

**ENFORCEMENT AND COMPOUNDING
COMMITTEE REPORT
April 18, 2017**

Amy Gutierrez, PharmD, Licensee Member, Chair
Allen Schaad, Licensee Member, Vice Chair
Greg Lippe, Public Member
Stan Weisser, Licensee Member
Valerie Muñoz, Public Member
Ricardo Sanchez, Public Member

I. Call to Order, Establishment of Quorum, and General Announcements

II. Public Comments on Items Not on the Agenda/Agenda Items for Future Meetings

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

III. Enforcement Matters

a. University of California, San Diego's Pilot Program to Permit Patients to Access Medications from an Automated Drug Delivery System Not Immediately Adjacent to the Pharmacy

Background

At the 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 drug delivery system (ADDS) 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 for first time fills.

Since that time the committee has received quarterly updates on the study, including usage of the system. At this meeting, the committee will hear the final report of the study.

As authorized by the board, UCSD has collected data through the first quarter of 2017 and will report its findings at this meeting and to the full board at the May 2017 Board Meeting. The board has permitted UCSD to continue operating the kiosk until the board makes a decision about the expanded use of the ADDS is made.

1. Discussion and Consideration of the Final Report from the Pilot Program

Attachment 1

At this meeting, the committee will review the final report of this study conducted by the study's researcher, Jan Hirsch, BSP Pharm, PhD. Dr. Hirsch will provide the presentation in person. Kim Allen from Sharp and Sara Lake from Asteres will also be present to respond to questions.

A copy of the final report is provided in **Attachment 1**.

2. Discussion and Consideration of Possible Future Action Based on the Pilot Program

During this portion of the meeting, the committee will discuss what recommendations it wishes to make to the board.

The use of automation technology presents opportunities and challenges to pharmacy regulators. Currently this study is being conducted to explore possible options to 16 California Code of Regulations section 1713 - specifically regarding the provisions in subsections (d) and (e):

1713. Receipt and Delivery of Prescriptions and Prescription Medications Must be To or From Licensed Pharmacy

- (a) Except as otherwise provided in this Division, no licensee shall participate in any arrangement or agreement, whereby prescriptions, or prescription medications, may be left at, picked up from, accepted by, or delivered to any place not licensed as a retail pharmacy.
- (b) A licensee may pick up prescriptions at the office or home of the prescriber or pick up or deliver prescriptions or prescription medications at the office of or a residence designated by the patient or at the hospital, institution, medical office or clinic at which the patient receives health care services. In addition, the Board may, in its sole discretion, waive application of subdivision (a) for good cause shown.
- (c) A patient or the patient's agent may deposit a prescription in a secure container that is at the same address as the licensed pharmacy premises. The pharmacy shall be responsible for the security and confidentiality of the prescriptions deposited in the container.
- (d) A pharmacy may use an automated delivery device to deliver previously dispensed prescription medications provided:**
 - (1) Each patient using the device has chosen to use the device and signed a written consent form demonstrating his or her informed consent to do so.**
 - (2) A pharmacist has determined that each patient using the device meets inclusion criteria for use of the device established by the pharmacy prior to delivery of prescription medication to that patient.**

- (3) The device has a means to identify each patient and only release that patient's prescription medications.**
- (4) The pharmacy does not use the device to deliver previously dispensed prescription medications to any patient if a pharmacist determines that such patient requires counseling as set forth in section 1707.2(a)(2).**
- (5) The pharmacy provides an immediate consultation with a pharmacist, either in-person or via telephone, upon the request of a patient.**
- (6) The device is located adjacent to the secure pharmacy area.**
- (7) The device is secure from access and removal by unauthorized individuals.**
- (8) The pharmacy is responsible for the prescription medications stored in the device.**
- (9) Any incident involving the device where a complaint, delivery error, or omission has occurred shall be reviewed as part of the pharmacy's quality assurance program mandated by Business and Professions Code section 4125.**
- (10) The pharmacy maintains written policies and procedures pertaining to the device as described in subdivision (e).**
- (e) Any pharmacy making use of an automated delivery device as permitted by subdivision (d) shall maintain, and on an annual basis review, written policies and procedures providing for:**
 - (1) Maintaining the security of the automated delivery device and the dangerous drugs within the device.**
 - (2) Determining and applying inclusion criteria regarding which medications are appropriate for placement in the device and for which patients, including when consultation is needed.**
 - (3) Ensuring that patients are aware that consultation with a pharmacist is available for any prescription medication, including for those delivered via the automated delivery device.**
 - (4) Describing the assignment of responsibilities to, and training of, pharmacy personnel regarding the maintenance and filing procedures for the automated delivery device.**
 - (5) Orienting participating patients on use of the automated delivery device, notifying patients when expected prescription medications are not available in the device, and ensuring that patient use of the device does not interfere with delivery of prescription medications.**
 - (6) Ensuring the delivery of medications to patients in the event the device is disabled or malfunctions.**
- (f) Written policies and procedures shall be maintained at least three years beyond the last use of an automated delivery device.**
- (g) For the purposes of this section only, "previously-dispensed prescription medications" are those prescription medications that do not trigger a non-discretionary duty to consult under section 1707.2(b)(1), because they have been previously dispensed to the patient by the pharmacy in the same dosage form, strength, and with the same written directions.**

Authority cited: Sections 4005, 4075, and 4114 Business and Professions Code. Reference: Sections 4005, 4052, 4116 and 4117 Business and Professions Code.

