual prescriber to whom the pharmacy furnishes, and with regard to ~~for~~ all prescribers to whom the pharmacy furnishes, ~~taken as a whole,~~ is an amount which the pharmacy is capable of compounding in compliance with pharmaceutical standards for integrity, potency, quality and strength of the compounded drug ~~product~~ preparation; and

(6) Does not exceed an amount the pharmacy can reasonably and safely compound.

(d) No pharmacy or pharmacist shall compound a drug preparation that:

(1) Is classified by the FDA as demonstrably difficult to compound;

(2) Appears on an FDA list of drugs that have been withdrawn or removed from the market because such drugs or components of such drugs have been found to be unsafe or not effective; or

(3) Is a copy or essentially a copy of one or more commercially available drug products, unless that drug product appears on an ASHP (American Society of Health-System Pharmacists) or FDA list of drugs that are in short supply at the time of compounding and at the time of dispense, and the compounding of that drug preparation is justified by a specific, documented medical need made known to the pharmacist prior to compounding. The pharmacy shall retain a copy of the documentation of the shortage and the specific medical need in the pharmacy records for three years from the date of receipt of the documentation.

~~(d)~~(e) A drug ~~product~~ preparation shall not be compounded until the pharmacy has first prepared a written master formula ~~record~~ document that includes at least the following elements:

(1) Active ingredients to be used.

(2) Equipment to be used.

(3) ~~Expiration dating requirements.~~ The maximum allowable beyond use date for the preparation, and the rationale or reference source justifying its determination.

(4) Inactive ingredients to be used.

(5) ~~Process and/or procedure~~ Specific and essential compounding steps used to prepare the drug.

(6) Quality reviews required at each step in preparation of the drug.

(7) Post-compounding process or procedures required, if any.

(8) Instructions for storage and handling of the compounded drug preparation.

~~(e)~~(f) Where a pharmacy does not routinely compound a particular drug ~~product~~ preparation, the master formula record for that ~~product~~ preparation may be recorded on the prescription document itself.

~~(f)~~(g) The pharmacist performing or supervising compounding is responsible for the integrity, potency, quality, and labeled strength of a compounded drug ~~product~~ preparation until ~~it~~ the beyond use date indicated on the label, so long as label instructions for storage and handling are followed after the preparation is dispensed.

~~(g)~~(h) All chemicals, bulk drug substances, drug products, and other components used for drug compounding shall be stored and used according to compendia~~l~~ and other applicable requirements to maintain their integrity, potency, quality, and labeled strength.

~~(h)~~(i) Every compounded drug ~~product~~ preparation shall be given a~~n expiration~~ beyond use date representing the date or date and time beyond which the compounded drug preparation should not be used, stored, transported or administered, and determined based on the professional judgment of the pharmacist performing or supervising the compounding.~~, in the professional judgment of the pharmacist performing or supervising the compounding, it should not be used.~~

(1) For non-sterile compounded drug preparation(s), the beyond use date ~~This "beyond use date" of the compounded drug product~~ shall not exceed any of the following: ~~180 days from preparation or~~

(A) the shortest expiration date or beyond use date of any ~~component~~ ingredient in the compounded drug ~~product~~ preparation,

(B) the chemical stability of any one ingredient in the compounded drug preparation;

(C) the chemical stability of the combination of all ingredients in the compounded drug preparation,

(D) 180 days for non-aqueous formulations,

(E) 14 days for water-containing oral formulations, and

(F) 30 days for water-containing topical/dermal and mucosal liquid and semisolid formulations.

(2) For sterile compounded drug preparations, the beyond use date shall not exceed any of the following:

(A) The shortest expiration date or beyond use date of any ingredient in the sterile compounded drug product preparation,

(B) The chemical stability of any one ingredient in the sterile compounded drug preparation,

(C) The chemical stability of the combination of all ingredients in the sterile compounded drug preparation, and

(D) The beyond use date assigned for sterility in section 1751.8.

(3) Extension of a beyond use date is only allowable when supported by the following:

(A) Method Suitability Test,

(B) Container Closure Integrity Test, and

(C) Stability Studies

~~unless a longer later date is supported by stability studies of~~

(4) In addition to the requirements of paragraph three (3), the ~~finished~~ drugs or compounded drug ~~products~~ preparations tested and studied shall be ~~using the same~~ identical ~~components~~ in ingredients, specific and essential compounding steps, quality reviews, and packaging as the finished drug or compounded drug preparation.

(5) Shorter dating than set forth in this subsection may be used if it is deemed appropriate in the professional judgment of the responsible pharmacist.

~~(i)~~(j) The pharmacist performing or supervising compounding is responsible for the proper preparation, labeling, storage, and delivery of the compounded drug ~~product~~ preparation.

~~(j)~~ (k) Prior to allowing any drug product preparation to be compounded in a pharmacy, the pharmacist-in-charge shall complete a self-assessment for compounding pharmacies developed

by the board (Incorporated by reference is "Community Pharmacy & Hospital Outpatient Pharmacy Compounding Self-Assessment" Form 17M-39 Rev. 02/12.) as required by Section 1715 of Title 16, Division 17, of the California Code of Regulations. That form contains a first section applicable to all compounding, and a second section applicable to sterile injectable compounding. The first section must be completed by the pharmacist-in-charge before any compounding is performed in the pharmacy. The second section must be completed by the pharmacist-in-charge before any sterile ~~injectable~~ compounding is performed in the pharmacy. The applicable sections of the self-assessment shall subsequently be completed before July 1 of each odd-numbered year, within 30 days of the start date of a new pharmacist-in-charge or change of location, and within 30 days of the issuance of a new pharmacy license. The primary purpose of the self-assessment is to promote compliance through self-examination and education.

(l) Packages of ingredients, both active and inactive, that lack a supplier's expiration date are subject to the following limitations:

(1) such ingredients cannot be used for any non-sterile compounded drug preparation more than three (3) years after the date of receipt by the pharmacy.

(2) such ingredients cannot be used for any sterile compounded drug preparation more than one (1) year after the date of receipt by the pharmacy.

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code, Sections 1735, 1735.1, 1735.8, and 1751.1-1751.8 of Title 16, Division 17, of the California Code of Regulations.

To Amend § 1735.3 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735.3. ~~Records~~ Recordkeeping ~~of~~ for Compounded Drug ~~Products~~ Preparations.

(a) For each compounded drug ~~product~~ preparation, ~~the~~ pharmacy records shall include:

(1) The master formula ~~record~~ document.

(2) A compounding log consisting of a single document containing all of the following:

(A) Name and Strength of the compounded drug preparation.

(B) The date the drug ~~product~~ preparation was compounded.

~~(3)~~(C) The identity of ~~the~~ any pharmacy personnel ~~who compounded the~~ engaged in compounding the drug ~~product~~ preparation.

~~(4)~~(D) The identity of the pharmacist reviewing the final drug ~~product~~ preparation.

~~(5)~~(E) The quantity of each ~~component~~ ingredient used in compounding the drug ~~product~~ preparation.

~~(6)~~(F) The manufacturer, expiration date and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. If the manufacturer does not supply an expiration date for any component, the records shall include the date of receipt of the component in the pharmacy, and the limitations of section 1735.2, subdivision (l) shall apply.

(i) Exempt from the requirements in this paragraph (1735.3(a)(2)(F)) are sterile ~~products~~ preparations compounded ~~on a one- time basis~~ in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code and stored in accordance with standards for "Redispensed CSPs" found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP37-NF32) Through 2nd Supplement (~~35~~ 37th Revision, Effective ~~May~~ December 1, ~~2012~~ 2014), hereby incorporated by reference~~, to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code~~.

~~(7)~~(G) A pharmacy-assigned unique reference or lot number for the compounded drug ~~product~~ preparation.

~~(8)~~(H) The ~~expiration~~ beyond use date or beyond use date and time of the final compounded drug ~~product~~ preparation, expressed in the compounding ~~record~~ document in a standard date and time format.

~~(9)~~(I) The final quantity or amount of drug ~~product~~ preparation compounded for dispensing.

(J) Documentation of quality reviews and required post-compounding process and procedures.

(b) Pharmacies shall maintain records of the proper acquisition, storage, and destruction of chemicals, bulk drug substances, drug products, and components used in compounding.

(c) Active ingredients shall be obtained from a supplier registered with the Food and Drug Administration (FDA). All other ~~C~~chemicals, bulk drug substances, and drug products~~, and components~~ used to compound drug ~~products~~ preparations shall be obtained, whenever possible, from ~~reliable~~ FDA- registered suppliers. The pharmacy shall acquire and retain ~~any available~~ certificates of purity or analysis, either written in English or translated into English, for chemicals, bulk drug substances, and drug products~~, and components~~ used in compounding. Certificates of purity or analysis are not required for drug products that are approved by the FDA. Any certificates of purity or analysis acquired by the pharmacy shall be matched to the corresponding chemical, bulk drug substance, or drug products received.

(d) Pharmacies shall maintain and retain all records required by this article in the pharmacy in a readily retrievable form for at least three years from the date the record was ~~created~~ last in effect. If only recorded and stored electronically, on magnetic media, or in any other computerized form, the records shall be maintained as specified by Business and Professions Code section 4070 subsection (c).

Authority cited: Sections 4005, 4127, and 4169, Business and Professions Code.
Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

To Amend § 1735.4 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735.4. Labeling of Compounded Drug ~~Products~~ Preparations.

(a) Each compounded drug preparation shall be affixed with a container label prior to dispensing that contains at least:

(1) Name of the compounding pharmacy and dispensing pharmacy (if different);

(2) Name (brand or generic) and strength, volume, or weight of each active ingredient. For admixed IV solutions, the intravenous solution utilized shall be included;

(3) Instructions for storage, handling, and administration. For admixed IV solutions, the rate of infusion shall be included;

(4) The beyond use date for the drug preparation;

(5) The date compounded; and

(6) The lot number or pharmacy reference number.

~~In addition to the labeling information required under Business and Professions Code section 4076 and under California Code of Regulations section 1707.5, the label of a compounded drug product preparation shall contain the generic or brand name(s) of the principal all active ingredient(s).~~

(b) Any compounded drug preparation dispensed to a patient or readied for dispensing to a patient shall also include on the label the information required under Business and Professions Code section 4076 and California Code of Regulations, title 16, section 1707.5.

~~A statement that the drug has been compounded by the pharmacy shall be included on the container or on the receipt provided to the patient.~~

(c) Any compounded drug preparation dispensed to a patient or readied for dispensing to a patient shall also include, on the container label or on a receipt provided to the patient, a statement that the drug has been compounded by the pharmacy. ~~Drug products preparations compounded into unit-dose containers that are too small or otherwise impractical for full compliance with subdivisions (a) and (b) shall be labeled with at least the name(s) of the active ingredient(s), concentration or strength, volume or weight of the~~

~~preparation, pharmacy reference or lot number, and expiration date.~~

(d) Prior to dispensing drug preparations compounded into unit-dose containers that are too small or otherwise impractical for full compliance with subdivisions (a), (b), and (c) shall be labeled with at least the name of the compounding pharmacy and dispensing pharmacy, if different, the name(s) of the active ingredient(s), strength, volume or weight of the preparation, pharmacy reference or lot number, and beyond use date, and shall not be subject to minimum font size requirements. Once dispensed, outer packaging must comply with 1735.4(a) – (c).

(e) All hazardous agents shall bear a special label which states "Chemotherapy - Dispose of Properly" or "Hazardous – Dispose of Properly."

Note: Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4076 and 4127, Business and Professions Code.

To Amend § 1735.5 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735.5. Compounding Policies and Procedures.

(a) Any pharmacy engaged in compounding shall maintain ~~a~~ written policy~~y~~ies and procedures ~~manual~~ for compounding that establishes procurement procedures, methodologies for the formulation and compounding of drugs, facilities and equipment cleaning, maintenance, operation, and other standard operating procedures related to compounding. Any material failure to follow the pharmacy's written policies and procedures shall constitute a basis for disciplinary action.

(b) The policy~~y~~ies and procedures ~~manual~~ shall be reviewed and such review shall be documented on an annual basis by the pharmacist-in-charge. ~~and~~ The policies and procedures ~~manual~~ shall be updated whenever changes in policies and procedures ~~processes~~ are implemented.

(c) The policy~~y~~ies and procedures ~~manual~~ shall include at least the following:

(1) Procedures for notifying staff assigned to compounding duties of any changes in ~~processes or to the~~ policy~~y~~ies or procedures ~~manual~~.

(2) ~~Documentation of a~~ A written plan for recall of a dispensed compounded drug ~~product~~ preparation where subsequent ~~verification~~ information demonstrates the potential for adverse effects with continued use ~~of a compounded drug product~~. The plan shall ensure that all affected doses can be accounted for during the recall and shall provide steps to identify which patients received the affected lot or compounded drug preparation(s).

(3) ~~The p~~ Procedures for maintaining, storing, calibrating, cleaning, and disinfecting equipment used in compounding, and for training on these procedures as part of the staff training and competency evaluation process.

(4) Procedures for evaluating, maintaining, certifying, cleaning, and disinfecting the facility (physical plant) used for compounding, and for training on these procedures as part of the staff training and competency evaluation process.

(~~4~~5) Documentation of the methodology used to ~~test~~ validate integrity, potency, quality, and labeled strength of compounded drug ~~products~~ preparations. The methodology must be appropriate to compounded drug preparations.

(~~5~~6) Documentation of the methodology and rationale or reference source used to determine appropriate ~~expiration~~ beyond use dates for compounded drug ~~products~~ preparations.

(7) Dates and signatures reflecting all annual reviews of the policies and procedures by the pharmacist-in-charge.

(8) Dates and signatures accompanying any revisions to the policies and procedures approved by the pharmacist-in-charge.

(9) Policies and procedures for storage of compounded drug preparations in the pharmacy and daily documentation of all room, refrigerator, and freezer temperatures within the pharmacy.

(10) Policies and procedures regarding ensuring appropriate functioning of refrigeration devices, monitoring refrigeration device temperatures, and actions to take regarding any out of range temperature variations within the pharmacy.

(11) Policies and procedures for proper garbing when compounding with hazardous products. This shall include when to utilize double shoe covers.

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, ~~and~~ 4127, and 4301, Business and Professions Code.

To Amend § 1735.6 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735.6. Compounding Facilities and Equipment.

(a) Any pharmacy engaged in compounding shall maintain written documentation regarding the facilities and equipment necessary for safe and accurate compounding of compounded drug ~~products~~ preparations. This shall include records of maintenance and cleaning of the facilities and equipment. Where applicable, this shall also include records of certification(s) of facilities or equipment.

(b) Any equipment used to compound drug ~~products~~ preparations shall be stored, used, ~~and~~ maintained, and cleaned in accordance with manufacturers' specifications.

(c) Any equipment that weighs, measures, or transfers ingredients used to compound drug ~~products~~ preparations for which calibration or adjustment is appropriate shall be calibrated prior to use, on a schedule and by a method determined by the manufacturer's specifications, to ensure accuracy. Documentation of each such calibration shall be recorded ~~in writing~~ in a form which is not alterable and these records of calibration shall be maintained and retained in the pharmacy.

(d) Any pharmacy engaged in any hazardous drug compounding shall maintain written documentation regarding appropriate cleaning of facilities and equipment to prevent cross-contamination with non-hazardous drugs.

(e) Hazardous drug compounding shall be completed in an externally vented physically separate room with the following requirements:

(1) Minimum of 30 air changes per hour except that 12 air changes per hour are acceptable for segregated compounding areas with a BSC or CACI when products are assigned a BUD of 12 hrs or less or when non sterile products are compounded; and

(2) Maintained at a negative pressure of 0.01 to 0.03 inches of water column relative to all adjacent spaces (rooms, above ceiling, and corridors); and

(3) Each PEC in the room shall also be externally vented; and

(4) All surfaces within the room shall be smooth, seamless, impervious, and non-shedding.

(f) Where compliance with the January 1, 2017 amendments to Article 4.5 or Article 7, requires physical construction or alteration to a facility or physical environment, the board or its designee may grant a waiver of such compliance for a period of time to permit such physical change(s). Application for any waiver shall be made by the licensee in writing, and the request shall identify the provision(s) requiring physical construction or alteration, and the timeline for any such change(s). The board or its designee may grant the waiver when, in its discretion, good cause is demonstrated for such waiver.

Note: Authority cited: Sections 4005 and 4127, Business and Professions Code.
Reference: Sections 4005, 4036, 4037, 4051, 4052 and 4127, Business and Professions Code.

To Amend § 1735.7 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735.7. Training of Compounding Staff.

(a) A pharmacy engaged in compounding shall maintain documentation demonstrating that personnel involved in compounding have the skills and training required to properly and accurately perform their assigned responsibilities and documentation demonstrating that all personnel involved in compounding are trained in all aspects of policies and procedures. This training shall include but is not limited to support personnel (e.g. institutional environmental services, housekeeping), maintenance staff, supervising pharmacist and all others whose jobs are related to the compounding process. ~~Any pharmacy engaged in compounding shall maintain written documentation sufficient to demonstrate that pharmacy personnel have the skills and training required to properly and accurately perform their assigned responsibilities relating to compounding.~~

(b) The pharmacy shall develop and maintain an ongoing competency evaluation process for pharmacy personnel involved in compounding, and shall maintain documentation of any and all training related to compounding undertaken by pharmacy personnel.
(c) Pharmacy personnel assigned to compounding duties shall demonstrate knowledge about processes and procedures used in compounding prior to compounding any drug ~~product~~ preparation.

Note: Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052 and 4127, Business and Professions Code.

To Amend § 1735.8 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735.8. Compounding Quality Assurance.

(a) Any pharmacy engaged in compounding shall maintain, as part of its written policies and procedures, a written quality assurance plan designed to monitor and ensure the integrity, potency, quality, and labeled strength of compounded drug ~~products~~ preparations.
(b) The quality assurance plan shall include written procedures for verification, monitoring, and review of the adequacy of the compounding processes and shall also include written documentation of review of those processes by qualified pharmacy personnel.
(c) The quality assurance plan shall include written standards for qualitative and quantitative analysis of compounded drug preparations to ensure integrity, potency, quality, and labeled strength, including the frequency of testing ~~analysis of compounded drug products~~. All qualitative and quantitative analysis reports for compounded drug ~~products~~ preparations shall be retained by the pharmacy and ~~collated~~ maintained along with the compounding log ~~record~~ and master formula document. The quality assurance plan shall include a schedule for routine testing and analysis of specified compounded drug preparations to ensure integrity, potency, quality, and labeled strength, on at least an annual basis.
(d) The quality assurance plan shall include a written procedure for scheduled action in the

event any compounded drug ~~product~~ preparation is ever discovered to be ~~below~~ outside minimum standards for integrity, potency, quality, or labeled strength.

(e) The quality assurance plan shall include a written procedure for responding to out-of-range temperature variations within the pharmacy and within patient care areas of a hospital where furnished drug is returned for redispensing.

Note: Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052 and 4127, Business and Professions Code.

To Amend § 1751 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

Article 7. Sterile ~~Injectable~~ Compounding

1751. Sterile ~~Injectable~~ Compounding; Compounding Area; Self-Assessment.

(a) Any pharmacy engaged in compounding sterile ~~injectable~~ drug ~~products~~ preparations shall conform to the parameters and requirements stated by Article 4.5 (Section 1735 et seq.), applicable to all compounding, and shall also conform to the parameters and requirements stated by this Article 7 (Section 1751 et seq.), applicable solely to sterile ~~injectable~~ compounding.

(b) Any pharmacy compounding sterile ~~injectable~~ drug ~~products~~ preparations shall have a ~~designated~~ compounding area designated for the preparation of sterile ~~injectable~~ drug ~~products~~ preparations that is in a restricted location where traffic has no impact on the performance of the PEC(s). The cleanroom, including the walls, ceilings, and floors, shall be constructed in accordance with Section 1250.4 of Title 24, Part 2, Chapter 12, of the California Code of Regulations. The pharmacy shall be ventilated in a manner in accordance with Section 505.5 of Title 24, Part 4, Chapter 5 of the California Code of Regulations. ~~which shall meet the following standards:~~ The environments within the pharmacy shall meet the following standards:

(1) ~~Clean Room and Work Station Requirements, shall be in accordance with Section 1250 of Title 24, Part 2, Chapter 12, of the California Code of Regulations.~~

~~(2) Walls, ceilings and floors shall be constructed in accordance with Section 1250 of Title 24, Part 2, Chapter 12, of the California Code of Regulations.~~

~~(3) Be ventilated in a manner in accordance with Section 505.12 of Title 24, Chapter 5 of the California Code of Regulations.~~

~~(4) Be~~ Each ISO environment shall be certified ~~annually~~ at least every six months by a qualified technician ~~who is familiar with the methods and procedures for certifying laminar air flow hoods and clean room requirements, in accordance with standards adopted by the United States General Services Administration~~ in accordance with Section 1751.4. Certification records must be retained ~~for at least 3 years~~ in the pharmacy.

~~(5)~~ (2) ~~The pharmacy shall be arranged in accordance with Section 1250 of Title 24, Part 2, Chapter 12, of the California Code of Regulations.~~ Items related to the compounding of sterile ~~injectable~~ drug ~~products~~ preparations within the compounding area shall be stored in such a way as to maintain the integrity of an aseptic environment.

~~(6)~~ (3) A sink shall be included in accordance with Section 1250.4 of Title 24, Part 2, Chapter 12, of the California Code of Regulations. Sinks and drains shall not be present in any ISO Class 7 or better cleanroom, nor in a segregated sterile compounding area within three feet of an ISO Class 5 or better PEC, with the exception of emergency eye-rinsing stations. A sink may be located in an ante-area. When the PEC in the segregated sterile compounding area is a CAI or CACI and the documentation provided by the manufacturer shows it meets the requirements listed in 1751.4(f)(1)-(3) the sterile compounding area is exempt from the room requirement listed in 1751(b)(3).

~~(7)~~ (4) There shall be a refrigerator and~~, /or~~ where appropriate, a freezer, of sufficient capacity to meet the storage requirements for all material requiring refrigeration or freezing, and a backup plan to ensure continuity of available compounded drug preparations in the event of a power outage.

~~(c) Any pharmacy compounding a sterile injectable drug product preparation from one or more non-sterile ingredients shall comply with Business and Professions Code section 4127.7.~~

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127 ~~and 4127.7~~, Business and Professions Code; Sections 1735, 1735.1-1735.8., and 1751.1-1751.8. of Title 16, Division 17, of the California Code of

Regulations; and Section 18944, Health and Safety Code.

To Amend § 1751.1 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.1. Sterile ~~Injectable~~ Compounding Recordkeeping Requirements.

(a) ~~Pharmacies compounding sterile injectable products for future use pursuant to section 1735.2 shall, in addition to those records required by section 1735.3, make and keep records indicating the name, lot number, amount, and date on which the products were provided to a prescriber.~~

~~(b)~~ In addition to the records required by section 1735.3 ~~and subdivision (a)~~, any pharmacy engaged in any compounding of ~~for~~ sterile drug ~~products~~ preparations ~~compounded from one or more non-sterile ingredients,~~ shall maintain the following records, which must be ~~must be made and kept by~~ readily retrievable, within the pharmacy:

(1) ~~The~~ Documents evidencing training and competency evaluations of employees in sterile ~~product~~ drug preparation policies and procedures.

(2) Results of hand hygiene and garbing assessments with integrated gloved fingertip testing.

(3) Results of assessments of personnel for aseptic techniques including results of media-fill tests and gloved fingertip testing performed in association with media-fill tests.

(4) Results of viable air and surface sampling.

(5) Video of smoke studies in all ISO certified spaces.

(6) Documents indicating daily documentation of room, ~~R~~ refrigerator, and freezer temperatures appropriate for sterile compounded drug preparations consistent with the temperatures listed in section 1735.1 for:

(A) Controlled room temperature.

(B) Controlled cold temperature.

(C) Controlled freezer temperature.

(7) Certification(s) of the sterile compounding environment(s).

(8) Documents indicating daily documentation of air pressure differentials or air velocity

measurements between all adjoining ISO rooms or areas, including those associated with compounding aseptic (containment) isolators, and air pressure differentials or air velocity measurements between all rooms or spaces with an immediate entry or opening to ISO rooms or areas.

(9) Other facility quality control ~~logs~~ records specific to the pharmacy's policies and procedures (e.g., cleaning logs for facilities and equipment).

(10) Logs or other documentation of ~~I~~inspections for expired or recalled ~~pharmaceutical products or raw ingredients~~ chemicals, bulk drug substances, drug products, or other ingredients.

(11) Preparation records including the master formula document ~~work sheet~~, the preparation compounding log ~~work sheet~~, and records of end-product evaluation testing and results.

(b) Pharmacies compounding sterile drug preparations for future use pursuant to section 1735.2 shall, in addition to those records required by section 1735.3, make and keep records indicating the name, lot number, and amount of any drug preparation compounded for future use, the date on which any preparation was provided to a prescriber, and the name, address, license type and number of the prescriber.

(c) Pharmacies shall maintain and retain all records required by this article in the pharmacy in a readily retrievable form for at least three years from the date the record was created. If only recorded and stored electronically, on magnetic media, or in any other computerized form, the records shall be maintained as specified by Business and Professions Code section 4070 subsection (c).

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

To Amend § 1751.2 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.2. Sterile ~~Injectable~~ Compounding Labeling Requirements.

In addition to the labeling information required under Business and Professions Code section 4076 and California Code of Regulations, title 16, sections 1707.5 and 1735.4, a pharmacy ~~which~~ that compounds sterile ~~injectable~~ drug ~~products~~ preparations shall include the following information on the label~~s~~ for each such ~~those products~~ preparation:

(a) The ~~T~~telephone number of the pharmacy. ~~, except~~ The telephone number is not required on the label for sterile ~~injectable~~ drug ~~products~~ preparations ~~dispensed~~ administered ~~for~~ to inpatients ~~of a~~ within the hospital ~~pharmacy~~.

~~(b) Name and concentration of ingredients contained in the sterile injectable drug product.~~

(~~c~~b) Instructions for storage, ~~and~~ handling, and administration.~~:~~

(~~d~~c) All ~~cytotoxic~~ hazardous agents shall bear a special label which states "Chemotherapy - Dispose of Properly" or "~~Cytotoxic~~ Hazardous – Dispose of Properly."

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4076 and 4127, Business and Professions Code.

To Amend § 1751.3 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.3. Sterile ~~Injectable~~ Compounding Policies and Procedures.

(a) Any pharmacy engaged in compounding sterile drug preparations shall maintain written policies and procedures for compounding. Any material failure to follow the pharmacy's written policies and procedures shall constitute a basis for disciplinary action. In addition to the elements required by section 1735.5, there shall be written policies and procedures regarding the following:

(1) Action levels for colony-forming units (CFUs) detected during viable surface sampling, glove

fingertip, and viable air sampling and actions to be taken when the levels are exceeded.

(2) Airflow considerations and pressure differential monitoring.

(3) An environmental sampling plan and procedures specific to viable air, surface and gloved fingertip sampling as well as nonviable particle sampling.

(4) Cleaning and maintenance of ISO environments and segregated compounding areas.

(5) Compounded sterile drug preparation stability and beyond use dating.

(6) Compounding, filling, and labeling of sterile drug preparations.

(7) Daily and monthly cleaning and disinfection schedule for the controlled areas and any equipment in the controlled area as specified in section 1751.4.

(8) Depyrogenation of glassware (if applicable)

(9) Facility management including certification and maintenance of controlled environments and related equipment.

(10) For compounding aseptic isolators and compounding aseptic containment isolators, documentation of the manufacturer's recommended purge time.

(11) Hand hygiene and garbing.

(12) Labeling of the sterile compounded drug preparations based on the intended route of administration and recommended rate of administration.

(13) Methods by which the supervising pharmacist will fulfill his or her responsibility to ensure the quality of compounded drug preparations.

(14) Orientation, training, and competency evaluation of staff in all aspects of the preparation of sterile drug preparations including didactic training and knowledge/competency assessments that include at minimum: hand hygiene and garbing; decontamination (where applicable); cleaning and disinfection of controlled compounding areas; and proper aseptic technique, demonstrated through the use of a media-fill test performed by applicable personnel; and aseptic area practices.

(15) Preparing sterile compounded drug preparations from non-sterile components (if applicable). This shall include sterilization method suitability testing for each master formula document.

(16) Procedures for handling, compounding and disposal of hazardous agents. The written

policies and procedures shall describe the pharmacy protocols for cleanups and spills in conformity with local health jurisdiction standards.

(17) Procedures for handling, compounding and disposal of infectious materials. The written policies and procedures shall describe the pharmacy protocols for cleanups and spills in conformity with local health jurisdiction standards.

(18) Proper use of equipment and supplies.

(19) Quality assurance program compliant with sections 1711, 1735.8 and 1751.7.

(20) Record keeping requirements.

(21) Temperature monitoring in compounding and controlled storage areas.

(22) The determination and approval by a pharmacist of ingredients and the compounding process for each preparation before compounding begins.

(23) Use of automated compounding devices (if applicable).

(24) Visual inspection and other final quality checks of sterile drug preparations.

~~(a) Any pharmacy engaged in compounding sterile injectable drug products shall maintain a written policy and procedures manual for compounding that includes, in addition to the elements required by section 1735.5, written policies and procedures regarding the following:~~

~~(1) Compounding, filling, and labeling of sterile injectable compounds.~~

~~(2) Labeling of the sterile injectable product compounded drug preparations based on the intended route of administration and recommended rate of administration.~~

~~(3) Equipment and supplies.~~

~~(4) Training of staff in the preparation of sterile injectable products.~~

~~(5) Procedures for handling cytotoxic agents.~~

~~(6) Quality assurance program.~~

~~(7) Record keeping requirements.~~

~~(b) The ingredients and the compounding process for each preparation must be determined in writing before compounding begins and must be reviewed by a pharmacist.~~

~~(c) Pharmacies compounding sterile injectable drug products preparations shall have written policies and procedures for the disposal of infectious materials and/or materials containing cytotoxic hazardous residues. The written policies and procedures shall describe the pharmacy~~

~~protocols for cleanups and spills in conformity with local health jurisdiction standards.~~

(b) For lot compounding, the pharmacy shall maintain written policies and procedures that includes, in addition to the elements required by section 1735.5 and 1751.3(a), written policies and procedures regarding the following:

(1) Use of master formula documents and compounding logs.

(2) Appropriate documentation.

(3) Appropriate sterility and potency testing.

(c) For non-sterile-to-sterile batch compounding, the pharmacy shall maintain written policies and procedures for compounding that includes, in addition to the elements required by section 1735.5, 1751.3(a), and 1751.7(e), written policies and procedures regarding the following:

(1) Process validation for chosen sterilization methods.

(2) End-product evaluation, quantitative, and qualitative testing.

(d)~~(1) All written p~~Policies and procedures shall be immediately available to all personnel involved in ~~these~~ compounding activities and to board inspectors.

~~(d)(2)~~(e) All personnel involved must read the policies and procedures before compounding sterile ~~injectable products~~ drug preparations.~~, and any~~ All personnel involved must read all additions, revisions, and deletions to the written policies and procedures~~ must be communicated to all personnel involved in sterile compounding~~. Each review must be documented by a signature and date.

~~(3) Policies and procedures must address at least the following:~~

~~(A) Competency evaluation.~~

~~(B) Storage and handling of products and supplies.~~

~~(C) Storage and delivery of final products.~~

~~(D) Process validation.~~

~~(E) Personnel access and movement of materials into and near the controlled area~~

~~(F) Use and maintenance of environmental control devices used to create the critical direct compounding area for manipulation of sterile products (e.g., laminar airflow workstations, biological safety cabinets, class 100 cleanrooms, and barrier isolator~~

~~workstations).~~

~~(G) Regular cleaning schedule for the controlled areas and any equipment in the controlled area and the alternation of disinfectants. Pharmacies subject to an institutional infection control policy may follow that policy as it relates to cleaning schedules and the alternation of disinfectants in lieu of complying with this subdivision.~~

~~(H) Disposal of packaging materials, used syringes, containers, and needles to enhance sanitation and avoid accumulation in the controlled area.~~

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

To Amend § 1751.4 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.4. Facility and Equipment Standards for Sterile ~~Injectable~~ Compounding.

(a) No sterile ~~injectable~~ drug ~~product~~ preparation shall be compounded if it is known, or reasonably should be known, that the compounding environment fails to meet criteria specified in the pharmacy's written policies and procedures for the safe compounding of sterile ~~injectable~~ drug ~~products~~ preparations.

(b) During the compounding of ~~preparation of~~ sterile ~~injectable~~ drug ~~products~~ preparations, access to the areas designated ~~area or cleanroom~~ for compounding must be limited to those individuals who are properly attired.

(c) All equipment used in the areas designated ~~area or cleanroom~~ for compounding must be made of a material that can be easily cleaned and disinfected.

(d) Cleaning shall be done using a germicidal detergent and sterile water. The use of a sporicidal agent is required to be used at least monthly.

(1) All ISO Class 5 surfaces, work table surfaces, carts, counters, and the cleanroom floor shall be cleaned at least daily. After each cleaning, disinfection using a suitable sterile agent shall occur on all ISO Class 5 surfaces, work table surfaces, carts, and counters.

(2) Walls, ceilings, storage shelving, tables, stools, and all other items in the ISO Class 7 or ISO Class 8 environment shall be cleaned at least monthly.

(3) Cleaning shall also occur after any unanticipated event that could increase the risk of contamination.

(4) All cleaning materials, such as wipers, sponges, and mops, shall be non-shedding and dedicated to use in the cleanroom, or ante-area, and segregated sterile compounding areas and shall not be removed from these areas except for disposal.

(e) Disinfection, using a suitable sterile agent, shall also occur on all surfaces in the ISO Class 5 PEC frequently, including:

(1) At the beginning of each shift;

(2) At least every 30 minutes when compounding involving human staff is occurring or before each lot;

(3) After each spill; and

(4) When surface contamination is known or suspected.

~~(d) Exterior workbench surfaces and other hard surfaces in the designated area, such as walls, floors, ceilings, shelves, tables, and stools, must be disinfected weekly and after any unanticipated event that could increase the risk of contamination.~~

(f) Pharmacies preparing sterile compounded preparations require the use of a PEC that provides ISO Class 5 air or better air quality. Certification and testing of primary and secondary engineering controls shall be performed no less than every six months and whenever the device or area designated for compounding is relocated, altered or a service to the facility is performed that would impact the device or area. Certification must be completed by a qualified technician who is familiar with certification methods and procedures in accordance with CETA Certification Guide for Sterile Compounding Facilities (CAG-003-2006-13, Revised May 20, 2015). Certification records must be retained for at least 3 years. Unidirectional compounding aseptic isolators or compounding aseptic containment isolators may be used outside of an ISO Class 7 cleanroom if the isolator is certified to meet the following criteria:

(1) Particle counts sampled approximately 6-12 inches upstream of the critical exposure site shall maintain ISO Class 5 levels during compounding operations.

(2) Not more than 3520 particles (0.5 um and larger) per cubic meter shall be counted during material transfer, with the particle counter probe located as near to the transfer door as possible without obstructing transfer.

(3) Recovery time to achieve ISO Class 5 air quality shall be documented and internal procedures developed to ensure that adequate recovery time is allowed after material transfer before and during compounding operations.

Compounding aseptic isolators that do not meet the requirements as outlined in this subdivision or are not located within an ISO Class 7 cleanroom may only be used to compound preparations that meet the criteria specified in accordance with subdivision (d) of Section 1751.8 of Title 16, Division 17, of the California Code of Regulations.

(g) Pharmacies preparing ~~parenteral cytotoxic~~ sterile hazardous agents shall do so in accordance with Section 505.~~12~~5.1 of Title 24, Chapter 5, of the California Code of Regulations, requiring a ~~laminar air flow hood~~ negative pressure PEC. Additionally, each PEC used to compound hazardous agents shall be externally vented. The ~~hood~~ negative pressure PEC must be certified ~~annually~~ every six months by a qualified technician who is familiar with CETA Certification Guide for Sterile Compounding Facilities (CAG-003-2006-13, Revised May 20, 2015). ~~the methods and procedures for certifying laminar air flow hoods and cleanroom requirements, in accordance with National Sanitation Foundation Standard 49 for Class II (Laminar Flow) Biohazard Cabinetry, as revised May, 1983 (available from the National Sanitation Foundation, 3475 Plymouth Road, P.O. Box 1468, Ann Arbor, Michigan 48106, phone number (313) 769-8010) or manufacturer's specifications. Certification records must be retained for at least 3 years.~~ Any drug preparation that is compounded in a PEC where hazardous drugs are prepared must be labeled as hazardous, regardless of whether the drug ingredients are considered hazardous.

(1) During the hazardous drug compounding that is performed in a compounding aseptic containment isolator, full hand hygiene and garbing must occur. Garbing shall include hair cover, facemask, beard cover (if applicable), polypropylene or low shedding gown that closes in the back, shoe covers, and two pairs of sterile ASTM D6978-05 standard gloves.

(h) If a compounding aseptic isolator is certified by the manufacturer to maintain ISO Class 5

air quality during dynamic operation conditions during compounding as well as during the transfer of ingredients into and out of the compounding aseptic isolator, then it may be placed into a non-ISO classified room. Individuals that use compounding aseptic isolators in this manner must ensure appropriate garbing, which consists of donning sterile gloves over the isolator gloves immediately before non-hazardous compounding. These sterile gloves must be changed by each individual whenever continuous compounding is ceased and before compounding starts again.

(i) Compounding aseptic isolator and compounding aseptic containment isolator used in the compounding of sterile drug preparations shall use non-turbulent unidirectional air flow patterns. A smoke patterned test shall be used to determine air flow patterns.

(j) Viable surface sampling shall be done at least every six months for all sterile-to-sterile compounding and quarterly for all non-sterile-to-sterile compounding. Viable air sampling shall be done by volumetric air sampling procedures which test a sufficient volume of air (400 to 1,000 liters) at each location and shall be done at least once every six months. Viable surface and viable air sampling shall be performed by a qualified individual who is familiar with the methods and procedures for surface testing and air sampling. Viable air sampling is to be performed under dynamic conditions that simulate actual production. Viable surface sampling is to be performed under dynamic conditions of actual compounding. When the environmental monitoring action levels are exceeded, the pharmacy shall identify the CFUs at least to the genus level in addition to conducting an investigation pursuant to its policies and procedures. Remediation shall include, at minimum, an immediate investigation of cleaning and compounding operations and facility management.

(k) The sterile compounding area in the pharmacy shall have a comfortable and well-lighted working environment, which includes a room temperature of 20-24 degrees Celsius (68-75 degrees Fahrenheit) or cooler to maintain comfortable conditions for compounding personnel when attired in the required compounding garb.

(l) A licensee may request a waiver of these provisions as provided in section 1735.6(f).

Note: Authority Cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052 and 4127, Business and Professions Code; and Section 18944, Health and Safety Code.

To Amend § 1751.5 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.5. Sterile ~~Injectable~~ Compounding Attire.

~~(a) When preparing cytotoxic agents, gowns and gloves shall be worn.~~

~~(b)~~ (a) When compounding sterile drug ~~products~~ preparations ~~from one or more non-sterile ingredients~~ the following standards must be met:

(1) ~~Cleanroom garb~~ Personal protective equipment consisting of a ~~low~~ non-shedding ~~coverall~~ gown, head cover, face mask, facial hair covers (if applicable), and shoe covers must be worn inside the designated area at all times. For hazardous compounding double shoe covers are required.

(2) ~~Cleanroom garb~~ Personal protective equipment must be donned and removed ~~outside the designated area~~ in an ante-area or immediately outside the segregated compounding area.

(3) Personnel shall don personal protective equipment in an order that proceeds from those activities considered the dirtiest to those considered the cleanest. The following order is to be followed unless the pharmacy has a procedure in place that documents a method equivalent to or superior to the method described here: The donning of shoe covers or dedicated shoes, head and facial hair covers and face masks shall be followed by the washing of hands and forearms up to the elbows for 30 seconds with soap and water, drying hands, and then the donning of a non-shedding gown.