Considering the results of this study and other factors of concern to each member, the committee should consider the following items as discussion items and may create additional items as well:

1. Should ADDs be allowed in expanded areas instead of being limited to “adjacent to the pharmacy counter,” and if so, what provisions are needed?
2. Should any expanded use of ADDs be allowed only for refills? If allowed for first-time fills, how will consultation be handled?
3. What should occur with the current ADDs device at Sharp until the board determines a resolution?
4. Is an additional study needed to explore additional topics?
5. Is expanded use of such technology in a patient’s interest?

b. Discussion and Consideration of the CURES 2.0 Prescription Drug Monitoring Program

During this portion of the meeting, the committee will discuss California’s prescription drug monitoring system for controlled substances, CURES.

The CA Department of Justice, which operates CURES, converted to the exclusive support of only CURES 2.0 only at the beginning of March. The new CURES 2.0 system contains features that were not available to pharmacists in the prior system. At the January Enforcement Committee Meeting, the Department of Justice provided an overview of the new system and highlighted the new features that can be accessed by pharmacists. For example, enrollment in CURES is now a much simpler online registration process.

Executive Officer Herold is one of three DCA staff who sit as members of the six-member change control board for CURES (the executive director of the Medical Board and a senior manager from the DCA executive office are the other DCA representatives).

Ms. Herold will provide an update on CURES access and use at this meeting.

At the January 2017 Board Meeting, the board identified multiple items for future change with respect to the CURES program and for staff to pursue statutory changes. These changes are:

1. Include the days’ supply of medication in the PAR (patient activity report).
2. Permit prescribers to view the prescriptions where they are identified as the prescriber.
3. Reduce period to report dispensing data to within 48 hours.
4. Add Schedule V prescriptions for reporting to the CURES system.

Discussion has occurred with CURES staff (at DOJ) on each of these items. Item 1 has been achieved: Pharmacists can now see the days' supply of medication on the PAR reports.

The board also strongly supported the movement to a cross-state information sharing system for controlled substances data. Forty-three states have signed agreements to use the system available through the National Association of Boards of Pharmacy.

c. Presentation by Stericycle of a New Device for Destruction of Controlled Substances in Health Care Facilities

Recently board staff viewed a demonstration by Stericycle of a new process/device for use in health care facilities to waste controlled substances. For informational purposes, a short presentation will be provided during this committee meeting.

d. Discussion and Consideration of the Use of Automated Drug Delivery Systems (ADDS) – Follow up from the February 2017 Board Meeting

Attachment 2

The board convened a special board meeting in February to focus on new technology that has been introduced to provide medications to patients. The board's goal is to seek ways to allow pharmacies to provide better quality care and service to patients while maintaining security and protecting the public from diversion of controlled substances and other prescription drugs. The board directed the Enforcement and Compounding Committee to continue to explore this topic and bring recommendations for action to a future board meeting.

Business and Professions Code [section 4186](#), Health and Safety Code [section 1261.6](#) and other statutes set specific requirements for pharmacies operating ADDS devices in licensed health facilities. Among other requirements, ADDS machines must "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." Key provisions specify who is responsible for stocking an ADDS with medication and how restocking may be done outside the health facility.

Because many ADDS devices today offer features not addressed in pharmacy law, the board invited vendors to present information about technological features and how the devices are affected by existing statutes. This year, there are at least two bills introduced in the California Legislature to authorize the use of expanded ADDS devices to provide medications in new ways. One of these bills is sponsored by the board (SB 443, Hernandez) to allow county fire departments to establish ADDS in fire stations to replenish ambulances and emergency vehicles.

At this meeting, the Enforcement and Compounding Committee will have an opportunity to discuss the various devices and their features. Dr. Gutierrez has developed a grid to facilitate this discussion, which is available in **Attachment 2**. The discussion will be framed around

three categories: Options and Features Currently Available, Refilling of ADDS in Skilled Nursing Facilities, and Next Steps by the Committee or Board.

1. Options and Features Currently Available:

Please refer to **Attachment 2**.

During the board's Technology Summit, Board Assistant Executive Officer Anne Sodergren generated a series of questions to help frame the discussion. Whereas these questions are in some ways contained in the grid developed by President Gutierrez, these questions are provided below to serve as a secondary point of reference for the committee in approaching this topic.

Vendor: imgRx, Medifriend RX

1. Should the board allow an ADDS owned and operated by a pharmacy to be used in the types of clinics listed in 4180 (licensed as nonprofit or free clinics)? If so, what if any type of license should the board issue?
2. Should the board allow someone other than an employee of the pharmacy that owns the ADDS to access the system for purposes of replenishing the drugs?
3. Is the board comfortable with the machine being loaded by the machine via a remote camera with pharmacist review?
4. Is there a benefit to limit the types of drugs used by the machine for this purpose, e.g., 340B, no controlled substances?
5. Should patient consultation be required before the drug is dispensed?
6. Should the board specify what health care professional can provide the drug to the patient?
7. Should the board limit this provision to one ADDS per location?
8. Should the board specify any type of ratio of ADDS/remote pharmacist?

Vendor: Cubex

1. Should the board allow someone other than pharmacy personnel to stock a machine, with safeguards of automation considered? Should the board specify that it be a nurse?
2. Should the board specify the specific safeguards the system must have to allow for this?
3. Should we limit this to SNFs?

Vendor: Becton Dickinson: Ascribe Rx

1. Should the board expand the environments where the device can be used - - including assisted living facilities, jails, and multi-doctors' offices.
2. Should the board allow someone other than pharmacy personnel to load a machine, with safeguards of automation considered? Should the board specify that it be a pharmacy technician or nurse?

Vendor: Omnicell

1. Would the board consider expanding use to Residential Care, Fire Departments? If so, who owns the device and is responsible?
2. Can a nurse restock and access the device?

Vendor: Asteres Inc.

1. Would the board allow for the placement of ADDS remote from the pharmacy? If so, should the board require licensure of the ADDS so that it could be used in a non-licensed site (e.g., work site)?