~~(3)~~ (4) Compounding personnel shall not wear any wrist, Hhand, finger, ~~and~~ or ~~wrist~~ other visible ~~jewelry must be eliminated~~ jewelry, piercing, headphones, earbuds, or personal electronic device. ~~If jewelry cannot be removed then it must be thoroughly cleaned and covered with a sterile glove.~~

~~(4) Head and facial hair must be kept out of the critical area or be covered.~~

(5) ~~Gloves made of low-shedding materials are required.~~ Sterile gloves that have been tested for compatibility with disinfection with isopropyl alcohol are required. Hand cleansing with a persistently active alcohol-based product followed by the donning of sterile gloves may occur within the ante or cleanroom. Gloves are to be routinely disinfected with sterile 70 percent isopropyl alcohol before entering or re-entering the PEC and after contact with non-sterile objects. Gloves shall also be routinely inspected for holes, punctures, or tears and replaced immediately if such are detected.

(6) Individuals experiencing exposed rashes, sunburn, weeping sores, conjunctivitis, active respiratory infections or other communicable disease, or those wearing cosmetics, nail polish, or artificial nails shall be excluded from the ISO Class 5 and ISO Class 7 compounding areas until their conditions are remedied.

~~(c) The requirements of subdivision (b) do not apply if a barrier isolator is used to compound sterile injectable products from one or more non-sterile ingredients.~~

(b) When preparing hazardous agents, appropriate gowns and personal protective equipment shall be worn regardless of the PECs used (e.g., biological safety cabinet and compounding aseptic containment isolator).

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

To Amend § 1751.6 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.6 ~~Training of Sterile Injectable Compounding Staff, Patient, and Caregiver.~~ **Sterile Compounding Consultation; Training of Sterile Compounding Staff**.

(a) Consultation shall be available to the patient and/or primary caregiver concerning proper use, storage, handling, and disposal of sterile ~~injectable~~ drug ~~products~~ preparations and related supplies furnished by the pharmacy.

(b) The pharmacist-in-charge shall ~~be responsible to~~ ensure that all pharmacy personnel

engaging in compounding sterile ~~injectable~~ drug ~~products~~ preparations ~~shall~~ have training and demonstrated competence in the safe handling and compounding of sterile ~~injectable~~ drug ~~products~~ preparations, including ~~cytotoxic~~ hazardous agents if the pharmacy compounds products with ~~cytotoxic~~ hazardous agents.

(c) Records of training and demonstrated competence shall be available for each individual and shall be retained for three years beyond the period of employment.

(d) The pharmacist-in-charge shall be responsible to ensure the continuing competence of pharmacy personnel engaged in compounding sterile ~~injectable~~ drug ~~products~~ preparations.

(e) Pharmacies that compound sterile drug ~~products from one or more non-sterile ingredients~~ preparations must comply with the following training requirements:

(1) The pharmacy must establish and follow a written program of training and performance evaluation designed to ensure that each person working in the designated area has the knowledge and skills necessary to perform their assigned tasks properly. This program of training and performance evaluation must address at least the following:

(A) Aseptic technique.

(B) Pharmaceutical calculations and terminology.

(C) Sterile ~~product~~ preparation compounding documentation.

(D) Quality assurance procedures.

(E) Aseptic preparation procedures.

(F) Proper hand hygiene, gowning and gloving technique.

(G) General conduct in the controlled area (aseptic area practices).

(H) Cleaning, sanitizing, and maintaining of the equipment and ~~used in~~ the controlled area.

(I) Sterilization techniques for compounding sterile drug preparations from one or more non-sterile ingredients.

(J) Container, equipment, and closure system selection.

(2) Each person ~~assigned to the controlled area~~ engaged in sterile compounding must successfully complete practical skills training in aseptic technique and aseptic area practices using models that are comparable to the most complex manipulations to be performed by the individual. Each pharmacist responsible for, or directly supervising and controlling, aseptic

techniques or practices, must demonstrate the skills needed to ensure the sterility of compounded drug preparations. Evaluation must include written testing and a written protocol of periodic routine performance checks involving adherence to aseptic area policies and procedures. Each person's proficiency and continuing training needs must be reassessed at least every 12 months. Results of these assessments must be documented and retained in the pharmacy for three years.

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

To Amend § 1751.7 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.7. Sterile ~~Injectable~~ Compounding Quality Assurance and Process Validation.

(a) Any pharmacy engaged in compounding sterile ~~injectable~~ drug ~~products~~ preparations shall maintain, as part of its written policies and procedures, a written quality assurance plan including, in addition to the elements required by section 1735.8, a documented, ongoing quality assurance program that monitors personnel performance, equipment, and facilities. The end product shall be examined on a periodic sampling basis as determined by the pharmacist-in-charge to assure that it meets required specifications. The ~~Q~~quality ~~A~~assurance ~~P~~program shall include at least the following:

(1) Procedures for ~~C~~cleaning and sanitization of the ~~parenteral~~ ~~medication~~ sterile preparation area.

~~(2) The storage of compounded sterile injectable products in the pharmacy and periodic documentation of refrigerator temperature.~~

~~(3)~~(2) Actions to be taken in the event of a drug recall.

~~(4)~~(3) ~~Written justification of~~ Documentation justifying the chosen ~~expiration~~ beyond use dates for compounded sterile ~~injectable~~ drug ~~products~~ preparations.

(b)(1) The pharmacy and each individual involved in the compounding of sterile drug

preparations must successfully demonstrate competency on aseptic technique and aseptic area practices before being allowed to prepare sterile drug preparations. The validation process shall be carried out in the same manner as normal production, except that an appropriate microbiological growth medium is used in place of the actual product used during sterile preparation. The validation process shall be representative of the types of manipulations, products and batch sizes the individual is expected to prepare and include a media-fill test. The validation process shall be as complicated as the most complex manipulations performed by staff and contain the same amount or greater amount of volume transferred during the compounding process. The same personnel, procedures, equipment, and materials must be used in the testing. Media used must have demonstrated the ability to support and promote growth. Completed medium samples must be incubated in a manner consistent with the manufacturer's recommendations. If microbial growth is detected, then each individual's sterile preparation process must be evaluated, corrective action taken and documented, and the validation process repeated.

(2) Each individual's competency must be revalidated at least every twelve months for sterile to sterile compounding and at least every six months for individuals compounding sterile preparations from non-sterile ingredients.

(3) The pharmacy's validation process on aseptic technique and aseptic area practices must be revalidated whenever:

(A) the quality assurance program yields an unacceptable result,

(B) there is any change in the compounding process, the Primary Engineering Control (PEC), or the compounding environment. For purposes of this subsection, a change includes, but is not limited to, when the PEC is moved, repaired or replaced, when the facility is modified in a manner that affects airflow or traffic patterns, or when improper aseptic techniques are observed.

(4) The pharmacy must document the validation and revalidation process.

~~Each individual involved in the preparation of sterile injectable drug products preparations must first successfully demonstrate competency by successfully performing aseptic media-fill tests complete a validation process on technique before being allowed to prepare sterile~~

~~injectable drug products preparations. The validation process shall be carried out in the same manner as normal production, except that an appropriate microbiological growth medium is used in place of the actual product used during sterile preparation. The validation process shall be representative of all types of manipulations, products and batch sizes the individual is expected to prepare. The media-fill testing process shall be as complicated as the most complex manipulations performed by staff and contain the same amount or greater of volume transferred during the compounding process. The same personnel, procedures, equipment, and materials must be involved. Media used must have demonstrated the ability to support and promote growth. Completed medium media samples must be incubated in a manner consistent with the manufacturer's recommendations. If microbial growth is detected, then the employee's sterile preparation process must be evaluated, corrective action taken and documented, and the validation process media-fill testing repeated. Personnel competency must be revalidated at least every twelve months for sterile to sterile compounding and at least every six months for individuals compounding sterile products from non-sterile ingredients. Aseptic work practice assessments via media-fill tests must be revalidated, as appropriate to the circumstance or personnel found to be deficient, whenever the quality assurance program yields an unacceptable result, when the compounding process changes, equipment used in the compounding of sterile injectable drug products preparations is repaired or replaced, the facility is modified in a manner that affects airflow or traffic patterns, or whenever improper aseptic techniques are observed. Revalidation must be documented.~~

(c) All sterile compounding personnel must successfully complete an initial competency evaluation. In addition, immediately following the initial hand hygiene and garbing procedure, each individual who may be required to do so in practice must successfully complete a gloved fingertip (all fingers on both hands) sampling procedure (zero colony forming units for both hands) at least three times before initially being allowed to compound sterile drug preparations.

(d) Re-evaluation of garbing and gloving competency shall occur at least every 12 months for personnel compounding products made from sterile ingredients and at least every six months for personnel compounding products from non-sterile ingredients.

~~(c)~~ (e)(1) Batch-produced sterile drug preparations compounded from one or more non-sterile ingredients, except as provided in paragraph (2), shall be subject to documented end product testing for sterility and pyrogens and shall be quarantined until the end product testing confirms sterility and acceptable levels of pyrogens. Sterility testing shall be USP chapter 71 compliant and pyrogens testing shall confirm acceptable levels of pyrogens per USP chapter 85 limits, before dispensing. This requirement of end product testing confirming sterility and acceptable levels of pyrogens prior to dispensing shall apply regardless of any sterility or pyrogen testing that may have been conducted on any ingredient or combination of ingredients that were previously non-sterile. Exempt from pyrogen testing are topical ophthalmic and inhalation preparations.

(2) The following non-sterile-to-sterile batch drug preparations do not require end product testing for sterility and pyrogens:

(A) Preparations for self-administered ophthalmic drops in a quantity sufficient for administration to a single patient for 30 days or less pursuant to a prescription.

(B) Preparations for self-administered inhalation in a quantity sufficient for administration to a single patient for 5 days or less pursuant to a prescription.

~~Batch-produced sterile injectable drug products compounded from one or more non-sterile ingredients shall be subject to documented end product testing for sterility and pyrogens and shall be quarantined until the end product testing confirms sterility and acceptable levels of pyrogens.~~

~~(d) Batch-produced sterile to sterile transfers shall be subject to periodic testing through process validation for sterility as determined by the pharmacist-in-charge and described in the written policies and procedures.~~

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

To Amend § 1751.8 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.8. Beyond Use Dating for Sterile Compounded Drug Preparations.

In conformity with and in addition to the requirements and limitations of section 1735.2, subdivision (h), every sterile compounded drug preparation shall be given and labeled with a beyond use date that does not exceed the shortest expiration date or beyond use date of any ingredient in sterile compounded drug preparation, nor the chemical stability of any one ingredient in the sterile compounded drug preparation, nor the chemical stability of the combination of all ingredients in the sterile compounded drug preparation, and that, in the absence of passing a sterility test in accordance with standards for sterility testing found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP37-NF32) Through 2nd Supplement (37th Revision, Effective December 1, 2014), hereby incorporated by reference, that would justify an extended beyond use date, conforms to the following limitations:

(a) The beyond use date shall specify that storage and exposure periods cannot exceed 48 hours at controlled room temperature, 14 days at controlled cold temperature, and 45 days in solid frozen state, where the sterile compounded drug preparation is compounded solely with aseptic manipulations and all of the following apply:

(1) The preparation is compounded entirely within an ISO Class 5 PEC located in an ISO Class 7 cleanroom with an ante-area or compounded entirely within a CAI which meets the requirements in 1751.4(f)(1)-(3), using only sterile ingredients, products, components, and devices; and

(2) The compounding process involves transferring, measuring, and mixing manipulations using not more than three commercially manufactured packages of sterile preparations and not more than two entries into any one sterile container or package of sterile preparations or administration containers/devices to prepare the drug preparation; and

(3) Compounding manipulations are limited to aseptically opening ampules, penetrating disinfected stoppers on vials with sterile needles and syringes or spiked transfer devices, and transferring sterile liquids in sterile syringes to sterile administration devices, package

containers of other sterile preparations, and containers for storage dispensing.

(b) The beyond use date shall specify that storage and exposure periods cannot exceed 30 hours at controlled room temperature, 9 days at controlled cold temperature, and 45 days in solid frozen state, where the sterile compounded drug preparation is compounded solely with aseptic manipulations and all of the following apply:

(1) The preparation is compounded entirely within an ISO Class 5 PEC located in an ISO Class 7 cleanroom with an ante-area or compounded entirely within a CAI which meets the requirements in 1751.4(f)(1)-(3), using multiple individual or small doses of sterile preparations combined or pooled to prepare a compounded sterile preparation that will be administered either to multiple patients or to one patient on multiple occasions; and

(2) The compounding process involves complex aseptic manipulations other than the single-volume transfer; and

(3) The compounding process requires unusually long duration such as that required to complete dissolution or homogenous mixing.

(c) The beyond use date shall specify that storage and exposure periods cannot exceed 24 hours at controlled room temperature, 3 days at controlled cold temperature, and 45 days in solid frozen state, where the sterile compounded drug preparation is compounded solely with aseptic manipulations using non-sterile ingredients, regardless of intervening sterilization of that ingredient and the following applies:

(1) The preparation is compounded entirely within an ISO Class 5 PEC located in an ISO Class 7 cleanroom with an ante-area or compounded entirely within a CAI which meets the requirements in 1751.4(f)(1)-(3).

(d) The beyond use date shall specify that storage and exposure periods cannot exceed 12 hours where the sterile compounded drug preparation is compounded solely with aseptic manipulations and all of the following apply:

(1) The preparation was compounded entirely within an ISO Class 5 PEC that is located in a segregated sterile compounding area and restricted to sterile compounding activities, using only sterile ingredients, components, and devices, by personnel properly cleansed and garbed; and

(2) The compounding process involves simple transfer of not more than three commercially manufactured packages of sterile nonhazardous preparations or diagnostic radiopharmaceutical preparations from the manufacturer's original containers; and

(3) The compounding process involves not more than two entries into any one container or package (e.g., bag, vial) of sterile infusion solution or administration container/device.

(e) Where any sterile compounded drug preparation was compounded either outside of an ISO class 5 PEC or under conditions that do not meet all of the requirements for any of subdivisions (a) through (d), the sterile compounded drug preparation shall be labeled "for immediate use only" and administration shall begin no later than one hour following the start of the compounding process. Unless the "immediate use" preparation is immediately and completely administered by the person who prepared it or immediate and complete administration is witnessed by the preparer, the preparation shall bear a label listing patient identification information, the names and amounts of all ingredients, the name or initials of the person who prepared the compounded sterile preparation, and the exact one-hour beyond use date and time. If administration has not begun within one hour following the start of the compounding process, the compounded sterile preparation shall be promptly, properly, entirely, and safely discarded. This provision does not preclude the use of a PEC to compound an "immediate use" preparation. A PEC used solely to compound 'immediate use' preparations need not be placed within an ISO Class 7 cleanroom, with an ante-area. Such "immediate use" preparations shall be compounded only in those limited situations where there is a need for immediate administration of a sterile preparation compounded outside of an ISO class 5 environment and where failure to administer could result in loss of life or intense suffering. Any such compounding shall be only in such quantity as is necessary to meet the immediate need and the circumstance causing the immediate need shall be documented in accordance with policies and procedures.

(f) The beyond use date for any compounded allergen extracts shall be the earliest manufacturer expiration date of the individual allergen extracts.

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

To Add § 1751.9 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.9 Single-Dose and Multi-Dose Containers; Limitations on Use

(a) Single-dose ampules are for immediate use only, and once opened shall not be stored for any time period.

(b) Unless otherwise specified by the manufacturer, any single-dose container of a compounded sterile drug preparation other than an ampule, such as a bag, bottle, syringe or vial, shall be used in its entirety or its remaining contents shall be labeled with a beyond use date and discarded within the following time limit, depending on the environment:

(1) When needle-punctured in an environment with air quality worse than ISO Class 5, within one (1) hour;

(2) When needle-punctured in an environment with ISO Class 5 or better air quality, within six (6) hours. A container must remain within the ISO Class 5 or better air quality to be used for the full six hours, unless otherwise specified by the manufacturer.

(3) If the puncture time is not noted on the container, the container must immediately be discarded.

(c) Unless otherwise specified by the manufacturer, a multi-dose container stored according to the manufacturer's specifications shall be used in its entirety or its remaining contents shall be labeled with a beyond use date and discarded within twenty eight (28) days from initial opening or puncture. Any multi-dose container not stored according to the manufacturer's specifications shall be discarded immediately upon identification of such storage circumstance. If any open container is not labeled with a beyond use date or the beyond use date is not correct, the container must immediately be discarded.

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

To Amend § 1751.10 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

~~1751.8.~~ 1751.10. Sterile ~~Injectable~~ Compounding Reference Materials.

In any pharmacy engaged in compounding sterile ~~injectable~~ drug ~~products~~ preparations, there shall be current and appropriate reference materials regarding the compounding of sterile ~~injectable~~ drug ~~products~~ preparations located in or immediately available to the pharmacy.

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

To Add Article 7.5 of Division 17 of Title 16 of the California Code of Regulations to read as follow

Article 7.5 Furnishing for Home Administration

To Amend § 1751.10 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

~~1751.10.~~ 1752. Furnishing to Parenteral Patient at Home.

Subject to all provisions of this article, a pharmacist may carry and furnish to a patient at home dangerous drugs, other than controlled substances, and devices for parenteral therapy when the dangerous drug or device is one currently prescribed for the patient.

Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code.

To Amend § 1751.11 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

~~1751.11.~~ 1753. Furnishing to Home Health Agencies and Licensed Hospices.

Subject to the following conditions, a licensed pharmacy may furnish to a home health agency licensed under provisions of Chapter 8 (commencing with section 1725 of Division 2 of the Health and Safety Code) or to a hospice licensed under provisions of Chapter 8.5 (commencing with section 1745 of Division 2 of the Health and Safety Code) dangerous drugs for parenteral therapy other than controlled substances, in a portable container for furnishing to patients at home for emergency treatment or adjustment of parenteral drug therapy by the home health agency or licensed hospice.

(a) The pharmacy, having ownership and responsibility for the portable containers, shall ensure that each portable container is:

(1) furnished by a registered pharmacist;

(2) sealed in such a manner that a tamper-proof seal must be broken to gain access to the drugs;

(3) under the effective control of a registered nurse, pharmacist or delivery person at all times when not in the pharmacy;

(4) labeled on the outside of the container with a list of the contents;

(5) maintained at an appropriate temperature according to United States Pharmacopeia Standards (1995, 23rd Revision), and protected at all times from extreme temperatures that could damage the contents.

(b) The portable container may contain up to:

(1) 1000mL of 0.9% sodium chloride intravenous infusion in containers of a size determined by the pharmacy;

(2) 1000mL of 5% dextrose in water injection in containers of a size determined by the

pharmacy;

(3) two vials of urokinase 5000 units;

(4) Each of the following items shall be in sealed, unused containers; the furnishing pharmacy may select any or all of these dangerous drugs in up to five dosage units for inclusion in the sealed, portable container:

(A) heparin sodium lock flush 100 units/mL;

(B) heparin sodium lock flush 10 units/mL;

(C) epinephrine HCl solution 1:1,000;

(D) epinephrine HCl solution 1:10,000;

(E) diphenhydramine HCl 50mg/mL;

(F) methylprednisolone 125mg/2mL;

(G) normal saline, preserved, up to 30 mL vials;

(H) naloxone 1mg/mL 2 mL;

(I) droperidol 5mg/2mL;

(J) prochlorperazine 10mg/2mL;

(K) promethazine 25mg/mL;

(L) dextrose 25gms/50mL;

(M) glucagon 1mg/mL;

(N) insulin (human) 100 units/mL;

(O) bumetamide 0.5mg/2mL;

(P) furosemide 10mg/mL;

(Q) EMLA Cream 5 gm tube;

(R) Lidocaine 1 percent 30mL vials.

(5) The pharmacy shall ensure that the specific dangerous drugs and quantities to be included in the portable container are listed in the home health agency's or licensed hospice's policy~~y~~ies and procedures.

(c) The pharmacy shall not supply a portable container to a home health agency or licensed hospice which does not:

(1) implement and maintain policies and procedures for:

(A) the storage, temperature stability and transportation of the portable container;
(B) the furnishing of dangerous drugs from the portable container upon the written or oral authorization of a prescriber; and
(C) a specific treatment protocol for the administration of each medication contained in the portable container.
(2) have the policies, procedures and protocols reviewed and revised (as needed) annually by a group of professional personnel including a physician and surgeon, a pharmacist and a registered nurse.
(d) A copy of these policies, procedures and protocols shall be maintained by the furnishing pharmacy from each home health agency or licensed hospice for which the pharmacy furnishes portable containers.
(e) In cases where a drug has been administered to a patient pursuant to the oral order of a licensed prescriber, the pharmacy shall ensure that the oral order is immediately written down by the registered nurse or pharmacist and communicated by copy or fax within 24 hours to the furnishing pharmacy, with a copy of the prescriber-signed document forwarded to the dispensing pharmacy within 20 days.
(f) The pharmacy shall ensure that within seven days (168 hours) after the seal has been broken on the portable container, the home health agency's director of nursing service or a registered nurse employed by the home health agency or licensed hospice returns the container to the furnishing pharmacy. The furnishing pharmacy shall then perform an inventory of the drugs used from the container, and if the container will be reused, must restock and reseal the container before it is again furnished to the home health agency or licensed hospice.
(g) The furnishing pharmacy shall have written policies and procedures for the contents, packaging, inventory monitoring, labeling and storage instructions of the portable container.
(h) The furnishing pharmacy shall ensure that the home health agency or licensed hospice returns the portable containers to the furnishing pharmacy at least every 60 days for verification of product quality, quantity, integrity and expiration dates, or within seven days (168 hours) after the seal has been broken.

(i) The furnishing pharmacy shall maintain a current inventory and record of all items placed into and furnished from the portable container.

Note: Authority cited: Sections 4005 and ~~and~~ 4057, Business and Professions Code. Reference: Sections 4040, 4057, 4081 and 4332, Business and Professions Code.

To Amend § 1751.12 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

~~1751.12~~ 1754. Obligations of a Pharmacy Furnishing Portable Containers.

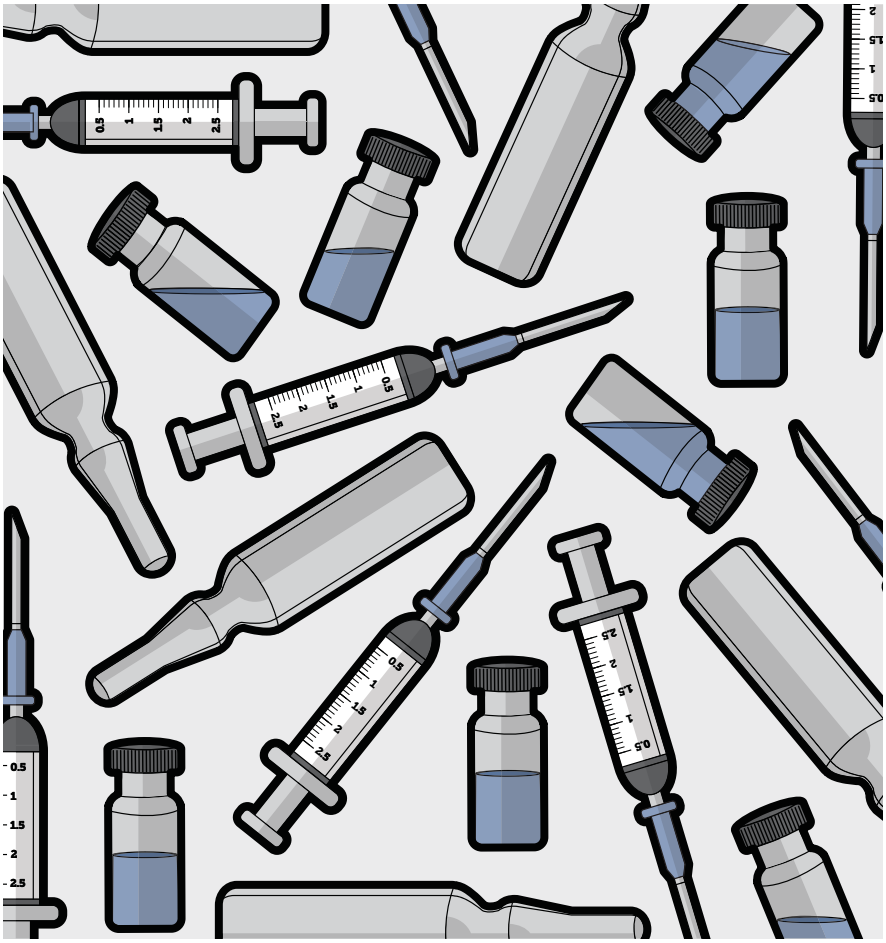
(a) A licensed pharmacy shall not issue portable containers to any home health agency or licensed hospice unless the home health agency or licensed hospice complies with provisions of section ~~1751.11~~ 1753.

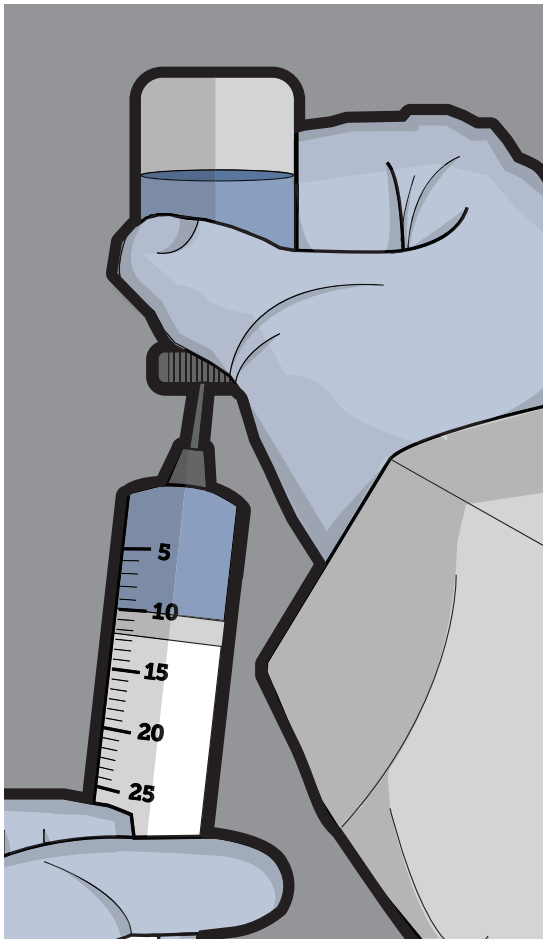
(b) A licensed pharmacy shall cease to furnish portable containers to a home health agency or licensed hospice if the home health agency or licensed hospice does not comply with provisions of section ~~1751.11~~ 1753.

Note: Authority cited: Sections 4005 and 4057, Business and Professions Code. Reference: Sections 4040, 4057, 4081 and 4332, Business and Professions Code.

Attachment 9

A report from THE PEW CHARITABLE TRUSTS | March 2016





Best Practices for State Oversight of Drug Compounding

Contents

The Pew Charitable Trusts

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Overview

In 2012 and 2013, contaminated injections compounded at a single pharmacy in Massachusetts were associated with 64 deaths and 753 illnesses in a nationwide outbreak of fungal meningitis. This unprecedented tragedy has driven state and federal officials to re-examine laws and regulations governing drug compounding—the traditional pharmacy practice of creating custom medicines to meet a patient's unique medical needs.

Although the Food and Drug Administration (FDA) enforces federal laws that apply to pharmaceutical products, states are in most cases the primary regulators of pharmacy compounding. In response to the meningitis outbreak and similar events—The Pew Charitable Trusts has identified over 25 reported compounding incidents associated with patient harm or deaths since 2001—numerous states are revisiting compounding oversight systems to ensure they are sufficiently robust. But state regulatory approaches and enforcement systems vary. For example, states apply different quality standards for compounding or inspect pharmacies on different schedules.

States must also consider how to address federal legislation on compounding, the Drug Quality and Security Act of 2013[1] (DQSA), which established a new type of company, an "outsourcing facility," that is allowed to compound supplies of medicine without receiving patient-specific prescriptions, permitting operation on a larger scale. To do this, outsourcing facilities must meet FDA's applicable current Good Manufacturing Practices (cGMP) regulations—the quality requirements for drug manufacturers—and register with FDA, among other obligations. Although FDA will have oversight responsibility for outsourcing facilities, states must still make decisions about how to recognize these companies in their jurisdictions and what oversight, if any, they wish to exert as the new sector is established.

The DQSA also clarifies the enforceability of federal law that traditional pharmacies may compound only pursuant to prescriptions, or in limited quantities in anticipation of receiving a prescription, to be exempt from FDA's drug approval, manufacturing, and labeling standards. Federal law does not permit traditional pharmacies to supply compounded drugs without prescriptions.

In 2014, Pew convened an advisory committee of state regulators and experts to examine state oversight of compounding and develop best practices. The committee reviewed several regulatory topics, including inspections of compounding pharmacies, requirements for quality, expectations for pharmacist training, and compounding without a prescription. The committee also discussed how states should harmonize these requirements with federal law and regulations, particularly on issues such as definition and recognition of the new outsourcing facility category.

Based on the advisory committee process, this document identifies the best practices that are most meaningful to patient safety and the most achievable—recognizing, however, that state funding may place limitations on oversight systems. The best practices provide a resource to state regulators, policymakers, and interested stakeholders who are reviewing oversight practices, and also support greater harmonization across states—a valuable pursuit, given the interstate movement of compounded drugs, to ensure evenly-applied oversight and help counter an incentive for businesses to locate in states with less rigorous regulations.

Best practice recommendations are described in each section of this report and include:

- Application of U.S. Pharmacopeial Convention (USP) quality standards on compounding.
- Training in sterile compounding for pharmacists who perform or supervise it.
- Annual inspections of facilities that perform sterile compounding.

- State mechanisms, such as separate licensure, to identify and apply specific standards to facilities performing sterile compounding.
- Recognition and definition of outsourcing facilities in a manner aligned with federal law.
- Harmonization of policies on compounding without prescriptions with federal law.
- Meaningful oversight of sterile compounding that occurs in physicians' offices.
- Mechanisms to track the compounding activities conducted by pharmacies within the state.

The Advisory Panel's Work

To develop best practices for state oversight of drug compounding, The Pew Charitable Trusts convened an advisory committee whose members included leaders from five state boards of pharmacy and the National Association of Boards of Pharmacy, plus an expert in compounding quality systems. (See a full list in the acknowledgments section.) The committee's goal was to develop practices that are meaningful, achievable, and important for patient safety and that take into account lessons learned from the 2012-13 meningitis outbreak linked to compounded injections and the regulatory oversight established by the Drug Quality and Security Act in 2013.

The committee identified and refined best practices through iterative review and discussion. First, Pew circulated a draft document to the committee that identified regulatory categories and potential standards for initial consideration; members then provided written feedback on this document. Committee members then met in person Oct. 9, 2014, at Pew's offices to review each regulatory area and potential standard in-depth. During that meeting, the group found a substantial degree of consensus on many of the regulatory categories. After the meeting, Pew again updated the best practices document and circulated it for two additional rounds of written review.

The best practices identified in this report were significantly informed by the advisory committee process and reflect a high level of consensus among the experts. However, the recommendations in this report are Pew's and may not represent the views of every participant. Where important differences of opinion were identified within the committee, they are described in the text that precedes the best practices for each category.

Best practices for state oversight of drug compounding

Quality standards

The U.S. Pharmacopeial Convention has established widely recognized quality standards for pharmacy compounding of sterile and nonsterile preparations—USP chapters <797> and <795>, respectively, as well as Chapter <800> on the compounding, handling, and administration of drugs that present physical or health hazards. Although many states reference or incorporate USP standards in their pharmacy laws and regulations,

many others do not, creating an uneven landscape of quality requirements. Furthermore, states may be even less likely to have regulatory safeguards that apply to compounding that occurs outside of a pharmacy, such as in a doctor's office. The advisory committee agreed that all traditional compounding facilities, whether an independent pharmacy, hospital pharmacy, or doctor's office, should comply, at minimum, with all applicable USP standards. Compounders that register with FDA as outsourcing facilities are in a separate category, because they are required by federal law to comply with cGMPs. However, states that elect to license and/or inspect outsourcing facilities may also wish to establish cGMPs as the required quality standard.

The committee also emphasized that drug compounding is an interstate operation; pharmacies may prepare medicines in one state and ship them to another. States can encounter oversight challenges if an out-of-state pharmacy shipping into their jurisdiction is held to a different quality or regulatory standard than in-state compounders.

Repackaged Drugs and Preparations Using Biologics

Federal law on compounding, which covers traditional pharmacies and outsourcing facilities, does not address repackaging or preparations made from biological products. The FDA is developing guidance to address these activities; depending on final language some quality elements, such as beyond-use dating (i.e., the date beyond which a compounded drug should not be used), may differ from USP standards. As delineated within the original statute, FDA guidance on repackaging also supersedes federal law (Section 506F of the Food, Drug, and Cosmetic Act*) that addresses hospital repackaging of drugs into smaller amounts to extend the supply during a shortage. States should examine FDA guidance closely to ensure their standards are aligned with federal expectations.

* http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm434174.pdf

Harmonized minimum quality standards across states would help address challenges in regulating out-of-state pharmacies and ensure that all traditional pharmacy compounding met strong baseline criteria for preparing safe drugs and protecting patients. Committee members emphasized the importance of minimum standards for sterile compounding, in particular, and identified core elements of USP Chapter <797>, the key standard for sterile compounding. They include:

- Personnel-related controls: hand hygiene, garbing (wearing protective garments), aseptic technique, and training.
- Environment-related controls: facility design and construction, cleaning, environmental monitoring, and equipment certification and calibration.
- Process-related controls: sterilization procedures and verification, control of components and materials, standard operating procedures, and documentation.

Advisory committee members noted that although minimum standards for traditional pharmacy compounding should be the same nationwide, states should be able to implement additional requirements. But regardless of

whether states choose to go beyond USP, they must ensure that any updates to USP standards are reflected in state law or regulations. USP regularly updates standards; for example, in September 2015 USP published a proposed revision to Chapter <797>.[2]

Best practice standards for states

- States should require traditional compounding pharmacies to comply, at minimum, with all applicable USP standards, including general chapters <795> and <797>, new chapter <800> when complete, and other referenced chapters.
- States should hold out-of-state traditional compounding pharmacies that ship into the state to USP standards at a minimum.
- States should ensure that revisions of USP standards are reflected in state requirements.

Equipment certification and laboratory accreditation

Compounders preparing sterile products must control the air quality in their facilities and keep contaminants at acceptable, low levels. USP <797> currently includes an expectation that sterile compounding facilities and critical air control devices be certified at least every six months by a qualified individual using standard testing protocols, such as those endorsed by the Controlled Environment Testing Association (CETA).[3] The advisory committee supported requiring the use of CETA testing standards for certification in all cases.

Compounders may use external labs to test products for sterility, endotoxins, and potency. Labs that are not appropriately rigorous in testing practices may produce compromised test results. Investigations following the 2012-13 meningitis outbreak revealed quality problems at several external testing labs used by compounding facilities. FDA issued inspectional findings to five contract labs in 2012 and 2013, in several cases noting that labs were not following USP standards for sterility testing. The advisory committee also recommended appropriate accreditation, which can help ensure that labs are meeting sufficient standards to produce reliable test results.

Best practice standards for states

- States should require that all sterile compounding facilities and critical air control devices be certified by a qualified individual at least every six months (as required by USP <797>) using standard testing protocols, such as those endorsed by CETA.
- States should require that sterile compounders use only external testing labs that are clinical or environmental labs with appropriate accreditation.[4] Labs should also meet the International Organization for Standardization and the International Electrotechnical Commission 17025:2005[5] quality standard, General Requirements for the Competence of Testing and Calibration Laboratories.

Pharmacist training on sterile compounding

Although USP <797> requires compounders to train personnel and regularly evaluate them through compounding simulations known as media fills, the committee recommended that states set more specific expectations for specialized training in sterile compounding for pharmacists engaging in that activity. This could be done by requiring a certain number of hours of continuing education in sterile compounding or through a certification program, if one were to be developed. Of note, proposed revisions to USP <797> include new detailed training expectations for personnel involved in sterile compounding activity.[6]

Some states have made changes in this regard. As of 2014, Massachusetts requires that five out of 20 continuing education hours be devoted to sterile compounding.[7] To renew a license in Texas, pharmacists engaging in high-risk sterile compounding, such as preparing sterile drugs from nonsterile ingredients, must receive four out of 30 required hours of continuing education in the practice, and pharmacists engaged in low- or medium-risk sterile compounding must have two hours of specific training.[8]

A pharmacist's compliance with training requirements can be checked during state audits of compounding facilities, though it may not always be easy for a state to match pharmacists it licensed to the facilities where the pharmacists work. Therefore, compounding facilities should be required to keep records demonstrating that all pharmacists engaged in sterile compounding on-site are qualified and have had appropriate training.

Requirements for training may help increase course offerings; the advisory committee noted that few courses in sterile compounding are available today. The committee supported encouraging the Accreditation Council for Pharmacy Education (ACPE)[9] to adopt a core curriculum standard on compounding that is taught in conformance with applicable USP standards. The advisory panel also saw value in developing specialty certification programs for sterile compounding.

Best practice standards for states

- In addition to USP <797> training expectations, states should require pharmacists who perform or supervise sterile compounding to receive regular specialized training in the practice, whether through continuing education or certification programs.
- Training must include classroom and practical components and must cover core elements of USP <797>. (See section on quality standards.)
- States should require compounders to document that all personnel engaging in or supervising sterile compounding are qualified and have had appropriate training. Compounders should provide such documentation upon request.

Recommendations for other stakeholders: ACPE should adopt core curriculum standards for schools of pharmacy that include training on nonsterile and sterile compounding, in conformance with USP requirements.

Inspections

Site inspections are the most important tool used by states to assess pharmacy compliance with laws and regulations on compounding, whether in a community, specialty, or hospital setting. The advisory committee discussed several important aspects of inspections, including frequency, process, inspector qualifications, documentation, and follow-up.

The committee supported annual inspection of sterile compounding pharmacies as a best practice but acknowledged that some states may find this difficult because of resource constraints. States should work to allocate sufficient resources to achieve this level of oversight and could consider various funding sources, such as budget allocations from state funds, pharmacy registration fees, or pharmacy inspection fees, among others. Where resources are limited, the committee supported a risk-based approach, in which oversight of higher-risk activities, such as preparing sterile drugs using nonsterile starting ingredients, is prioritized. An additional option for states is having compounders perform annual compliance self-assessments, which could be useful additional documentation that states could review during or between inspections. States should also conduct facility inspections if a compounding pharmacy remodels or relocates.

Inspections of compounders should be unannounced and long enough to include direct observation of compounding activity. If a facility is not performing compounding on the day of the inspection, state inspectors should require compounders to simulate or compound for observation the sterile products that are most challenging to make. Inspectors should also review results of prior media fills simulating these most-challenging preparations, which are required under USP <797>. While states may not have the resources to regularly take samples of compounded products for testing, the committee felt it was important that states have the ability to test drugs as needed during inspections and investigations. The state should work to allocate sufficient funding and, if needed, authority to achieve this.

Inspectors should use a formalized inspection document that adequately describes what was observed and indicates the level of compliance with specific quality standards. Because regulators must assess compliance by not only compounding pharmacies within the state, but also compounders shipping into their state from other locations, the committee saw value in the development of a standard form to help states understand and rely on each other's inspections.

The committee supported allowing states to use trusted third parties to conduct inspections when needed, but emphasized that these third parties must be qualified and that inspections must assess adherence at minimum to USP standards. Auditors, whether with the state or a third party, must be competent to assess the type of activity they are inspecting, whether sterile compounding, nuclear/radiopharmaceuticals compounding, or other activities.

Best practice standards for states

Frequency

- States should inspect nonsterile compounding facilities at least every two years and sterile compounding facilities yearly. States should have sufficient staff and funding to achieve these frequencies.
- When resources are constrained, states should use a risk-based assessment to prioritize inspections, emphasizing high-risk compounding (e.g., preparing sterile drugs from nonsterile ingredients). States may also review documents to supplement in-person inspections.
- States should also conduct facility inspections if the compounding pharmacy remodels or relocates, and such changes must be reported to the state. Before sterile products can be released from a remodeled or relocated facility, a successful inspection should be required.
- Out-of-state pharmacies should be subject to the same frequency of inspections as in-state pharmacies, whether conducted by the state or a third party.