Vendor: MedAvail

1. Should the board write a new statute to overhaul all ADDS?
2. Should the board expand the provisions similar to the imgRX request?
3. Should the board allow use in the following settings: urgent care, certain clinics, surgical clinics, ER to provide outpatient dispensing, physician offices? If so, should it be required to have a pharmacist perform a final check and provide consultation before the drug is released? Should the device be limited to stocking noncontrolled drugs only? Should the board limit who can own and operate the unit. Should it be licensed?
4. How can the technologies meet the language translation requirement?
5. How should the board handle medications that require reconstitution?

Vendor: Arxium:

1. Would the board allow a technician to restock the medication that has been repackaged in the pharmacy if the repackaged container has a temper evident seal on it?
2. Would the board allow a technician can do a monthly inspection of the machine while a pharmacist still performs the quarterly review?
3. Would the board consider allowing the pharmacist to be outside of California - services like order verification?

Vendor: PharMerica Corporation

1. Would you allow a pharmacy technician, intern or nursing staff to restock?

2. Refilling of ADDS in Skilled Nursing Facilities

Attachment 3

In skilled nursing facilities, ADDS are sometimes installed to permit the furnishing of emergency medications or to start initial doses to patients receiving care in the facilities.

At a prior meeting, discussion included a review of California law regarding Health and Safety Code section 1261.1. At the prior meeting, board attorneys indicated their view that drugs in the ADDS are the stock of the pharmacy and because of that, the pharmacy is responsible for restocking the device (pharmacist, pharmacist intern, or

pharmacy technician under pharmacist supervision). However, board staff is aware that some skilled nursing facilities are using nursing staff or perhaps other employees to refill the ADDS.

At this meeting the committee will resume discussion on this topic. A copy of Health and Safety Code section 1261.6 is provided in **Attachment 3**.

3. Next Steps by the Committee or Board

During this portion of the meeting, the committee will discuss how it will proceed with the use of ADDS to provide patients with medications in different settings.

e. **Discussion and Consideration of a Proposed Regulation to Add Title 16 California Code of Regulations Section 1715.65 Related to Inventory Reconciliation of Controlled Substances**

Attachment 4

For over one year, the board has been discussing proposed new regulation requirements to ensure pharmacies more closely monitor and periodically count controlled substances as a means to reduce drug losses and to identify any losses sooner. The regulation in its current form requires the counting of all Schedule II controlled substances every 90 days.

At the January 2017 Board Meeting, the board asked the committee to review the regulation's text to determine if the board can improve its clarity. The board also asked the committee to consider whether the board should initiate a new rulemaking to amend section 1715.6 and determine if the board should replace the requirement to report any controlled substances drug loss to the board with "a significant" loss.

A chronology for the section 1715.65 regulation is:

Board approves initial version of regulation:	July 28, 2016
Proposed text released for 45-day public comment:	September 16-October 31, 2016
Board reviews comments and modifies text:	December 14, 2016
Modified text released for 15-day comment:	December 23, 2016-January 7, 2017
Board refers text to Enforcement Committee:	January 24, 2017

Attachment 4 contains the current proposed text of the regulation, and a summary of the draft minutes from the January 2017 Board Meeting.

Below for the committee's consideration, and indicated in highlight (or shadow), are the staff-proposed modifications – which are minor -- to the text of the regulation. In its current form, the reconciliation regulation would:

- Require pharmacies, including inpatient pharmacies, and clinics licensed by the board under sections 4180 and 4190) to count every quarter all schedule II drugs in the licensee's possession. This will also include medications in ADDS machines owned by a pharmacy.

- Requires that the reconciliation be signed by the PIC or, in the case of a clinic, the professional director. All records must be kept for three years and be readily retrievable.
- Reaffirm the reporting of losses as required by other sections of CA and federal law.
- Require that a new PIC perform an inventory reconciliation of all Schedule II controlled substances within 30 days of becoming PIC, and encourage the outgoing PIC to perform a similar reconciliation before leaving his or her PIC position.

If the committee is satisfied with these parameters (requiring a reconciliation report for Schedule II controlled substances every 90 days), the committee can recommend that the board adopt the language. The changes indicated below are editorial and would not require a 15-day comment period.

1715.65. Inventory Reconciliation 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:
 - 1) A physical count, not an estimate, of all quantities of 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;
 - 2) A review of all acquisitions and dispositions of Schedule II controlled substances since the last Inventory Reconciliation Report;
 - 3) A comparison of (1) and (2) to determine if there are any variances; and
 - 4) All records used to compile each Inventory Reconciliation Report shall be maintained in the pharmacy or clinic for at least three years in a readily retrievable form.
- d) A pharmacy or clinic shall report in writing identified losses and possible causes, shall be identified in writing and reported to the board and, when appropriate, to the Drug Enforcement Administration within 30 days unless the cause of the loss is theft, diversion, or self-use in which case the report shall be made within 14 days. If the pharmacy or clinic is unable to identify the cause of the loss, further investigation shall be undertaken to identify the cause and security improvements necessary to prevent additional losses of controlled substances.
- e) Likely Possible causes of overages shall be identified in writing and incorporated into the Inventory Reconciliation Report.

- e)f) The Inventory Reconciliation Report shall be dated and signed by the individual(s) performing the inventory, and countersigned by the pharmacist-in-charge or professional director (if a clinic) and be readily retrievable in the pharmacy or clinic for three years. A countersignature is not required if the pharmacist-in-charge or professional director personally completed the inventory reconciliation report.
- f)g) A new pharmacist-in-charge of a pharmacy shall complete an inventory reconciliation report within 30 days of becoming pharmacist in-charge as identified in subdivision (c) within 30 days of becoming pharmacist-in-charge. Whenever possible an outgoing pharmacist-in-charge also should complete an inventory reconciliation report as required in subdivision (c).
- g)h) For inpatient hospital pharmacies, a separate quarterly Inventory Reconciliation Report shall be required for Schedule II controlled substances stored within the pharmacy and for each pharmacy satellite location.
- h)i) The pharmacist-in-charge of an inpatient hospital pharmacy or of a pharmacy servicing onsite or offsite automated drug delivery systems shall ensure that:
- 1) All controlled substances added to an automated drug delivery system are accounted for;
 - 2) Access to automated drug delivery systems is limited to authorized facility personnel;
 - 3) An ongoing evaluation of discrepancies or unusual access associated with controlled substances is performed; and
 - 4) Confirmed losses of controlled substances are reported to the board; and
 - 5) ~~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.~~

Regarding the review of section 1715.6: this section requires the reporting to the board of any loss of controlled substances. The text of section 1715.6 is provided below:

1715.6. Reporting Drug Loss.

The owner shall report to the Board within thirty (30) days of discovery of any loss of the controlled substances, including their amounts and strengths.

Meanwhile DEA requirements specify immediate reporting of significant controlled substances losses to the DEA. The board uses the broader standard of reporting any loss to the board, in part to remove the ambiguity of a pharmacy’s ability to determine what is a “significant” loss is. For example, a large pharmacy could lose several thousand controlled substances and still not consider this a “significant” loss. The board does not typically investigate a single small loss reported to it.

This board’s current regulation regarding the reporting of any controlled substances loss in section 1715.6 has been a requirement since before 1990, and it likely reflects the actions the board took in the early to mid-1980s to address pill mill pharmacies in LA. Among the board’s actions at that time was also a strengthened corresponding responsibility law, which is the California version of law that is in place today. Board staff believes section 1715.6 is an important regulation to ensure pharmacies keep close watch on their inventories, and it removes the ambiguity in evaluating what

would be considered a significant loss. It is also commensurate with the philosophy in why the board is pursuing the inventory reconciliation regulation to require closer monitoring of controlled substances inventories in pharmacies.

As background, former Board Member Marsha Cohen and former liaison Deputy Attorney General Bill Marcus state the following information about a pharmacy's obligation to count and report drug losses, which reflects longstanding board policy in this area (*from Marcus & Cohen's Pharmacy Law for California Pharmacists, 7th Edition*). See particularly the last paragraph of this excerpt:

"A pharmacy (or any licensed entity or person handling dangerous drugs) is always responsible for an accurate accounting for the drugs it should have on hand (sections 4080, 4081(b)). In order to maintain such an accounting, the pharmacy must keep accurate records of acquisitions and dispositions of dangerous drugs these records must include drugs lost by any means.

From time to time, a pharmacy will lose some drugs, for such reason as adverse weather conditions, fire or other building damage, deterioration, or theft, for example. Minor accounting discrepancies can arise from an accumulation of minor filling errors or record keeping errors over a period of time. However, the pharmacy and pharmacist should institute changes in pharmacy operations, such as better security, whenever inexplicable or sizeable losses begin to occur.

The pharmacy must keep accurate records of all losses. If the pharmacy cannot match stock on hand to its records of acquisitions and dispositions, it is in violation of the law (section 4081(a)). A significant discrepancy, especially involving controlled substances, is likely to lead to disciplinary action.

Controlled substances lost in transit and prior to receipt are the responsibility of the supply, which must any lost or missing controlled substances to DEA (DEA Pharmacist's Manual, p. 17). If controlled substances are destroyed or damaged in transit, the loss is generally not reportable to DEA as a loss or theft of drugs, at least if their disposal or their transfer to a reverse distributor for destruction is reported to DEA (on form 41), thus maintaining accuracy in record-keeping.

The pharmacy and the responsible pharmacist, usually the pharmacist-in-charge, must watch for evidence of loss or theft and take security measures to guard against theft and diversion of controlled substances (21 CFR section 1301.71, 1301.75). They must maintain vigilance with respect to all persons employed by or with access to the pharmacy. DEA regulations also require all pharmacy employees (not just pharmacists) to notify their employers if they know of drug diversion from the pharmacy by a fellow employee (21 CFR 1301.91).

A pharmacy must have procedures in place to protect the public when a licensed person employed in or by the pharmacy is discovered or known to be chemically, physically or mentally impaired to the extent that it affects his or her ability to

practice his or her profession or occupation safely now when it is discovered or known that a licensed employee has engaged in theft, diversion, or self-use (section 4104(a)). The pharmacy must have written policies and procedures for detecting impairment, theft, diversion or self-use by such licensed individuals (section 4104(b)). The pharmacy must report to the Board within 14 days any of the following:

- Admission by a licensed individual of chemical, mental or physical impairment or any video or documentary evidence of such impairment to the extent it affects the ability to practice;
- Admission by a licensed individual of theft, diversion or self-use of dangerous drugs or any video or documentary evidence of such conduct; or
- Any termination of a licensed individual for such impairment or conduct (4104(c)).

A person who makes a required or authorized report to the Board about loss, theft, diversion, or employee self-use of drugs is immune from civil or criminal liability that might arise from doing so (4104(e)).

Board regulations require immediate and careful documentation of any loss of drugs and a report to the Board within 30 days (section 1715.6). A significant loss of controlled substances of controlled substances must be reported to the DEA with one business day. The criteria a registrant should consider to determine whether a loss is “significant” include the quantity lost in relation to the type of business: which controlled substances were lost and whether they are likely candidates for diversion; whether the loss can be associated with specific individuals or attributed to “unique” activities; whether there is a pattern of losses over time, whether the losses appear to be random and the results of any efforts to resolved the losses; and local trends and other indicators of the potential for diversion of the lost drugs (21 CFR sections 1301.74, 1301.76(b)); DEA Form 106). Careful contemporaneous records of loss will allow the pharmacy to explain any discrepancy to a state or federal inspector and allay suspicion of pharmacy misconduct or failure to responds properly and promptly to the cause of the problems.”

f. Discussion and Consideration of March 11, 2017, Training Provided by the Board and DEA on CURES and Prescription Drug Abuse, and Possible Future Training

Attachment 5

On March 11, 2017, the board, Drug Enforcement Administration and UCSD provided a day-long conference on prescription drug abuse, corresponding responsibility and preventing drug losses from a pharmacy. There were nearly 200 attendees who earned six hours of continuing education

credit for attending this training, and another 132 individuals who earned one additional hour of continuing education to secure the training needed to provide naloxone under California protocol.