Process

- Inspections should be conducted by state regulators or by a trusted, qualified third party approved by the state.
- Inspections should include examinations specific to the compounding activity, such as sterile or high-risk compounding, with sterile compounding activities assessed for minimum core components of USP <797>. (See section on quality standards.)
- States should utilize a formalized inspection document that adequately describes what was observed on an inspection to ensure compounder adherence to appropriate quality standards for the activities being conducted.
- Inspections should be unannounced.

- Inspections should be long enough (or include return visits) to permit direct observation of the highest-risk compounding activity performed at the site. If this is not possible, states should require compounders to simulate, or compound for observation, the sterile products most challenging to make. States should also review the results of prior media fill (compounding simulations) tests that simulate the compounder's most challenging sterile product processes.
- States should have the ability to take and test samples of sterile compounded drugs when needed, such as for inspections or investigations. States should have sufficient funding and, if needed, authority to support these activities. States should have a relationship with a qualified lab to perform analyses.

Inspections by regulators in other states or by third parties

- If the state relies on another state or a third party to perform inspections, the inspection process must sufficiently assess, and the inspection report must demonstrate compliance with, USP standards at minimum. Inspection reports must describe the specific criteria reviewed and whether compliance was met.
- States should approve in advance any third parties permitted to conduct inspections and regularly confirm that these inspectors are meeting qualification criteria.
- Third-party inspectors should provide the state with timely notification of any compliance failures and with all documentation related to the inspection.

Inspector qualifications

- State and third-party inspectors should be competent to examine the type of facility they are reviewing. This includes pharmacies engaging in traditional sterile compounding or handling of nuclear/radiopharmaceuticals (knowledge of and experience inspecting for applicable USP requirements), or outsourcing facilities for states that elect to inspect them (knowledge of and experience in inspecting for relevant cGMPs). States may also choose to rely on FDA inspections of outsourcing facilities (see outsourcing facilities section).
- Inspectors should receive initial training before conducting inspections and ongoing follow-up training to stay current with updated standards. Training should include a classroom component and practical experience. States should allocate sufficient financial resources to support both initial and follow-up training for state inspectors. Third-party inspectors must be able to show proof of training.

Documentation of inspections and findings

- States should document all inspections and inspectional findings in writing, which should include an inspection report form or checklist clearly indicating the standards reviewed and observed; documentation may also include additional narrative as needed.
- States should give compounders a written description of any problems discovered during inspections and request a written response describing how problems will be addressed. States should follow up with facilities to ensure appropriate responses and actions.

Recommendations for other stakeholders: The National Association of Boards of Pharmacy (NABP), or another similar credible organization, should work with states to create a standardized inspection form to support harmonization of state oversight.

Pharmacy licensure

Pharmacy licensure is an important way for states to set both the general and activity-specific requirements that compounders must meet. States should conduct an inspection prior to initial licensure of a compounding pharmacy and before compounding activity begins at a licensed pharmacy. For out-of-state pharmacies, states may conduct their own inspection, rely on an inspection by the state where the pharmacy is located, or use a qualified third-party inspection. Given the additional quality standards necessary to safely perform sterile compounding, states should have the ability to track sterile compounding and enforce specific standards in a targeted way. Most members of the advisory committee believe this is best achieved by establishing a separate licensure category for sterile compounders. Suspending a separate sterile compounding license is simpler than restricting just the sterile compounding activity of a facility that may also conduct nonsterile compounding or have retail operations that should be allowed to continue. Licensure suspension also makes it easier for regulators in other states, where the pharmacy may ship products, to take conforming disciplinary action. Finally, separate licensure supports fees specific to sterile compounding.

Best practice standards for states

Pre-licensure inspection

- States should conduct an inspection prior to initial licensure of a traditional compounding pharmacy and before compounding activity begins at a licensed traditional pharmacy.
- States may rely on FDA licensure and inspections for outsourcing facilities. However, if the state elects to license and inspect outsourcing facilities before licensure, inspections must be to cGMP standards (see outsourcing facilities section).

Specific licensure requirements for sterile compounding

- States should have a mechanism to identify facilities that engage in sterile compounding that ship or dispense drugs in the state and must have a targeted ability to enforce standards specific to sterile compounding. The optimal way to achieve this is through separate licensure for sterile compounders.
- Licensure requirements should include quality standards for sterile compounding (i.e., USP <797>).

Out-of-state pharmacies

- States should independently license out-of-state compounding pharmacies, which should be inspected prior to initial licensure or before compounding activity begins at a licensed traditional pharmacy.
- If the state cannot conduct an inspection before initial licensure, it may rely on an inspection report by the state where the pharmacy is located or an inspection by a qualified third party. In either case, the inspection must have been performed in the previous year, and the report must sufficiently demonstrate compliance with USP standards at minimum and describe the specific criteria reviewed and whether compliance was met.

Outsourcing facilities

Outsourcing facilities, the category of FDA-regulated compounders created by the Drug Quality and Security Act of 2013, may compound drugs without prescriptions if they register with FDA and meet applicable cGMPs, the quality standards applied to drug manufacturers. The ability to compound without prescriptions enables outsourcing facilities to meet legitimate provider needs for standing supplies of compounded medicines. Congress created this new type of FDA-regulated facility to address the emergence over the past several years

of nontraditional compounding pharmacies operating without appropriate oversight. Traditional pharmacies normally compound drugs to meet individual patient needs. When compounded drugs are created in large batches and sold across the country, any contamination has the potential to affect thousands of patients. Because public exposure is increased, traditional pharmacy quality standards applied by states are not sufficient. Stricter protections are warranted.

Outsourcing facilities are not considered manufacturers or distributors under federal law, nor are they necessarily pharmacies, although they are not prevented from holding a state pharmacy license. The advisory committee considered both the optimal way in which states should recognize outsourcing facilities and what oversight states should provide.

Regarding how states recognize outsourcing facilities, a majority on the committee felt that states should incorporate a definition in harmony with federal law, though this was not an area of perfect agreement. Updating statutes and/or regulations to include an outsourcing facility category and definition is not necessarily simple for all states, although some, such as New York, have done it.[10] Other states are regulating outsourcing facilities as compounding pharmacies, manufacturers, or distributors—existing categories that afford them continued control. However, because outsourcing facilities ship their products across state lines, these variations can create significant challenges and confusion. Differing licensure requirements placed on a facility by different states may even directly contradict each other.

Aligning state definitions of outsourcing facilities with federal law would help support harmonized recognition across states and would help prevent confusion about what outsourcing facilities are, what standards they must meet (e.g., cGMPs), and what they are allowed to do (e.g., compound without prescriptions). Regardless of alignment with federal law, some states may wish to require separate registration or licensure to keep track of outsourcing facilities within their borders, as many states do for pharmaceutical manufacturing companies.

Regarding oversight and inspections of outsourcing facilities, the committee said the ultimate goal is for states to rely on FDA as the primary provider of oversight, but it noted transitional oversight challenges. For example, although state inspection frequencies range widely, some states are accustomed to inspecting sterile compounding pharmacies—the category many outsourcing facilities fell into before the Drug Quality and Security Act—frequently, perhaps once a year. By comparison, FDA has historically inspected drug manufacturing sites once every two to three years. States may be reluctant to halt inspections of outsourcing facilities because they do not yet have confidence in FDA's oversight. But continued state inspections are also a challenge because outsourcing facilities must meet Good Manufacturing Practices, quality standards that state inspectors generally are not trained to know. The committee agreed that states that wish to directly inspect outsourcing facilities should be trained on cGMPs and could seek collaboration and support from FDA and the National Association of Boards of Pharmacy. Other options for states are to review inspection reports showing cGMP compliance or simply rely on FDA's oversight of these facilities.

Best practice standards for states

- States should recognize outsourcing facilities in regulation or statute and incorporate a state law definition that is aligned with federal law.
- If states wish to formally track outsourcing facilities that do business in their state via separate registration or licensure, registration with FDA should be a prerequisite.
- All production at an outsourcing facility must meet applicable cGMPs. States may:
    - Rely on FDA to conduct oversight.

    - Require an inspection report demonstrating compliance with cGMPs.
    - Conduct their own inspections. States that wish to inspect outsourcing facilities must ensure inspectors have the appropriate training to assess adherence to applicable cGMP standards.
- Outsourcing facilities that conduct patient-specific compounding and dispensing must also be licensed as a pharmacy with the state, but the quality standard applied to the facility must be cGMP, not USP <797>. Records of compounded products prepared based on a patient-specific prescription must be maintained separately from records of non-patient-specific compounded products, so that these distinct records are readily retrievable.

Compounding without prescriptions and other violations of federal law

Compounding is traditionally done pursuant to a patient prescription. Federal law allows compounding pharmacies to be exempt from requirements placed on drug manufacturers, such as the FDA drug approvals process, if compounding is done pursuant to a patient prescription or in limited quantities before the receipt of a patient prescription. Federal law allows compounding without a prescription only if a plant registers with FDA as an outsourcing facility and meets cGMP standards.

In contrast to federal law, some states allow compounding pharmacies to sell a certain amount of products without prescriptions for use in doctors' offices and clinics, often referred to as "office stock" or "office use" compounding. Addressing this disparity between federal and state law may be challenging, but a majority of committee members agreed that states should seek to harmonize their policies with federal law and regulations. The committee also felt that states should take a public health approach to enforcement: States should focus oversight resources on plants compounding drugs without prescriptions in larger batches, where any contamination represents a greater public health risk. The Drug Quality and Security Act brings nontraditional compounding under FDA oversight, and thus higher-quality standards, to protect patients. Continuing to allow unrestricted compounding without prescriptions outside of this system undermines the new federal oversight category because it removes the incentive to participate.

The committee considered how states should address centralized compounding services that serve a large health system network, but it did not identify a clear best practice. States, FDA, and health system stakeholders should collaborate to determine whether centralized hospital pharmacies that compound sterile products for use within their health system without receiving patient prescriptions should register with FDA as an outsourcing facility, or whether state oversight is sufficient to ensure safety. Considerations when making this decision should include the volume of output, the number of hospitals and patients served, and whether the central pharmacy compounds drugs with beyond-use dating that exceeds defaults established in USP <797>.

In addition to compounding without prescriptions, states should be vigilant for other ways pharmacies may exceed the bounds of traditional practice and violate federal law, such as compounding copies of commercially available drugs, compounding drugs on FDA's list of products that have been withdrawn or removed from the market due to safety or efficacy concerns, or compounding drugs on FDA's list of drugs too difficult to compound safely. States should communicate with FDA about any facility they think is operating outside of traditional practice. The Drug Quality and Security Act requires FDA to work with the National Association of Boards of Pharmacy to establish a mechanism for states to report these issues to the agency.

Best practice standards for states

Compounding without prescriptions

- States should align laws and regulations with federal laws and regulations on compounding and dispensing/distributing without prescriptions.
- States should prioritize enforcement oversight on higher-risk activities—such as compounding pharmacies producing products without prescriptions on a larger scale—that in the event of contamination can affect more patients.
- States should establish policies that support provider purchasing of compounded drugs without prescriptions only from FDA-registered outsourcing facilities.

Compounding in violation of federal law

- State regulators should identify any compounding entities that operate in violation of federal law and either require them to cease this activity or, if appropriate, register with FDA as an outsourcing facility. State regulators should report to FDA any facilities that refuse to either cease activities in violation of federal law or, if appropriate, register with FDA as an outsourcing facility.

Physician's office compounding

Drug compounding most commonly occurs at pharmacies, but it may also take place in a doctor's office. State pharmacy regulators manage the oversight of compounding within pharmacies but do not normally have jurisdiction over medical practices, which are regulated by state medical boards. If a doctor's office employs a pharmacist to compound, the state board of pharmacy may have a greater ability to exert control through licensure, but not always. Differing state laws on whether physicians are allowed to dispense drugs complicates matters further.

The advisory committee affirmed that quality standards must be the same wherever compounding occurs and expressed concern that compounding in doctors' offices is not always regulated or tracked well. States should have a mechanism to identify and oversee doctor's office compounding, whether done through the board of pharmacy or board of medicine. The committee recommended that this issue also be addressed through collaboration between the Federation of State Medical Boards and the National Association of Boards of Pharmacy.

The committee also acknowledged that special considerations are necessary for compounding drugs in a doctor's office that for medical reasons must be administered immediately after preparation. It also agreed that an exemption from full USP quality standards may be appropriate in this case, because a contaminant, if present, would not have time to proliferate to harmful levels when the drug is used immediately. Practitioners compounding in doctors' offices, however, must still have appropriate training and must be held to a standard of care that includes good hand hygiene and aseptic technique. States should be careful to ensure that special allowances for immediate-use compounding do not inadvertently encourage this practice outside of what is medically necessary. Some studies suggest drugs prepared outside of controlled pharmacy environments, such as in hospital wards, may be at higher risk for contamination.[11] Because nurses may also be asked to compound for physicians, consideration should be given to involving state boards of nursing as well.

Best practice standards for states

- Physicians' offices that compound should be held to the same standards as other compounding facilities, including quality standards (e.g., USP <797>) and reporting standards.
- The state should have a mechanism for knowing which doctors' offices are conducting sterile compounding and should inspect these offices to ensure compliance. This oversight can be done by the state medical board or the state board of pharmacy. If by the state medical board, inspectors must receive appropriate training.
- There should be an exemption for compliance by physicians' offices with full USP <797> for immediate-use drugs (which are administered within the hour as defined by USP). However, practitioners compounding in doctors' offices must still have training and be held to a standard of care that includes good hand hygiene and aseptic technique, per USP standards. The immediate-use exemption cannot apply to hazardous drugs.

Recommendations for other stakeholders: The Federation of State Medical Boards should work with the National Association of Boards of Pharmacy to address physician's office compounding and identify appropriate oversight systems, whether through state medical boards, state boards of pharmacy, or other appropriate entities.

Reporting activities and adverse events

To meaningfully regulate compounding activity within the state, regulators need complete information about what activities are occurring at which facilities. The advisory committee discussed what information would be valuable to regularly receive from compounders and what would be important to have upon request. Traditional pharmacy compounders should regularly report their intended compounding practices to the state, including sterile and high-risk compounding, as well as compounding drug products that are in short supply. This could be done through licensure and licensure renewal or through a separate reporting process.

States can also benefit from information about the volume of drugs compounded in the previous year to monitor the scale of compounding operations. Advisory committee members felt that annual reporting of production volume information was not needed, but this information should be available to state regulators upon request. States may also have interest in knowing what activities occur at the outsourcing facilities in their jurisdictions. Outsourcing facilities must submit annual reports to FDA on the volume and type of products they produce, and these facilities should also make their reports available to states upon request.

Traditional compounding pharmacies should also report adverse events and voluntary recalls to the state. States should review voluntary recalls to ensure that actions taken to carry out the recall sufficiently address any risk to patients. States that elect to license outsourcing facilities may also elect to require these facilities to report adverse events to the state. Federal law requires outsourcing facilities to report adverse events to FDA.

Best practice standards for states

Activity reporting

- States should be able to track the type of compounding activities conducted by pharmacies in the state including sterile, nonsterile, and high-risk compounding. States should require compounders to report this information to the state, whether through licensure application or renewal, or through a separate activity reporting mechanism.
- States should have the authority to request reports from traditional compounding pharmacies on the number and volume of compounded products sold or dispensed in the state and, for in-state pharmacies, outside the

state in the previous year, including the drug's active ingredients, strength, and dosage form. States should be able to request this information outside of an inspection.

- States should have the authority to request the reports outsourcing facilities give to FDA identifying the drugs compounded in the previous six months, including the drug's active ingredients, strength, and dosage form.

Adverse event and recalls reporting

- Traditional compounding pharmacies should be required to report serious adverse events (as defined by FDA)[12] to the state board of pharmacy within 24 hours.
- Traditional compounding pharmacies should be required to report voluntary recalls to the state and FDA within 24 hours. The state should review voluntary recalls to ensure that actions taken to communicate with providers and/or remove products from the market sufficiently mitigate risk to patients.
- States that elect to license outsourcing facilities may also decide to require these facilities to report serious adverse events to the state.

State authorities and sanctions

States need appropriate authorities to execute oversight of drug compounding, such as the power to seize and quarantine products and, when there is the potential for serious patient harm, to order the cessation of activity to protect the public in advance of a hearing. States should also have the ability to mandate the recall of a compounded drug when there is potential for patient harm. States should further consider appropriate administrative, civil, and criminal penalties for violations of compounding regulations. States that elect to license outsourcing facilities may also elect to clarify the authorities that apply to these facilities and the products they make.

Members of the advisory committee also underscored the importance of receiving enforcement information from other states and FDA. A central clearinghouse of publicly available enforcement actions taken against compounding pharmacies and outsourcing facilities would be a helpful resource for state regulators. In some cases, however, state law may constrain what information regulators are able to share publicly or with each other.

Best practice standards for states

State authorities

- States should have the authority to quarantine products.
- States should have the authority to seize products.
- States should have the authority to suspend activity the state believes to be in violation of applicable law or regulation in advance of a hearing when the potential for serious patient harm exists.
- States should have the authority to mandate recalls of compounded drugs when there is potential or confirmed harm to a patient.
- States should have the authority to require compounders to notify providers and patients about recalled products to protect public health.
- States should have the authority to share information with other regulators, both federal and state, to support oversight and investigations.

Sanctions and penalties

- States should post sanctions and disciplinary actions on a public website.

Recommendations for other stakeholders: An independent third party, such as the National Association of Boards of Pharmacy, should establish a central resource of public enforcement actions taken against compounding pharmacies and outsourcing facilities by state regulators, as well as product recalls. FDA enforcement actions, which the agency already posts publicly, could also be incorporated.

Conclusion

This best practices document, developed with an advisory committee of state regulators and experts (see acknowledgments), identifies the most important state practices in the regulation of compounding. Although 2013 federal legislation created a new role for FDA to oversee compounding facilities producing standing supplies of drugs without prescriptions, states remain the primary regulator of traditional pharmacy compounding. As such, states are responsible for establishing appropriate oversight systems to protect patients from the risk of contaminated or substandard compounded products. In the wake of the 2012-13 nationwide fungal meningitis outbreak linked to compounded injections, states should examine existing systems closely and address any identified gaps.

States should hold compounding pharmacies to appropriate minimum quality standards and must regularly send qualified inspectors to ensure compliance. States should have systems to track the compounding activities in their state and should set meaningful training expectations for pharmacists, especially those who compound sterile drugs. States should also communicate with each other and harmonize oversight to better address interstate movement of compounded drugs. Finally, states should ensure that their policies on compounding without a prescription are aligned with federal law. They should work with FDA to identify compounding that violates these standards or production plants that exceed traditional pharmacy practice and should be regulated by FDA as outsourcing facilities.

Appendix

Best Practices for State Oversight of Drug Compounding

Quality standards

States should require traditional compounding pharmacies to comply, at minimum, with all applicable U.S. Pharmacopeial (USP) Convention standards, including general chapters <795> and <797>, new chapter <800> when complete, and other referenced chapters.

States should hold out-of-state traditional compounding pharmacies that ship into the state to USP standards at a minimum.

States should ensure that revisions of USP standards are reflected in state requirements.

Equipment certification and lab accreditation

States should require that all sterile compounding facilities and critical air control devices be certified by a qualified individual at least every six months (as required by USP <797>) using standard testing protocols such as those endorsed by the Controlled Environment Testing Association (CETA).

States should require that sterile compounders use only external testing labs that are clinical or environmental labs with appropriate accreditation.* Labs should also meet the International Organization for Standardization and the International Electrotechnical Commission 17025:2005† quality standard, General Requirements for the Competence of Testing and Calibration Laboratories.

Pharmacist training

In addition to USP <797> training expectations, states should require pharmacists who perform or supervise sterile compounding to receive regular specialized training in the practice, whether through continuing education or certification programs.

Training must include classroom and practical components and must cover core elements of USP <797> (see section on quality standards).

States should require compounders to document that all personnel engaging in or supervising sterile compounding are qualified and have had appropriate training. Compounders should provide such documentation upon request.

Recommendation for other stakeholders: Accreditation Council for Pharmacy Education (ACPE) should adopt core curriculum standards for schools of pharmacy that include training on nonsterile and sterile compounding, in conformance with USP requirements.

* Appropriate accreditation for clinical labs could include, for example, Clinical Laboratory Improvement Amendments accreditation or College of American Pathologists accreditation. Appropriate accreditation for environmental labs could include, for example, review by the American Association for Laboratory Accreditation, American Industrial Hygiene Association's Laboratory Accredited Programs LLC, or National Environmental Laboratory Accreditation Conference accreditation.

† The nonprofit International Organization for Standardization creates standardized international specifications for numerous types of business operations and products across many industry sectors.

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Inspections

Frequency

States should inspect nonsterile compounding facilities at least every two years and sterile compounding facilities yearly. States should have sufficient staff and funding to achieve these frequencies.

When resources are constrained, states should use a risk-based assessment to prioritize inspections, emphasizing high-risk compounding (e.g., preparing sterile drugs from nonsterile ingredients). States may also review documents to supplement in-person inspections.

States should also conduct facility inspections if the compounding pharmacy remodels or relocates, and such changes must be reported to the state. Before sterile products can be released from a remodeled or relocated facility, a successful inspection should be required.

Out-of-state pharmacies should be subject to the same frequency of inspections as in-state pharmacies, whether conducted by the state or a third party.

Process

Inspections should be conducted by the state or by a trusted, qualified third party approved by the state.

Inspections should include examinations specific to the compounding activity, such as sterile or high-risk compounding, with sterile compounding activities assessed for minimum core components of USP <797> (see section on quality standards).

States should utilize a formalized inspection document that adequately describes what was observed on an inspection to ensure compounder adherence to appropriate quality standards for the activities being conducted.

Inspections should be unannounced.

Inspections should be long enough (or include return visits) to permit direct observation of the highest risk compounding activity performed at the site. If this is not possible, states should require compounders to simulate, or compound for observation, the sterile products most challenging to make. States should also review the results of prior media fill (compounding simulations) tests that simulate the compounder's most challenging sterile product processes.

States should have the ability to take and test samples of sterile compounded drugs when needed, such as for inspections or investigations. States should have sufficient funding and, if needed, authority to support these activities. States should have a relationship with a qualified lab to perform analysis.

Recommendation for other stakeholders: The National Association of Boards of Pharmacy, or other similar credible organization, should work with states to create a standardized inspection form to support harmonization of state oversight.

Inspections by regulators in other states or by third parties

If the state relies on another state or a third party to perform inspections, the inspection process must sufficiently assess, and the inspection report must demonstrate compliance with, USP standards at minimum. Inspection reports must describe the specific criteria reviewed and whether compliance was met.

States should approve in advance any third parties permitted to conduct inspections and regularly confirm that these inspectors are meeting qualification criteria.

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Third-party inspectors should provide the state with timely notification of any compliance failures and with all documentation related to the inspection.

Inspector qualifications

State and third-party inspectors should be competent to examine the type of facility they are reviewing. This includes pharmacies engaging in traditional sterile compounding or handling nuclear/radiopharmaceuticals (knowledge of and experience in inspecting for applicable USP requirements), or outsourcing facilities for those states that elect to inspect them (knowledge of and experience in inspecting for relevant current Good Manufacturing Practices). States may also choose to rely on FDA inspections of outsourcing facilities (see outsourcing facilities section).

Inspectors should receive initial training before conducting inspections and ongoing follow-up training to stay current with updated standards. Training should include a classroom component and practical experience. States should allocate sufficient financial resources to support both initial and follow-up training for state inspectors. Third-party inspectors must be able to show proof of training.

Documentation of inspections and findings

States should document all inspections and inspectional findings in writing, which should include an inspection report form or checklist clearly indicating the standards reviewed and observed; documentation may also include additional narrative as needed.

States should give compounders a written description of any problems discovered during inspections and request a written response describing how problems will be addressed. States should follow up with facilities to ensure appropriate responses and actions.

Pharmacy licensure

Pre-licensure inspection

States should conduct an inspection before initial licensure of a traditional compounding pharmacy and before compounding activity begins at a licensed traditional pharmacy.

States may rely on FDA licensure and inspections for outsourcing facilities. However, if the state elects to license and inspect outsourcing facilities before licensure, inspections must be to cGMP standards (see outsourcing facilities section).

Specific licensure requirements for sterile compounding

States should have a mechanism to identify facilities that engage in sterile compounding that ship or dispense drugs in the state and must have a targeted ability to enforce standards specific to sterile compounding. The optimal way to achieve this is through separate licensure for sterile compounders.

Licensure requirements should include quality standards for sterile compounding (i.e., USP <797>).

Out-of-state pharmacies

States should independently license out-of-state pharmacies, which should be inspected before initial licensure or before compounding activity begins at a licensed traditional pharmacy.

If the state cannot conduct an inspection before initial licensure, it may rely on an inspection report by the state where the pharmacy is located or on an inspection by a qualified third party. In either case, the inspection must have been performed in the previous year, and the report must sufficiently demonstrate compliance with USP standards at minimum and describe the specific criteria reviewed and whether compliance was met.

Outsourcing facilities

States should recognize outsourcing facilities in regulation or statute and incorporate a state law definition that is aligned with federal law.

If states wish to formally track outsourcing facilities that do business in their state via separate registration or licensure, registration with FDA should be a prerequisite.

All production at an outsourcing facility must meet applicable cGMPs. States may:

- Rely on FDA to conduct oversight.
- Require an inspection report demonstrating compliance with cGMPs.
- Conduct their own inspections. States that wish to inspect outsourcing facilities must ensure inspectors have the appropriate training to assess adherence to applicable cGMP standards.

Outsourcing facilities that conduct patient-specific compounding and dispensing must also be licensed as a pharmacy with the state, but the quality standard applied to the facility must be cGMP, not USP <797>. Records of compounded products prepared based on a patient-specific prescription must be maintained separately from records of non-patient-specific compounded products, so that these distinct records are readily retrievable.

Compounding without prescriptions, violations of federal law

Compounding without prescriptions

States should align laws and regulations with federal laws and regulations on compounding and dispensing/distributing without prescriptions.

States should prioritize enforcement oversight on higher-risk activities—such as compounding pharmacies producing products without prescriptions on a larger scale—that in the event of contamination can affect more patients.

States should establish policies that support provider purchasing of compounded drugs without prescriptions only from FDA-registered outsourcing facilities.

Compounding in violation of federal law

State regulators should identify any compounding entities that operate in violation of federal law and either require them to cease this activity or, if appropriate, register with FDA as an outsourcing facility. State regulators should report to FDA any facilities that refuse to either cease activities in violation of federal law or, if appropriate, register with FDA as an outsourcing facility.

Physician's office compounding

Physicians' offices that compound should be held to the same standards as other compounding facilities, including quality standards (e.g., USP <797>) and reporting standards.

The state should have a mechanism for knowing which doctors' offices are conducting sterile compounding and should inspect these offices to ensure compliance. This oversight can be done by the state medical board or state board of pharmacy. If by the state medical board, inspectors must receive appropriate training.

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There should be an exemption for compliance by physicians' offices with full USP <797> for immediate-use drugs (which are administered within the hour, as defined by USP). However, practitioners compounding in doctors' offices must still have training and be held to a standard of care that includes good hand hygiene and aseptic technique, per USP standards. The immediate-use exemption cannot apply to hazardous drugs.

Recommendation for other stakeholders: The Federation of State Medical Boards should work with the National Association of Boards of Pharmacy to address physician's office compounding and identify appropriate oversight systems, whether through state medical boards, state boards of pharmacy, or other appropriate entities.

Activity and adverse event reporting

Activity reporting

States should be able to track the type of compounding activities conducted by pharmacies in the state including sterile, nonsterile, and high-risk compounding. States should require compounders to report this information to the state, whether through licensure application or renewal, or through a separate activity reporting mechanism.

States should have the authority to request reports from traditional compounding pharmacies on the number and volume of compounded products sold or dispensed in the state and, for in-state pharmacies, outside the state in the previous year, including the drug's active ingredients, strength, and dosage form. States should be able to request this information outside of an inspection.

States should have the authority to request the reports outsourcing facilities give to FDA identifying the drugs compounded in the previous six months, including the drug's active ingredients, strength, and dosage form.

Adverse event and recalls reporting

Traditional compounding pharmacies should be required to report serious adverse events (as defined by FDA)‡ to the state board of pharmacy within 24 hours.

Traditional compounding pharmacies should be required to report voluntary recalls to the state and FDA within 24 hours. The state should review voluntary recalls to ensure that actions taken to communicate with providers and/or remove products from the market sufficiently mitigate risk to patients.

States that elect to license outsourcing facilities may also decide to require these facilities to report serious adverse events to the state.

‡ U.S. Food and Drug Administration, "What Is a Serious Adverse Event?" updated Jan. 10, 2014, http://www.fda.gov/Safety/MedWatch/HowToReport/ucm053087.htm. FDA defines a serious adverse event associated with the use of a medical product in a patient as a death, life-threatening event, hospitalization, disability or permanent damage, congenital anomaly or birth defect, or an event that may require medical or surgical intervention to prevent one of these outcomes.

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State authorities and sanctions

State authorities

States should have the authority to quarantine products.

States should have the authority to seize products.

States should have the authority to suspend activity the state believes to be in violation of applicable law or regulation in advance of a hearing when the potential for serious patient harm exists.

States should have the authority to mandate recalls of compounded drugs when there is potential or confirmed harm to a patient.

States should have the authority to require compounders to notify providers and patients about recalled products to protect public health.

States should have the authority to share information with other regulators, both federal and state, to support oversight and investigations.

Sanctions and penalties

States should post sanctions and disciplinary actions on a public website.

Recommendation for other stakeholders: An independent third party, such as the National Association of Boards of Pharmacy, should establish a central resource of public enforcement actions taken against compounding pharmacies and outsourcing facilities by state regulators, as well as product recalls. FDA enforcement actions, which the agency already posts publicly, could also be incorporated.

Endnotes

1 U.S. Congress, H.R. 3204, Drug Quality and Security Act, https://www.congress.gov/bill/113th-congress/house-bill/3204.

2 United States Pharmacopeial Convention, "General Chapter <79 7> Pharmaceutical Compounding—Sterile Preparations: Notice of Intent to Revise," Sept. 25, 2015, http://www.usp.org/usp-nf/notices/general-chapter-797-proposed-revision.

3 Controlled Environment Testing Association, "What Is CETA?" http://www.cetainternational.org/#what. CETA is a nonprofit trade association "devoted to promoting and developing quality assurance within the controlled environment testing industry."

4 Appropriate accreditation for clinical labs could include, for example, Clinical Laboratory Improvement Amendments accreditation or College of American Pathologists accreditation. Appropriate accreditation for environmental labs could include review by the American Association for Laboratory Accreditation, American Industrial Hygiene Association's Laboratory Accredited Programs LLC, or National Environmental Laboratory Accreditation Conference accreditation.

5 The nonprofit International Organization for Standardization creates standardized international specifications for numerous type s of business operations and products across many industry sectors.

6 United States Pharmacopeial Convention, "General Chapter <79 7> Pharmaceutical Compounding—Sterile Preparations: Notice of Intent to Revise."

7 An Act Relative to Pharmacy Practice in the Commonwealth, Commonwealth of Massachusetts, 2014 Session Law, Chapter 159, https: // malegislature.gov/Laws/SessionLaws/Acts/2014/Chapter159.

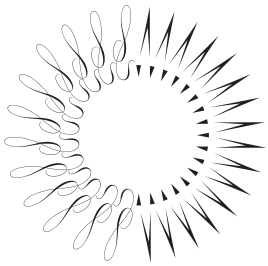
8 Continuing Education Requirements, Texas Administrative Code, Title 22, Part 15, Chapter 295, Rule Section 295.8, http://texreg.sos.state.tx.us/public/readtac$ext.TacPage?sl=R&app=9&p_dir=&p_rloc=&p_tloc=&p_ploc=&pg=1&p_tac=&ti=22&pt=15&ch=295&rl=8; and Additional Continuing Education Requirements, Texas State Board of Pharmacy (June 2015), http://www.pharmacy.texas.gov/files_pdf/Specific_CE_Requirements.pdf.

9 The Accreditation Council for Pharmacy Education is "the national agency for the accreditation of professional degree programs in pharmacy and providers of continuing pharmacy education" (https://www.acpe-accredit.org/about/default.asp).

10 Special Provisions Relating to Outsourcing Facilities, New York State Education Department, Education Law, Article 137, Pharm acy, Section 6831, http://www.op.nysed.gov/prof/pharm/article137.htm.

11 Cyril Stucki et al., "Microbial Contamination of Syringes During Preparation: The Direct Influence of Environmental Cleanliness and Risk Manipulations on End-Product Quality," *American Journal of Health-System Pharmacy* 66 (2009): 2032-2036.

12 U.S. Food and Drug Administration, "What Is a Serious Adverse Event?" last modified Jan. 10, 2014, http://www.fda.gov/Safety/MedWatch/HowToReport/ucm053087.htm. FDA defines a serious adverse event associated with the use of a medical product in a patient as a death, life-threatening event, hospitalization, disability or permanent damage, congenital anomaly or birth defect, or an event that may require medical or surgical intervention to prevent one of these outcomes.



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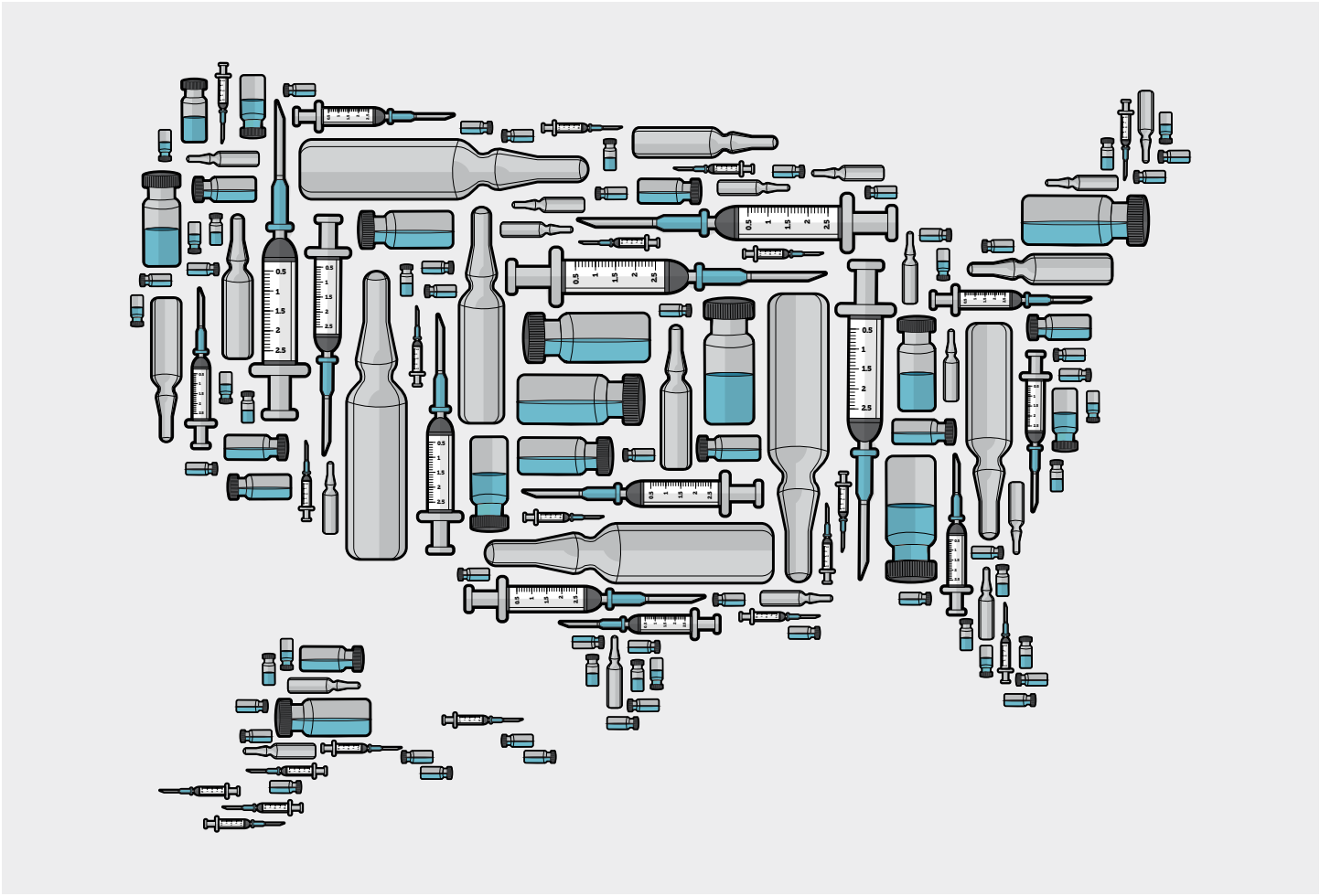

National Assessment of State Oversight of Sterile Drug Compounding

Contents

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Overview

Drug compounding is a long-standing practice wherein a pharmacist "combines, mixes, or alters ingredients of a drug to create a medication tailored to the needs of an individual patient."[1] While the Food and Drug Administration (FDA) has the authority to enforce applicable federal laws over pharmacies, states remain the principal regulators of pharmacy practice, including pharmacy compounding activity. Relevant laws and regulations are updated at the discretion of each state and jurisdiction. This study, commissioned by The Pew Charitable Trusts and conducted by researchers from the University of Illinois at Chicago, assesses the national landscape of state policies on compounding sterile drugs—such as medicines that are injected or infused into the body.

Between 2012 and 2013,[2] an outbreak involving hundreds of patient illnesses and dozens of deaths linked to tainted compounded injections drove state and federal officials to re-examine oversight of sterile drug compounding, particularly when it exceeds traditional practice in scale and risk.[3] However, until now there has been no single central repository for information describing policy and practice across states.

This study collected data from publicly available websites and from a questionnaire on state oversight that was completed by representatives from 43 of the 51 state boards of pharmacy (50 states plus the District of Columbia) in spring and summer 2015.

The study found that states vary significantly in their policies for sterile compounding. While some policy areas showed greater alignment across states, such as the application of recognized quality standards, others differed notably, including disparate systems to oversee out-of-state compounding pharmacies. Some states have updated their standards in the wake of the 2012-13 outbreak and to conform to new federal law. The Drug Quality and Security Act of 2013, among other reforms, added a new category of compounders called outsourcing facilities that can compound supplies of drugs without obtaining prescriptions. However, the state policy landscape remains fluid: New policies are not uniform. Some states are still working to advance change, and others have yet to act. This remains a transitional time for compounding drug policy in many states, which should be weighed in the interpretation of the findings of this study.

Among the notable findings and themes of this research:

- About half of the respondents (representing 21 of 43 states, or 49 percent) reported that they required sterile compounding to fully conform to the widely recognized quality standards set by the U.S. Pharmacopeial Convention (USP) in its General Chapter <797> Pharmaceutical Compounding—Sterile Preparations. Thirteen respondents (30 percent) reported that their states mandated at least some part of USP Chapter <797>. Just over half of respondents (representing 24 of 43 states, or 56 percent) reported that their states tracked the number of pharmacies that perform sterile compounding.
- The majority of respondents (representing 26 of 43 states, or 60 percent) said their states did not require pharmacies to report serious adverse events and reactions related to sterile compounding.
- Twenty-eight respondents (65 percent) said their states allowed pharmacies to compound without patient-specific prescriptions. Most of these states (21 of the 43 respondents, or 49 percent) had specific limits on this practice, but with varying degrees of restriction—such as a narrow allowance for emergency veterinary use only, compared with a broader allowance for any drug that is not commercially available. State policies permitting compounding without a prescription for human use conflict with recently clarified federal law.
- Nine respondents (21 percent) said their state required pharmacies to have a separate license or registration to perform sterile compounding.

- Twelve respondents (28 percent) reported that when inspecting sterile compounding pharmacies in the state, they prioritized inspections for pharmacies where high-risk sterile compounding occurs.
- Sterile compounding sometimes takes place in physician offices or clinics, which are normally regulated by a state board of medicine. When asked, only one state reported that their state had a mechanism to track nonpharmacy locations where sterile compounding occurs, and only seven respondents (17 percent) reported that physician offices were held to the same compounding quality standards as pharmacies.