A copy of the agenda is provided as **Attachment 5**. Evaluations of this training were positive. Staff will schedule additional training sessions in other areas of California in the next fiscal year.

g. Report Submitted to the Assembly Budget Committee Regarding the Board's Prescription Drug Abuse Team

Attachment 6

During the Legislature's 2016-17 state budget negotiations, the board was asked to provide a report on the initial results of the formation of a specific team of investigators to proactively identify and initiate investigations involving prescription drugs. This report was due in April 2017. A copy of this report is provided in **Attachment 6**. The report is being provided to you for information only.

The report asked for information on five items:

1. Narrative description of the preceding year's activities related to combatting prescription drug abuse.
2. Funding and expenses information including the budgeted, allocated and expended money.
3. Number of positions and responsibilities.
4. Number of cases and disposition of cases referred to the Office of the Attorney General (AG) as a result of a case opened from a coroner report.
5. Number of hours spent combating prescription drug abuse, including separately identifying the total number of hours spent reviewing coroners reports and submitting public records requests to obtain the reports.

IV. Compounding Matters

a. Discussion and Consideration of Statistics Regarding Outcomes of Board of Pharmacy Compounding Inspections

During this portion of the meeting, Supervising Inspector Christine Acosta will provide a presentation describing the number and type of violations identified involving compounding during Board of Pharmacy inspections since the beginning of July 2016.

b. Discussion and Consideration of Waiver Requests for Compounding Construction Compliance Delays Pursuant to Title 16 California Code of Regulations, Sections 1735 et seq. and 1751 et seq.

Attachment 7

Title 16 of the California Code of Regulations (CCR) section 1735.6 (f) states that where compliance with California's compounding regulations require physical construction or alteration to a facility or physical environment, the board may grant a waiver for a period of time to permit the required physical changes. There is a related provision in CCR section

1751.4 dealing with sterile compounding. A copy of the waiver application form is provided in **Attachment 7**.

1. Update

Status of waiver requests received as of 3/30/17:

- Processed: Total: 509
 - Processed without LSC 98 (98/509=19%)
 - HSP Processed: 213 (213/509= 41.85%)
 - PHY processed: 242 (242/509= 47.54%)
- Outcomes:
 - Denied: 47 (47/509= 9.24%)
 - Withdrawn: 45 (42/509=8.84%)
 - Approved: 289 (289/509= 56.77%)
 - In process: 128 (128/509= 25%)
- Overview Perspective:
 - Waivers received
 - HSP: 213/480 = 44.3% HSPs applied for a waiver
 - PHY: 242/6586= 3.67% PHYs applied for a waiver
 - NRP: 15/ 513= 2.92% of NRPs applied for a waiver
- Pending review:
 - Unprocessed emails with waiver attachments: 92

2. Process for Review of Waiver Requests

Towards the end of 2016, the board established a waiver process. Application for any waiver must be made in writing, identify the provisions requiring physical construction or alteration, and provide a timeline for any such changes. The board is able to grant the waiver for a specified period when, in its discretion, good cause is demonstrated for the waiver.

At the October 2016 Board Meeting, the board delegated authority to the executive officer to process waiver requests with parameters from the board. The board further delegated authority for a committee assigned by the president (to include the president and Board Member Schaad) to hear waiver requests.

Initially staff met with Dr. Gutierrez, Mr. Schaad and usually representatives of the Office of Statewide Health Planning and the California Department of Public Health to normalize the reviewing and processing of the waiver requests. This process has now been refined to have the initial review performed by staff led by the executive officer, who approves or denies the waiver request. (The California Department of Public Health and the Office of Statewide Health Planning also typically have staff participate.) If a waiver is denied by the executive officer, there is an appeal process which will be reviewed by two board members, currently Board Members Schaad and Law.

The approval or denial of the waiver request is provided in writing. There is an ability for a pharmacy to appeal a denied waiver a second time.

The goal of the construction waiver process is to secure full compliance at the earliest possible time.

c. Update on the Board’s Progress in Implementing California Business and Professions Code Section 4129 et seq., regarding Licensure of Outsourcing Facilities

Effective January 1, 2017, the board received the authority to license in state and nonresident outsourcing facilities. This is an entirely new function and type of licensee than we have licensed in the past. The board will receive three new staff (two inspectors, one supervising inspector) for this program beginning July 1. Currently interviews are being scheduled to hire the staff needed for this program, and an inspector has been promoted into the supervising inspector position.

Additionally, training is being created to train staff on inspecting outsourcing facilities. We believe that the board will be positioned to inspect and license outsourcing facilities before July 1.

Currently, the board has received 28 applications for outsourcers (five of these are in California). There are currently 68 outsourcing facilities listed on the FDA’s website.

d. Discussion and Consideration of the United States Government Accountability Office’s March 31, 2017 E-Supplement Report to Congressional Committees on Drug Compounding: *FDA Has Taken Steps to Implement Compounding Law, but Some States and Stakeholders Reported Challenges*

Attachment 8

This item is provided for informational purposes.