The variations in sterile compounding policy across states suggest that an opportunity exists to review state oversight systems for potential weaknesses, and consequently to advance regulatory practices to better protect patients. This study is intended to provide helpful information to policymakers and stakeholders in pursuit of that goal.

Background

Traditional pharmacy compounding involves the specialized preparation of a drug tailored to the needs of an individual patient. Compounding is distinct from commercial drug manufacturing, in which standardized drug products are approved by FDA and produced on a large scale. Pharmacists may prepare customized drugs in a number of ways, such as by combining or diluting existing drugs, or creating a drug product from bulk active chemicals. Compounding is considered a fundamental skill for pharmacists,[4] and like other licensed health care professions, pharmacy practice is regulated by the state. State pharmacy law is typically enforced by a state board of pharmacy.[5]

Meaningful quality standards are important for all forms of compounded drugs, including pills, syrups, and topical creams. But rigorous standards are critical for drugs that are injected or infused into the body, and therefore must be sterile to minimize the risk of infection. The preparation of sterile injectables and IV infusion products by a pharmacist or other practitioner emerged as a practice in the early 20th century primarily in the hospital setting, where those products were used.[6] However, as the complexity of sterile preparations increased and demand grew, outsourced sterile compounding became a commercial enterprise.[7]

Pharmaceutical manufacturers were among the first companies to enter the outsourced compounding services market in the 1980s and 1990s, establishing pharmacies to prepare sterile medications for hospitals. Other compounding pharmacies also began to supply doctors' offices and clinics.[8] Some of these outsourcers were providing supplies of compounded drugs without patient prescriptions, which created an oversight and enforcement challenge for FDA.[9] There was no explicit federal regulatory framework for compounding pharmacies, and the agency became increasingly concerned about appropriate oversight of businesses that looked more like manufacturers than traditional compounders.[10]

In 1997, Congress introduced new federal policy on compounding as part of the Food and Drug Administration Modernization Act, adding Section 503A to the Federal Food, Drug, and Cosmetic Act (FDCA).[11] Under this section, compounders must obtain a prescription for an individually identified patient in order to receive exemptions from several FDA requirements, including new drug approval processes, labeling with adequate directions for use, and adherence to FDA Current Good Manufacturing Practices (CGMPs). Among other provisions to distinguish compounding from commercial manufacturing, Section 503A prohibited compounders from "advertising, promoting, or soliciting prescriptions."[12]

However, soon after the passage of Section 503A, several pharmacies challenged the restrictions on advertising in court, claiming a free-speech violation.[13] This led to a series of conflicting rulings resulting in invalidation of the

law in some parts of the country. In 2001, the U.S. Court of Appeals for the 9th Circuit upheld a lower court ruling that the advertising provision was unconstitutional and further said that the provision could not be separated from the rest of the section, rendering it inoperable.[14] In 2002, the Supreme Court affirmed this ruling and did not address whether the advertising provisions could be separated from the rest of the section, leaving the 9th Circuit's decision in place.[15]

In response to the invalidation of Section 503A, FDA reissued a Compliance Policy Guide.[16] The guide stated that FDA would generally defer to state boards of pharmacy to oversee traditional pharmacy compounding but would enforce federal drug law over entities that crossed the line into drug manufacturing based on certain criteria, such as offering compounded drugs for wholesale.[17] Later, in 2008, the U.S. Court of Appeals for the 5th Circuit ruled that the advertising restrictions were invalid but that the rest of Section 503A should remain in effect.[18] This created additional ambiguity about the enforceability of federal law in different jurisdictions.

Compounding practice across the U.S. became complex and diverse as states pursued varied regulatory approaches.[19] FDA continued to harbor concerns regarding the quality and safety of compounded products. In 2001, the agency tested sterile preparations sold online by 12 compounding pharmacies for quality, purity, and potency.[20] They found that 34 percent of the 29 samples failed quality and safety tests, most frequently for potency. In contrast, the failure rate cited by FDA among commercial manufacturers was less than 2 percent.[21] Between 1990 and 2005, the agency discovered more than 240 serious illnesses and deaths associated with compounded products.[22] It also stated that this estimate might be an underrepresentation because pharmacists and physicians were not required to report adverse events to FDA.[23]

Between 2012 and 2013, 753 patients were sickened—64 of whom died—during an outbreak of fungal meningitis and other infections attributed to tainted steroid injections made by a large compounding pharmacy center in Massachusetts.[24] A subsequent examination identified numerous other incidents involving over 300 adverse events, including 26 deaths since 2001.[25] In the aftermath of the 2012-13 outbreak policymakers, including the U.S. Congress, and other groups moved to examine underlying issues around drug compounding and identify solutions.[26] Since the outbreak, FDA has conducted over 200 inspections of compounding facilities and issued approximately 60 warning letters.[27]

Congressional investigations identified several urgent issues related to (1) the need to distinguish between traditional compounding activities and those that resemble manufacturing; (2) reconsideration of appropriate oversight and quality standards for nontraditional compounding; and (3) the need for sufficient enforcement of standards by state and federal officials. Over the course of 2013, Congress developed legislation intended to address these concerns. On Nov. 27, 2013, the Drug Quality and Security Act (DQSA) was signed into law by President Barack Obama.[28] The law's first major component was the Compounding Quality Act (CQA).

The CQA clarified the distinction between traditional compounding pharmacies, which prepare drugs pursuant to individual prescriptions to meet specific patient needs and are regulated under Section 503A of the FDCA, and companies selling supplies of compounded drugs without patient-specific prescriptions. These latter are now regulated as part of a new "outsourcing facility" sector under Section 503B and are required to meet stricter quality controls. FDA implementation of the law is active and ongoing. Following passage of the DQSA, Pew commissioned a report, "Quality Standards for Large-Scale Sterile Compounding Facilities,"[29] to review the differences between traditional compounding pharmacies and operations that supply compounded drugs without prescriptions on a larger scale. The report describes the stringent standards that are critical to ensuring drug quality and patient safety in facilities that make standing supplies of drugs with the potential to reach many thousands of patients.

The Compounding Quality Act and New Outsourcing Facility Sector

The Compounding Quality Act (CQA) created a new type of compounder known as an "outsourcing facility" (OF) under Section 503B of the FDCA.[30] In exchange for submitting to more stringent FDA oversight and adherence to formal CGMPs, OFs are permitted to sell unlimited quantities of compounded drugs without a prescription anywhere in the U.S. and are exempt from the drug approvals process.[31] OFs are subject to several requirements and limitations: They may not sell drugs through wholesalers[32] and are not allowed to compound copies of drug products already on the market,[33] including a drug made using an active ingredient that is part of an approved medicine, unless the product is on the drug shortage list.[34] Further, while OFs may take an FDA-approved drug out of its packaging and alter it when required for patient care, they may not compound using a bulk chemical active ingredient unless it is on an FDA list identifying bulk drug substances for which there is a clinical need.[35] Compounding at an OF must be done under the supervision of a licensed pharmacist,[36] and OFs must also follow new labeling requirements (including the drug name, dosage form, and strength, and a statement that the drug is compounded),[37] report any adverse drug events to FDA,[38] be inspected by FDA based on a set of risk factors,[39] and pay FDA an annual fee.[40] As of Oct. 29, 2015, 55 compounding entities had registered as outsourcing facilities.[41]

The CQA also reaffirmed the applicability of Section 503A of the FDCA by removing the contested advertising provisions. Section 503A stipulates that traditional pharmacies—unlike OFs under 503B—must compound based on an individual patient prescription, or in limited quantities (not defined) before the receipt of a prescription, in order to receive exemptions from CGMP, drug approval, and labeling requirements.[42] Section 503A also directs FDA to develop a memorandum of understanding with state regulatory agencies to address the inordinate interstate distribution of compounded drugs.

The CQA helped clarify that FDA has primary oversight of all commercial pharmaceutical manufacturing as well as the new outsourcing facility compounding sector, while states are primarily responsible for regulating the practice of pharmacy, including compounding by traditional pharmacies. FDA also retains authority to enforce applicable federal law over pharmacies.

Each state has laws and regulations setting pharmacy standards and requirements, and addressing issues related to the authority pharmacies are granted to compound products for patients. But until now, there has been no single public repository for information describing state policies.

This report aims to describe state oversight of sterile compounding practices using publicly available data, and information solicited from state regulatory bodies. The authors worked with each state to characterize current efforts to oversee sterile compounding, as well as anticipated policy changes in certain areas in response to the 2013 federal law.

Methodology

The research team convened an expert advisory panel (EAP) to develop a questionnaire aimed at eliciting current state practices related to the oversight of sterile compounding practices; this panel was also consulted on how to best approach each state and implement data collection. The EAP consisted of eight individuals with extensive experience in pharmacy and compounding practice, jurisprudence, regulation, research methods and questionnaire design, and pharmaceutical policy in the U.S. health care system. The research protocol was reviewed and approved by the institutional review board at the University of Illinois at Chicago.

The questionnaire was developed through an iterative process in which questions and response options were generated, revised for clarity, and grouped into themes. Each theme related to an aspect of sterile compounding practices oversight: quality standards, monitoring and enforcement, compounding without patient-specific prescriptions (also called office stock compounding), licensure, inspection and inspector training, and compounding in physician offices or clinics.

Questionnaire items were reviewed and revised multiple times, with some items eliminated for reasons of redundancy and relevance. The final questionnaire consisted of 50 items. To minimize respondent burden, the research team pre-populated questionnaire responses from publicly available sources (i.e., state government websites on legislation and regulation) prior to contacting the state. These responses were then verified, or modified as needed, by the state contacts completing the questionnaire.

A list of potential respondents was compiled with input from the EAP; it included experts in pharmacy compounding regulation for each state, primarily executive directors of state boards of pharmacies. These individuals were contacted by the research team via telephone to explain the purpose of the questionnaire, and they were invited to participate. The questionnaire was administered through either a Web-based version developed in Qualtrics (Provo, Utah), which was sent by the research team to the respondent via an email link, or by telephone with an interviewer-administered questionnaire, depending upon respondent choice. The questionnaire was shared with external reviewers for comment prior to deployment, and pilot tested with respondents from five state boards of pharmacy. Minimal modifications were made in response to feedback from external reviewers.

Those who agreed to complete the Web-based questionnaire were sent a personal email summarizing the voluntary nature of participation, some information about the questionnaire, and a link to it. Follow-up reminder emails with the questionnaire link, and/or telephone calls, were made to respondents every week until the questionnaire was completed, the respondent declined to participate, or the respondent did not complete the questionnaire before the final deadline had passed.

Once the primary data collection phase ended, all respondents were sent a summary of their questionnaire responses for verification. For states not participating in the primary data collection phase, a copy of the questionnaire pre-filled with publicly available information was sent to the state board of pharmacy director, or equivalent. In early August 2015, state contacts were again asked to verify the accuracy of the information collected for their state and given two weeks to provide comments.

Current landscape of sterile compounding state oversight

Characteristics of participating states

After the final outreach to all 51 individual state boards of pharmacy (which includes the District of Columbia), 43 of the states (84 percent) had completed the questionnaire. Eight states (Alaska, Delaware, Florida, Georgia, Maine, North Carolina, Ohio, and Wisconsin) did not complete the questionnaire. Some of these states simply declined to participate, while others were willing to complete it but were unable to respond in a timely manner. The results were generally representative of the main regions of the United States: Northeast (eight of nine states and the District of Columbia, or 89 percent), Midwest (10 of 12 states, or 83 percent), South (13 of 17 states, or 76 percent), and West (12 of 13 states, or 92 percent). According to 2014 U.S. census data, the states that responded to our questionnaire represented the majority of the population in each region: Northeast (97 percent), Midwest (74 percent), South (66 percent), and West (99 percent). Additional characteristics of the 50 states and the District of Columbia are provided in Table 1, which presents pharmacy counts in each state using information from the National Council for Prescription Drug Programs (NCPDP) Pharmacy Provider Database. This database contains over 75,000 pharmacies and is used by many prescription processors, pharmacy benefit managers, health plans, and government entities. Table 1 also presents the number of sterile compounding pharmacies in each state where this information was provided by respondents. Pharmacies performing sterile compounding as a percentage of all pharmacies in each state ranged from 3 to 24 percent.

Results from this group of 43 participating states are described and discussed below. Data from all states, including those not participating in the questionnaire, are available in Appendix B. Information for nonparticipant states was retrieved for tables in this appendix from public websites, to the extent possible.

Table 1

Number of Pharmacies, and Pharmacies That Perform Compounding, in All U.S. States and the District of Columbia

State	Total number of pharmacies (NCPDP* data)	Number of pharmacies that list compounding functions (NCPDP* data)	Number of pharmacies performing sterile compounding (state-provided data)	Percentage of all pharmacies that perform sterile compounding
AK	153	36		
AL	1,527	588	224	15%
AR	799	260	48	6%
AZ	1,288	472		
CA	7,278	2,751	934	13%
CO	996	319	167	17%

(continued on next page)

State	Total number of pharmacies (NCPDP* data)	Number of pharmacies that list compounding functions (NCPDP* data)	Number of pharmacies performing sterile compounding (state-provided data)	Percentage of all pharmacies that perform sterile compounding
CT	761	332		
DC	160	48	15	9%
DE	218	91		
FL	5,966	2,322		
GA	2,768	1,102		
HI	316	65		
IA	862	466	90	10%
ID	380	149	90	24%
IL	2,699	1,303		
IN	1,393	467		
KS	722	335		
KY	1,299	598		
LA	1,323	435		
MA	1,277	616		
MD	1,411	678	190	13%
ME	321	198		
MI	2,663	1,581		
MN	1,290	650		
MO	1,465	706		
MS	915	263		
MT	312	123		
NC	2,546	880		
ND	220	113		
NE	548	275		

(continued on next page)

State	Total number of pharmacies (NCPDP* data)	Number of pharmacies that list compounding functions (NCPDP* data)	Number of pharmacies performing sterile compounding (state-provided data)	Percentage of all pharmacies that perform sterile compounding
NH	299	157	43	14%
NJ	2,167	1,236	180	8%
NM	427	149		
NV	652	160	35	5%
NY	5,202	2,877		
OH	2,623	1,066		
OK	1,024	387	195	19%
OR	837	362		
PA	3,736	1,759		
RI	268	101	8	3%
SC	1,436	526	122	8%
SD	253	116		
TN	1,952	735	305	16%
TX	5,298	1,928	723	14%
UT	580	230		
VA	1,849	699	172	9%
VT	168	116		
WA	1,473	553	80	5%
WI	1,307	654		
WV	615	306		
WY	147	58		

Note:

* Data are from the National Council for Prescription Drug Programs (NCPDP) Pharmacy Provider Database. Counts of pharmacies listing compounding activity may be an overestimation because they include entities that perform any compounding, not just pharmacies specializing in this practice. It is also possible that they are an underestimation because providing this information was optional.

Quality standards

Conforming to scientifically sound standards, such as those established by the U.S. Pharmacopeial Convention (USP), is critical to preventing dangerous contaminations, especially for sterile compounding. Deficiencies in sterile compounding practices can, and have, led to patient harm and death. The USP has established widely recognized quality standards for pharmacy compounding: USP Chapters <797> (sterile preparations) and <795> (nonsterile preparations). (See sidebar.)

United States Pharmacopeia Chapter <797>

The USP has developed standards to help compounding practitioners adhere to widely accepted, scientifically sound procedures and practices. USP standards can be legally enforceable when incorporated into or referenced by state laws or regulations.

The USP Chapter <797> provides procedures and requirements for compounding sterile preparations. It describes conditions and practices to prevent patient harm resulting from microbial contamination, excessive bacterial endotoxins,[43] variability in intended strength, unintended chemical and physical contaminants, and ingredients of inappropriate quality in compounded sterile preparations. Chapter <797> describes appropriate sterile gowning, cleaning procedures, environmental controls such as airflow, and monitoring practices to detect and prevent unsafe levels of contaminants in the air and on equipment and surfaces. Adherence to quality standards is essential to the safe preparation of sterile drugs.

Of note, the USP is currently working to update its standards for sterile compounding and published a proposed revision to Chapter <797> in September of 2015.[44] The USP is also working to develop Chapter <800>, which will cover the compounding of hazardous drugs.[45]

Our study found that most regulatory bodies (34 of 43 states, or 79 percent) referenced or incorporated USP <797> standards for sterile compounding in their laws and regulations. However, 13 of these 34 respondents (or 38 percent) indicated that the state does not require USP <797> in its entirety. Seven of the eight states reporting that they do not require USP <797> indicated that they will require the standard under pending policy changes. (See Table 2.)

Table 2

State Requirement of USP Chapter <797> on Sterile Compounding, and State Definitions of Compounding for the Purposes of Meeting This Requirement

	Number	Percentage*
Does the state mandate USP Chapter <797> on sterile compounding or equivalent for pharmacies that perform sterile compounding? (n = 43)		
Yes	21	49%
Yes, but not in its entirety	13	30%
No, but will under pending policy change	7	16%
No	1	2%
Don't know	1	2%
How is compounding defined by the states for the purpose of meeting USP Chapter <797> standards? Select all that apply. (n = 43)		
Constrained to 2 or more ingredients	14	33%
Repackaging	7	16%
Reconstituting, diluting, or pooling	10	23%
Other	17	40%

Note:

* Because of rounding, percentages may not always add to 100 percent.

At the time of the study, there were notable differences in how respondents defined compounding for the purposes of meeting USP <797> standards. (See Table 2.) State definitions included varying criteria, such as the combination of two or more ingredients, repackaging, reconstitution, diluting, or pooling. As a consequence, drugs prepared in one state may not be held to the same standard as those prepared in another, depending on the definition of compounding. This has implications for the quality standards applied to products shipped across state lines. For example, a repackaged sterile product made in a state that does not consider this compounding, and thus not subject to USP <797> standards, could be sent to a state that does require USP compliance for sterile repackaging. This presents an additional challenge for state regulators, who are already confronted with the task of how to best ensure the safety of compounded drugs shipped from other states. Minimum quality standards that are consistent across both drug preparation activities and states would help ensure that compounders within and outside of the state prepare safe drug products and protect the public from potential harms.

Table 3

Examples of State Requirements for Specific Minimum Training on Sterile Compounding Beyond Training Expectations Set Forth in USP Chapter <797>

Must receive five hours of continuing education, live, with written test, and must be monitored compounding in a hood [enclosed workspace with air controls] with written evaluation. Must receive passing grade on written monitoring evaluation.
To engage in the practice of sterile compounding, a minimum of one CPE hour must be ACPE accredited and related to the practice of sterile compounding.
Rule requires all individuals to obtain practical and/or academic training in the compounding and dispensing of sterile preparations, and further complete a minimum of one hour of accredited CE on an annual basis.
Have appropriate practical and didactic training in sterile compounding, clean room technology, laminar flow technology, quality assurance technique, and clinical applications of IV drug therapy.
Shall have didactic and practical training in sterile preparation compounding prior to compounding and annually thereafter.
All personnel, including pharmacists, pharmacists who supervise compounding personnel, pharmacy interns, and pharmacy technicians, shall have completed didactic and experiential training with competency evaluation through demonstration and testing (written or practical) as required by USP/NF (USP General Chapters: Pharmaceutical Compounding—Sterile Preparations). Pharmacy technicians shall complete 100 hours.
All sterile compounding personnel (pharmacy technicians and pharmacists) must have proof of personal competency in the art of sterile compounding completed annually.
To renew their license/registration, all pharmacists and pharmacy technicians must complete two hours of ACPE-accredited continuing education relating to one or more listed areas in sterile preparation if the pharmacy technician is engaged in compounding low- and medium-risk sterile preparations; or four hours if the pharmacy technician is engaged in compounding high-risk sterile preparations.

In response to questions regarding training requirements for pharmacists conducting sterile compounding, a majority of respondents (28 of 43 states, or 65 percent) reported that they did not mandate specific expectations for specialized training in sterile compounding, beyond what is currently required in USP <797>, as a condition of competency for pharmacists engaging in such activity. Ten states (23 percent of respondents) reported specific training requirements: Alabama, California, Idaho, Louisiana, Maryland, Missouri, New Jersey, New Mexico, South Carolina, and Texas. For example, as of September 2015, Texas indicated that it will require all pharmacists and pharmacy technicians who conduct sterile compounding to complete annual training in this practice (see Table 3 for additional examples). The number of hours required will depend on whether the practitioner is engaged in low- and medium-risk sterile preparations (two hours) or high-risk sterile preparations (four hours).[46] Both Texas and New Jersey clarified in their questionnaire responses that they assess compliance with specific sterile compounding training requirements during facility inspections.

Research suggests that many pharmacy schools and educational programs for pharmacists and technicians lack appropriate hands-on training in aseptic technique and sterile compounding. In 2005, 82 accredited U.S. pharmacy schools were surveyed regarding the extent to which they provided didactic and laboratory instruction related to compounded sterile preparations. Among the 53 schools that responded, 88 percent taught students about USP <797>; however, only 13 percent felt that their students had been adequately trained in sterile compounding prior to graduation.[47] Given this potential gap in education, it is possible that some pharmacists may not recognize deficiencies in their own sterile compounding practices.

Monitoring and enforcement

To effectively oversee compounding activity, state regulators need reliable information about facilities that compound and their ability to meaningfully respond to any safety deficiencies. In this regard, the monitoring and enforcement tools available to state regulatory bodies were uneven. Twenty-four of 43 respondents (56 percent) reported tracking the number of pharmacies performing sterile compounding in their state, and 17 of them provided a count. Slightly fewer respondents (19 of 43, or 44 percent) said their state tracked the number of out-of-state pharmacies shipping or dispensing compounded drugs into the state. Sixteen respondents (37 percent) reported that they did not track compounding pharmacies. (See Table 4.) Reliable data on total number of sterile compounding pharmacies in the U.S. remain elusive. There is no central repository of information tracking pharmacies that perform sterile compounding; NCPDP, the source this study used for counts of pharmacies performing compounding in each state, started collecting data in May 2011 on the specific type of compounding activity pharmacies performed, but these data have limitations. Compounding data is self-reported by pharmacies and questions about specific compounding services are currently optional.[48]

Few states (five, or 12 percent) responding to the questionnaire reported that they separately tracked sterile compounding violations. They are Alabama, Arizona, California, Maryland, and New Jersey. While most states indicated that they report pharmacy violations on a public website (36 states, or 84 percent), only three states—California, Massachusetts, and New Mexico—said they list compounding-related violations separately. (See Table 4.)

Most states did not require pharmacies performing sterile compounding to report voluntary recalls, either to the state only (7 percent do), FDA (7 percent), or both (9 percent). Reporting requirements were slightly more common for adverse events: 30 percent of states required sterile compounding pharmacies to report serious adverse events to the state, to FDA, or to both. (See Table 4.) Adverse event reporting is required by federal law for pharmaceutical companies and outsourcing facilities.[49] It can be used to identify problems that may affect other patients who received drugs from the same batch. While traditional compounding produces one-

Table 4

State Tracking and Reporting Requirements for Sterile Compounding Activity, Violations, Recalls, and Adverse Events

	Number	Percentage*
Does your state ... Select all that apply. (n = 43)		
Track the number of pharmacies in the state that perform compounding?	18	42%
Track the number of pharmacies in the state that perform sterile compounding?	24	56%
Track the number of out-of-state pharmacies that ship or dispense compounded drugs to providers or patients into the state?	19	44%
None of the above	16	37%
Don't know	3	7%
Does your state track sterile compounding-related violations separately from other pharmacy violations? (n = 43)		
Yes	5	12%
No	34	79%
Don't know	4	9%
Does your state list disciplinary actions related to pharmacy and/or compounding-related violations on a public website? (n = 43)		
Pharmacy violations listed	36	84%
Compounding violations separately listed	3	7%
Does your state require pharmacies that perform sterile compounding to report voluntary recalls to the state or FDA? (n = 43)		
To the state and FDA	4	9%
To the state only	3	7%
To FDA only	3	7%
Neither	25	58%
Don't know	8	19%
Does your state require pharmacies that perform sterile compounding to report serious adverse events to the state or FDA's MedWatch program? (n = 43)		
State and MedWatch	3	7%
State only	7	16%
MedWatch only	3	7%
Neither	26	60%
Don't know	4	9%

Note:

* Because of rounding, percentages may not always add to 100 percent.

Table 5

State Authorities Regarding Pharmacies That Perform Sterile Compounding

For pharmacies that perform sterile compounding, does your state have the authority to ...	Number	Percentage
Mandate a recall (n = 43)		
Yes	13	30%
No	19	44%
Don't know	11	26%
Issue a cease-and-desist order (n = 42*)		
Yes	37	88%
No	4	10%
Don't know	1	2%
Request reports from pharmacies that perform sterile compounding on the number of sterile products prepared (n = 43)		
Yes	38	88%
No	3	7%
Don't know	2	5%

Note:

* One state chose not to answer this question.

off medications for individual patients, mandatory reporting could still signal quality concerns associated with a specific facility.

With respect to enforcement authority, most respondents (88 percent) reported that the state had the power to request reports of sterile products prepared by pharmacies. An ability to know the amount of sterile compounded products that pharmacies ship out of state may be relevant to state participation in an anticipated FDA-state memorandum of understanding system to address the inordinate interstate distribution of compounded drugs. As required under Section 503A of the FDCA, FDA is working to develop a standard memorandum of understanding for this purpose.

Most respondents had the authority to issue cease-and-desist orders (88 percent), but approximately two-thirds (70 percent) were unable to mandate a recall of compounded drugs or were unsure of their explicit authority to do so. (See Table 5.) This may reflect a technical lack of recall authority rather than an inability to advance a recall, given that state regulators ultimately control licensure and may use this to request pharmacy actions when there is a real or perceived emergent threat to public health. In addition, other state officials, such as state governors, have the ability to take action when public health is threatened.[50] Understanding recall authority is important as it is a powerful tool to ensure that drug compounders are compliant with state regulations having

implications for protecting public health. Similar to adverse event reporting, the need for an effective recall system is greater for facilities making standardized or batched medicines, which can affect more patients.

Compounding without prescriptions and the new outsourcing facility sector

Section 503A of the FDCA does not allow the compounding of drugs for human use without a prescription, also known as office stock or office use compounding. This is only allowed if a facility registers with FDA as an outsourcing facility under Section 503B of the FDCA and meets CGMP standards. However, there was some legal uncertainty about the enforceability of Section 503A until the passage of the DQSA in 2013, and states may still be working to adapt their regulations. Our study found that nearly two-thirds of respondents allowed traditional compounding pharmacies to produce drugs without prescriptions to at least some extent. (See Table 6.) Ten respondents reported that their policies did not allow compounding without prescriptions: the District of Columbia, Hawaii, Illinois, Maryland, Missouri, Montana, New York, Rhode Island, Washington, and West Virginia. Based on public websites, Maine (a nonrespondent state) also prohibits compounding without a prescription.[51] An additional three states—Minnesota, Louisiana, and New Mexico—reported that compounding without prescriptions was allowed only for veterinary use, and based on public information North Carolina took the same position.[52] Finally, Nebraska indicated in its response that pharmacies engaging in this practice should be FDA-registered outsourcing facilities to comply with federal regulations. Other limits placed on compounding without prescriptions were less restrictive, such as allowing any quantity justified by a doctor's prescribing habits. (See Table 6.)

Although states may have written policies prohibiting compounding without a patient-specific prescription, this study did not assess whether or how such policies were enforced. In addition, in some cases states appeared to conflate anticipatory compounding—compounding before the receipt of an anticipated valid prescription—with compounding a supply of a drug without a prescription to be stocked by a doctor's office or clinic. While federal law allows for anticipatory compounding, it still requires the compounder to receive a prescription prior to dispensing the compounded drug to the patient.

Notably, few respondents (7 percent) reported pending policy changes on compounding by pharmacies without a patient-specific prescription. The few states that did report changes were evenly split between prohibiting the practice, limiting it, or allowing it. Regulatory disparity both between states and with federal law may make attempts to harmonize the oversight of compounding without prescriptions (office stock compounding) challenging. Under the DQSA, in exchange for submitting to more stringent oversight, the new outsourcing facility category is now the only group allowed to legally compound without prescriptions. If states allow compounding by traditional pharmacies without patient-specific prescriptions, it could remove incentives for companies to participate in the new outsourcing facility system.

State approaches to recognizing outsourcing facilities (OFs) varied, and only seven states had developed a specific OF licensure or registration category at the time of data collection. Five of these states reported this through our questionnaire: California (bill pending in Legislature), Idaho, Mississippi, New York, and Tennessee. Based on the review of public websites, Delaware and Florida also have an OF category, although this was not confirmed by a state contact. Additionally, 12 respondents reported that they were currently developing an OF licensure or registration category. Other states were mixed: Some required OFs to license as manufacturers, some as wholesalers, and some as pharmacies, while some permitted multiple licensure categories. (See Tables 7 and 8.) Federal law neither prohibits nor requires pharmacy licensure for OFs. If OFs maintain a traditional pharmacy practice as well as an outsourcing facility, continued licensure as a pharmacy is likely to be appropriate. In some cases, state licensure requirements may be mutually exclusive, for example, if one state

Table 6

State Policies on Compounding Without Patient-Specific Prescriptions

	Number	Percentage
Does your state allow pharmacies to compound without patient-specific prescriptions? (n = 43)		
Yes	7	16%
Yes, with specific limits	21	49%
Depends on pending policy change	3	7%
No	10	23%
Don't know	2	5%

Selected examples of specific limits placed on compounding without patient-specific prescriptions by states
Potentially more restrictive
Veterinary emergency only
Nonsterile compounding that is not dispensed to patient
For emergency only
Potentially less restrictive
For noncommercially available drugs
For in-office use only
Under direct supervision of physician only
Only 5 or 10% of total pharmacy's monthly sales
Based on prescriber habits
Only for anticipatory prescription orders

does not permit OF licensure as a pharmacy whereas another state requires it. This puts OFs that wish to be licensed by both states in an unworkable compliance situation.

There also appeared to be some uncertainty among states regarding how to address facilities performing sterile compounding without patient-specific prescriptions that are not registered as an OF with FDA, as federal law requires. While approximately half of respondents reported that they would take some action, this was fairly evenly split between requiring these facilities to register with FDA, informing the agency of their existence, or disciplining the facility. Four states, Maryland, Minnesota, Tennessee, and West Virginia, reported that they would take all three actions. Nine states (21 percent) said they would take none of these actions. (See Table 8.)

Table 7

State Licensure or Registration Policy for Facilities That Register With FDA Under the Outsourcing Facility Category of Drug Compounders

	Number	Percentage*
How does your state license or register facilities that register with FDA under the new federal outsourcing facility (OF) category of drug compounders? (n = 43)		
State law or regulation has a specific outsourcing facility licensure or registration category	5	12%
State is currently developing a specific outsourcing facility licensure or registration category	12	28%
State licenses or registers outsourcing facilities as manufacturers	4	9%
State licenses or registers outsourcing facilities as wholesalers	4	9%
State does not license or register outsourcing facilities	5	12%
State licenses or registers outsourcing facilities as pharmacies	2	5%
State licenses or registers outsourcing facilities as manufacturers and wholesalers	2	5%
Other	5	12%
Don't know	4	9%

Note:

* Because of rounding, percentages may not always add to 100 percent.

Table 8

State Actions to Address Facilities Not Registered With FDA That Perform Sterile Compounding Without Patient-Specific Prescriptions

	Number	Percentage
How does your state address facilities that perform sterile compounding without patient-specific prescriptions that are not registered with FDA? Select all that apply. (n = 42*)		
State requires these facilities to register as outsourcing facilities	13	31%
State informs FDA of such facilities	10	24%
State takes disciplinary action	13	31%
None of the above	9	21%
Don't know	9	21%

Note:

* One state chose not to answer this question.

This mixed response was true even for the subset of states that allow some degree of compounding without a prescription. However, of the seven states that allowed this practice without limitation, none reported that they would take disciplinary action; one reported that it would require registration with FDA, and one indicated that it would inform the agency of such facilities.

Licensure

Pharmacy licensure is an important method for states to set both the general and activity-specific requirements that drug compounders must meet, as well as monitor the activity of compounders. Separate licensure for sterile compounding pharmacies is one approach to more closely targeting oversight and enforcement activities—for example, it could allow a regulator to address sterile compounding violations at a pharmacy without shutting down other activities. However, separate licensure systems are yet to be widely adopted. One in five respondents required pharmacies to have a separate licensure to perform sterile compounding. (See Table 9.) Some of these policies were recently enacted: In December 2014, the Massachusetts Legislature passed a law that established separate licensure for sterile compounding pharmacies both in and out of state.[53] Regulations to implement the law also stipulate that out-of-state pharmacies cannot dispense any sterile compounded drug into Massachusetts unless they hold a "Nonresident Sterile Compounding Pharmacy" license. Whether or not they perform compounding, licensure or registration of out-of-state pharmacies is the norm across states. (See Table 9.)

Table 9

State Licensure of Pharmacies That Perform Sterile Compounding and Nonresident Pharmacies

	Number	Percentage
Does your state have a separate license or other requirement (e.g., permit) for pharmacies that perform sterile compounding? (n = 43)		
Yes	9	21%
No	32	74%
Don't know	2	5%
Does your state independently license out-of-state pharmacies that ship or dispense products to providers or patients inside of the state? (n = 43)		
Yes	43	100%

Inspections and inspector training

Facility inspection is a key instrument that regulatory bodies can use to assess pharmacy compliance with laws and regulations on compounding—it protects the public by ensuring that appropriate quality standards are met. This study explores state policies on important aspects of inspections of pharmacies that perform sterile compounding. The most commonly reported circumstances that triggered inspections of such pharmacies in the state were initial licensure, when a pharmacy remodels or moves locations, occurrences of complaints or incidents, and licensure renewal. (See Table 10.) Respondents generally required that inspections occur at least every 12 months, though 10 states reported an inspection frequency of every two years or longer, and several states reported no specific frequency.

Table 10

Criteria Driving State Inspections of In-State Pharmacies That Perform Sterile Compounding

	Number	Percentage*
What specific circumstances trigger the state to conduct inspections for in-state pharmacies that perform sterile compounding? Select all that apply. (n = 43)		
Initial licensure	34	79%
Licensure renewal	11	26%
When pharmacy remodels or moves location	29	67%
When a complaint or incident occurs	30	70%
Other	3	7%
None of the above	4	9%
Unsure	2	5%
How frequently does the state conduct routine inspections for in-state pharmacies that perform sterile compounding? (n = 43)		
At least every 6 months	0	0%
At least every 1 year	23	53%
At least every 2 years	7	16%
At least every 3 years	2	5%
At least every 5 years	1	2%
No specific frequency	7	16%
Don't know	3	7%

Note:

* Because of rounding, percentages may not always add to 100 percent.

The number of reported pharmacy inspector FTEs (full-time equivalents—a unit representing a full-time employee) in each of the states responding ranged from one to 50. To better understand these differences in the context of the number of pharmacies within the state, the researchers divided the number of pharmacies in each state in the NCPDP database by the number of pharmacy inspectors reported by the state. The number of pharmacies per inspector ranged from 40 to 900, with a mean of 230 (standard deviation = 159) and a median of 183. It is worthwhile to note that differences in state policy and inspector workload allocation also affect how oversight is conducted. In addition, in some cases states may outsource inspections to third parties to improve their oversight reach.

Inspections require resources, and insufficient funding can affect inspection frequency, as well as staff hiring and training. In any situation, but particularly when resources are limited, states may seek to prioritize oversight of compounding pharmacies based on risk. Approximately one-quarter of respondents (12 states, or 28 percent) reported prioritizing inspections for in-state pharmacies where high-risk sterile compounding occurs. However, respondents generally did not report higher than annual inspection frequencies for these high-risk facilities. One state, Colorado, reported inspecting these facilities every six months.

The questionnaire also asked regulators how drug compounders shipping into their state from other locations were assessed for compliance, which may or may not include an in-person inspection (Table 11), and respondents varied in their approaches. While some states such as California[54] conduct their own inspections of out-of-state pharmacies, many states reported relying on inspections by the state where the pharmacy is located (49 percent), and/or inspections by a third party (53 percent), and states may also combine approaches. States

Table 11

Methods Used by States to Examine Out-of-State Pharmacy Compliance With Applicable Standards

	Number	Percentage
How does the state verify that out-of-state pharmacies performing sterile compounding comply with their applicable regulations? Select all that apply. (n = 43)		
Compliance is not verified	5	12%
Inspection performed by National Association of Boards of Pharmacy's Verified Pharmacy Program	22	51%
Inspection performed by a third party, approved in advance by the state	10	23%
Inspection performed by a third party, not approved in advance by the state	3	7%
Review of inspection report by another state, conducted in the past ____ years	21	49%
The pharmacy must provide self-evaluation or attestation of compliance	3	7%
Other	6	14%

that relied on inspection reports from another state had different requirements for how recent the inspection must be, ranging from 90 days to four years. Most respondents relying on a third party reported working with the National Association of Boards of Pharmacy's Verified Pharmacy Program. Five respondents (12 percent) reported that they did not verify the compliance of out-of-state sterile compounders. The frequency for assessing the compliance of out-of-state pharmacies varied considerably, with 40 percent of respondents indicating that there was no specific time frame. (See Table 12.) However, it is possible that some states may have interpreted this question as "frequency of inspection," which is one of several possible strategies of assessing compliance.

Table 12

Criteria Driving State Compliance Assessment of Out-of-State Pharmacies Performing Sterile Compounding

	Number	Percentage
What specific circumstances trigger the state to assess compliance with state requirements for out-of-state pharmacies that perform sterile compounding? Select all that apply. (n = 43)		
Initial licensure	31	72%
Licensure renewal	20	47%
When pharmacy remodels or moves location	14	33%
When a complaint or incident occurs	29	67%
None of the above	1	2%
Don't know	5	12%
How frequently does the state assess compliance with state standards for out-of-state pharmacies that perform sterile compounding?* (n = 43)		
At least every 6 months	0	0%
At least every 1 year	10	23%
At least every 2 years	7	16%
At least every 3 years	1	2%
At least every 5 years	0	0%
No specific frequency	17	40%
Don't know	8	19%

Note:

* Some states may have interpreted this question as "frequency of in-person inspection," not including regular, required review of inspections by other states or third parties.

Table 13

Characteristics of State Inspections of Pharmacies Performing Sterile Compounding

	Number	Percentage*
How long do inspections of pharmacies that perform sterile compounding usually last? (n = 43)		
Less than 4 hours	9	19%
4-8 hours	20	47%
1-3 days	3	7%
Other	6	14%
Don't know	5	12%
Are inspections of pharmacies that perform sterile compounding announced? (n = 43)		
Yes	0	0%
No	37	86%
Sometimes	3	7%
Don't know	3	7%
Is direct observation of sterile compounding activity required during inspections of pharmacies that perform sterile compounding, even if it must be simulated? (n = 43)		
Yes	10	23%
No	27	63%
Don't know	6	14%
Does the state have the ability to take and test samples of sterile compounded drugs for inspections or investigations? (n = 43)		
Yes	18	42%
No	15	35%
Don't know	10	23%

Note:

* Because of rounding, percentages may not always add to 100 percent.

Table 14

Factors Evaluated During Inspections of Pharmacies Performing Sterile Compounding

	Number	Percentage
What factors are evaluated during a sterile compounding inspection? Select all that apply. (n=43)		
Equipment certification and calibration	39	91%
Environmental monitoring	38	88%
Cleaning	38	88%
Standard operating procedures	37	86%
Training	37	86%
Documentation	37	86%
Facility design and construction	36	84%
Aseptic technique	36	84%
Hand hygiene	34	79%
Garbing	34	79%
Sterilization procedures and verification	33	77%
Control of components and materials	32	74%
All major inspection areas	24	56%
Other	5	12%
Don't know	4	9%

Tables 13 and 14 summarize additional characteristics of inspections for sterile compounding pharmacies. Inspections of sterile compounding pharmacies typically lasted for less than eight hours. (See Table 13.) Only the District of Columbia, Minnesota, and Washington reported that inspections of sterile compounding pharmacies usually lasted from one to three days. Virginia reported that hospital pharmacy inspections usually take two days. Most states held inspections that were unannounced but did not require direct observation of sterile compounding activity, even if by simulation. Ten jurisdictions reported that they required direct observation of sterile compounding activity during inspections: California, the District of Columbia, Indiana, Maryland, Montana, New Jersey, Oklahoma, Rhode Island, Tennessee, and Washington. Given the additional

quality standards required to safely compound sterile drug products, observation of compounding activity, whether actual or simulated, is relevant to an inspector's ability to meaningfully assess compounder compliance with state regulations.

Respondents generally indicated that inspection factors included important sterile compounding topics covered by USP <797> (Table 14), which is interesting given that only about half of respondents reported mandating USP <797> in its entirety. However, these questions did not assess the specific requirement for each inspection factor assessed by the state, so they cannot be used to evaluate alignment with USP <797>. Finally, when issues are discovered during inspection, most respondents (79 percent) required a written response from the pharmacy describing how the issues were addressed, and a majority (67 percent) also needed an additional on-site inspection to verify compliance. (See Table 15.) The ability of states to take samples of compounded products for testing also varied. This may be due, in part, to the high costs of sample testing, which can be prohibitive depending on state resource constraints.

Majorities of respondents reported that their states required that inspectors who assess sterile compounding be licensed pharmacists (70 percent), have prior experience within a pharmacy (60 percent), and have training on applicable USP standards (58 percent). (See Figure 1.) Interestingly, among states that mandated full or partial compliance with USP <797> (21 and 13 respondents, respectively) for sterile compounding, only 14 of 21 (67 percent) and 6 of 13 (46 percent) required that their inspectors to be trained in applicable USP standards. Lack of a requirement does not mean that states never secure such training for inspectors, but insufficient training can undermine the state's ability to recognize a violation through inspection.

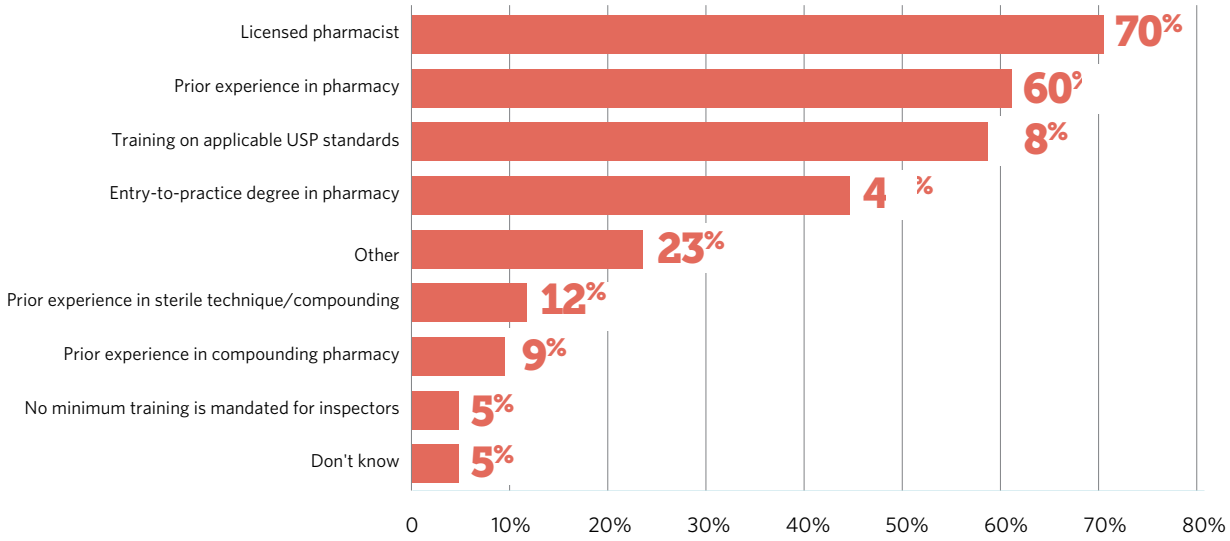
Table 15

State Follow-Up With Pharmacies Performing Sterile Compounding in Violation of State Regulations

	Number	Percentage
How does the state follow up with pharmacies to ensure that violations are addressed? Select all that apply. (n = 43)		
State conducts on-site inspection to verify that issues are addressed	29	67%
State requires written response from pharmacy describing how issues are addressed	34	79%
Other	8	19%
Don't know	2	5%

Figure 1

State-Required Training for Inspectors of Pharmacies That Perform Sterile Compounding (n=43)



Finally, given states' reliance on one another's inspections, they arguably would benefit from better harmonization of inspection protocols, minimum inspector training, and the ability to share information related to oversight and investigations. Our study found variability in the authority of states to share information about inspections, investigations, and enforcement concerns related to drug compounding with in-state, out-of-state, and federal officials. Twenty-six, 28, and 30 respondents reported that they could share information with in-state, federal, and other state officials, respectively (corresponding to 60 percent, 65 percent, and 70 percent of the 43 respondents). One respondent reported no authority to share information. (See Table 16.) Third parties, such as the National Association of Boards of Pharmacy, are engaged in efforts to establish clearinghouses of inspection information for states to access, and to facilitate state recognition of one another's inspections through harmonized inspection checklists.

Physician office or clinic compounding

Drug compounding generally occurs in pharmacies but may also take place in doctors' offices or clinics. Regardless of where sterile compounding is practiced, quality assurance is critical. Some research suggests that the frequency of contamination of parenteral (injected or infused) drug preparations is higher in clinical environments (e.g., hospital unit or operating room) than in controlled pharmacy environments.[55] Only one respondent state, Idaho, reported that its state board of pharmacy oversaw compounding that occurs within doctors' offices; most states were not certain that any meaningful oversight system exists, even by state medical boards. (See Table 17.) There is little to no clarity on which quality standards apply to sterile compounding in physician offices, and often no mechanisms exist to track adverse events in these settings. (See Figure 2.)

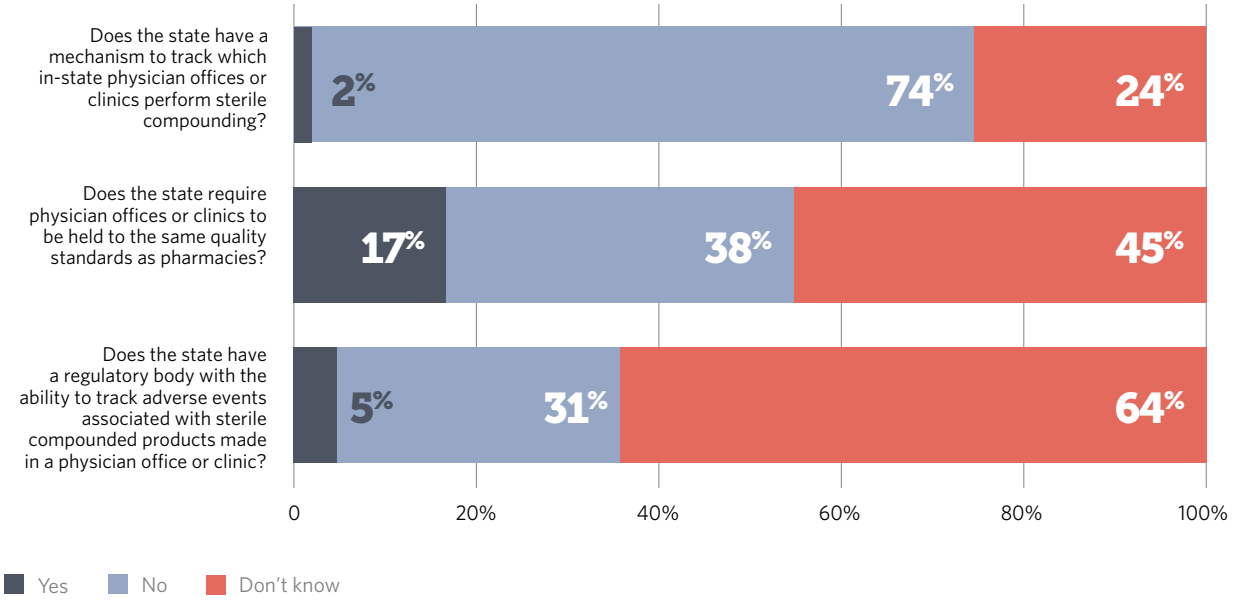
Table 16

State Authority to Share Inspection Information Related to Drug Compounding

	Number	Percentage*
Does the state have the authority to share information about inspections, investigations, and enforcement concerns related to drug compounding with other regulators and officials at the state or federal level? Select all that apply. (n = 43)		
State has no authority to share	1	2%
Can share on a public website	10	23%
Can share with in-state officials	26	60%
Can share with federal officials	28	65%
Can share with officials from other states	30	70%

Figure 2

State Oversight Systems for Sterile Compounding That Occurs in Physician Offices (n=42*)†



Note:

* One state chose not to answer this question.

† Because of rounding, percentages may not always add to 100 percent.

Table 17

State Body Responsible for Oversight of Sterile Compounding Occurring in Physician Offices

	Number	Percentage*
How do states provide oversight of physician offices or clinics that perform sterile compounding to ensure compliance with applicable standards? (n=43)		
Oversight provided by the state board of medicine	7	16%
Oversight provided by the state board of pharmacy	1	2%
There is no oversight system to ensure compliance	24	56%
Other	7	16%
Don't know	4	9%

Note:

* Because of rounding, percentages may not always add to 100 percent.

Conclusions

Although the national outbreak of meningitis linked to contaminated compounded injections has driven a number of individual states to revisit the regulation of sterile compounding, this study revealed substantial variability in state regulation and oversight. Although many states had adopted widely recognized USP quality standards, some applied them only in part, and some did not require them at all. Inspection practices varied in frequency and length, and the ratio of pharmacy inspectors to pharmacies ranged widely, revealing potentially uneven oversight practices across the nation. States also applied notably different policies on compounding without a prescription; some were permissive, and others were restrictive. While federal law passed in 2013 clarified that pharmacies may not compound without prescriptions unless they are registered with FDA, it appears that states have not moved quickly to synchronize their regulations to federal policy.

States bear the primary responsibility for oversight of pharmacy compounding in their jurisdictions. Significant variability in state oversight systems, particularly given the interstate movement of some compounded drugs, suggests that quality assurance practices to protect patients may be inconsistent.

Many states are currently considering policy changes, and this study was designed to provide a useful landscape assessment of oversight systems that states can use when considering both their own policies and those governing out-of-state pharmacies that ship to the state. The results suggest that states may benefit from additional tools that describe policy best practices, lessons learned from states successfully advancing change and effectively allocating resources, and up-to-date model legislation and regulation in conformance with changes to federal law. These tools could be a resource to individual states reviewing practices, and also

support greater harmonization across states, particularly regarding appropriate rigor in the oversight of sterile compounding practice. Ideally, best practices should inform broader research pursuits to assess the landscape of state oversight systems today and analyze their strengths and weaknesses. This study may be useful in providing a baseline that facilitates the evaluation of policy transitions with respect to state oversight of sterile compounding practices.

Study limitations

This study had several limitations. First, although the study achieved a response rate of more than 80 percent from the 50 states and the District of Columbia, eight states did not complete our questionnaire. Second, the study could not definitively ascertain the accuracy of some responses where information was not available on public websites. However, the research team was careful to select potential respondents based on the experiences of our expert advisory panel.

Furthermore, state boards of pharmacy are responsible for defining state oversight of pharmacy compounding practice, and therefore respondents from these regulatory bodies should be authorities on the most current status of their jurisdiction. The authors are therefore confident that respondents participating in this study were among the most appropriate and knowledgeable sources of information available on current state oversight practices. Owing to rigorous follow-up and diligence, there were no missing responses to individual questions; however, two respondents reported as being "unsure" on several questions. This may have reflected an inability to answer questions before the questionnaire deadline, rather than uncertainty among regulators about their state's policy or authority. In addition, one question regarding state oversight of out-of-state facilities was not understood uniformly by respondents, potentially limiting our ability to interpret responses to that particular question, as noted in Table 12. Finally, responses to questions on whether compounding without prescriptions was permitted in states may reflect differing interpretations of what constitutes a full prohibition on compounding without prescriptions.

Appendix A: Glossary of terms

503B facility. See *outsourcing facility*.

Adverse event. Any undesirable experience associated with the use of a medical product in a patient.

Anticipatory compounding. Creation of a drug product prior to receipt of a prescription, based on a history of receiving such prescriptions. A prescription is received before the compounder dispenses or distributes the product. (This is distinct from office stock compounding, in which the compounder dispenses or distributes products to a provider without ever receiving prescriptions.)

Current Good Manufacturing Practice (CGMP). Minimum requirements for the methods, facilities, and controls used in the manufacturing, processing, and packing of a drug product. They are enforced in the United States by FDA, under Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (21 USCS § 351).

Drug Quality and Security Act (DQSA). On Nov. 27, 2013, President Obama signed the Drug Quality and Security Act, legislation with two titles: Title I contains important provisions relating to the oversight of compounding of human drugs, and Title II creates a drug serialization and tracking system.

Food and Drug Administration (FDA). The Food and Drug Administration (FDA) is an agency within the U.S. Department of Health and Human Services responsible for, among other things, protecting the public health by ensuring that human and veterinary drugs, vaccines and other biological products, and medical devices intended for human use are safe and effective.[56]

Good Manufacturing Practice. See *Current Good Manufacturing Practice.*

High-risk sterile compounding. Includes compounding activities that present potentially higher risk of compromised sterility in the end product, such as the preparation of sterile drugs from nonsterile components.

In-state pharmacy. Licensed pharmacy physically located within the state. May be referred to as a resident pharmacy.

Nonresident pharmacy. See *out-of-state pharmacy*.

Office stock compounding. Creating standardized drug products to be kept as stock in a doctor's office or hospital. By definition, these products are not compounded, dispensed, or distributed by a compounder pursuant to an individual patient prescription. Normally this is differentiated from anticipatory compounding, in which the product is prepared in advance of receiving a prescription but is not dispensed or distributed by a compounder until the prescription is received. FDA's current position is that office stock compounding is not permitted under federal law—Section 503A of the Federal Food, Drug, and Cosmetic Act specifies that traditional compounders may only receive exemptions from federal drug approval requirements if they compound pursuant to an individual patient prescription.

Out-of-state pharmacy. Licensed pharmacy not physically located within the state. Also referred to as nonresident pharmacy.

Outsourcing facility. Under Section 503B of the Drug Quality and Security Act, a compounder can become an "outsourcing facility," defined as a facility at one geographic location or address that (1) is engaged in the compounding of sterile drugs, (2) has elected to register as an outsourcing facility, and (3) complies with all of the requirements of Section 503B. Major requirements include registration with FDA, reporting of adverse

events and products compounded to FDA, and payment of fees to FDA. Outsourcing facilities are permitted to compound and distribute drugs without receiving individual patient prescriptions, but they are not exempt from current Good Manufacturing Practices. They may hold a pharmacy license but are not required to do so under federal law.

Physician office compounding. Compounding that occurs in a physician's office, either by a physician or by another practitioner for that physician.

Recalls. Actions taken by a firm to remove a product from the market. Recalls may be conducted on a firm's own initiative or by regulator request. FDA does not currently have the statutory authority to mandate a drug recall. State authorities here may differ.

Resident pharmacy. Licensed pharmacy physically located within the state. May be referred to as in-state pharmacy.

Serious adverse event. As defined by FDA, an adverse event that results in death, hospitalization (initial or prolonged), disability or permanent damage, or congenital anomaly or birth defect; is life-threatening; or requires an intervention to prevent permanent impairment or damage.[57]

State board of pharmacy. A state licensing board that develops, implements, and enforces standards relating to pharmacy practice.

United States Pharmacopeial Convention (USP). Scientific nonprofit organization that sets standards for the identity, strength, quality, and purity of medicines, food ingredients, and dietary supplements manufactured, distributed, and consumed worldwide. The USP's drug standards are enforceable in the United States by FDA and are used in more than 140 countries.

USP <795>. Chapter of the USP that provides compounders with guidance on applying good compounding practices for the preparation of nonsterile compounded formulations for dispensing and/or administration to humans or animals.

USP <797>. Chapter of the USP that describes conditions and practices to prevent harm to patients that could result from microbial contamination, excessive bacterial endotoxins, variability in intended strength, unintended chemical and physical contaminants, and ingredients of inappropriate quality in compounded sterile preparations.

USP <800>. Proposed chapter of the USP that provides compounders with standards to protect personnel and the environment when handling hazardous drugs.

Appendix B: Complete tables on state oversight of sterile compounding

Table B.1

Quality Standards Responses by State

B.1	Quality standards for pharmacies that perform sterile compounding		Pharmacist training requirements
	Does the state mandate USP Chapter <797> on sterile compounding or equivalent?	Legislation or regulation that mandates USP Chapter <797> on sterile compounding or equivalent	For pharmacists who perform sterile compounding, does the state set specific minimum expectations for regular training on sterile compounding, beyond USP requirements (such as a minimum number of hours of continuing education devoted to sterile compounding)? And if so, what are these standards?
AK*	Yes, but not in its entirety	12 AAC 52.430 and 12 AAC 52.440 and sterile pharmaceuticals guidelines	Unsure
AL	Yes, but not in its entirety	The state has a clause which says pharmacies must follow all USP standards and we have been functioning under that requirement to enforce USP <797>. We are presently rewriting our legislation and debating whether or not we will state simply to follow USP <797> or write specific requirements which mimic USP <797>.	Yes—must receive 5 hours continuing education, live, with written test and must be monitored compounding in a hood with written evaluation. Must receive passing grade on written monitoring evaluation.
AR	Yes, but not in its entirety	07-02-0002 http://pharmacyboard.arkansas.gov/licenseeInfo/Documents/lawBook/mergedLawbook.pdf	No
AZ	Unsure	NA	Unsure
CA	Yes, but not in its entirety	Chapter 9 Division 2 Article 7.5, Portions of 16 CA Code of Regulations 1735 et seq. and 1751 et seq.; Also regulations currently undergoing substantial revision	Yes—annual assessment; See 16 CA Code of Regulations Section 1751.6
CO	Yes, but not in its entirety	3 CCR 719-1, chapter 21	No
CT	Yes	Public Act No 14-224 Sc (4)c Sec 20-576-66	Unsure
DC	No, but will under pending policy change	NA	No
DE*	Yes, but not in its entirety	Only under hospital inspection form http://regulations.delaware.gov/AdminCode/title24/2500.shtml	No
FL*	Yes	64B16-27.797	Unsure
GA*	Yes	Rules and Regulations of State of Georgia: Chapter 480-11-.02 Compounded Drug Preparations	Yes—pharmacists who engage in drug compounding, and any other pharmacy personnel, supervised by pharmacists, who assist in drug compounding, shall be competent and proficient in compounding procedures and shall maintain that proficiency through current awareness and training and documentation of that training

B.1	Quality standards for pharmacies that perform sterile compounding		Pharmacist training requirements
	Does the state mandate USP Chapter <797> on sterile compounding or equivalent?	Legislation or regulation that mandates USP Chapter <797> on sterile compounding or equivalent	For pharmacists who perform sterile compounding, does the state set specific minimum expectations for regular training on sterile compounding, beyond USP requirements (such as a minimum number of hours of continuing education devoted to sterile compounding)? And if so, what are these standards?
	Yes	Hawaii Administrative Rules § 16-95-110 Grounds for revocation, suspension, refusal to renew or restore, denial, or conditioning of license or permit. (17) Failure to comply with the pharmaceutical compounding requirements found in Chapter 795 (nonsterile preparations) and 797 (sterile preparations) of the United States Pharmacopeia National Formulary, as amended.	No
	No, but will under pending policy change	NA	No
	No	NA	Yes—to engage in the practice of sterile compounding, a minimum of one (1) of the CPE hours must be ACPE-accredited and related to the practice of sterile compounding
	No, but will under pending policy change	NA	No
	Yes	IAC-1-Rule 30. Sterile Pharmaceuticals; Preparation and Dispensing	No
	No, but will under pending policy change	NA	No
	Yes	KRS 217	No
	Yes	LAC 46:L III.2535	Yes—rule requires all individuals obtain practical and/or academic training in compounding and dispensing of sterile preparations and further complete minimum of 1 hour of accredited CE on annual basis
	Yes	247 CMR 6.01.(5)c	No
	Yes	COMAR 10.34.19	Yes—have appropriate practical and didactic training in sterile compounding, clean room technology, laminar flow technology, quality assurance technique, and clinical applications of IV drug therapy. COMAR 10.34.19.05A
	Yes	Chapter 37: Licensure of Sterile Compounding Pharmacies. 10. Operational Requirements	No
	Yes	Act 280 of 2014	No
	Yes	6800.3300 Compounding Standards Subpart 2	No

B.1	Quality standards for pharmacies that perform sterile compounding		Pharmacist training requirements
	Does the state mandate USP Chapter <797> on sterile compounding or equivalent?	Legislation or regulation that mandates USP Chapter <797> on sterile compounding or equivalent	For pharmacists who perform sterile compounding, does the state set specific minimum expectations for regular training on sterile compounding, beyond USP requirements (such as a minimum number of hours of continuing education devoted to sterile compounding)? And if so, what are these standards?
MO	Yes, but not in its entirety	20 CSR 2220-2.200	Yes—personnel trained for risk level of sterile compounding (Risk level 1, 2, and 3)
MS	No, but will under pending policy change	NA	No
MT	Yes	24.174.841 (not legislation—a rule that went into effect March 2015 in definition)	Unsure
NC*	Yes	NCBOP-Pharmacy Rules. 21 NCAC 46 .2801, Section.2800 Compounding	No
ND	Yes, but not in its entirety	61-02-01-03. Pharmaceutical compounding standards	No
NE	Yes, but not in its entirety	Legislative Bill 37 (LB 37), effective Aug. 30, 2015	No
NH	Yes	NH RSA 318:14-a Compounding and NH Pharmacy Rules Chapter 400 part Ph 404	No
NJ	Yes, but not in its entirety	NJAC 13:39 Subchapter 11	Yes—shall have didactic and practical training in sterile preparation compounding prior to compounding and annually thereafter, 13:39-11:16(a)
NM	Yes	26-1-2.L.NMSA	Yes—all personnel, including pharmacists, pharmacists who supervise compounding personnel, pharmacist interns, and pharmacy technicians, shall have completed didactic and experiential trainings with competency evaluation through demonstration and testing (written or practical) as required by USP/NF (USP General Chapters: Pharmaceutical Compounding-Sterile Preparations). Pharmacy technicians shall complete 100 hours.
NV	Yes, but not in its entirety	Chapter 639—Pharmacists and Pharmacy NAC 639.67015 Establishment of policies and procedures	No
NY	Yes	Our NYS guidelines inform whether a product was prepared competently	No
OH*	Yes	Ohio Administrative Code (OAC) Drug Compounding 4729-16-07	Yes—there shall be a documented, ongoing quality assurance control program that monitors personnel performance, equipment, finished compounded drug products, and facilities

B.1	Quality standards for pharmacies that perform sterile compounding		Pharmacist training requirements
	Does the state mandate USP Chapter <797> on sterile compounding or equivalent?	Legislation or regulation that mandates USP Chapter <797> on sterile compounding or equivalent	For pharmacists who perform sterile compounding, does the state set specific minimum expectations for regular training on sterile compounding, beyond USP requirements (such as a minimum number of hours of continuing education devoted to sterile compounding)? And if so, what are these standards?
OK	Yes	535:15-10-54. CSP microbial contamination risk levels, 535:15-10-61. Beyond use dating.	No
OR	Yes, but not in its entirety	Oregon Administrative Rules Chapter 855 855-045-0200 (3) pharmacists engaging in compounding should adhere to those guidelines that apply to their practice setting and in all situations comply with the spirit of USP <795> and USP <797>	No
PA	No, but will under pending policy change	NA	No
RI	Yes, but not in its entirety	R5-19.1-PHAR	No
SC	No, but will under pending policy change	H3349	Yes—all sterile compounding personnel (pharmacy technicians and pharmacists) must have proof of personal competency in the art of sterile compounding completed on an annual basis
SD	Yes, but not in its entirety	ARSD 20:51:31	No
TN	Yes	Public Chapter 266	No
TX	Yes	22 TAC §291.133	Yes—all pharmacists must complete through a single course a minimum of 20 hours of instruction and experience in the areas listed in paragraph (4)(D) of this subsection. Such training shall be obtained through completion of a recognized course in an accredited college of pharmacy or a course sponsored by an ACPE-accredited provider as well as OJT. Technicians must complete a 40-hour ACPE or ASHP course and OJT. In addition, to renew their license/registration, all pharmacists and pharmacy technicians must complete two hours of ACPE-accredited continuing education relating to one or more of the areas listed in paragraph (4)(D) of this subsection if the pharmacy technician is engaged in compounding low- and medium-risk sterile preparations; or four hours of ACPE-accredited continuing education relating to one or more of the areas listed in paragraph (4)(D) of this subsection if pharmacy technician is engaged in compounding high-risk sterile preparations.

B.1	Quality standards for pharmacies that perform sterile compounding		Pharmacist training requirements
	Does the state mandate USP Chapter <797> on sterile compounding or equivalent?	Legislation or regulation that mandates USP Chapter <797> on sterile compounding or equivalent	For pharmacists who perform sterile compounding, does the state set specific minimum expectations for regular training on sterile compounding, beyond USP requirements (such as a minimum number of hours of continuing education devoted to sterile compounding)? And if so, what are these standards?
UT	Yes	R156. Commerce, Occupational and Professional Licensing. R156-17b. Pharmacy Practice Act Rule. R156-17b-614a. Operating Standards—General Operating Standards, Class A and B Pharmacy (3)	No
VA	Yes	Regulations Governing Practice of Pharmacy Title 18. VAC110-20-321: Compounding—performed in accordance with USP-NF compounding for sterile and nonsterile drug products and §54.1-3410.2 of the Code of Virginia	No
VT	Yes	Administrative Rules of the Board of Pharmacy 13.22 USP <797> Compliance for Compounded Sterile Products	Unsure
WA	Yes	2013 HB 1800	No
WI*	No	NA	No
WV	Yes	Title 15 Series 1 Section 16	No
WY	Yes, but not in its entirety	WY Pharmacy Act Rules Chapter 17	Unsure

Note:

* Indicates that a state either declined to participate in the survey or did not complete the survey. The answers for these states' responses have been found on publicly available websites.

Table B.2

Monitoring and Enforcement Responses by State

B.2		AK*	AL	AR	AZ	CA	CO	CT	DC	DE*	FL*
Tracking facilities	Does your state track the number of in-state pharmacies that perform compounding?	Yes	Yes	No	Yes	No	Yes	No	Yes	No	Yes
	Does your state track the number of in-state pharmacies that perform sterile compounding?	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
		Yes	No	Yes	Yes	Yes	No	No	No	Yes	Yes
	Are sterile compounding-related violations tracked separately by the state?	Yes	Yes	No	Yes	Yes	No	Unsure	No	Unsure	Unsure
	Does the state list disciplinary actions related to pharmacy violations on a public website?	No	Yes	Yes	Yes	Yes	Yes	Unsure	No	Yes	Yes
	Does the state separately list disciplinary actions for compounding-related violations?	NA	No	No	No	Yes	No	NA	NA	Yes	Yes
Tracking violations		Cannot share information with any regulators or officials, either federal or state	Can share with in-state regulators and officials, and federal regulators and officials	Can share with other state regulators and officials	Can share with other state regulators and officials		Unsure	Unsure	Unsure	Unsure	
Pharmacy reporting		Yes, to the state and to MedWatch	No	No	No	Yes, to the state and to MedWatch	Yes, to the state only	Unsure	Yes, to the state and to MedWatch	Yes, to the state only	Yes, to MedWatch only
	Are pharmacies that perform sterile compounding required to report voluntary recalls to the state and/or FDA?	Unsure	Yes, to FDA only	No, to either	Unsure	Yes, to both	Unsure	Unsure	No, to either	Unsure	Unsure
	Does the state have the authority to mandate a recall?	Unsure	Yes	No	No	No	Unsure	Yes	Yes	Yes	Unsure
	Does the state have the authority to issue cease-and-desist orders?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Unsure
		Yes	Yes	Yes	Yes	Yes	Yes	Unsure	Yes	No	Unsure

B.2		GA*	HI	IA	ID	IL	IN	KS	KY	LA
Tracking facilities	Does your state track the number of in-state pharmacies that perform compounding?	Yes	No	Yes	No	No	No	Yes	No	No
	Does your state track the number of in-state pharmacies that perform sterile compounding?	No	No	Yes	Yes	No	No	Yes	No	No
	Does your state track the number of out-of-state pharmacies that ship or dispense compounded drugs to providers or patients in the state?	Yes	No	Yes	No	No	No	No	No	No
	Are sterile compounding-related violations tracked separately by the state?	Unsure	Unsure	No	No	No	No	No	No	No
	Does the state list disciplinary actions related to pharmacy violations on a public website?	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
	Does the state separately list disciplinary actions for compounding-related violations?	NA	No	No	No	No	NA	No	No	No
Tracking violations	Does the state have the authority to share information about inspections, investigations, and enforcement concerns related to drug compounding with other regulators and officials, both federal and state?	Unsure	Can share with in-state regulators and officials, other state regulators and officials, and federal regulators and officials	Can share with in-state regulators and officials, other state regulators and officials, federal regulators and officials, and on public websites	Can share with in-state regulators and officials, other state regulators and officials, federal regulators and officials, and on public websites	Can share with in-state regulators and officials, other state regulators and officials, and federal regulators and officials	Unsure	Can share with in-state regulators and officials, other state regulators and officials, and federal regulators and officials	Can share with in-state regulators and officials, other state regulators and officials, and federal regulators and officials	Can share with in-state regulators and officials, other state regulators and officials, and federal regulators and officials
Pharmacy reporting	Does the state require pharmacies that perform sterile compounding to report serious adverse events to the state and/or MedWatch?	Yes, to the state only	No	No	No	No	No	No	No	No
	Are pharmacies that perform sterile compounding required to report voluntary recalls to the state and/or FDA?	Yes, to the state only	Unsure	No, to either	No, to either	No, to either	No, to either	Yes, to both	No, to either	No, to either
State authorities	Does the state have the authority to mandate a recall?	Yes	Unsure	Yes	No	No	Yes	No	Yes	No
	Does the state have the authority to issue cease-and-desist orders?	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
	Does the state have the authority to request reports from pharmacies that perform sterile compounding on the number of sterile products they prepare?	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes

B.2		MA	MD	ME*	MI	MN	MO	MS	MT
Tracking facilities	Does your state track the number of out-of-state pharmacies that ship or dispense compounded drugs to providers or patients in the state?	Unsure	No	No	Yes	Yes	Yes	No	No
		Unsure	Yes	Yes	Yes	Yes	Yes	No	No
		Unsure	Yes	No	Yes	Yes	Yes	No	No
		Unsure	Yes	Unsure	No	No	No	No	No
		Yes	Yes	Yes	Yes	Yes	No	No	Yes
		Yes	No	Yes	No	No	NA	NA	No
Tracking violations	Does the state have the authority to share information about inspections, investigations, and enforcement concerns related to drug compounding with other regulators and officials, both federal and state?	Unsure	Can share with in-state regulators and officials, other state regulators and officials, and federal regulators and officials	Can share with in-state regulators and officials, other state regulators and officials, federal regulators and officials, and on public websites	Can share with in-state regulators and officials, other state regulators and officials, federal regulators and officials, and on public websites	Can share with in-state regulators and officials, other state regulators and officials, and federal regulators and officials	Can share with in-state regulators and officials, other state regulators and officials, and federal regulators and officials	Unsure	Cannot share information with any regulators or officials, either federal or state
Pharmacy reporting	Does the state require pharmacies that perform sterile compounding to report serious adverse events to the state and/or MedWatch?	Yes, to the state only	Yes, to the state only	Yes, to the state only	Yes, to the state only	No	No	No	No
	Are pharmacies that perform sterile compounding required to report voluntary recalls to the state and/or FDA?	Yes, to the state only	Yes, to FDA only	Yes, to the state only	Yes, to both	No, to either	Yes, to the state only	No, to either	No, to either
	Does the state have the authority to mandate a recall?	Unsure	Yes	Yes	Yes	No	No	Unsure	Unsure
State authorities	Does the state have the authority to issue cease-and-desist orders?	Yes	Yes	Unsure	Yes	Yes	NA†	Yes	Yes
	Does the state have the authority to request reports from pharmacies that perform sterile compounding on the number of sterile products they prepare?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

B.2		NC*	ND	NE	NH	NJ	NM	NV	NY
Tracking facilities	Does your state track the number of in-state pharmacies that perform compounding?	Unsure	Yes	No	Yes	No	No	Yes	Unsure
	Does your state track the number of in-state pharmacies that perform sterile compounding?	Unsure	Yes	No	Yes	Yes	No	Yes	Unsure
	Does your state track the number of out-of-state pharmacies that ship or dispense compounded drugs to providers or patients in the state?	Unsure	Yes	No	Yes	Yes	No	Yes	Unsure
Tracking violations	Are sterile compounding-related violations tracked separately by the state?	Unsure	No	No	No	Yes	No	No	No
	Does the state list disciplinary actions related to pharmacy violations on a public website?	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
	Does the state separately list disciplinary actions for compounding-related violations?	No	No	No	No	No	Yes	NA	No
	Does the state have the authority to share information about inspections, investigations, and enforcement concerns related to drug compounding with other regulators and officials, both federal and state?	Unsure	Can share with in-state regulators and officials, other state regulators and officials, federal regulators and officials, and on public websites	Can share with in-state regulators and officials, other state regulators and officials, federal regulators and officials, and on public websites	Can share with other state regulators and officials	Can share with in-state regulators and officials, other state regulators and officials, and federal regulators and officials	Can share with in-state regulators and officials, other state regulators and officials, federal regulators and officials, and on public websites	Can share with in-state regulators and officials, other state regulators and officials, and federal regulators and officials	Can share with other state regulators and officials, and with federal regulators and officials
Pharmacy reporting	Does the state require pharmacies that perform sterile compounding to report serious adverse events to the state and/or MedWatch?	Unsure	No	No	Yes, to MedWatch only	Yes, to the state only	Yes, to the state only	No	No
	Are pharmacies that perform sterile compounding required to report voluntary recalls to the state and/or FDA?	Unsure	No, to either	No, to either	Unsure	No, to either	No, to either	Unsure	No, to either
State authorities	Does the state have the authority to mandate a recall?	Yes	Yes	Unsure	Unsure	No	No	Yes	Unsure
	Does the state have the authority to issue cease-and-desist orders?	Unsure	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Does the state have the authority to request reports from pharmacies that perform sterile compounding on the number of sterile products they prepare?	Unsure	Yes	Yes	Yes	Yes	Yes	Yes	Yes

B.2		OH*	OK	OR	PA	RI	SC	SD	TN
Tracking facilities	Does your state track the number of in-state pharmacies that perform compounding?	Unsure	Yes	No	No	Yes	Yes	Yes	No
	Does your state track the number of in-state pharmacies that perform sterile compounding?	Unsure	Yes	No	No	Yes	Yes	Yes	Yes
	Does your state track the number of out-of-state pharmacies that ship or dispense compounded drugs to providers or patients in the state?	Unsure	Yes	No	No	Yes	Yes	Yes	Yes
	Are sterile compounding-related violations tracked separately by the state?	Unsure	No	No	No	No	No	No	No
	Does the state list disciplinary actions related to pharmacy violations on a public website?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Does the state separately list disciplinary actions for compounding-related violations?	NA	No	No	No	No	No	No	No
Tracking violations	Does the state have the authority to share information about inspections, investigations, and enforcement concerns related to drug compounding with other regulators and officials, both federal and state?	Unsure	Can share with in-state regulators and officials, other state regulators and officials, federal regulators and officials, and on public websites	Can share with other state regulators and officials	Unsure	Can share with in-state regulators and officials, other state regulators and officials, and federal regulators and officials	Can share with in-state regulators and officials, other state regulators and officials, and federal regulators and officials	Can share with in-state regulators and officials, other state regulators and officials, federal regulators and officials, and on public websites	Can share with federal regulators and officials
Pharmacy reporting	Does the state require pharmacies that perform sterile compounding to report serious adverse events to the state and/or MedWatch?	Yes, to the state only	No	No	No	Yes, to MedWatch only	No	Yes, to MedWatch only	No
	Are pharmacies that perform sterile compounding required to report voluntary recalls to the state and/or FDA?	Unsure	No, to either	No, to either	No, to either	Yes, to both	No, to either	Unsure	No, to either
	Does the state have the authority to mandate a recall?	Unsure	No	No	No	Yes	No	Unsure	No
State authorities	Does the state have the authority to issue cease-and-desist orders?	Unsure	Yes	No	Yes	Yes	Yes	Yes	Yes
	Does the state have the authority to request reports from pharmacies that perform sterile compounding on the number of sterile products they prepare?	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes

B.2		TX	UT	VA	VT	WA	WI*	WV	WY
Tracking facilities	Does your state track the number of in-state pharmacies that perform compounding?	Yes	No	Yes	Unsure	No	Unsure	No	No
	Does your state track the number of in-state pharmacies that perform sterile compounding?	Yes	No	Yes	Unsure	No	Unsure	No	No
	Does your state track the number of out-of-state pharmacies that ship or dispense compounded drugs to providers or patients in the state?	Yes	No	Yes	Unsure	No	Unsure	No	No
Tracking violations	Are sterile compounding-related violations tracked separately by the state?	No	No	No	No	Unsure	No	No	No
	Does the state list disciplinary actions related to pharmacy violations on a public website?	Yes	Yes	Yes	Yes	No	Unsure	Yes	Yes
	Does the state separately list disciplinary actions for compounding-related violations?	No	No	No	No	No	NA	No	No
	Does the state have the authority to share information about inspections, investigations, and enforcement concerns related to drug compounding with other regulators and officials, both federal and state?	Can share with in-state regulators and officials, other state regulators and officials, and federal regulators and officials	Can share with in-state regulators and officials, other state regulators and officials, federal regulators and officials, and on public websites	Can share with in-state regulators and officials, other state regulators and officials, federal regulators and officials, and on public websites	Unsure	Unsure	Unsure	Can share with in-state regulators and officials, other state regulators and officials, and federal regulators and officials	Unsure
Pharmacy reporting	Does the state require pharmacies that perform sterile compounding to report serious adverse events to the state and/or MedWatch?	Yes, to the state only	Yes, to the state and to MedWatch	No	Unsure	Unsure	No	Unsure	No
	Are pharmacies that perform sterile compounding required to report voluntary recalls to the state and/or FDA?	Yes, to the state only	Yes, to FDA only	No, to either	Unsure	No, to either	No, to either	No, to either	No, to either
State authorities	Does the state have the authority to mandate a recall?	Yes	No	No	Unsure	No	Unsure	Unsure	Yes
	Does the state have the authority to issue cease-and-desist orders?	Yes	Yes	No	Unsure	Yes	Unsure	No	Yes
	Does the state have the authority to request reports from pharmacies that perform sterile compounding on the number of sterile products they prepare?	Yes	Yes	Yes	Unsure	Yes	Unsure	No	Yes

Note:

* Indicates that a state either declined to participate in the survey or did not complete the survey. The answers for these states' responses have been found on publicly available websites.

† Indicates that the state opted to abstain from answering that specific question.