At the last Enforcement and Compounding Committee Meeting, the committee reviewed a GAO report on the FDA’s implementation of compounding law, titled: *Drug Compounding: FDA Has Taken Steps to Implement Compounding Law, but Some States and Stakeholders Reported Challenges* (GAO-17-64).

At the end of March 2017, the GAO released an e-supplement, which is a companion piece to the drug compounding report that was issued in November 2016.

The e-supplement is an Internet-only product that provides selected results from the GAO survey of state regulatory bodies on drug compounding, including additional data that are not included in the report.

The e-supplement is titled: *Drug Compounding: Survey of State Pharmacy Regulatory Bodies (GAO-17-363SP, March 2017), an E-supplement to GAO-17-64*. The information can be accessed at: <http://www.gao.gov/products/GAO-17-363SP>

These supplements provide details about the data compiled by the GAO for its November report. As an example, **Attachment 8** contains one example of some of the data displayed in these e-supplement tables.

e. Presentation by Road Runner Pharmacy Regarding Compounding for Veterinary Prescriber Office Use

Attachment 9

At a recent board meeting, Road Runner Pharmacy requested the opportunity to address the board on compounding for veterinary prescriber office use. They were invited to make a presentation at the next Enforcement and Compounding Committee Meeting.

At the time Road Runner Pharmacy approached the board requesting time to make a presentation, they read a statement seeking an exemption from the board's compounding regulations for veterinary compounding. A summary of this statement is provided below (note a copy of the referenced code section is provided in **Attachment 9**).

**Road Runner Summarized Statement for Enforcement Committee Meeting
Excerpt for January 24, 2017 Draft Board Meeting Minutes**

Morgan McCloud, representing Road Runner Veterinary Compounding Pharmacy located in Phoenix, Arizona, requested the board exempt veterinary compounding from some of the requirements in the compounding regulations.

Mr. McCloud reported to the board a colleague Jeremy Schmidt addressed the January 4, 2017, Enforcement and Compounding Committee regarding the recent adoption of new BUD dating and testing for compounding medications and the need for the veterinary community to be exempted from California Code of Regulations (CCR) section 1735.2. Method suitability tests and container closure integrity tests normally associated with sterile products are now mandated for nonsterile products if BUD dating extension is to occur. Additionally, stability studies in the same paragraph can be interpreted differently. Using stability indicators, a common process used in manufacturing could add as much as \$20,000 to the BUD analysis and would significantly raise costs to pet owners, of which most have no insurance dramatically decreasing pet patient care. Due to differences in the practice of veterinary medicine versus human medicine, the Enforcement and Compounding Committee agreed to add the topic to their agenda at the next committee meeting.

Mr. McCloud explained to the board the importance of the request for exemption and to ensure the board is aware of the impact of compounding medications within the veterinary community. He explained in the veterinary practice, it is expected for the veterinarian to have the

appropriate medication for the pets. Due to the wide range of patients seen by veterinarians and unavailability of select drugs and strengths, the treatments often come from compounded office stock. Mr. McCloud explained the newly required testing could add as much as \$30,000 annually per a medication leaving pets to go untreated due to the costs. Additionally, the requirement for the practitioner to explain why a compounded product over commercial product has been selected seems counterintuitive. Mr. McCloud continued that mandates requiring the office stock to indicate the number of patients the medication is to serve and quantities expected to administer in the clinic as well as the average volume dispensed for a 120-hour supply are illogical in the typical veterinary practice.

Mr. McCloud requested veterinary medications be exempted for these additional requirements because the medical needs for animals are met differently than those of humans. Due to the on-demand service nature of veterinary medicine, the unique nature of veterinary medicines and dosages, the unavailability of most commercial drugs to meet those needs, Road Runner Veterinary Compounding Pharmacy requests a consideration for exemption in veterinary practices or at least request the board place this item on the agenda for further discussion at the next meeting.

The board also has recently received several letters from entities indicating that the board's regulations are negatively impacting patients and their pets. Copies of these letters are provided in **Attachment 9**. The board has also received a few recent complaints from patients indicating that the board's regulations should be removed for veterinary compounding.

d. Discussion and Consideration of the Proposed Food and Drug Administration Rule, "List of Bulk Drug Substances That Can Be Used to Compound Drug Products in Accordance with Section 503A of the Federal Food, Drug, and Cosmetic Act" and Proposed Lists

Attachment 10

The next three agenda items address FDA guidance documents on compounding from bulk substances by compounding pharmacies, outsourcing facilities and use of bulk substances for veterinary use.

Under section 503A of the Food, Drug and Cosmetic Act, a bulk drug substance that is not the subject of a USP or NF monograph or is not a component of an FDA-approved drug cannot be used in compounding unless it appears on a list promulgated by the FDA. However, until the substance has been evaluated and either included or not included to the bulks list, the FDA does not intend to take action if the product fits specific criteria (page 9).

This specific guidance document establishes an interim list of bulk substances that may be

used by compounding pharmacies. The proposed rule also proposes other bulk drug substances the FDA has reviewed and classified as not to be added to the bulks list. Since December 2013, over 2,000 substances have been nominated to the FDA for listing on the bulks list, many of these can be used without inclusion on the bulks because they are subject of an applicable USP or NF monograph or are a component of an FDA-approved drug. Of 740 unique substances that have been reviewed by FDA:

- Approximately 315 are “already” eligible for compounding by pharmacies.
- One is not a bulk drug substance, but is a finished drug product which does qualify
- One is a biological which does not qualify.
- Four products have been withdrawn or removed from the market because they are unsafe or not effective.
- One is a Schedule I drug and not eligible.
- 350 substances were not submitted with adequate supporting evidence for the FDA to evaluate them.
- Additional substances (the remaining ones) FDA identified significant safety risks to use the products.

One of the conditions that must be met for a compounded drug product to be exempted from section 505 of the Food, Drug and Cosmetic Act, is that the produce is compounded by a pharmacist or physician using bulk drug substances that:

1. Comply with USP or National Formulary standards
2. If no monograph exists, the items are drug components of approved drugs
3. Or the product appears on a list developed by the FDA

The bulk drug substance must be manufactured in an FDA-approved plant and accompanied by a certificate of analysis.

Another purpose of this guidance is to establish another process by which bulk substances that do not fit the above criteria could be evaluated by the FDA and placed on an approved bulks list.

e. Discussion and Consideration of the Food and Drug Administration Rule “Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act – Guidance for Industry” and Proposed Lists

Attachment 11

A bulk drug substance cannot be used in compounding unless it is used to compound a drug that appears on the FDA drug shortage list at the time of compounding, distributing and dispensing, or appeared on the drug shortage list within 60 days of compounding.

According to this guidance document, the FDA is considering the following factors in developing a bulks list for outsourcers:

- Safety concerns about use of the bulk drug substance in compounding
- Whether the bulk drug substances was nominated by multiple parties or identified as necessary by medical professional organizations
- The efficiency with which the evaluation can be completed (ease of acquiring the information to conduct the review, available resources, and other logistical issues)

The FDA intends to publish in the *Federal Register* that describes its proposed position on each substance it has evaluated and why it will or will not add each to the outsourcing bulks list. It will seek the Pharmacy Compounding Advisory Committee’s review when it believes their input may be helpful.

The last pages of **Attachment 11** provides three lists: a list of substances that are under evaluation for the bulk drug substances list for outsourcers, bulk substances that raise significant safety risks, and a list that were nominated “without adequate support.”

f. Discussion and Consideration of the Food and Drug Administration Rule “Guidance for Industry Compounding Animal Drugs from Bulk Drug Substances” and Proposed Lists

Attachment 12

Regulations developed by the FDA for animal drugs specify that bulk drug substances cannot be used to compound animal drugs. However, the FDA also notes that because either no drug is approved for a specific animal species or a drug is available under extra label use provisions, an animal drug compounded from bulk drug substances may be an appropriate treatment option. Nevertheless the FDA states that the “unrestricted compounding of animal drugs from bulk drug substances has the potential to compromise food safety, place animals or humans at undue risk from unsafe or ineffective treatment, and undermine the incentives to develop and submit new animal drug applications to FDA containing data and information to demonstrate that the product is safe, effective, properly manufactured, and accurately labeled.”

The guidance provides that the FDA does not intend to take action if a state-licensed pharmacy, licensed veterinarian or outsourcer compounds animal drugs from bulk drug substances if operating under specified conditions. These include:

- If in a pharmacy, is compounded under the direct supervision of a pharmacist, after receipt of a prescription from a vet or based upon prescribed prior experience
- If the compounded product is not used for food producing animals,
- If the bulk substance is part of an approved animal or human drug, there is a change from the approved drug that produces a clinical difference for the animal.
- And numerous other factors detailed in the guidance.

V. Enforcement Statistics

a. Citations and Fines

Attachment 13

Attachment 13 contains statistics describing the citations with fines issued this year.

b. Medication Errors

No statistics specifically on medication errors are available as the packet is being compiled. A report on the medication errors observed during 2016/17 will be available after the fiscal year has ended and will be brought to this committee.

c. Other Enforcement Statistics

Attachment 14

Attachment 14 contains statistics describing the enforcement activities of the board.

Attachment 1

Study of Expanded Use of an Automated Delivery Device

STUDY RESULTS

April 18, 2017

Jan D. Hirsch, BPharm, PhD

UCSD Skaggs School of Pharmacy & Pharmaceutical Sciences



Outline

- Study Results
 - Pre-Kiosk Employee Survey
 - Satisfaction with Kiosk
 - Comparison Kiosk to Regular Counter
 - Return to Stock (RTS)
 - Time to Pick-Up
 - Consultations
- Next Steps