Table B.3

Office Use Compounding and Outsourcing Facilities Responses by State

		AL	AR	AZ	CA	CO
		Yes	Yes, but with specific limits	Yes	Yes	Yes, but with specific limits
	If the state applies specific limits to pharmacy compounding without patient specific prescriptions, what are these limits?	NA		NA	NA	10% of total sales, in-state only
	What is the name of legislation or regulation that addresses compounding without patient specific prescriptions?	Sec.08.80.045	Code of Alabama Title 34 Chapter 23, Section 160	07-02-0002—Good Compounding Practices. (I) Compounding for a prescriber's office use.	Not verified†	Business and Professions Code Section 4050-4068 4052. (a) Notwithstanding any other law, a pharmacist may: (1) Furnish a reasonable quantity of compounded drug product to a prescriber for office use by the prescriber. Also Title 16, California Code of Regulations Section 1735.2 (b) and (c), also Title 16 CA Code of Regulations 1735.2(c)—compounding for office use and for future furnishing	3 CCR 719-1 Rule 21.00.20
Outsourcing facilities		State does not license or register outsourcing facilities	State is currently developing a specific outsourcing facility licensure or registration category	By other means: They are working on future regulations to have potential for single outsourcing permit but currently licensed under our wholesaler and pharmacy permits. Statute for the wholesaler permits has already been updated to include language for outsourcing.	State does not license or register outsourcing facilities	State law or regulation has a specific outsourcing facility licensure or registration category	State licenses or registers outsourcing facilities as wholesalers
	What is the name of legislation or regulation that establishes the specific outsourcing facility licensure or registration category?	NA	NA	NA	NA	Senate Bill 619 (Morrell) still pending in Legislature	NA
Enforcement		Unsure	Take disciplinary action	None of the above	Unsure	None of the above	Unsure

B.3		CT	DC	DE*	FL*	GA*	HI
Compounding without prescriptions (also known as office stock)	Does the state allow pharmacies to compound without patient specific prescriptions, such as to provide a doctor with a stock of medicines to use in the office?	Unsure	No	Unsure	Yes, but with specific limits	Yes, but with specific limits	No
	If the state applies specific limits to pharmacy compounding without patient specific prescriptions, what are these limits?	NA	NA	NA	Can compound if it will be used in a treatment setting, is in a reasonable quantity and doesn't exceed the practitioner's anticipatory amount, and the pharmacy and practitioner enter into a written agreement	If there is a valid prescription or for anticipatory prescription drug based on routine	NA
	What is the name of legislation or regulation that addresses compounding without patient specific prescriptions?	NA	Definition of Compounding in DC Pharmacy Laws	NA	64B16-27.700 Definition of Compounding (3)	Georgia State Board of Pharmacy: Pharmaceutical Compounding 480-1.02	Nothing specific, interpretation of various pharmacy laws/rules that a valid prescription that is patient-specific is required for any pharmacy to "dispense" a prescription drug
Outsourcing facilities	How does the state license or register facilities that register with FDA under the new federal outsourcing facility (OF) category of drug compounders?	Unsure	State is currently developing a specific outsourcing facility licensure or registration category	State law or regulation has a specific outsourcing facility licensure or registration category	State law or regulation has a specific outsourcing facility licensure or registration category	Unsure	State does not license or register outsourcing facilities at this time
	What is the name of legislation or regulation that establishes the specific outsourcing facility licensure or registration category?	NA	NA	Section 5 outsourcing facility permit application: Section 503B	64B16-27.700 Definition (3)(g)	NA	NA
Enforcement	How does the state address facilities that perform sterile compounding without patient specific prescriptions that are not registered with FDA?	Unsure	Require those facilities to register with FDA as outsourcing facilities	None of the above	Require those facilities to register with FDA as outsourcing facilities and take disciplinary action	Unsure	None of the above

B.3		IA	ID	IL	IN	KS
Compounding without prescriptions (also known as office stock)	Does the state allow pharmacies to compound without patient specific prescriptions, such as to provide a doctor with a stock of medicines to use in the office?	Pending policy change: State will prohibit compounding without patient-specific prescriptions	Yes, but with specific limits	No	Yes, but with specific limits	Yes
	If the state applies specific limits to pharmacy compounding without patient specific prescriptions, what are these limits?	NA	If the compounded drug product is not sterile and not intended to be sterile; compounded drug product is not further dispensed or distributed by the practitioner; and quantity of compounded drug product distributed is limited to five percent (5%) of the total number of compounded drug products dispensed and distributed on an annual basis by the pharmacy, which may include a drug compounded for the purpose of, or incident to, research, teaching, or chemical analysis	NA	Referred to federal law	NA
	What is the name of legislation or regulation that addresses compounding without patient specific prescriptions?	NA	Section 230 05	Title 68: Professions and Occupations Chapter VII: Department of Financial and Professional Regulation Subchapter B: Professions and Occupations Part 1330 Pharmacy Practice Act Section 1330.640 Pharmaceutical Compounding Standards. These rules will be amended within the next year.	None	It is not addressed, so it isn't prohibited
Outsourcing facilities	How does the state license or register facilities that register with FDA under the new federal outsourcing facility (OF) category of drug compounders?	By other means: State licenses outsourcing facilities as pharmacies or wholesalers; the choice is left to the outsourcing facility	State law or regulation has a specific outsourcing facility licensure or registration category	State licenses or registers outsourcing facilities as manufacturers and wholesalers	State does not license or register outsourcing facilities	State licenses or registers outsourcing facilities as pharmacies
	What is the name of legislation or regulation that establishes the specific outsourcing facility licensure or registration category?	NA	740 Outsourcing facility and 615 Drug distribution 01.b and 070	NA	NA	NA
Enforcement	How does the state address facilities that perform sterile compounding without patient specific prescriptions that are not registered with FDA?	Unsure	Take disciplinary action	Take disciplinary action	Require those facilities to register with FDA as outsourcing facilities	None of the above

B.3		KY	LA	MA	MD	ME*	MI
Compounding without prescriptions (also known as office stock)	Does the state allow pharmacies to compound without patient specific prescriptions, such as to provide a doctor with a stock of medicines to use in the office?	Yes, but with specific limits	Yes, but with specific limits	Unsure	No	No	Yes, but with specific limits
	If the state applies specific limits to pharmacy compounding without patient specific prescriptions, what are these limits?	Only within Kentucky	For veterinarian use only; pharmacy may not distribute such products in excess of 5% of its total sales per month	NA	NA	NA	Limited quantities only
	What is the name of legislation or regulation that addresses compounding without patient specific prescriptions?	201 KAR 2:310	LAC 46:L III.2535	NA	Health Occupations Article, 12-101, Annotated Code of MD	Chapter 117: Maine Pharmacy Act Heading: PL 1987 c.710	Act 280 of 2014
Outsourcing facilities	How does the state license or register facilities that register with FDA under the new federal outsourcing facility (OF) category of drug compounders?	State licenses or registers outsourcing facilities as wholesalers	By other means: Another state agency licenses outsourcers as distributors; we only license as pharmacies if they dispense patient-specific preparations	Unsure	State licenses or registers outsourcing facilities as wholesalers	Unsure	State licenses or registers outsourcing facilities as manufacturers
	What is the name of legislation or regulation that establishes the specific outsourcing facility licensure or registration category?	NA	NA	NA	NA	NA	NA
Enforcement	How does the state address facilities that perform sterile compounding without patient specific prescriptions that are not registered with FDA?	Require those facilities to register with FDA as outsourcing facilities and inform FDA of such facilities	Take disciplinary action	Unsure	Require those facilities to register with FDA as outsourcing facilities, inform FDA of such facilities, and take disciplinary action	Unsure	None of the above

B.3		MN	MO	MS	MT
Compounding without prescriptions (also known as office stock)	Does the state allow pharmacies to compound without patient specific prescriptions, such as to provide a doctor with a stock of medicines to use in the office?	Yes, but with specific limits	No	Yes	No
	If the state applies specific limits to pharmacy compounding without patient specific prescriptions, what are these limits?	Only for drugs that are needed for emergency veterinarian use. Such drugs may be administered in the veterinary offices or dispensed in limited quantities. No other compounding for office use is permitted. Technically, all compounding for office use is illegal except as authorized by the rules of the Board. The Board will promulgate rules allowing for emergency veterinary compounding for "office use" but, for now, is exercising enforcement discretion and allowing such compounding pending promulgation of the rules.	NA	NA	NA
Outsourcing facilities	What is the name of legislation or regulation that addresses compounding without patient specific prescriptions?	Minnesota Statutes Section 151.253 addresses compounding and specifically prohibits compounding without receipt of patient-specific prescriptions	NA	Mississippi Pharmacy Practice Regulations Article XXXI Compounding Guidelines 1. General Provisions C	NA‡
	How does the state license or register facilities that register with FDA under the new federal outsourcing facility (OF) category of drug compounders?	State licenses or registers outsourcing facilities as manufacturers	By other means: Must be registered as a drug distributor	State law or regulation has a specific outsourcing facility licensure or registration category	State does not license or register outsourcing facilities
	What is the name of legislation or regulation that establishes the specific outsourcing facility licensure or registration category?	NA	NA	Mississippi Pharmacy Practice Regulations Article VI Practice of Pharmacy Permits 1. F. Sterile Product Outsourcing	NA
Enforcement	How does the state address facilities that perform sterile compounding without patient specific prescriptions that are not registered with FDA?	Require those facilities to register with FDA as outsourcing facilities, inform FDA of such facilities, and take disciplinary action	NA‡	Require those facilities to register with FDA as outsourcing facilities	Unsure

B.3		NC*	ND	NE	NH	NJ
Compounding without prescriptions (also known as office stock)	Does the state allow pharmacies to compound without patient specific prescriptions, such as to provide a doctor with a stock of medicines to use in the office?	Yes, but with specific limits	Yes, but with specific limits	Yes, but with specific limits	Yes, but with specific limits	Yes, but with specific limits
	If the state applies specific limits to pharmacy compounding without patient specific prescriptions, what are these limits?	For veterinary use only	Only used in the office and can't be dispensed to patients	Pharmacies should be FDA-registered outsourcing facilities to comply with federal regulations	Limited Quantities is defined in NH Pharmacy Rule Ph 404.02(u), "Limited quantities" means a batch with 50 or fewer dosage units provided to a hospital or practitioner to administer to their own patient.	Pending review, as federal law prohibits this practice
	What is the name of legislation or regulation that addresses compounding without patient specific prescriptions?	NCBOP-Pharmacy Rules. 21 NCAC 46 .2801, Section.2800 Compounding. North Carolina Board of Pharmacy FAQ clarifies office use compounding for human use is not permitted because it is not allowed under federal law.	61-02-01-03. Pharmaceutical compounding standards	LB 37; Section 45 1(c)—effective Aug. 30, 2015	NH RSA 318:14-a I: Products that are not commercially available may be compounded for hospital or office use but shall not be resold or dispensed; NH RSA 318:14-a(III) and NH Pharmacy Rule Ph 404.04(c)	Title 13:39 Subchapter 11.18 (sterile) and Subchapter 11A.6 (nonsterile)—Compounded Sterile Preparations for Prescriber practice use: May compound for licensed prescriber
Outsourcing facilities	How does the state license or register facilities that register with FDA under the new federal outsourcing facility (OF) category of drug compounders?	By other means: Every person doing business in NC and operating as a wholesaler, manufacturer, or repackager of prescription drugs and devices must register with the NC Department of Agriculture's Food and Drug Safety Division ("Outsourcing only" facility must be properly permitted by that office and FDA but need not obtain a pharmacy permit from the NCBOP)	State is currently developing a specific outsourcing facility licensure or registration category	State licenses or registers outsourcing facilities as manufacturers and wholesalers	State is currently developing a specific outsourcing facility licensure or registration category	By other means: Outsourcing facilities fall under the regulation of the New Jersey Department of Health, Wholesaler Division. Exact registration type determined by this agency.
	What is the name of legislation or regulation that establishes the specific outsourcing facility licensure or registration category?	NA	NA	NA	NA	NA
Enforcement	How does the state address facilities that perform sterile compounding without patient specific prescriptions that are not registered with FDA?	Unsure	Require those facilities to register with FDA as outsourcing facilities	Inform FDA of such facilities	None of the above	None of the above

B.3		NM	NV	NY	OH*	OK
Compounding without prescriptions (also known as office stock)	Does the state allow pharmacies to compound without patient specific prescriptions, such as to provide a doctor with a stock of medicines to use in the office?	Yes, but with specific limits	Yes, but with specific limits	No	Yes, but with specific limits	Pending policy change: State will limit compounding without patient-specific prescriptions
	If the state applies specific limits to pharmacy compounding without patient specific prescriptions, what are these limits?	Only for veterinarians. Nonsterile. For office use only	For in-office administration only	NA	For direct administration to patients as long as it is not greater than 5% of the pharmacy's total dollar amount of sales	NA
	What is the name of legislation or regulation that addresses compounding without patient specific prescriptions?	16.19.30.9.A.4 NMAC	Chapter 639—Pharmacists and Pharmacy Standards for Compounding and Dispensing Generally NAC 639.6702	Our law only authorizes patient-specific; Education Law Section 6810	4729-16-02 of the Administrative Code	NA
Outsourcing facilities	How does the state license or register facilities that register with FDA under the new federal outsourcing facility (OF) category of drug compounders?	State is currently developing a specific outsourcing facility licensure or registration category	State is currently developing a specific outsourcing facility licensure or registration category	State law or regulation has a specific outsourcing facility licensure or registration category	State licenses or registers outsourcing facilities as wholesalers	State is currently developing a specific outsourcing facility licensure or registration category
	What is the name of legislation or regulation that establishes the specific outsourcing facility licensure or registration category?	NA	NA	§63.8 Registration of nonresident establishments. Education Law §6831. Special provisions relating to outsourcing facilities	Yes	NA
Enforcement	How does the state address facilities that perform sterile compounding without patient specific prescriptions that are not registered with FDA?	Take disciplinary action	Require those facilities to register with FDA as outsourcing facilities	Require those facilities to register with FDA as outsourcing facilities and take disciplinary action	Require those facilities to register with FDA as outsourcing facilities	Require those facilities to register with FDA as outsourcing facilities

B.3		OR	PA	RI	SC	SD	TN
Compounding without prescriptions (also known as office stock)	Does the state allow pharmacies to compound without patient specific prescriptions, such as to provide a doctor with a stock of medicines to use in the office?	Yes, but with specific limits	Pending policy change: State will allow compounding without patient-specific prescriptions	No	Yes	Yes, but with specific limits	Yes, but with specific limits
	If the state applies specific limits to pharmacy compounding without patient specific prescriptions, what are these limits?	Need Board-approved Shared Service Agreement	NA	NA	NA	Based on the prescribers' habits	Only for non-commercially available products
	What is the name of legislation or regulation that addresses compounding without patient specific prescriptions?	Oregon Administrative Rules Chapter 855 855-045-0230 General Requirements (b) Dispense a compounded product only subject to a valid prescription except as provided in OAR 855-045-0220(4), and only when, in their professional judgment, it results from a valid prescriber-patient relationship	NA	Rules and Regulations Pertaining to Pharmacists, Pharmacies and Manufacturers, Wholesalers and Distributors, Section 19.5	40-43-81c (CC)(2)(e)	SDCL 36-11-2	Public Chapter 266
Outsourcing facilities	How does the state license or register facilities that register with FDA under the new federal outsourcing facility (OF) category of drug compounders?	State licenses or registers outsourcing facilities as manufacturers	State licenses or registers outsourcing facilities as wholesalers	State does not license or register outsourcing facilities	Unsure	State is currently developing a specific outsourcing facility licensure or registration category	State law or regulation has a specific outsourcing facility licensure or registration category
	What is the name of legislation or regulation that establishes the specific outsourcing facility licensure or registration category?	NA	NA	NA	NA	NA	Not verified†
Enforcement	How does the state address facilities that perform sterile compounding without patient specific prescriptions that are not registered with FDA?	Require those facilities to register with FDA as outsourcing facilities and take disciplinary action	Inform FDA of such facilities	Inform FDA of such facilities and take disciplinary action	None of the above	Unsure	Require those facilities to register with FDA as outsourcing facilities, inform FDA of such facilities, and take disciplinary action

B.3		TX	UT	VA	VT	WA
Compounding without prescriptions (also known as office stock)	Does the state allow pharmacies to compound without patient specific prescriptions, such as to provide a doctor with a stock of medicines to use in the office?	Yes	Yes, but with specific limits	Yes, but with specific limits	Yes, but with specific limits	No
	If the state applies specific limits to pharmacy compounding without patient specific prescriptions, what are these limits?	NA	But only for anticipatory prescription orders	A pharmacist may provide a reasonable amount of compounded products to practitioners of medicine, osteopathy, podiatry, or dentistry to administer to their patients, either personally or under direct and immediate supervision, if there is critical need to treat an emergency condition, or as allowed by federal law or regulations. A pharmacist may also provide compounded products to practitioners of veterinary medicine for office-based administration to their patients.	Only for anticipatory stock	NA
	What is the name of legislation or regulation that addresses compounding without patient specific prescriptions?	Texas Pharmacy Act, Occupations Code, Chapter 562, Subchapter D	R156. Commerce, Occupational and Professional Licensing. R156-17b. Pharmacy Practice Act Rule. R156-17b-614a. Operating Standards—General Operating Standards, Class A and B Pharmacy (3).	§54.1-3410.2	Administrative Rules of the Board of Pharmacy 10.23 Drugs Compounded in a Pharmacy (C)	Legislation HB 1800 in 2013
Outsourcing facilities	How does the state license or register facilities that register with FDA under the new federal outsourcing facility (OF) category of drug compounders?	State is currently developing a specific outsourcing facility licensure or registration category	State licenses or registers outsourcing facilities as pharmacies	State is currently developing a specific outsourcing facility licensure or registration category	Unsure	State is currently developing a specific outsourcing facility licensure or registration category
	What is the name of legislation or regulation that establishes the specific outsourcing facility licensure or registration category?	NA	NA	NA	NA	NA
Enforcement	How does the state address facilities that perform sterile compounding without patient specific prescriptions that are not registered with FDA?	Inform FDA of such facilities	Take disciplinary action	Unsure	Unsure	Inform FDA of such facilities

B.3		WI*	WV	WY
Compounding without prescriptions (also known as office stock)	Does the state allow pharmacies to compound without patient-specific prescriptions, such as to provide a doctor with a stock of medicines to use in the office?	Unsure	No	Yes, but with specific limits
	If the state applies specific limits to pharmacy compounding without patient specific prescriptions, what are these limits?	NA	NA	Must be administered in the office
	What is the name of legislation or regulation that addresses compounding without patient-specific prescriptions?	NA	Violation of 30-5-4 sub 12 (definition of compounding)	WY Pharmacy Act Rules Chapter 13 Section 3 (d)
Outsourcing facilities	How does the state license or register facilities that register with FDA under the new federal outsourcing facility (OF) category of drug compounders?	Unsure	State licenses or registers outsourcing facilities as manufacturers	State is currently developing a specific outsourcing facility licensure or registration category
	What is the name of legislation or regulation that establishes the specific outsourcing facility licensure or registration category?	NA	NA	NA
Enforcement	How does the state address facilities that perform sterile compounding without patient-specific prescriptions that are not registered with FDA?	Unsure	Require those facilities to register with FDA as outsourcing facilities, inform FDA of such facilities, and take disciplinary action	None of the above

Note:

* Indicates that a state either declined to participate in the survey or did not complete the survey. The answers for these states' responses have been found on publicly available websites.

† Indicates that the state did not respond to an email regarding further clarification that was needed to adequately address what the question was intended for. On those questions, the answer was defaulted to "Not verified."

‡ Indicates that the state opted to abstain from answering that specific question.

Table B.4

Licensure Responses by State

	Sterile compounding	Out-of-state pharmacies
	Is there a separate license or other requirement (e.g. permit) for pharmacies that perform sterile compounding?	Does the state independently license or register out-of-state pharmacies that ship or dispense products to providers or patients in the state?
AK*	No	Yes
AL	Yes	Yes
AR	No	Yes
AZ	Unsure	Yes
CA	Yes	Yes
CO	No	Yes
CT	No	Yes
DC	No	Yes
DE*	No	Yes
FL*	Yes	Yes
GA*	No	Yes
HI	No	Yes
IA	No	Yes
ID	No	Yes
IL	No	Yes
IN	No	Yes
KS	No	Yes
KY	No	Yes
LA	No	Yes
MA	Unsure	Yes
MD	No	Yes
ME*	Yes	Yes
MI	Yes	Yes
MN	Yes	Yes
MO	Yes	Yes
MS	No	Yes
MT	No	Yes
NC*	No	Yes
ND	No	Yes
NE	No	Yes
NH	No	Yes
NJ	No	Yes
NM	No	Yes
NV	No	Yes
NY	No	Yes
OH*	No	Yes
OK	Yes	Yes
OR	No	Yes
PA	No	Yes
RI	No	Yes
SC	No	Yes
SD	No	Yes
TN	Yes	Yes
TX	Yes	Yes
UT	No	Yes
VA	No	Yes
VT	No	Yes
WA	No	Yes
WI*	No	Yes
WV	Yes	Yes
WY	No	Yes

Note:

* Indicates that a state either declined to participate in the survey or did not complete the survey. The answers for these states' responses have been found on publicly available websites.

Table B.5

Inspectorate and Inspector Training Responses by State

B.5	Number of pharmacy inspectors and number of pharmacies					Minimum training requirements for inspectors who assess pharmacies that perform sterile compounding							
		Based on NCPDP data†											
	How many inspectors (full-time equivalents, FTEs) does the state employ who conduct pharmacy inspections?	Number of pharmacies	Number of pharmacies per pharmacy inspector (FTE)	Number of pharmacies that list com pounding functions	Number of pharmacies that per form sterile compounding	Entry to-practice degree in pharmacy (e.g., B.Sc. Pharm., Pharm.D.)	Licensed pharmacist	Training on applicable USP standards	Prior experience in pharmacy	Prior experience in compounding pharmacy	Prior experience in sterile technique/ compounding	No minimum training is mandated	Other
AK*	Unsure	153		36		Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure
AL	9	1,527	170	588	224	No	No	Yes	No	No	No	No	No
AR	3	799	266	260	48	Yes	Yes	Yes	Yes	No	No	No	No
AZ	5	1,288	258	472		No	Yes	No	Yes	No	No	No	No
CA	48	7,278	152	2,751	934	Yes	Yes	Yes	No	No	Yes	No	Yes, additional training in sterile compounding
CO	3	996	332	319	167	Yes	Yes	No	Yes	No	No	No	Yes, critical point boot camp and online training
CT	12	761	63	332		Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure
DC	4	160	40	48	15	No	Yes	Yes	Yes	Yes	Yes	No	No
DE*	Unsure	218		91		Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure
FL*	Unsure	5,966		2,322		Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure
GA*	Unsure	2,768		1,102		Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure

B.5	Number of pharmacy inspectors and number of pharmacies					Minimum training requirements for inspectors who assess pharmacies that perform sterile compounding							
		Based on NCPDP data†											
	How many inspectors (full-time equivalents, FTEs) does the state employ who conduct pharmacy inspections?	Number of pharmacies	Number of pharmacies per pharmacy inspector (FTE)	Number of pharmacies that list com pounding functions	Number of pharmacies that per form sterile compounding	Entry to-practice degree in pharmacy (e.g., B.Sc. Pharm., Pharm.D.)	Licensed pharmacist	Training on applicable USP standards	Prior experience in pharmacy	Prior experience in compounding pharmacy	Prior experience in sterile technique/ compounding	No minimum training is mandated	Other
HI	1	316	316	65		No	No	No	No	No	No	Yes	No
IA	8	862	108	466	90	No	Yes	No	No	No	No	No	No
ID	3	380	127	149	90	No	No	No	No	No	No	No	Yes, NABP training
IL	3	2,699	900	1,303		Yes	Yes	No	Yes	No	No	No	No
IN	5	1,393	279	467		No	No	Yes	No	No	No	No	No
KS	2	722	361	335		Yes	Yes	Yes	Yes	Yes	Yes	No	No
KY	5	1,299	260	598		Yes	Yes	Yes	No	No	Yes	No	Yes, sterile compounding boot camp
LA	5	1,323	265	435		Yes	Yes	Yes	Yes	Yes	Yes	No	No
MA	Unsure	1,277		616		Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure
MD	5	1,411	282	678	190	No	Yes	Yes	Yes	No	No	No	Yes, pharmacy technician license

B.5	Number of pharmacy inspectors and number of pharmacies					Minimum training requirements for inspectors who assess pharmacies that perform sterile compounding							
		Based on NCPDP data†											
	How many inspectors (full-time equivalents, FTEs) does the state employ who conduct pharmacy inspections?	Number of pharmacies	Number of pharmacies per pharmacy inspector (FTE)	Number of pharmacies that list com pounding functions	Number of pharmacies that per form sterile compounding	Entry to-practice degree in pharmacy (e.g., B.Sc. Pharm., Pharm.D.)	Licensed pharmacist	Training on applicable USP standards	Prior experience in pharmacy	Prior experience in compounding pharmacy	Prior experience in sterile technique/ compounding	No minimum training is mandated	Other
ME*	Unsure	321		198		Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure
MI	4	2,663	666	1,581		Yes	Yes	Yes	Yes	No	No	No	No
MN	7	1,290	184	650		Yes	Yes	Yes	Yes	No	Yes	No	Yes, sterile compounding inspection training
MO	8	1,465	183	706		Yes	Yes	Yes	Yes	No	No	No	Yes, annual training
MS	4	915	229	263		Yes	Yes	Yes	Yes	No	No	No	No
MT	2	312	156	123		Yes	Yes	Yes	Yes	No	No	No	No
NC*	12	2,546	212	880		No	No	Yes	No	No	Yes	No	No
ND	3	220	73	113		No	No	No	No	No	No	No	Yes, there is no set standard
NE	3	548	183	275		No	Yes	Yes	Yes	No	No	No	No
NH	3	299	100	157	43	No	Yes	Yes	Yes	No	No	No	No
NJ	6	2,167	361	1,236	180	No	No	No	Yes	No	No	No	Yes, NABP training
NM	6	427	71	149		No	Yes	No	Yes	No	No	No	No

B.5	Number of pharmacy inspectors and number of pharmacies					Minimum training requirements for inspectors who assess pharmacies that perform sterile compounding							
		Based on NCPDP data†											
	How many inspectors (full-time equivalents, FTEs) does the state employ who conduct pharmacy inspections?	Number of pharmacies	Number of pharmacies per pharmacy inspector (FTE)	Number of pharmacies that list com pounding functions	Number of pharmacies that per form sterile compounding	Entry to-practice degree in pharmacy (e.g., B.Sc. Pharm., Pharm.D.)	Licensed pharmacist	Training on applicable USP standards	Prior experience in pharmacy	Prior experience in compounding pharmacy	Prior experience in sterile technique/ compounding	No minimum training is mandated	Other
NV	4	652	163	160	35	Yes	Yes	Yes	Yes	No	No	No	No
NY	50	5,202	104	2,877		No	No	Yes	No	No	No	No	Yes, individualized training, pharmacy board members may assist
OH*	Unsure	2,623		1,066		Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure
OK	6	1,024	171	387	195	Yes	Yes	Yes	Yes	No	No	No	No
OR	5	837	167	362		Yes	Yes	No	Yes	No	No	No	Yes, 5 years' experience to qualify for an inspector position
PA	Unsure	3,736		1,759		No	Yes	No	No	No	No	No	No
RI	Unsure	268		101	8	No	No	No	No	No	No	No	Yes, no training is mandated, however, inspectors are sent to training
SC	5.5	1,436	261	526	122	Yes	Yes	Yes	Yes	No	No	No	No
SD	2	253	127	116		No	Yes	No	No	No	No	No	No
TN	8	1,952	244	735	305	Yes	No	Yes	Yes	No	No	No	No
TX	12	5,298	442	1,928	723	Yes	Yes	Yes	Yes	No	No	No	Yes, pharmacy technician license
UT	3	580	193	230		No	No	No	Yes	Yes	Yes	No	No

B.5	Number of pharmacy inspectors and number of pharmacies					Minimum training requirements for inspectors who assess pharmacies that perform sterile compounding							
		Based on NCPDP data†											
	How many inspectors (full-time equivalents, FTEs) does the state employ who conduct pharmacy inspections?	Number of pharmacies	Number of pharmacies per pharmacy inspector (FTE)	Number of pharmacies that list com pounding functions	Number of pharmacies that per form sterile compounding	Entry to-practice degree in pharmacy (e.g., B.Sc. Pharm., Pharm.D.)	Licensed pharmacist	Training on applicable USP standards	Prior experience in pharmacy	Prior experience in compounding pharmacy	Prior experience in sterile technique/ compounding	No minimum training is mandated	Other
VA	5	1,849	370	699	172	No	Yes	Yes	Yes	No	No	No	No
VT	1	168	168	116		No	No	No	No	No	No	Yes	No
WA	10	1,473	147	553	80	No	Yes	No	No	No	Yes	No	No
WI*	Unsure	1,307		654		Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure
WV	3.5	615	176	306		No	Yes	Yes	No	No	No	No	Yes, 5 years' experience is preferred
WY	1.5	147	98	58		Yes	Yes	Yes	Yes	No	No	No	Yes, NABP training

Note:

* Indicates that a state either declined to participate in the survey or did not complete the survey. The answers for these states' responses have been found on publicly available websites.

† Data from NCPDP Pharmacy Provider Database. Counts of pharmacies listing compounding activity may be an overestimation, as they include entities that perform any compounding, not just pharmacies specializing in this practice. It is also possible they are an underestimation, as this information was optional to provide.

Table B.6

Inspection Policy and Procedure Responses by State

B.6		AK*	AL	AR	AZ
Inspection protocols	How frequently does the state conduct routine inspections for in-state pharmacies that perform sterile compounding?	Unsure	At least every 2 years	At least every year	At least every year
			No	Unsure	Yes; At least every year
		Unsure	Initial licensure, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure	Initial licensure
	Are inspections of pharmacies that perform sterile compounding announced?	Unsure	No	No	No
	How long do inspections of pharmacies that perform sterile compounding usually last?	Unsure	4-8 hours	Other duration: Most last less than 4 hours, but some run over that time	Unsure
	Is direct observation of sterile compounding activity required during inspections of pharmacies that perform sterile compounding, even if it must be simulated?	No	No	No	No
	Does the state have the ability to take and test samples of sterile compounded drugs for inspections or investigations?	No	Yes	Unsure	No
		Unsure	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed	State requires written response describing how issues were addressed	State conducts on-site inspection to ensure that issues were addressed
	Do state inspectors conduct or coordinate inspections with FDA?	Unsure	Yes	Yes	Unsure
	Does the state board of pharmacy inspect hospital pharmacies that perform sterile compounding?	No	Yes	Sometimes	Yes
Inspections by third parties	Must inspection reports by third parties or other states demonstrate compliance with USP standards?	No	Yes	Unsure	NA
	Do third-party inspectors provide all information on compliance and any compliance failures that are observed?	Unsure	No	Unsure	NA

B.6		CA	CO	CT	DC
Inspection frequency	How frequently does the state conduct routine inspections for in-state pharmacies that perform sterile compounding?	At least every year	At least every year	Unsure	At least every year
	Does the state prioritize inspections of in-state pharmacies that perform high-risk sterile compounding? If so, how frequently are these prioritized inspections conducted?	No	Yes; At least every 6 months	Unsure	No
	What specific circumstances trigger the state to conduct inspections for in-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure	Unsure	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, when a complaint or incident occurs, and other circumstances: Damaged premises shall be inspected by the mayor to determine their continued suitability for pharmacy operations
Inspection protocols	Are inspections of pharmacies that perform sterile compounding announced?	No	No	Unsure	No
	How long do inspections of pharmacies that perform sterile compounding usually last?	4-8 hours	Less than 4 hours	Unsure	1-3 days
	Is direct observation of sterile compounding activity required during inspections of pharmacies that perform sterile compounding, even if it must be simulated?	Yes	No	Unsure	Yes
	Does the state have the ability to take and test samples of sterile compounded drugs for inspections or investigations?	Yes	Unsure	Unsure	Yes
	How does the state follow up with pharmacies to make sure that violations are addressed? (Includes other mechanisms reported by states in addition to response options provided.)	Other mechanisms: Could include submitting proof of correction, additional training of staff, additional inspections, citations and fines, license restriction	State requires written response describing how issues were addressed	State conducts on-site inspection to ensure that issues were addressed	State requires written response describing how issues were addressed
Inspections by third parties	Do state inspectors conduct or coordinate inspections with FDA?	Yes	Yes	Unsure	No
	Does the state board of pharmacy inspect hospital pharmacies that perform sterile compounding?	Yes	Yes	No	Yes
	Must inspection reports by third parties or other states demonstrate compliance with USP standards?	NA	Unsure	Yes	Yes
	Do third-party inspectors provide all information on compliance and any compliance failures that are observed?	NA	Unsure	Yes	Unsure

B.6		DE*	FL*	GA*	HI	IA
Inspection frequency	How frequently does the state conduct routine inspections for in-state pharmacies that perform sterile compounding?	At least every year	At least every year	Unsure	No specific frequency	No specific frequency
	Does the state prioritize inspections of in-state pharmacies that perform high-risk sterile compounding? If so, how frequently are these prioritized inspections conducted?	No	Unsure	Unsure	No	No
	What specific circumstances trigger the state to conduct inspections for in-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	Initial licensure and licensure renewal	Initial licensure, licensure renewal, and when a pharmacy remodels or moves location	Unsure	When a complaint or incident occurs and random inspections	Initial licensure, when a pharmacy remodels or moves location, and when a complaint or incident occurs
Inspection protocols	Are inspections of pharmacies that perform sterile compounding announced?	Unsure	Unsure	Unsure	No	No
	How long do inspections of pharmacies that perform sterile compounding usually last?	Unsure	Unsure	Unsure	Less than 4 hours	Other duration: It varies, depending on all services provided by the pharmacy; inspection not limited to sterile compounding practices
	Is direct observation of sterile compounding activity required during inspections of pharmacies that perform sterile compounding, even if it must be simulated?	Unsure	Unsure	Unsure	Unsure	No
	Does the state have the ability to take and test samples of sterile compounded drugs for inspections or investigations?	Yes	Yes	Unsure	Unsure	Yes
	How does the state follow up with pharmacies to make sure that violations are addressed? (Includes other mechanisms reported by states in addition to response options provided.)	Unsure	Unsure	Unsure	Unsure	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed
	Do state inspectors conduct or coordinate inspections with FDA?	Unsure	Unsure	Unsure	Unsure	Yes
	Does the state board of pharmacy inspect hospital pharmacies that perform sterile compounding?	Yes	Yes	Yes	Sometimes	Yes
Inspections by third parties	Must inspection reports by third parties or other states demonstrate compliance with USP standards?	No	Yes	Yes	Yes	No
	Do third-party inspectors provide all information on compliance and any compliance failures that are observed?	Unsure	Unsure	Unsure	NA	Unsure

B.6		ID	IL	IN	KS	KY
Inspection frequency	How frequently does the state conduct routine inspections for in-state pharmacies that perform sterile compounding?	At least every year	No specific frequency	At least every 3 years	At least every year	At least every year
	Does the state prioritize inspections of in-state pharmacies that perform high-risk sterile compounding? If so, how frequently are these prioritized inspections conducted?	No	Yes; No specific frequency	No	Yes; At least every year	No
	What specific circumstances trigger the state to conduct inspections for in-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	When a pharmacy remodels or moves location and when a complaint or incident occurs	Initial licensure, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure, when a pharmacy remodels or moves location, and when a complaint or incident occurs
Inspection protocols	Are inspections of pharmacies that perform sterile compounding announced?	No	No	No	No	No
	How long do inspections of pharmacies that perform sterile compounding usually last?	Less than 4 hours	4-8 hours	4-8 hours	4-8 hours	4-8 hours
	Is direct observation of sterile compounding activity required during inspections of pharmacies that perform sterile compounding, even if it must be simulated?	No	No	Yes	No	No
	Does the state have the ability to take and test samples of sterile compounded drugs for inspections or investigations?	Yes	Yes	No	No	No
	How does the state follow up with pharmacies to make sure that violations are addressed? (Includes other mechanisms reported by states in addition to response options provided.)	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed	State conducts on-site inspection to ensure that issues were addressed	State conducts on-site inspection to ensure that issues were addressed	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed
Inspections by third parties	Do state inspectors conduct or coordinate inspections with FDA?	Yes	Yes	Yes	Yes	Yes
	Does the state board of pharmacy inspect hospital pharmacies that perform sterile compounding?	Yes	Yes	Yes	Yes	Yes
	Must inspection reports by third parties or other states demonstrate compliance with USP standards?	No	No	Yes	No	No
	Do third-party inspectors provide all information on compliance and any compliance failures that are observed?	Unsure	NA	Yes	Unsure	NA

B.6		LA	MA	MD	ME*	MI
Inspection frequency	How frequently does the state conduct routine inspections for in-state pharmacies that perform sterile compounding?	At least every year	Unsure	At least every year	At least every year	No specific frequency
	Does the state prioritize inspections of in-state pharmacies that perform high-risk sterile compounding? If so, how frequently are these prioritized inspections conducted?	Yes; At least every year	Unsure	No	No	No
	What specific circumstances trigger the state to conduct inspections for in-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Unsure	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure, licensure renewal, and when a complaint or incident occurs	Initial licensure and when a complaint or incident occurs
Inspection protocols	Are inspections of pharmacies that perform sterile compounding announced?	No	Unsure	No	Unsure	No
	How long do inspections of pharmacies that perform sterile compounding usually last?	4-8 hours	Unsure	Less than 4 hours	Unsure	4-8 hours
	Is direct observation of sterile compounding activity required during inspections of pharmacies that perform sterile compounding, even if it must be simulated?	No	Unsure	Yes	Unsure	No
	Does the state have the ability to take and test samples of sterile compounded drugs for inspections or investigations?	Yes	Unsure	No	Yes	No
	How does the state follow up with pharmacies to make sure that violations are addressed? (Includes other mechanisms reported by states in addition to response options provided.)	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed. Other mechanisms: Depends on level of disciplinary action. Follow-up is made part of monitoring team if issue rises to disciplinary action; if not, state conducts education and ensures compliance.	State requires written response describing how issues were addressed	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed	State requires written response describing how issues were addressed	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed
Inspections by third parties	Do state inspectors conduct or coordinate inspections with FDA?	Yes	Unsure	No	Unsure	Yes
	Does the state board of pharmacy inspect hospital pharmacies that perform sterile compounding?	Yes	Unsure	Yes	Yes	Yes
	Must inspection reports by third parties or other states demonstrate compliance with USP standards?	Yes	Unsure	Yes	Unsure	Yes
	Do third-party inspectors provide all information on compliance and any compliance failures that are observed?	Unsure	Unsure	Unsure	Unsure	Unsure

B.6		MN	MO	MS	MT	NC*
Inspection frequency	How frequently does the state conduct routine inspections for in-state pharmacies that perform sterile compounding?	At least every 2 years	No specific frequency	At least every year	Unsure	At least every 5 years
	Does the state prioritize inspections of in-state pharmacies that perform high-risk sterile compounding? If so, how frequently are these prioritized inspections conducted?	Yes; At least every 2 years	Yes; At least every year	No	No	Yes; At least every year
	What specific circumstances trigger the state to conduct inspections for in-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	Initial licensure, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs	No specific circumstances (other than annual inspections)	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and other circumstances: change in ownership	Initial licensure and when a complaint or incident occurs
Inspection protocols	Are inspections of pharmacies that perform sterile compounding announced?	No	No	No	No	Unsure
	How long do inspections of pharmacies that perform sterile compounding usually last?	1-3 days	Other duration: It depends on the nature/scope of activities	Unsure	Less than 4 hours	Unsure
	Is direct observation of sterile compounding activity required during inspections of pharmacies that perform sterile compounding, even if it must be simulated?	No	Unsure	Unsure	Yes	Unsure
	Does the state have the ability to take and test samples of sterile compounded drugs for inspections or investigations?	Yes	Yes	Unsure	Unsure	Unsure
	How does the state follow up with pharmacies to make sure that violations are addressed? (Includes other mechanisms reported by states in addition to response options provided.)	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed. Other mechanisms: Responses depend on the nature of the violation.	State conducts on-site inspection to ensure that issues were addressed	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed	Unsure
Inspections by third parties	Do state inspectors conduct or coordinate inspections with FDA?	Yes	Yes	Yes	No	Unsure
	Does the state board of pharmacy inspect hospital pharmacies that perform sterile compounding?	Yes	Sometimes	Yes	Yes	Yes
	Must inspection reports by third parties or other states demonstrate compliance with USP standards?	Yes	NA	NA	NA	NA
	Do third-party inspectors provide all information on compliance and any compliance failures that are observed?	Unsure	NA†	Yes	Unsure	Unsure

B.6		ND	NE	NH	NJ	NM
Inspection frequency	How frequently does the state conduct routine inspections for in-state pharmacies that perform sterile compounding?	At least every year	At least every 5 years	At least every year	At least every year	At least every 2 years
	Does the state prioritize inspections of in-state pharmacies that perform high-risk sterile compounding? If so, how frequently are these prioritized inspections conducted?	No	No	No	No	No
	What specific circumstances trigger the state to conduct inspections for in-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	No specific circumstances (other than annual inspections)	Initial licensure, when a pharmacy remodels or moves location, and when a complaint or incident occurs	No specific circumstances (other than annual inspections)	Initial licensure, when a complaint or incident occurs, and when a pharmacy remodels or moves location	Initial licensure and when a pharmacy remodels or moves location
Inspection protocols	Are inspections of pharmacies that perform sterile compounding announced?	No	No	Sometimes	No	No
	How long do inspections of pharmacies that perform sterile compounding usually last?	Less than 4 hours	Other duration: It depends on the individual pharmacy	4-8 hours	4-8 hours	Less than 4 hours
	Is direct observation of sterile compounding activity required during inspections of pharmacies that perform sterile compounding, even if it must be simulated?	No	No	No	Yes	No
	Does the state have the ability to take and test samples of sterile compounded drugs for inspections or investigations?	Yes	Unsure	Yes	No	No
	How does the state follow up with pharmacies to make sure that violations are addressed? (Includes other mechanisms reported by states in addition to response options provided.)	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed	State requires written response describing how issues were addressed. Other mechanisms: Follow-up inspections may be conducted.	State requires written response describing how issues were addressed. Other mechanisms: Unannounced reinspections may occur depending on the nature of the violation.	State requires written response describing how issues were addressed
Inspections by third parties	Do state inspectors conduct or coordinate inspections with FDA?	No	Yes	Yes	Yes	No
	Does the state board of pharmacy inspect hospital pharmacies that perform sterile compounding?	Yes	Sometimes	Yes	Yes	Yes
	Must inspection reports by third parties or other states demonstrate compliance with USP standards?	Yes	Unsure	Yes	Yes	No
	Do third-party inspectors provide all information on compliance and any compliance failures that are observed?	Yes	Unsure	No	Yes	Yes

B.6		NV	NY	OH*	OK	OR
Inspection frequency	How frequently does the state conduct routine inspections for in-state pharmacies that perform sterile compounding?	At least every year	At least every 3 years	Unsure	At least every year	At least every year
	Does the state prioritize inspections of in-state pharmacies that perform high-risk sterile compounding? If so, how frequently are these prioritized inspections conducted?	No	Yes; At least every 2 years	Unsure	No	No
	What specific circumstances trigger the state to conduct inspections for in-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, when a complaint or incident occurs, and other circumstances: Whenever board requests	Initial licensure, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Unsure	Initial licensure, when a pharmacy remodels or moves location, and when a complaint or incident occurs	No specific circumstances (other than annual inspections)
Inspection protocols	Are inspections of pharmacies that perform sterile compounding announced?	No	No	Unsure	No	No
	How long do inspections of pharmacies that perform sterile compounding usually last?	4-8 hours	Other duration: It is variable	Unsure	4-8 hours	Less than 4 hours
	Is direct observation of sterile compounding activity required during inspections of pharmacies that perform sterile compounding, even if it must be simulated?	No	No	Unsure	Yes	No
	Does the state have the ability to take and test samples of sterile compounded drugs for inspections or investigations?	Yes	Yes	Unsure	Yes	No
	How does the state follow up with pharmacies to make sure that violations are addressed? (Includes other mechanisms reported by states in addition to response options provided.)	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed. Other mechanisms: annual inspections; review of self-assessment form; notes regarding discrepancies or deficiencies; correction of discrepancies or deficiencies.	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed	Unsure	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed	State requires written response describing how issues were addressed
Inspections by third parties	Do state inspectors conduct or coordinate inspections with FDA?	Yes	Yes	Unsure	Yes	Yes
	Does the state board of pharmacy inspect hospital pharmacies that perform sterile compounding?	Yes	Yes	Yes	Yes	Yes
	Must inspection reports by third parties or other states demonstrate compliance with USP standards?	Yes	NA	Unsure	Yes	Unsure
	Do third-party inspectors provide all information on compliance and any compliance failures that are observed?	NA	NA	Yes	Yes	No

B.6		PA	RI	SC	SD	TN
Inspection frequency	How frequently does the state conduct routine inspections for in-state pharmacies that perform sterile compounding?	At least every year	No specific frequency	At least every 2 years	At least every year	At least every year
	Does the state prioritize inspections of in-state pharmacies that perform high-risk sterile compounding? If so, how frequently are these prioritized inspections conducted?	No	Yes; No specific frequency	No	No	Yes; At least every year
	What specific circumstances trigger the state to conduct inspections for in-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	Initial licensure, when a pharmacy remodels or moves location, when a complaint or incident occurs, and random inspections	Initial licensure, when a complaint or incident occurs, and random inspections	Initial licensure, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs
Inspection protocols	Are inspections of pharmacies that perform sterile compounding announced?	Unsure	No	No	Sometimes	No
	How long do inspections of pharmacies that perform sterile compounding usually last?	Unsure	4-8 hours	Not verified‡	4-8 hours	4-8 hours
	Is direct observation of sterile compounding activity required during inspections of pharmacies that perform sterile compounding, even if it must be simulated?	Unsure	Yes	No	No	Yes
	Does the state have the ability to take and test samples of sterile compounded drugs for inspections or investigations?	Unsure	No	Yes	No	Yes
	How does the state follow up with pharmacies to make sure that violations are addressed? (Includes other mechanisms reported by states in addition to response options provided.)	Unsure	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed
Inspections by third parties	Do state inspectors conduct or coordinate inspections with FDA?	Yes	Yes	Yes	Yes	Yes
	Does the state board of pharmacy inspect hospital pharmacies that perform sterile compounding?	Yes	Yes	Yes	Yes	Yes
	Must inspection reports by third parties or other states demonstrate compliance with USP standards?	NA	Yes	No	Unsure	Yes
	Do third-party inspectors provide all information on compliance and any compliance failures that are observed?	NA	Yes	Unsure	NA	Yes

B.6		TX	UT	VA
Inspection frequency	How frequently does the state conduct routine inspections for in-state pharmacies that perform sterile compounding?	At least every 2 years	No specific frequency	At least every 2 years
	Does the state prioritize inspections of in-state pharmacies that perform high-risk sterile compounding? If so, how frequently are these prioritized inspections conducted?	Yes; At least every 2 years	No	No
	What specific circumstances trigger the state to conduct inspections for in-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure, when a pharmacy remodels or moves location, when a complaint or incident occurs, and random inspections	Initial licensure, when a pharmacy remodels or moves location, and when a complaint or incident occurs
Inspection protocols	Are inspections of pharmacies that perform sterile compounding announced?	No	No	No
	How long do inspections of pharmacies that perform sterile compounding usually last?	4-8 hours	4-8 hours	4-8 hours; hospitals usually take 2 days
	Is direct observation of sterile compounding activity required during inspections of pharmacies that perform sterile compounding, even if it must be simulated?	No	No	No
	Does the state have the ability to take and test samples of sterile compounded drugs for inspections or investigations?	Yes	Yes	No
	How does the state follow up with pharmacies to make sure that violations are addressed? (Includes other mechanisms reported by states in addition to response options provided.)	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed. Other mechanisms: For less serious violations, a warning notice is issued that requires a response from the pharmacy to indicate the correction. For more serious violations, the Board notifies the licensee of the Board's intent to institute disciplinary action, provides the licensee with the opportunity to show compliance. If the licensee is unable, they may consent to, and agree to the terms of, an Agreed Board Order. If the licensee does not wish to have an informal conference, a disciplinary hearing is scheduled.	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed	State requires written response describing how issues were addressed
Inspections by third parties	Do state inspectors conduct or coordinate inspections with FDA?	Yes	Yes	Yes
	Does the state board of pharmacy inspect hospital pharmacies that perform sterile compounding?	Yes	Sometimes	Yes
	Must inspection reports by third parties or other states demonstrate compliance with USP standards?	Yes	Unsure	Yes
	Do third-party inspectors provide all information on compliance and any compliance failures that are observed?	Yes	Unsure	Yes

B.6		VT	WA	WI*	WV	WY
Inspection frequency	How frequently does the state conduct routine inspections for in-state pharmacies that perform sterile compounding?	At least every 2 years	At least every year	At least every year	At least every year	At least every year
	Does the state prioritize inspections of in-state pharmacies that perform high-risk sterile compounding? If so, how frequently are these prioritized inspections conducted?	Unsure	Yes; At least every year	Unsure	No	No
	What specific circumstances trigger the state to conduct inspections for in-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	Initial licensure and when a pharmacy remodels or moves location	When a complaint or incident occurs	Unsure	Initial licensure and when a pharmacy remodels or moves location	Initial licensure and when a complaint or incident occurs
Inspection protocols	Are inspections of pharmacies that perform sterile compounding announced?	Sometimes	No	Unsure	No	No
	How long do inspections of pharmacies that perform sterile compounding usually last?	4-8 hours	Less than 4 hours	Unsure	Other duration: 12 hours; FDA-led inspections may vary	4-8 hours
	Is direct observation of sterile compounding activity required during inspections of pharmacies that perform sterile compounding, even if it must be simulated?	No	Yes	Unsure	No	No
	Does the state have the ability to take and test samples of sterile compounded drugs for inspections or investigations?	No	Unsure	Unsure	No	No
	How does the state follow up with pharmacies to make sure that violations are addressed? (Includes other mechanisms reported by states in addition to response options provided.)	State requires written response describing how issues were addressed	State conducts on-site inspection to ensure that issues were addressed	Unsure	State requires written response describing how issues were addressed. Other mechanisms: Under certain circumstances, state goes back to conduct on-site inspections.	State conducts on-site inspection to ensure that issues were addressed and requires written response describing how issues were addressed
Inspections by third parties	Do state inspectors conduct or coordinate inspections with FDA?	Yes	Yes	Unsure	Yes	No
	Does the state board of pharmacy inspect hospital pharmacies that perform sterile compounding?	Unsure	Yes	Unsure	Yes	Yes
	Must inspection reports by third parties or other states demonstrate compliance with USP standards?	Yes	No	No	No	Yes
	Do third-party inspectors provide all information on compliance and any compliance failures that are observed?	Unsure	Unsure	Unsure	No	Unsure

* Indicates that a state either declined to participate in the survey or did not complete the survey. The answers for these states' responses have been found on publicly available websites.

† Indicates that the state opted to abstain from answering that specific question.

‡ Indicates that the state did not respond to an email regarding further clarification that was needed to adequately address what the question was intended for. On those questions, the answer was defaulted to "Not verified."

Table B.7

Sterile Compounding Inspection Evaluation Responses by State

B.7	Factors evaluated during a sterile compounding inspection												
	Hand hygiene	Garbing	Aseptic technique	Training	Facility design and construc-tion	Cleaning	Environ-mental monitoring	Equipment certifica-tion and calibration	Steril-ization procedures and verification	Control of compo-nents and materials	Standard operating procedures	Documen-tation	Other
AK*	No	No	No	Yes	No	No	No	Yes	No	Yes	No	Yes	No
AL	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Hazardous product compounding, hazardous training, signed consent form, waste management, lists of which products are compounded and whether they are FDA-approved for compounding, invoices for bulk ingredients for source and certificate of analysis, shipping records and billing records to see who receives products and who pays for products; documentation for beyond use dating
AR	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No
AZ	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No
CA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
CO	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
CT	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure
DC	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	No
DE*	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure
FL*	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No
GA*	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure

B.7	Factors evaluated during a sterile compounding inspection												
	Hand hygiene	Garbing	Aseptic technique	Training	Facility design and construc-tion	Cleaning	Environ-mental monitoring	Equipment certification and calibration	Sterilization procedures and verification	Control of compo-nents and materials	Standard operating procedures	Documen-tation	Other
HI	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure
IA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
ID	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
IL	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No
IN	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
KS	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
KY	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
LA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
MA	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure
MD	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No
ME*	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure
MI	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No
MN	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
MO	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Other standards/issues that may affect the public health
MS	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure
MT	No	No	Yes	Yes	No	No	No	Yes	No	No	No	Yes	No
NC*	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
ND	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No

B.7	Factors evaluated during a sterile compounding inspection												
	Hand hygiene	Garbing	Aseptic technique	Training	Facility design and construction	Cleaning	Environ-mental monitoring	Equipment certification and calibration	Sterilization procedures and verification	Control of components and materials	Standard operating procedures	Docu-mentation	Other
NE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
NH	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
NJ	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Records of required ongoing training for personnel involved in CSP preparation
NM	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
NV	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
NY	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
OH*	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
OK	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
OR	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
PA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No
RI	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
SC	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
SD	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
TN	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No

B.7	Factors evaluated during a sterile compounding inspection												
	Hand hygiene	Garbing	Aseptic technique	Training	Facility design and construction	Cleaning	Environ-mental monitoring	Equipment certification and calibration	Sterilization procedures and verification	Control of components and materials	Standard operating procedures	Docu-mentation	Other
TX	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Specific initial training for both pharmacist and pharmacy technicians who compound sterile products; and all pharmacy personnel preparing sterile preparations shall perform didactic review and pass written and media-fill testing of aseptic manipulative skills initially followed by: every 12 months for low- and medium-risk level compounding; and every six months for high-risk level compounding
UT	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
VA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
VT	No	No	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	No
WA	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
WI*	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure	Unsure
WV	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
WY	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No	Risk level

Note:

* Indicates that a state either declined to participate in the survey or did not complete the survey. The answers for these states' responses have been found on publicly available websites.

Table B.8

Oversight of Nonresident (Out-of-State) Compounding Pharmacies Responses by State

B.8		AK*	AL	AR	AZ
Methods used to assess out-of-state pharmacy compliance	For out-of-state pharmacies performing sterile compounding, does the state verify compliance with their applicable regulations?	Yes	Yes	Yes	Yes
	Are inspections performed by the National Association of Boards of Pharmacy (NABP) used by the state to verify that out of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	Yes
	Are inspections performed by a third party approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No
	Are inspections performed by a third party not approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No
	Are reviews of inspection reports by another state, conducted in the past ____ years, done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations? If so, specify the number of years.	No	No	Yes; Within the past 2 years	Yes; Time period not specified
	Must the pharmacy provide self-evaluation or attestation of compliance to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Yes	Yes	Yes	No
	Are there other means used to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	Yes—planning to require copy of other inspections; research FDA documentation, NABP report, disciplinary action from other states	No	No
Frequency	How frequently does the state assess compliance for out-of state pharmacies that perform sterile compounding?	Unsure	No specific frequency	No specific frequency	Unsure
	What specific circumstances trigger the state to assess compliance for out-of-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	License renewal, when a facility remodels or moves location, and when a complaint or incident occurs	Initial licensure and when a complaint or incident occurs	Initial licensure and other circumstances: Working on this for renewal	When a complaint or incident occurs

B.8		CA	CO	CT	DC	DE*
Methods used to assess out-of-state pharmacy compliance	For out-of-state pharmacies performing sterile compounding, does the state verify compliance with their applicable regulations?	Yes	No	Unsure	Yes	Yes
	Are inspections performed by the National Association of Boards of Pharmacy (NABP) used by the state to verify that out of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	Unsure	Yes	No
	Are inspections performed by a third party approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	Unsure	No	No
	Are inspections performed by a third party not approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	Unsure	No	No
	Are reviews of inspection reports by another state, conducted in the past ____ years, done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations? If so, specify the number of years.	No	No	Unsure	No	No
	Must the pharmacy provide self-evaluation or attestation of compliance to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	Unsure	No	Yes
	Are there other means used to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	Unsure	No	No
Frequency	How frequently does the state assess compliance for out-of state pharmacies that perform sterile compounding?	At least every year	Unsure	Unsure	At least every 2 years	At least every year
	What specific circumstances trigger the state to assess compliance for out-of-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Unsure	Unsure	Licensure renewal	Unsure

B.8		FL*	GA*	HI	IA	ID
Methods used to assess out-of-state pharmacy compliance	For out-of-state pharmacies performing sterile compounding, does the state verify compliance with their applicable regulations?	Yes	Yes	No	Yes	Yes
	Are inspections performed by the National Association of Boards of Pharmacy (NABP) used by the state to verify that out of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	Yes
	Are inspections performed by a third party approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	Yes	No
	Are inspections performed by a third party not approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	Yes
	Are reviews of inspection reports by another state, conducted in the past ____ years, done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations? If so, specify the number of years.	Yes; Within the past 6 months for initial licensure, within the past year for renewal	Yes; Within the past 6 months for initial licensure, within the past 2 years for renewal	No	No	Yes; Within the past 3 years
	Must the pharmacy provide self-evaluation or attestation of compliance to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	No
	Are there other means used to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	No
Frequency	How frequently does the state assess compliance for out-of state pharmacies that perform sterile compounding?	At least every year	At least every 2 years	No specific frequency	At least every year	No specific frequency
	What specific circumstances trigger the state to assess compliance for out-of-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	Initial licensure and licensure renewal	Initial licensure and licensure renewal	When a complaint or incident occurs	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, when a complaint or incident occurs, and other circumstances: failure to provide acceptable inspection report	Initial licensure

B.8		IL	IN	KS	KY	LA
Methods used to assess out-of-state pharmacy compliance	For out-of-state pharmacies performing sterile compounding, does the state verify compliance with their applicable regulations?	Yes	Yes	Yes	Yes	Yes
	Are inspections performed by the National Association of Boards of Pharmacy (NABP) used by the state to verify that out of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	Yes	Yes	No	Yes
	Are inspections performed by a third party approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	No
	Are inspections performed by a third party not approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	No
	Are reviews of inspection reports by another state, conducted in the past ____ years, done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations? If so, specify the number of years.	No	No	Yes; Within the past year	Yes; Time period not specified	No
	Must the pharmacy provide self-evaluation or attestation of compliance to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	No
	Are there other means used to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Yes—must be licensed in home state	No	No	No	No
Frequency	How frequently does the state assess compliance for out-of state pharmacies that perform sterile compounding?	No specific frequency	Unsure	At least every year	No specific frequency	At least every year
	What specific circumstances trigger the state to assess compliance for out-of-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	When a complaint or incident occurs	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure, licensure renewal, and when a complaint or incident occurs	Initial licensure, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure and licensure renewal

B.8		MA	MD	ME*	MI	MN
Methods used to assess out-of-state pharmacy compliance	For out-of-state pharmacies performing sterile compounding, does the state verify compliance with their applicable regulations?	Unsure	Yes	Yes	Yes	Yes
	Are inspections performed by the National Association of Boards of Pharmacy (NABP) used by the state to verify that out of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Unsure	Yes	Yes	Yes	Yes
	Are inspections performed by a third party approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Unsure	Yes	No	Yes	Yes
	Are inspections performed by a third party not approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Unsure	No	No	Yes	No
	Are reviews of inspection reports by another state, conducted in the past ____ years, done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations? If so, specify the number of years.	Unsure	Yes; Within the past 90 days	No	Yes; Time period not specified	Yes; Within the past 2 years
	Must the pharmacy provide self-evaluation or attestation of compliance to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Unsure	No	No	No	No
	Are there other means used to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Unsure	No	No	No	No
Frequency	How frequently does the state assess compliance for out-of state pharmacies that perform sterile compounding?	Unsure	At least every 2 years	At least every year	No specific frequency	At least every year
	What specific circumstances trigger the state to assess compliance for out-of-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	Unsure	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure, licensure renewal, and when a complaint or incident occurs	Initial licensure, licensure renewal, and when a complaint or incident occurs	Initial licensure and licensure renewal

B.8		MO	MS	MT	NC*	ND
Methods used to assess out-of-state pharmacy compliance	For out-of-state pharmacies performing sterile compounding, does the state verify compliance with their applicable regulations?	Unsure	No	Yes	Unsure	Yes
	Are inspections performed by the National Association of Boards of Pharmacy (NABP) used by the state to verify that out of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Unsure	No	No	Unsure	Yes
	Are inspections performed by a third party approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Unsure	No	No	Unsure	No
	Are inspections performed by a third party not approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Unsure	No	No	Unsure	No
	Are reviews of inspection reports by another state, conducted in the past ____ years, done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations? If so, specify the number of years.	Unsure	No	No	Unsure	Yes; Within the past year
	Must the pharmacy provide self-evaluation or attestation of compliance to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Unsure	No	No	Unsure	Yes
	Are there other means used to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	The Board is unaware of any way to verify compliance with regulations in other states	No	No	Unsure	No
Frequency	How frequently does the state assess compliance for out-of state pharmacies that perform sterile compounding?	No specific frequency	No specific frequency	No specific frequency	Unsure	At least every year
	What specific circumstances trigger the state to assess compliance for out-of-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, when a complaint or incident occurs, and other circumstances: Multiple factors may result in a compliance assessment, including news reports, disciplinary actions, investigations, inquiries, anonymous tips, FDA recall notices, etc.	Unsure	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, when a complaint or incident occurs, and other circumstances: change in ownership	Unsure	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs

B.8		NE	NH	NJ	NM	NV
Methods used to assess out-of-state pharmacy compliance	For out-of-state pharmacies performing sterile compounding, does the state verify compliance with their applicable regulations?	Yes	Yes	Yes	Yes	Yes
	Are inspections performed by the National Association of Boards of Pharmacy (NABP) used by the state to verify that out of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	Yes	Yes	No	Yes
	Are inspections performed by a third party approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	Yes
	Are inspections performed by a third party not approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	Yes
	Are reviews of inspection reports by another state, conducted in the past ____ years, done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations? If so, specify the number of years.	No	Yes; Within the past 18 months	Yes; Within the past 2 years	Yes; Time period not specified	Yes; Within the past year
	Must the pharmacy provide self-evaluation or attestation of compliance to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	No
	Are there other means used to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Yes—Mail Service Pharmacy License application requests the last 2 inspections conducted by the regulatory agency of the home state in which the pharmacy is located	Yes—pharmacy must provide GAP analysis	No	No	No
Frequency	How frequently does the state assess compliance for out-of state pharmacies that perform sterile compounding?	Unsure	At least every year	At least every year	No specific frequency	At least every 2 years
	What specific circumstances trigger the state to assess compliance for out-of-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	Initial licensure and when a complaint or incident occurs	Initial licensure and licensure renewal	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure and when a complaint or incident occurs	Initial licensure and when a complaint or incident occurs

B.8		NY	OH*	OK	OR	PA
Methods used to assess out-of-state pharmacy compliance	For out-of-state pharmacies performing sterile compounding, does the state verify compliance with their applicable regulations?	Yes	Yes	Yes	Yes	No
	Are inspections performed by the National Association of Boards of Pharmacy (NABP) used by the state to verify that out of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Yes	No	Yes	No	No
	Are inspections performed by a third party approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	Yes	No	No
	Are inspections performed by a third party not approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	No
	Are reviews of inspection reports by another state, conducted in the past ____ years, done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations? If so, specify the number of years.	No	Yes; Within the past 2 years	Yes; Within the past 2 years	Yes; Within the past 3 years	No
	Must the pharmacy provide self-evaluation or attestation of compliance to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	No
	Are there other means used to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	No
Frequency	How frequently does the state assess compliance for out-of state pharmacies that perform sterile compounding?	At least every 3 years	At least every 2 years	No specific frequency	No specific frequency	No specific frequency
	What specific circumstances trigger the state to assess compliance for out-of-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	When a complaint or incident occurs	Unsure	Initial licensure, licensure renewal, and when a complaint or incident occurs	Initial licensure and when a complaint or incident occurs	No specific circumstances trigger an inspection

B.8		RI	SC	SD	TN	TX
Methods used to assess out-of-state pharmacy compliance	For out-of-state pharmacies performing sterile compounding, does the state verify compliance with their applicable regulations?	Yes	Yes	Yes	Yes	Yes
	Are inspections performed by the National Association of Boards of Pharmacy (NABP) used by the state to verify that out of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Yes	Yes	Yes	Yes	Yes
	Are inspections performed by a third party approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Yes	Yes	No	No	Yes
	Are inspections performed by a third party not approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	No
	Are reviews of inspection reports by another state, conducted in the past ____ years, done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations? If so, specify the number of years.	No	Yes; Within the past 2 years	Yes; Within the past 4 years	Yes; Within the past year	No
	Must the pharmacy provide self-evaluation or attestation of compliance to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	No
	Are there other means used to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	No
Frequency	How frequently does the state assess compliance for out-of state pharmacies that perform sterile compounding?	No specific frequency	At least every 2 years	At least every year	At least every 2 years	At least every 2 years
	What specific circumstances trigger the state to assess compliance for out-of-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	Initial licensure	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure, licensure renewal, when a pharmacy remodels or moves location, and when a complaint or incident occurs

B.8		UT	VA	VT	WA	WI*
Methods used to assess out-of-state pharmacy compliance	For out-of-state pharmacies performing sterile compounding, does the state verify compliance with their applicable regulations?	Yes	Yes	Yes	No	Unsure
	Are inspections performed by the National Association of Boards of Pharmacy (NABP) used by the state to verify that out of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	Yes	No	No	Unsure
	Are inspections performed by a third party approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	Yes	No	No	Unsure
	Are inspections performed by a third party not approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	Unsure
	Are reviews of inspection reports by another state, conducted in the past ____ years, done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations? If so, specify the number of years.	Yes; Within the past year	Yes; Within the past 6 months for initial licensure, within the past 2 years for renewal	Yes; Within the past 3 years	No	Unsure
	Must the pharmacy provide self-evaluation or attestation of compliance to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	Unsure
	Are there other means used to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No	No	No	Unsure
Frequency	How frequently does the state assess compliance for out-of state pharmacies that perform sterile compounding?	No specific frequency	At least every 2 years	Unsure	No specific frequency	Unsure
	What specific circumstances trigger the state to assess compliance for out-of-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	Initial licensure, when a pharmacy remodels or moves location, and when a complaint or incident occurs	Initial licensure and licensure renewal	Unsure	Initial licensure and when a complaint or incident occurs	Unsure

B.8		WV	WY
Methods used to assess out-of-state pharmacy compliance	For out-of-state pharmacies performing sterile compounding, does the state verify compliance with their applicable regulations?	Yes	Yes
	Are inspections performed by the National Association of Boards of Pharmacy (NABP) used by the state to verify that out of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	Yes
	Are inspections performed by a third party approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No
	Are inspections performed by a third party not approved in advance by the state done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No
	Are reviews of inspection reports by another state, conducted in the past ____ years, done to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations? If so, specify the number of years.	No	No
	Must the pharmacy provide self-evaluation or attestation of compliance to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	No	No
	Are there other means used to verify that out-of-state pharmacies that perform sterile compounding comply with their applicable regulations?	Yes—FDA oversight as well	Yes—disciplinary actions must be provided
Frequency	How frequently does the state assess compliance for out-of state pharmacies that perform sterile compounding?	Unsure	At least every year
	What specific circumstances trigger the state to assess compliance for out-of-state pharmacies that perform sterile compounding? (Includes other circumstances reported by states in addition to response options provided.)	When a complaint or incident occurs	Initial licensure, licensure renewal, and when a complaint or incident occurs

Note:

* Indicates that a state either declined to participate in the survey or did not complete the survey. The answers for these states' responses have been found on publicly available websites.

Table B.9

Physician Office/Clinic Compounding Responses by State

B.9		AK*	AL	AR	AZ	CA	CO	CT	DC	DE*	FL*	GA*	HI
Physician office or clinic compounding	How does the state provide oversight of physician offices or clinics that perform sterile compounding to ensure compliance with applicable standards?	Unsure	There is no oversight system to ensure compliance	There is no oversight system to ensure compliance	Unsure	There is no oversight system to ensure compliance	There is no oversight system to ensure compliance	Unsure	There is no oversight system to ensure compliance	Unsure	Unsure	Other: Oversight provided by the state board of medicine, oversight provided by the state board of pharmacy	Unsure
	Does the state have a mechanism to track which in-state physician offices or clinics perform sterile compounding?	Unsure	No	Unsure	Unsure	No	Unsure	Unsure	No	Unsure	Unsure	Unsure	No
	Are physician offices or clinics that perform sterile compounding held to the same quality standards as pharmacies that perform sterile compounding, such as USP Chapter 797?	Unsure	No	Unsure	Unsure	No	Unsure	Unsure	Unsure	Unsure	Unsure	Yes	Unsure
	Does the state board of medicine or other state regulatory body have the ability to track adverse events associated with sterile compounded products made in a physician office or clinic?	Unsure	No	Unsure	Unsure	Unsure	Unsure	Unsure	No	Unsure	Unsure	Unsure	Unsure

B.9		IA	ID	IL	IN	KS	KY	LA	MA	MD	ME*	MI	MN
Physician office or clinic compounding	How does the state provide oversight of physician offices or clinics that perform sterile compounding to ensure compliance with applicable standards?	There is no oversight system to ensure compli-ance	Oversight provided by the state board of pharmacy	There is no oversight system to ensure compli-ance	There is no oversight system to ensure compli-ance	There is no oversight system to ensure compli-ance	There is no oversight system to ensure compli-ance	Oversight provided by the state board of medicine	Unsure	Oversight provided by the state board of medicine	Unsure	Other: Oversight informed by allega-tions and complaints	Other: The Board of Pharmacy may have the authority to pro-vide oversight, but that authority is not clear. Consequently, the Board is not currently conducting inspections of sterile compounding done in offices and clinics.
	Does the state have a mechanism to track which in-state physician offices or clinics perform sterile compounding?	No	No	No	No	No	No	No	Unsure	Unsure	Unsure	No	No
	Are physician offices or clinics that perform sterile compounding held to the same quality standards as pharmacies that perform sterile compounding, such as USP Chapter 797?	Unsure	Yes	No	No	No	Unsure	Unsure	Unsure	Unsure	Unsure	No	No
	Does the state board of medicine or other state regulatory body have the ability to track adverse events associated with sterile compounded products made in a physician office or clinic?	Unsure	Yes	No	Unsure	Unsure	No	Unsure	Unsure	Unsure	Unsure	Yes	Unsure

B.9		MO	MS	MT	NC*	ND	NE	NH	NJ	NM	NV	NY	OH*
Physician office or clinic compounding	How does the state provide oversight of physician offices or clinics that perform sterile compounding to ensure compliance with applicable standards?	Other: Missouri Board of Pharmacy does not have jurisdiction over physician offices	Oversight provided by the state board of medicine	Oversight provided by the state board of medicine	Unsure	There is no oversight system to ensure compliance	Other: Currently, only offices/clinics that possess a dispensing practitioner's pharmacy license will be inspected on drugs that are dispensed and charged to patients	Other: The Board of Pharmacy conducts inspections and reports findings to appropriate licensing board	Other: Clinics are under the regulation of the New Jersey Department of Health. Physician offices are under the regulation of the Board of Medical Examiners.	Other: Private physician offices are not inspected. But clinics are registered with NMBOP.	There is no oversight system to ensure compliance	There is no oversight system to ensure compliance	Oversight provided by the state board of pharmacy
	Does the state have a mechanism to track which in-state physician offices or clinics perform sterile compounding?	NA†	No	No	Unsure	No	No	No	Unsure	No	No	No	Yes
	Are physician offices or clinics that perform sterile compounding held to the same quality standards as pharmacies that perform sterile compounding, such as USP Chapter 797?	NA†	No	No	Unsure	Yes	Yes	Yes	Unsure	Yes	Unsure	Unsure	Unsure
	Does the state board of medicine or other state regulatory body have the ability to track adverse events associated with sterile compounded products made in a physician office or clinic?	NA†	Unsure	No	Unsure	Unsure	Unsure	Unsure	Unsure	No	Unsure	No	Yes

B.9		OK	OR	PA	RI	SC	SD	TN	TX	UT	VA	VT
Physician office or clinic compounding	How does the state provide oversight of physician offices or clinics that perform sterile compounding to ensure compliance with applicable standards?	There is no oversight system to ensure compliance	There is no oversight system to ensure compliance	There is no oversight system to ensure compliance	There is no oversight system to ensure compliance	There is no oversight system to ensure compliance	There is no oversight system to ensure compliance	Oversight provided by the state board of medicine	Oversight provided by the state board of medicine	There is no oversight system to ensure compliance	Oversight provided by the state board of medicine	There is no oversight system to ensure compliance
	Does the state have a mechanism to track which in-state physician offices or clinics perform sterile compounding?	No	No	No	No	No	No	No	Unsure	No	Yes	Unsure
	Are physician offices or clinics that perform sterile compounding held to the same quality standards as pharmacies that perform sterile compounding, such as USP Chapter 797?	No	No	Unsure	Yes	Unsure	Unsure	No	Unsure	Yes	No	Unsure
	Does the state board of medicine or other state regulatory body have the ability to track adverse events associated with sterile compounded products made in a physician office or clinic?	Unsure	No	Unsure	No	Unsure	Unsure	Unsure	Unsure	No	No	Unsure

B.9		WA	WI*	WV	WY
Physician office or clinic compounding	How does the state provide oversight of physician offices or clinics that perform sterile compounding to ensure compliance with applicable standards?	There is no oversight system to ensure compliance	Unsure	There is no oversight system to ensure compliance	There is no oversight system to ensure compliance
	Does the state have a mechanism to track which in-state physician offices or clinics perform sterile compounding?	No	Unsure	Unsure	No
	Are physician offices or clinics that perform sterile compounding held to the same quality standards as pharmacies that perform sterile compounding, such as USP Chapter 797?	No	Unsure	No	No
	Does the state board of medicine or other state regulatory body have the ability to track adverse events associated with sterile compounded products made in a physician office or clinic?	Unsure	Unsure	No	No

Note:

* Indicates that a state either declined to participate in the survey or did not complete the survey. The answers for these states' responses have been found on publicly available websites.

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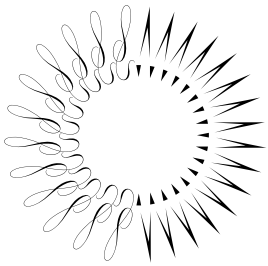

THE PEW CHARITABLE TRUSTS

Attachment 10

Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact Sara Rothman, CDER Office of Unapproved Drugs and Labeling Compliance (OUDLC) at 301-796-3110.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Office of Compliance/OUDLC

April 2016
Compounding and Related Documents

Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

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Compounding and Related Documents

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Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION AND SCOPE

This guidance sets forth the Food and Drug Administration's (FDA or Agency) policy concerning certain prescription requirements for compounding human[2] drug products for identified individual patients under section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act or Act). It addresses compounding after the receipt of a prescription for an identified individual patient, compounding before the receipt of a prescription for an identified individual patient (anticipatory compounding), and compounding for office use (or "office stock").

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

[1] This guidance has been prepared by multiple offices in the Center for Drug Evaluation and Research (CDER) and in consultation with the Office of Regulatory Affairs at the Food and Drug Administration.

[2] This guidance does not apply to drugs compounded for use in animals, to biological products subject to licensure in a biologics license application, or to repackaged drug products. For proposed policies pertaining to compounding drug products from bulk drug substances for use in animals, see FDA's draft guidance, *Compounding Animal Drugs from Bulk Drug Substances*. For proposed policies pertaining to mixing, diluting, and repackaging biological products, see FDA's draft guidance, *Mixing, Diluting, and Repackaging Biological Products Outside the Scope of an Approved Biologics License Application*. For proposed policies pertaining to repackaged drug products, see FDA's draft guidance, *Repackaging of Certain Human Drug Products by Pharmacies and Outsourcing Facilities*. FDA guidances are available on the FDA website at http://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

A. Overview

1. Compounding Under the FD&C Act

Sections 503A and 503B of the FD&C Act address human drug compounding.

Section 503A, added to the FD&C Act by the Food and Drug Administration Modernization Act in 1997, describes the conditions that must be satisfied for human drug products compounded by a licensed pharmacist in a State licensed pharmacy or Federal facility, or by a licensed physician, to be exempt from the following three sections of the FD&C Act:

- section 501(a)(2)(B) (concerning CGMP requirements);
- section 502(f)(1) (concerning the labeling of drugs with adequate directions for use; and
- section 505 (concerning the approval of drugs under new drug applications (NDAs) or abbreviated new drug applications (ANDAs)).

A list of the conditions that must be met for a compounded drug product to qualify for the exemptions in section 503A of the FD&C Act appears in the guidance, *Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act*.

Section 503B, added to the FD&C Act by the Drug Quality and Security Act in 2013, created a new category of compounders called *outsourcing facilities*. Section 503B of the FD&C Act describes the conditions that must be satisfied for human drug products compounded by or under the direct supervision of a licensed pharmacist in an outsourcing facility to qualify for exemptions from three sections of the FD&C Act:

- section 502(f)(1);
- section 505; and
- section 582 (concerning track and trace requirements).

In contrast to drug products compounded under section 503A of the FD&C Act, drug products compounded by outsourcing facilities under section 503B are not exempt from CGMP requirements in section 501(a)(2)(B). Outsourcing facilities are also subject to FDA inspections according to a risk-based schedule, specific adverse event reporting requirements, and other conditions that help to mitigate the risks of the drug products they compound.

The guidance, *For Entities Considering Whether to Register As Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act*, lists the conditions that are set forth in section 503B of the FD&C Act.

2. Compounding, Generally

Compounded drug products can serve an important role for patients whose clinical needs cannot be met by an FDA-approved drug product, such as a patient who has an allergy and needs a medication to be made without a certain dye, or an elderly patient or a child who cannot swallow a tablet or capsule and needs a medicine in a liquid dosage form that is not otherwise available.

Drug products for identified individual patients can be compounded consistent with section 503A by licensed pharmacists in state-licensed pharmacies and Federal facilities, or by licensed physicians. Drug products can also be compounded by compounders known as *outsourcing facilities* under section 503B of the FD&C Act.

In general, when a compounded drug product is clinically necessary for a patient, a prescriber writes a prescription for a compounded drug product, and the patient brings the prescription to a pharmacy, where a licensed pharmacist fills the prescription. In an inpatient setting, such as in a hospital, a prescriber may write an order for a compounded drug product on a patient's chart. Sometimes, a physician may compound a drug in the office for administration to his or her patient after the patient presents at the physician's office with a clinical need for the compounded drug.

In other cases, a pharmacist may compound a drug product before receipt of a prescription for an identified individual patient in anticipation of receiving such a prescription, based on knowledge of what prescriptions the pharmacist has historically been asked to fill. The pharmacist then provides the drug product to a patient or a prescriber upon receipt of a prescription. Similarly, a physician may compound a drug product to hold in his or her office in anticipation of patients in his or her practice presenting with a need for the compounded drug, based on the amount of the compounded drug that the physician has historically administered or dispensed. The physician then administers or dispenses the compounded drug to his or her patients after making a notation the patients' charts.

Sometimes, it is necessary for health care practitioners in hospitals, clinics, offices, or other settings to have certain compounded drug products on hand that they can administer to a patient who presents with an immediate need for the compounded drug product. For example, if a patient presents at an ophthalmologist's office with a fungal eye infection, timely administration of a compounded antifungal medication may be critical to preventing vision loss. In such a case, the prescriber may need to inject the patient with a compounded drug product immediately, rather than writing a prescription and waiting for the drug product to be compounded and shipped to the prescriber.[3]

In other cases, compounded drug products may need to be administered by a health care practitioner in his or her office because it would not be safe for the patient to take the drug home for self-administration, and it would not be practical for the patient to bring a prescription for the compounded drug product to a pharmacy and then return to the health care practitioner for administration.

3. Risks Associated with Compounded Drug Products

Although compounded drugs can serve an important need, they pose a higher risk to patients than FDA-approved drugs. Compounded drug products are not FDA-approved, which means

[3] Such compounding would be subject to all of the conditions of section 503A or 503B, including provisions concerning compounding drug products that are essentially copies of commercially available drug products (section 503A(b)(1)(D)) or drug products that are essentially copies of approved drugs (section 503B(a)(5)).

they have not undergone FDA premarket review for safety, effectiveness, and quality. In addition, licensed pharmacists and licensed physicians who compound drug products in accordance with section 503A are not required to comply with current good manufacturing practice (CGMP) requirements. Furthermore, FDA does not interact with the vast majority of licensed pharmacists and licensed physicians who compound drug products and seek to qualify for the exemptions under section 503A of the FD&C Act for the drug products they compound (see section 3, below) because these compounders are not licensed by FDA and generally do not register their compounding facilities with FDA. Therefore, FDA is often not aware of potential problems with their compounded drug products or compounding practices unless it receives a complaint such as a report of a serious adverse event or visible contamination.

In 2012, contaminated injectable drug products that a compounding pharmacy shipped to patients and health care practitioners across the country caused a fungal meningitis outbreak that resulted in more than 60 deaths and 750 cases of infection.[4] This was the most serious of a long history of outbreaks associated with contaminated compounded drugs. Since the 2012 fungal meningitis outbreak, FDA has investigated numerous other outbreaks and other serious adverse events, including deaths, associated with compounded drugs that were contaminated or otherwise compounded improperly.

FDA has also identified many pharmacies that compounded drug products under insanitary conditions whereby the drug products may have been contaminated with filth or rendered injurious to health, and that shipped the compounded drug products made under these conditions to patients and health care providers across the country, sometimes in large amounts.[5] The longer a compounded sterile drug product that has been contaminated is held by a pharmacist or physician before distribution, or held in inventory in a health care facility before administration, the greater the likelihood of microbial proliferation and increased patient harm. Because of these and other risks, the FD&C Act places conditions on compounding that must be met for compounded drugs to qualify for the exemptions in section 503A. Among these conditions are that:

- compounding is for an identified individual patient,
- drugs compounded in advance of receiving prescriptions are compounded only in limited quantities, and
- drugs are distributed pursuant to a patient-specific prescription.

These conditions are meant to help ensure that compounding under section 503A is based on individual patient needs, and that entities purportedly operating under section 503A are not actually operating as conventional manufacturers.

[4] See http://www.cdc.gov/HAI/outbreaks/meningitis.html.

[5] See FDA actions, including warning letters and injunctions, related to insanitary conditions at compounding facilities, on FDA's website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm339771.htm

B. The Prescription Requirement in Section 503A(a) of the FD&C Act[6]

A compounded drug product may be eligible for the exemptions under section 503A of the FD&C Act only if it is, among other things, "compounded for an identified individual patient based on the receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient." To qualify for the exemptions under section 503A, the drug product must also be compounded by a licensed pharmacist in a state-licensed pharmacy or a Federal facility, or by a licensed physician (section 503A(a)).

Section 503A(a) describes two situations in which a drug product can be compounded: (1) based on the receipt of a valid prescription order for an identified individual patient (section 503A(a)(1)); or (2) in limited quantities before the receipt of a valid prescription order for an identified individual patient (section 503A(a)(2)). As discussed further in section III.C of this guidance document, section 503A does not provide for distributing a compounded drug product before receiving a valid prescription order for an identified individual patient.

The *prescription requirement* under section 503A is a critical mechanism to distinguish compounding by a licensed pharmacist or licensed physician from conventional manufacturing, and to ensure that drug products compounded under section 503A, which are not FDA-approved, not labeled with adequate directions for use, and not made in accordance with CGMP requirements, are provided to a patient only based on individual patient need.

The prescription requirement is also an important factor that distinguishes compounding by a licensed pharmacist in a state-licensed pharmacy or a Federal facility, or by a licensed physician under section 503A from compounding by an outsourcing facility under section 503B of the FD&C Act. Section 503B states that an outsourcing facility may or may not obtain prescriptions for identified individual patients (section 503B(d)(4)(C)). Outsourcing facilities, which are subject to CGMP requirements and other important conditions, can compound drug products to fulfill the needs described in section II.A.1 for health care practitioners to have drug products on hand that are not compounded for identified individual patients.

1. Compounding After Receipt of a Valid Prescription Order

As described in section II.A.1, a prescriber may write a prescription for an identified individual patient who needs a compounded drug product. In most cases, either the prescriber or the patient will then bring or send the prescription to the pharmacy, where the pharmacist will compound the drug product for the patient and provide it to the prescriber or patient according to the prescription. For a patient in an inpatient setting, a prescriber may place an order in the patient's chart for a compounded drug product, which will likely be provided by the health care facility

[6] For information concerning how the FDA intends to apply the prescription requirement in section 503A of the FD&C Act to compounding within a hospital or health system, see the draft guidance for industry, *Hospital and Health System Compounding Under the Federal Food, Drug, and Cosmetic Act*. Once finalized, this guidance will describe FDA's current thinking on this topic.

pharmacy. In an office setting, a physician may compound a drug after making a notation in the chart of a patient in his practice who presents with a need for the compounded medication. This type of compounding is covered under section 503A(a)(1) of the FD&C Act,[7] which provides for compounding by a licensed pharmacist in a State-licensed pharmacy or a Federal facility, or a licensed physician, on the prescription order for an individual patient made by a licensed physician or other licensed practitioner authorized by state law to prescribe drugs.

2. Compounding Before Receipt of a Valid Prescription Order

Sometimes, based on a history of receiving prescriptions for a particular drug product to be compounded for an identified individual patient, and in the context of an established relationship with a particular prescriber or patient, a pharmacist or physician will compound a batch of drugs in anticipation of receiving another patient-specific prescription. The compounder then provides the drugs to a patient or healthcare provider when a prescription for an identified individual patient is received. This is known as *anticipatory compounding*. Section 503A(a)(2) of the FD&C Act provides for compounding by a licensed pharmacist or licensed physician in "limited quantities before the receipt of a valid prescription order for such individual patient" if:

- The compounding is based on a history of the licensed pharmacist or licensed physician receiving valid prescription orders for the compounding of the human drug product;

and

- The orders have been generated solely within an established relationship between the licensed pharmacist or licensed physician and either such patient for whom the prescription order will be provided or the physician or other licensed practitioner who will write such prescription order.

Anticipatory compounding can be beneficial because larger batch sizes can increase efficiency and reduce the likelihood of human error that is associated with compounding many small batches of a drug product after the receipt of individual prescriptions for the same drug. However, anticipatory compounding also has risks. For example, if a problem occurs during compounding, such as contaminating a drug product that is supposed to be sterile, it could affect numerous patients, and not just one. Because drug products compounded in accordance with section 503A are exempt from CGMP requirements, there is an inherently greater chance of a production mistake or contamination. Restricting production to limited quantities serves to limit the number of patients likely to be affected by such a mistake.

The limitations on anticipatory compounding in section 503A (i.e., compounding must be in "limited quantities" and based on an "established relationship") help to protect patients from product quality issues. These limitations on anticipatory compounding also help to distinguish licensed pharmacists or licensed physicians compounding drug products under section 503A for

[7] If applicable state and federal requirements are met, outsourcing facilities can also compound drug products pursuant to prescriptions for identified individual patients under section 503B of the FD&C Act. However, that is not the subject of this guidance document.

individual patients from conventional manufacturers, who generally produce larger quantities of drugs that are distributed without a prescription through a wholesaler to pharmacies, which then dispense them to individual patients pursuant to a prescription order.

The anticipatory compounding limitations also differentiate licensed pharmacists and licensed physicians compounding under section 503A from compounders registered as outsourcing facilities under section 503B of the FD&C Act. As explained above, outsourcing facilities are subject to increased Federal oversight and quality standards, including CGMP requirements, which reduce the risks of quality problems such as production mistakes or contamination. Under section 503B, an outsourcing facility can distribute compounded drug products to health care facilities and healthcare practitioners without first receiving prescriptions for identified individual patients.

With these principles in mind, FDA sets forth its policy with regard to the prescription requirement in section 503A.

III. POLICY

A. Receipt of a Valid Prescription Order or a Notation Approved by the Prescriber Under Section 503A

For purposes of section 503A, a *valid prescription order* for a compounded drug product means a valid prescription order from a licensed physician or other licensed practitioner authorized by state law to prescribe drugs (prescriber). It also includes a valid order or notation written by a prescriber in a patient's chart in an inpatient setting and a valid order or notation by a physician who compounds a drug for his or her own patient written in that patient's chart. [8]

If it is not obvious from a prescription order that the prescription is for a compounded drug product, a pharmacist may consult with the prescriber to determine whether the patient needs a compounded drug and make an appropriate notation on the prescription order.[9] To serve as a basis for compounding under section 503A, a notation must document the prescriber's determination that a compounded drug is necessary for the identified patient (section 503A(a)). We recommend using the following statement:

"Per [type of communication] with [name of prescriber] on [date], [name of prescriber] has advised that compounded [name of drug] is necessary for the treatment of [name of patient]."

[8] Prescription orders that are not valid would not satisfy the prescription requirement in section 503A and cannot serve as the basis for anticipatory compounding. See, in addition, section 301(ccc)(2), which states that, with respect to a drug to be compounded pursuant to section 503A or 503B, the intentional falsification of a prescription, as applicable, is a prohibited act.

[9] FDA anticipates that in general, it will be clear whether a prescription is for a compounded drug product. An example of a circumstance in which this may be unclear, and the compounder may consult with the prescriber, is if a compounder receives a prescription for an FDA-approved drug product, but determines that the product is not medically appropriate for the patient and needs to be compounded (e.g., if the FDA-approved drug product is an oral capsule, but the patient has difficulty swallowing capsules and needs the drug in a liquid dosage form).

Furthermore, to meet the prescription requirement, a prescription must identify the patient for whom the drug has been prescribed. If the identity of the patient is not given or is not clear, it will not satisfy this requirement. For example, a prescription would not satisfy the requirement if it is written for the prescriber, when the prescriber is not also the patient. If the identity of the patient who will receive the drug is not clear from the prescription, the compounder should contact the prescriber for clarification and must not distribute the drug unless the identity of the patient is clarified.

B. When a Drug Can Be Compounded Under Section 503A

1. Compounding After Receipt of a Valid Prescription Order

Unless a drug product is compounded in limited quantities before the receipt of a valid prescription order under the conditions described in section 503A(a)(2) of the FD&C Act, which are also described in section III.B.2 of this guidance, to qualify for the exemptions under section 503A, the drug product must be compounded *after* the licensed pharmacist or licensed physician receives a valid prescription order for an individual patient. We understand this to be compounding "on" the receipt of a valid prescription order, as provided in section 503A(a)(1). [10]

2. Compounding Before Receipt of a Valid Prescription Order

If a drug product is not compounded after the receipt of a valid prescription order for an identified individual patient as described in section 503A(a)(1) of the FD&C Act and section III.B.1 of this guidance, the drug product can be compounded under section 503A of the Act by a licensed pharmacist or licensed physician in limited quantities before the receipt of a valid prescription order for such individual patient (section 503A(a)(2)(A)), if all of the conditions of section 503A are met, including the following conditions:

- The compounding is based on a history of the licensed pharmacist or licensed physician receiving valid prescription orders[11] for the compounding of the human drug product; and

- The orders have been generated solely within an established relationship between the licensed pharmacist or licensed physician and either such patient for whom the prescription order will be provided or the prescriber who will write such prescription order[12] (see section 503A(a)(2)(B)).

[10] This includes a physician compounding a drug for his or her own patient after writing a prescription order (e.g., an order written in the patient's chart) for the compounded drug.

[11] This includes orders that a physician writes in the charts of his or her patients.

[12] When a physician compounds drugs for his or her own patients, FDA considers the "established relationship" provision of section 503A(a)(2) to have been satisfied because the licensed physician and the "prescriber who will write such prescription order" are the same individual.

This means that anticipatory compounding under section 503A is done in limited quantities, based on an expectation that the licensed pharmacist or licensed physician will receive a patient-specific prescription for the particular drug product, written for a patient or by a prescriber with whom the compounder has a relationship.

At this time we do not intend to consider a compounder to have exceeded the limited quantity condition in section 503A(a)(2) if:

- The compounder holds for distribution[13] no more than a 30-day supply of a particular compounded drug product (i.e., units of a compounded drug product that the compounder believes it will distribute over a 30-day period) to fill valid prescriptions it has not yet received; and

- The amount of the supply is based on the number of valid prescriptions that the compounder has received for identified individual patients in a 30-day period over the past year that the compounder selected.

Under this policy, if a compounder does not exceed the quantities described above, FDA also does not intend to determine whether anticipatory compounding was based on the expectation that the compounder would receive another prescription for the drug product for a particular patient or prescriber with whom the compounder has established a history.

The following example illustrates FDA's policy on anticipatory compounding under section 503A(a)(2):

> A compounder regularly receives valid prescription orders from a particular prescriber or prescribers, or for a particular patient or patients, for compounded drug X. The highest number of units of drug X for which the compounder has received patient-specific prescriptions in a 30-day period in the last year is 500 units. Compounding up to 500 units of drug X in advance of receiving prescriptions for the drug, and holding no more than that amount to fill new patient-specific prescriptions as the compounder receives them, would be consistent with this policy.
>
> A physician who compounds drugs for his or her own patients routinely sees patients who need compounded drug X. The highest number of units of drug X that the physician has dispensed or administered to patients after making a notation in the patients' charts in a 30-day period in the last year is 500 units. Compounding up to 500 units of drug X in advance of making such notations in patients' charts (i.e., before patients present at the physician's office with a need for the compounded drug), and holding no more than that amount to dispense or administer to patients, would be consistent with this policy.

C. When a Compounded Drug Product Can Be Distributed Under Section 503A

[13] *For distribution* means drug product that is available for immediate distribution and does not include drug product that is being held pending receipt of the results of release testing such as sterility testing.

Compounding under section 503A(a) must be "for an identified patient based on the receipt of a valid prescription order" – either "on the receipt of a prescription order for such individual patient" or, under certain conditions, "before the receipt of a valid prescription order for such individual patient." This means that for each drug compounded under section 503A, the compounder must obtain a patient-specific prescription order. We therefore understand that the compounder can fill a prescription for compounded drugs under section 503A only pursuant to such a patient-specific prescription. We recognize that some state boards of pharmacy may authorize the writing of prescriptions that do not include individual patient names. Such prescriptions, however, do not meet the requirement of a patient-specific prescription in section 503A. Under section 503B, outsourcing facilities can fill such prescriptions if they meet the requirements of applicable state and Federal laws.

D. Office Stock/Office Use

As discussed in section II.A.1 of this guidance, some compounded drug products are kept in stock by hospitals, clinics, or health care practitioners to administer to patients who present with an immediate need for a compounded drug product. Hospitals, clinics, and health care practitioners can obtain non-patient-specific compounded drug products from outsourcing facilities registered under section 503B.[14] Outsourcing facilities, which are subject to CGMP requirements, FDA inspections according to a risk-based schedule, specific adverse event reporting requirements, and other conditions that provide greater assurance of the quality of their compounded drug products, may, but need not, obtain prescriptions for identified individual patients prior to distribution of compounded drug products (section 503B(d)(4)(C)).[15] Therefore, outsourcing facilities can compound and distribute sterile and non-sterile[16] non-patient-specific drug products to hospitals, clinics, and health care practitioners for office use.[17]

Section 503A(a)(2) provides a pathway for anticipatory compounding in limited quantities. A licensed pharmacist or licensed physician can compound a drug product in advance of receiving a valid prescription order for an identified individual patient, in accordance with the conditions described in section 503A(a)(2) of the FD&C Act, to have a supply of the drug product ready to provide to a patient or prescriber (or, in the case of a physician, to administer to a patient) when a patient-specific prescription order is presented for the compounded drug product. This can

[14] See also FDA's draft guidance, *Hospital and Health System Compounding Under the Federal Food, Drug, and Cosmetic Act* for FDA's proposed policies regarding the application of section 503A of the FD&C Act to drug products compounded for use within a hospital or health system.

[15] Although an outsourcing facility may send prescription drugs to health care facilities without obtaining prescriptions for identified individual patients, drugs produced by outsourcing facilities remain subject to the requirements in section 503(b) of the FD&C Act. Therefore, an outsourcing facility cannot dispense a prescription drug to a patient without a prescription.

[16] Section 503B defines *outsourcing facility*, in part, as a facility that is engaged in the compounding of sterile drugs (section 503B(d)(4)(A)(i)). Therefore, an entity that only compounds non-sterile drugs does not meet the definition of *outsourcing facility*.

[17] Distribution of compounded drug products by outsourcing facilities is subject to the limitations described in section 503B(a)(8), among other conditions.

reduce the time it would take for a compounded drug product to be made available to a patient upon receipt of a valid prescription order for that patient.

E. Recordkeeping

The licensed pharmacist or licensed physician seeking to compound a drug product under section 503A should maintain records to demonstrate compliance with the prescription requirement in section 503A(a)(1) of the FD&C Act and the basis for any anticipatory compounding. For example, this includes records of valid prescription orders, and of prescription orders bearing notations that the compounded drug product is necessary for the identified individual patient as described in section III.A of this guidance and section 503A(a) of the FD&C Act.

This also includes records of the calculations performed to determine the limited quantities of drug products compounded before the receipt of valid prescription orders under the enforcement policy described in section III.B.2 of this guidance and section 503A(a)(2) of the FD&C Act. These records should clearly reflect the quantity of a particular drug product compounded in advance of receiving prescription orders for identified individual patients that the compounder has kept on hand as stock for distribution and the basis for the quantity the compounder kept in stock. Under the enforcement policy described in section III.B.2, this would include the quantity of the drug product distributed pursuant to prescription orders for identified individual patients during the reference period that the licensed pharmacist or licensed physician selected (i.e., a 30-day period within the last year).

Attachment 11

Facility Definition Under Section 503B of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact Sara Rothman (CDER) at 301-796-3110.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

April 2016
Compounding and Related Documents

Facility Definition Under Section 503B of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

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Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance is intended for entities that are registered or are considering registering with the Food and Drug Administration (FDA or Agency) as an outsourcing facility under section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act).[2] Section 503B defines an outsourcing facility, in part, as "a facility at one geographic location or address." FDA has received questions from outsourcing facilities and other stakeholders about the meaning of this term, such as whether multiple suites used for compounding human drugs at a single street address constitute one or multiple facilities, or whether a single location where human drugs are compounded can be subdivided into separate operations compounding under different standards. FDA is issuing this guidance to answer these questions.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

Section 503B, added to the FD&C Act by the Drug Quality and Security Act in 2013, created a new category of compounders called *outsourcing facilities*. Section 503B describes the conditions that must be satisfied for human drug products compounded by or under the direct

[1] This guidance has been prepared by multiple offices in the Center for Drug Evaluation and Research (CDER) and in consultation with the Office of Regulatory Affairs at the Food and Drug Administration.

[2] A new section 503B was added to the FD&C Act by the Drug Quality and Security Act (DQSA). See Pub. L. No.113-54, § 102(a), 127 Stat. 587, 587-588 (2013).

supervision of a licensed pharmacist in an outsourcing facility to qualify for exemptions from three sections of the FD&C Act:

- section 502(f)(1) (concerning labeling requirements);
- section 505 (concerning drug approval requirements); and
- section 582 (concerning Drug Supply Chain Security Act requirements).

Section 503B(d)(4) of the FD&C Act defines an outsourcing facility as a facility at one geographic location or address that— (i) is engaged in the compounding of sterile drugs; (ii) has elected to register as an outsourcing facility; and (iii) complies with all of the requirements of this section. In addition, an outsourcing facility is not required to be a licensed pharmacy, and it may or may not obtain prescriptions for identified individual patients.[3] Because drugs compounded by outsourcing facilities are not exempt from section 501(a)(2)(B) of the FD&C Act, outsourcing facilities are subject to current good manufacturing practice (CGMP) requirements.[4,5]

One of the conditions that must be met for a compounded drug to qualify for the exemptions under section 503B is that it must be compounded in an outsourcing facility in which the compounding of drugs occurs only in accordance with this section (section 503B(a)(11)). FDA's final guidance document, *For Entities Considering Whether to Register As Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act*,[6] clarifies that:

> If you register a facility as an outsourcing facility, you are indicating your intent for the facility's compounded drugs to be regulated under section 503B of the FD&C Act. Under section 503B(a)(11), a compounded drug can only qualify for the exemptions from sections 502(f)(1), 505, and 582 of the FD&C Act if ***all*** of the facility's compounded drugs are compounded in accordance with section 503B (page 4).

The guidance further states that:

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[3] See section 503B(d)(4)(C).

[4] See section 503B(a).

[5] FDA has issued a draft guidance entitled, *Current Good Manufacturing Practice — Interim Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act* ("Interim CGMP Guidance"). The Interim CGMP Guidance, when finalized, will describe FDA's expectations regarding outsourcing facilities and the CGMP requirements in 21 CFR parts 210 and 211 until more specific CGMP regulations for outsourcing facilities are promulgated.

> All FDA guidances are available on the FDA guidance Webpage at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm. FDA updates guidances regularly. To ensure that you have the most recent version, please check this web page.

[6] See the guidance *For Entities Considering Whether to Register As Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act*.

> By registering as an outsourcing facility, an entity is electing to have its compounded drugs regulated under section 503B of the FD&C Act, not section 503A. Drugs compounded at an outsourcing facility are not eligible for the exemptions provided in section 503A, even if the conditions in that section are met with respect to the particular drug (page 5).

Some outsourcing facilities compound drugs both according to patient-specific prescriptions as well as in response to orders that are not patient-specific, as section 503B permits them to do.[7] FDA has been asked whether an outsourcing facility can create a separate area within its facility for compounding according to patient specific prescriptions under section 503A, and not follow CGMP requirements in that area. For example, can the drugs be compounded according to patient-specific prescriptions in an adjacent area or room, or in a separate suite, but with the same staff and the same components used in 503B compounding? The CGMP regulations[8] contain requirements for facility design, staff training and competency testing, control of incoming components, aseptic processing, air quality, environmental monitoring, and related requirements designed to ensure the quality of the finished product. The application of different CGMP requirements or the different conditions in section 503A and 503B to commingled compounding activities can cause confusion about what requirements apply and could lead to the production of substandard drugs.

For that reason, and because it is a condition of eligibility for the exemptions in section 503B that all of the drug products compounded in an outsourcing facility must be compounded in accordance with section 503B and with CGMP requirements, this guidance clarifies what constitutes a "facility."

III. POLICY

Section 503B(d) defines an outsourcing facility, in part, as "a facility at one geographic location or address." FDA interprets "facility at one geographic location or address" to mean a business or other entity under one management, direct or indirect, engaged in human drug compounding at a geographic location or street address. The agency considers all activities, equipment, appurtenances, and materials part of such a facility if they are related to human drug compounding under the supervision of the facility's management at the same street address, or in the same building, or in buildings located in close proximity to one another.

As noted above, all drug products compounded in an outsourcing facility are regulated under section 503B[9] and subject to CGMP requirements.[10] These conditions cannot be avoided by segregating or subdividing compounding within an outsourcing facility. For example, even if an

[7] See note 3, supra.

[8] See CGMP regulations at Title 21, Parts 210 and 211 of the Code of Federal Regulations.

[9] See section 503B(a)(11).

[10] See section 503B(a).

outsourcing facility divides its site at one street address into multiple sections with temporary or permanent physical barriers, conducts patient-specific and non-patient specific compounding in different areas (e.g., in different hoods or different rooms), or conducts patient specific and non-patient specific compounding on different days or different times of the day, all of the drug products compounded at that street address must meet the conditions of section 503B or none of the outsourcing facility's drug products would qualify for the exemptions in section 503B. Furthermore, all of the drug products compounded at that street address must be compounded in accordance with CGMP requirements or the outsourcing facility could be cited for violations of section 501(a)(2)(B) of the FD&C Act.

A. Segregating Compounding of Drug Products Under Section 503A From Compounding of Drug Products Under Section 503B

FDA is interpreting facility in this way to be consistent with the intent of section 503B. To be eligible for the exemptions in section 503B(a), a drug product must be compounded in an outsourcing facility in which drugs are compounded only in accordance with section 503B (see section 503B(a)(11)). Outsourcing facilities may or may not obtain prescriptions for identified individual patients, and they are not subject to the interstate distribution restrictions in section 503A. Therefore, the intent of this provision is to ensure that all drugs compounded at an outsourcing facility without the restrictions in section 503A (e.g., the prescription requirement and the restrictions on interstate distribution) are compounded in accordance with CGMP requirements, labeled appropriately, subject to adverse event reporting, and otherwise compounded in accordance with the conditions of section 503B.

If compounding under sections 503A and 503B were to take place in the same geographic location or address, it could appear that all drug products compounded in the outsourcing facility were being made under higher standards, when in fact some or all were made under lesser controls (e.g., the drugs produced under the conditions of 503A would not be produced in accordance with CGMP requirements).

In addition, this definition is designed to prevent commingling of compounding activities under sections 503A and 503B to evade the conditions of section 503B and CGMP requirements. A drug product compounded under section 503A may be indistinguishable from a drug product compounded under section 503B except for the conditions under which it is compounded. It is important to be able to follow the production of drug products compounded in an outsourcing facility to ensure that the products are made under CGMP requirements from the time the bulk drug substances are received at the facility through production of the finished dosage form. If a firm compounds drug products in the same general location under different standards, it will be difficult to ensure that all of the products were made under the correct standards, particularly if the activities are commingled (e.g., because compounding under both standards draws on the same supplies, equipment, personnel, storage, or processing areas), or if compounded drug products are marketed under the same firm name or from the same location. And because drug products compounded under section 503A must be compounded in accordance with a prescription while drug products made under section 503B may or may not be compounded in accordance with a prescription, if the drug products are made in neighboring suites in the same

building, it may be impossible to determine whether a prescription was obtained for the a particular product before it was distributed. The agency's interpretation also provides clarity during inspections with regard to which standards apply to the location that is being inspected.

It is in the best interest of the public health to be clear about the separation between 503A and 503B facilities to ensure that those obtaining the drugs will know the standards under which they were compounded. Furthermore, the public health is best served, and an important objective of section 503B is achieved, if all drug products compounded in an outsourcing facility, whether patient-specific or non-patient specific, are compounded in accordance with CGMP requirements and other requirements imposed in section 503B of the FD&C Act.

B. Compounding Drug Products Under Section 503B and Conventionally Manufacturing Drug Products at the Same Facility

If a conventional manufacturer registers a facility as an outsourcing facility and makes both approved drug products and compounded drug products in the outsourcing facility, the compounded drug products would need to meet the conditions of section 503B to qualify for the exemptions from sections 502(f)(1), 505, and 582.[11]

All of the drug products produced at the facility would be subject to the CGMP requirements in 21 CFR parts 210 and 211. As stated above,[12] FDA has issued a draft guidance that, when finalized, will describe FDA's expectations regarding outsourcing facilities and these CGMP requirements. When a facility both manufactures conventional drug products and compounds drug products under section 503B, the policies described in this guidance would apply to the facility's compounded drug products, except with respect to CGMP requirements that must be implemented throughout a manufacturing facility and cannot be applied differently to different drug products in the same facility, such as environmental monitoring and pressure differential monitoring requirements.

The compounding of drug products under section 503B and the manufacture of approved drug products in the same facility does not present the complications described above regarding the compounding of drug products under sections 503A and 503B in the same facility. For example, an outsourcing facility could not commingle its compounded and approved drug products to avoid manufacturing the approved drug products in accordance with applicable CGMP requirements or to avoid compounding drug products in accordance with the conditions of section 503B. An outsourcing facility's compounded drug products are easily differentiated from its approved drug products; the approved drug products are the subject of approved drug applications and are listed with FDA under section 510 of the FD&C Act, while the compounded drug products are unapproved and are generally not listed. Furthermore, outsourcing facilities

[11] We do not read "compounding" in section 503B(a)(11) of the Act to refer to the manufacture of an approved drug product. Therefore, a drug product may be compounded in an outsourcing facility in accordance with section 503B even if an approved drug product is manufactured in that outsourcing facility not in accordance with section 503B.

[12] See footnote 5.

must label compounded drug products with the statement, "This is a compounded drug,"[13] so purchasers of compounded drug products from an outsourcing facility that also manufactures approved drug products will know that the drug products that they purchased were compounded. FDA verifies during inspections that outsourcing facilities are producing their compounded and approved drug products in accordance with the applicable standards, including that the drug products are labeled appropriately.

[13] See section 503B(a)(10).

Attachment 12

Hospital and Health System Compounding Under the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

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For questions regarding this draft document contact Sara Rothman, CDER Office of Unapproved Drugs and Labeling Compliance (OUDLC) at 301-796-3110.

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Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
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Hospital and Health System Compounding Under the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

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Guidance for Industry[1]

This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. INTRODUCTION AND SCOPE

Pharmacies located within a hospital or standalone pharmacies that are part of a health system frequently provide compounded drug products for administration within the hospital or health system. Some of these compounders have registered with FDA as outsourcing facilities under section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act or the Act) and others are state-licensed pharmacies subject to section 503A of the FD&C Act. This guidance describes how FDA intends to apply section 503A of the FD&C Act to drugs compounded by licensed pharmacists or physicians in state-licensed hospital or health system pharmacies for use within the hospital or health system.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

A. Overview

1. Compounding Under the FD&C Act

Sections 503A and 503B of the FD&C Act address human drug compounding.

[1] This guidance has been prepared by multiple offices in the Center for Drug Evaluation and Research (CDER) and in consultation with the Office of Regulatory Affairs at the Food and Drug Administration.

Section 503A, added to the FD&C Act by the Food and Drug Administration Modernization Act in 1997, describes the conditions that must be satisfied for human drug products compounded by a licensed pharmacist in a State licensed pharmacy or Federal facility, or by licensed physician, to be exempt from the following three sections of the FD&C Act:

- section 501(a)(2)(B) (concerning current good manufacturing practice (CGMP) requirements);
- section 502(f)(1) (concerning the labeling of drugs with adequate directions for use); and
- section 505 (concerning the approval of drugs under new drug applications or abbreviated new drug applications).

A list of the conditions that must be met for a compounded drug product to qualify for the exemptions in section 503A of the FD&C Act appears in the guidance, *Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act*.[2]

Section 503B, added to the FD&C Act by the Drug Quality and Security Act in 2013, created a new category of compounders called *outsourcing facilities*. Section 503B of the FD&C Act describes the conditions that must be satisfied for human drug products compounded by or under the direct supervision of a licensed pharmacist in an outsourcing facility to qualify for exemptions from three sections of the FD&C Act:

- section 502(f)(1);
- section 505; and
- section 582 (concerning track and trace requirements).

The guidance, *For Entities Considering Whether to Register As Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act* lists the conditions that are set forth in section 503B of the FD&C Act.

Because drugs compounded by outsourcing facilities are not exempt from section 501(a)(2)(B) of the FD&C Act, outsourcing facilities are subject to CGMP requirements, among other requirements under the FD&C Act (section 503B(a)).[3] In addition, outsourcing facilities will be inspected by FDA on a risk-based schedule (section 503B(b)(4)). An outsourcing facility is not required to be a licensed pharmacy and may or may not obtain prescriptions for identified individual patients.[4]

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[2] All FDA guidances are available on the FDA guidance Webpage at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm. FDA updates guidances regularly. To ensure that you have the most recent version, please check this web page.

[3] FDA has issued a draft guidance for industry *Current Good Manufacturing Practice—Interim Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act.* Once finalized, that guidance will represent the Agency's thinking on this topic.

[4] Although an outsourcing facility may send prescription drugs to health care facilities without obtaining prescriptions for identified individual patients, drugs produced by outsourcing facilities remain subject to the

2. Compounding in Hospitals and Health Systems

Compounded drug products can serve an important role for patients whose clinical needs cannot be met by an FDA-approved drug product, such as a patient who has an allergy and needs a medication to be made without a certain dye, or an elderly patient or a child who cannot swallow a pill and needs a medicine in a liquid form that is not otherwise available.

Hospital and health system[5] drug compounding and distribution practices vary. For example, some hospital pharmacies compound drugs only for use in the hospital in which the pharmacy is located (e.g., for the treatment of patients admitted to the hospital, or for use in the hospital's emergency room), while other hospital and health system pharmacies compound and distribute their compounded drug products to other facilities within their health system (e.g., to other hospitals, clinics, infusion centers, or long-term care facilities within the health system for administration or dispensing).

In some cases, a hospital or health system pharmacy compounds drugs only after receipt of a prescription or order for an identified individual patient. Hospital and health system pharmacies may also compound drugs and distribute them within the hospital or health system before the receipt of a patient-specific prescription. The hospital or health system then holds the drug products until a patient presents with a need for the drug, for example in an operating room, where emergency procedures cannot be scheduled in advance, or in emergency departments.

Many hospitals and health systems purchase compounded drug products from compounders that have registered with FDA as outsourcing facilities under section 503B of the FD&C Act. Outsourcing facilities are subject to increased federal oversight through FDA inspection on a risk-based schedule, and quality standards CGMP requirements) that help to assure the quality of their compounded drug products. Some hospital and health system compounders have registered with FDA as outsourcing facilities to serve as centralized compounding facilities where drug products are compounded with or without first receiving patient-specific prescriptions, and they then distribute the drugs within their health system or to affiliated health care facilities.

3. Risks Associated with Compounded Drug Products

Although compounded drugs can serve an important need, they pose a higher risk to patients than FDA-approved drugs. Compounded drug products are not FDA-approved, which means they have not undergone FDA premarket review for safety, effectiveness, and quality. In

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requirements in section 503(b) of the FD&C Act. Therefore, an outsourcing facility cannot dispense a prescription drug to a patient without a prescription.

[5] FDA regards a health system as collection of hospitals that are owned and operated by the same entity and that share access to databases with drug order information for their patients. There is no definition of "health system" that applies to all sections of the FD&C Act. However, this is the definition of a "health system" used in section 506F of the Act concerning hospital repackaging of drugs in shortage.

addition, licensed pharmacists and licensed physicians who compound drug products in accordance with section 503A are not required to comply with CGMP requirements. Furthermore, FDA does not interact with the vast majority of licensed pharmacists and licensed physicians who compound drug products and seek to qualify for the exemptions under section 503A of the FD&C Act for the drug products they compound because these compounders are not licensed by FDA and generally do not register their compounding facilities with FDA. Therefore, FDA is often not aware of potential problems with their compounded drug products or compounding practices unless it receives a complaint such as a report of a serious adverse event or visible contamination.

In 2012, contaminated injectable drug products that a compounding pharmacy shipped to patients and healthcare practitioners across the country caused a fungal meningitis outbreak that resulted in over 60 deaths and over 750 cases of infection.[6] This was the most serious of a long history of outbreaks associated with contaminated compounded drugs. Since the 2012 fungal meningitis outbreak, FDA has investigated numerous other outbreaks and other serious adverse events, including deaths, associated with compounded drugs that were contaminated or otherwise compounded improperly.

FDA has also identified many pharmacies that compounded drug products under insanitary conditions whereby the drug products may have been contaminated with filth or rendered injurious to health and that shipped the compounded drug products made under these conditions to patients and health care providers in large volumes across the country.[7] The longer a compounded sterile drug product that is contaminated is held by a pharmacist or physician before distribution, or the longer it is held in inventory in a healthcare facility before administration, the greater the likelihood of microbial proliferation and increased patient harm.

As noted previously, compounders that elect to become outsourcing facilities must register with FDA, must comply with CGMP requirements, and are inspected by FDA according to a risk-based schedule. This mitigates the risk that their drug products will be contaminated or otherwise made under substandard conditions.

Because compounded drugs have not undergone premarket review for safety, effectiveness, and quality, they should only be used when an FDA-approved product is not available to meet the medical needs of an individual patient. As described further below, the exemptions under sections 503A and 503B of the FD&C Act are only available to compounded drugs that meet certain conditions.

B. The Prescription Requirement in Hospitals and Health Systems

[6] See http://www.cdc.gov/HAI/outbreaks/meningitis.html

[7] See FDA actions, including warning letters and injunctions, related to insanitary conditions at compounding facilities, on FDA's website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm339771.htm

As described above, compounded drug products are not approved and, therefore, do not undergo premarket review for safety, effectiveness, and quality. In addition, drug products compounded by licensed pharmacists and licensed physicians under section 503A of the FD&C Act are exempt from CGMP requirements. As reflected in the policies set forth below, FDA believes that the conditions in sections 503A and 503B provide important protections to patients, including those treated in a hospital or other facility within a health system, from the risks associated with compounded drugs and help ensure that compounders do not operate like conventional manufacturers. Therefore, FDA generally intends to apply these conditions to compounding in health system and hospital pharmacies, and sets forth an enforcement policy below regarding the prescription requirement in section 503A.

The prescription requirement in section 503A ensures that drug products are only exempt from three key provisions of the FD&C Act designed to assure safety, efficacy, and quality if they are compounded for identified individual patients. However, as stated above, FDA recognizes that a hospital may need to maintain a supply of certain compounded drug products within the hospital but outside of the pharmacy (e.g., in an emergency department or operating room) in anticipation of a patient presenting with a critical need for the drug when there is no time for the hospital pharmacy to compound and provide the drug upon receipt of a prescription or order for that patient.

FDA also recognizes that certain characteristics of hospital pharmacies differentiate them from pharmacies that are not owned and controlled by hospitals, and from conventional manufacturers. For example, generally, the scope of distribution of drug products compounded by hospital pharmacies is limited. Hospital pharmacies usually compound drug products based on orders from practitioners who work in the hospital, distribute the drug products only within the hospital or to related healthcare facilities under common ownership and control and located within close proximity to the hospital, and administer them only to patients within the hospital or healthcare facility. Because the hospital or healthcare facility and the pharmacy are under common ownership and control, the hospital or healthcare facility is responsible for both the compounding of the drug and treatment of the patient, and the cause of any compounding-related adverse events can be more readily identified. FDA believes that the policies set forth in this guidance, based on the way a hospital pharmacy normally functions with regard to compounding for its patients, will prevent hospital pharmacies from operating like conventional manufacturers.

III. POLICY

A. Hospital or Health System Compounding Under Section 503A of the FD&C Act

To qualify for the exemptions under section 503A of the FD&C Act from sections 501(a)(2)(B), 502(f)(1), and 505(a), a drug product compounded by a licensed pharmacist in a state-licensed pharmacy or Federal facility, or by a licensed physician, must be compounded in accordance with all of the provisions of section 503A. Section 503A does not distinguish between stand-alone pharmacies and pharmacies within hospitals and health systems. Therefore, the provisions of section 503A apply to pharmacists, pharmacies, and physicians that compound drugs within a hospital or a health system that is not registered as an outsourcing facility under section 503B.

Drug products compounded by a licensed pharmacist or licensed physician that are not compounded in accordance with all of the provisions of section 503A may be subject to regulatory action for violations of the new drug approval, adequate directions for use, and CGMP requirements of the FD&C Act.

For example, under section 503A, a licensed pharmacist or a licensed physician within a hospital or health system must compound drug products for an identified individual patient. The compounding must either be (a) after the receipt of a valid prescription or order for an identified individual patient or (b) in limited quantities in advance of receipt of a valid prescription or order for an identified individual patient, and the drug must be distributed after receipt of the prescription or order.

However, FDA does not intend to take action if a hospital pharmacy distributes compounded drug products without first receiving a patient-specific prescription or order provided that:

(1) The drug products are distributed only to healthcare facilities that are owned and controlled by the same entity that owns and controls the hospital pharmacy and that are located within a 1 mile radius of the compounding pharmacy;
(2) The drug products are only administered within the healthcare facilities to patients within the healthcare facilities[8], pursuant to a patient specific prescription or order; and
(3) The drug products are compounded in accordance with all other provisions of section 503A, and any other applicable requirements of the FD&C Act and FDA regulations (e.g., the drug products are not made under insanitary conditions (section 501(a)(2)(A)) or misbranded (e.g., section 502(g)).

The 1-mile radius in our policy is intended to distinguish a hospital campus from a larger health system. As explained in section II.B of this guidance, certain characteristics of hospital pharmacies distinguish them from conventional manufacturers. However, a health system pharmacy that compounds drug products without patient-specific prescriptions for facilities within its health system across a broader geographic area could function as a large manufacturing operation, but without the necessary standards to assure drug quality. If such a pharmacy contaminates or otherwise adulterates or misbrands a compounded drug, the drug has the potential to harm many patients. Outsourcing facilities, which are subject to CGMP requirements and other conditions that help to assure drug quality, can compound and distribute drug products to healthcare facilities nationwide without first receiving prescriptions for identified individual patients.

B. Hospital or Health System Compounding Under Section 503B of the FD&C Act

A compounder can register as an outsourcing facility if it intends to provide compounded drugs to facilities such as other hospitals or clinics outside the 1 mile radius of the pharmacy in which the drug is compounded without first obtaining a prescription for an identified individual patient.

[8] This does not include dispensing a drug product to a patient for use outside the hospital.

To qualify for the exemptions under section 503B from sections 502(f)(1), 505, and 582 of the FD&C Act, hospitals and health system compounders that elect to register with FDA as outsourcing facilities must comply with all of the provisions of section 503B. Outsourcing facilities must also comply with CGMP requirements in section 501(a)(2)(B) of the FD&C Act.