Kiosk = ScriptCenter

ScriptCenter Kiosk Sharp Memorial Hospital



First Floor Lobby Sharp Memorial Hospital



Study Design

- Pre-Kiosk Implementation Survey (Sharp Employees) October-November 2015

Study Start

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

Month 1: March

Month 6: August

Month 10: December

Regular Counter

- RTS rate*

Kiosk

- RTS rate
- Consultation Log
- Time to Pickup
- Kiosk Patient Satisfaction

Regular Counter

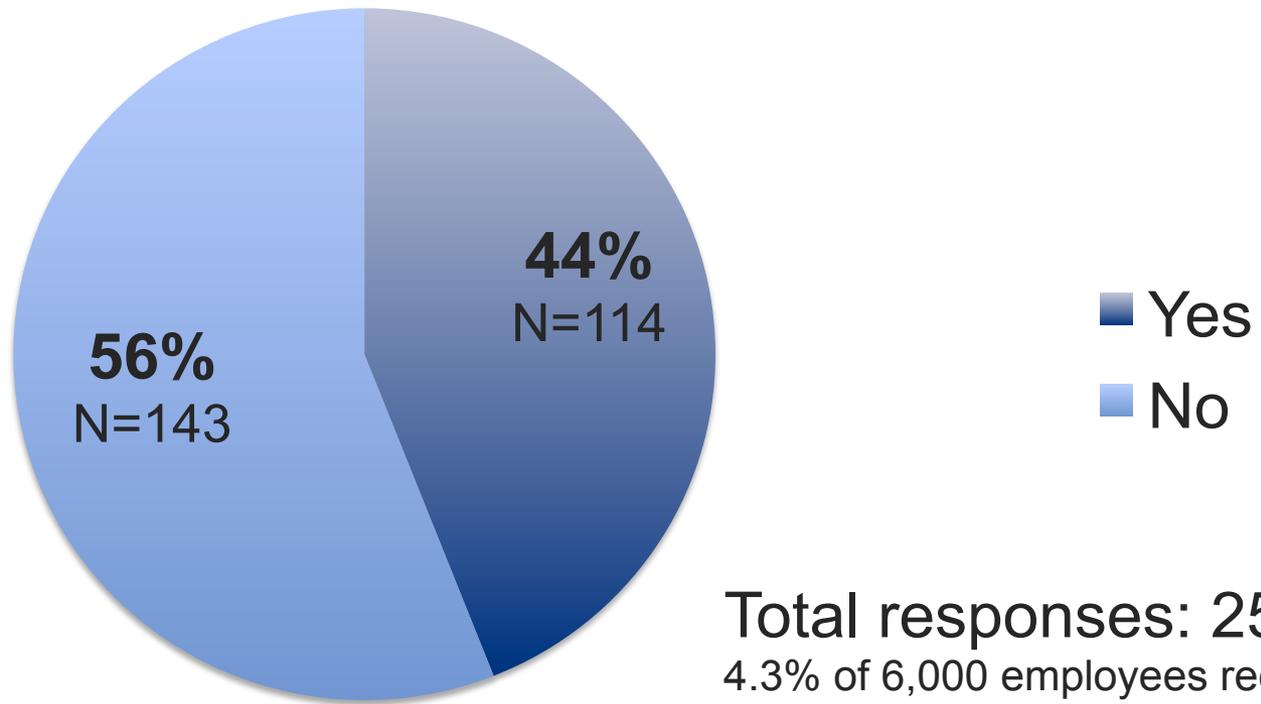
- RTS rate*
- Consultation Log (Sample: New Rx's weeks of 5/23&6/6 &12/5)
- Time to Pickup*

Kiosk Go Live Date: 1/20/16
Study Start: 3/1/16

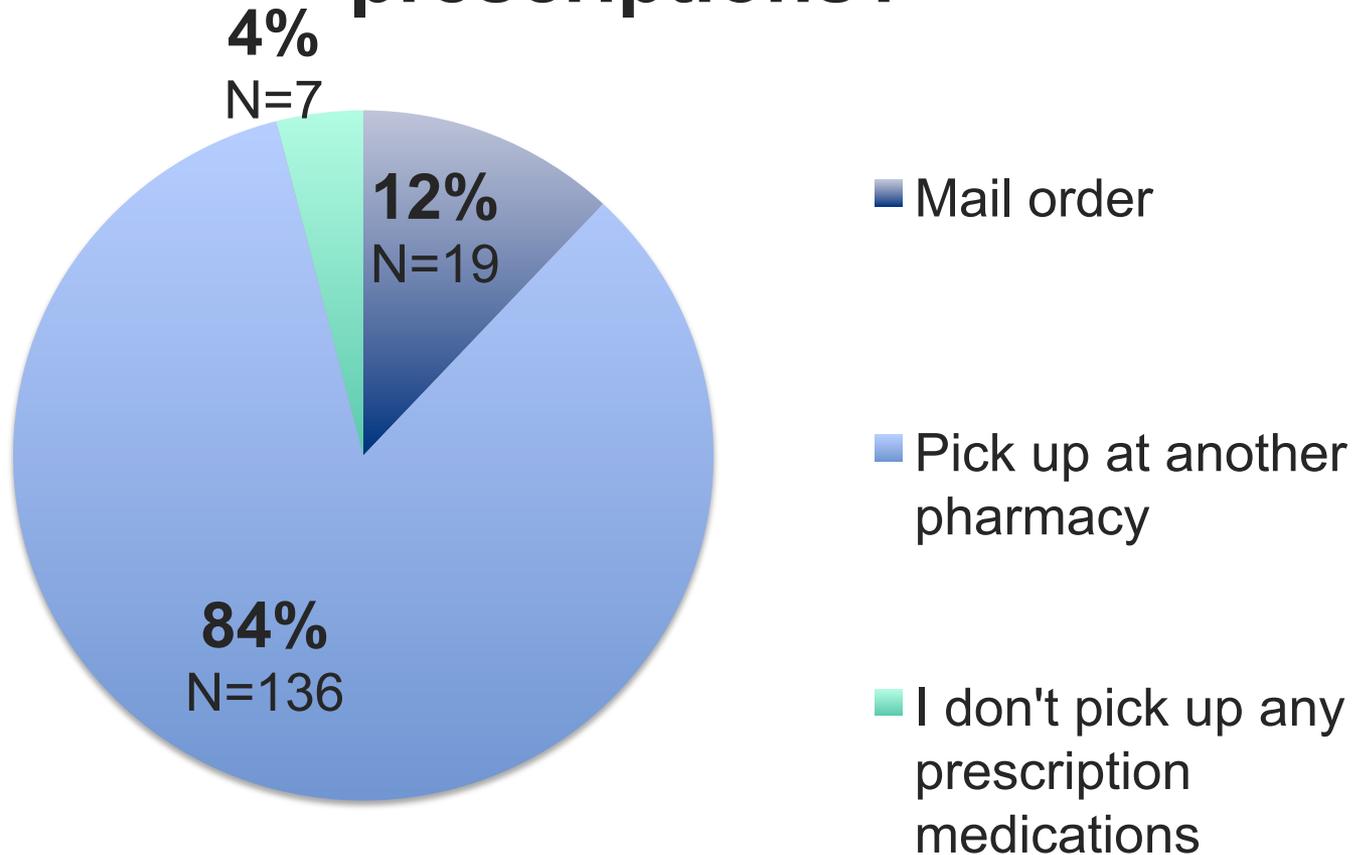
Pre-Kiosk Employee Survey Results

October – November 2015

Do you pick up your or your family's prescriptions from a Sharp Rees-Stealy pharmacy?

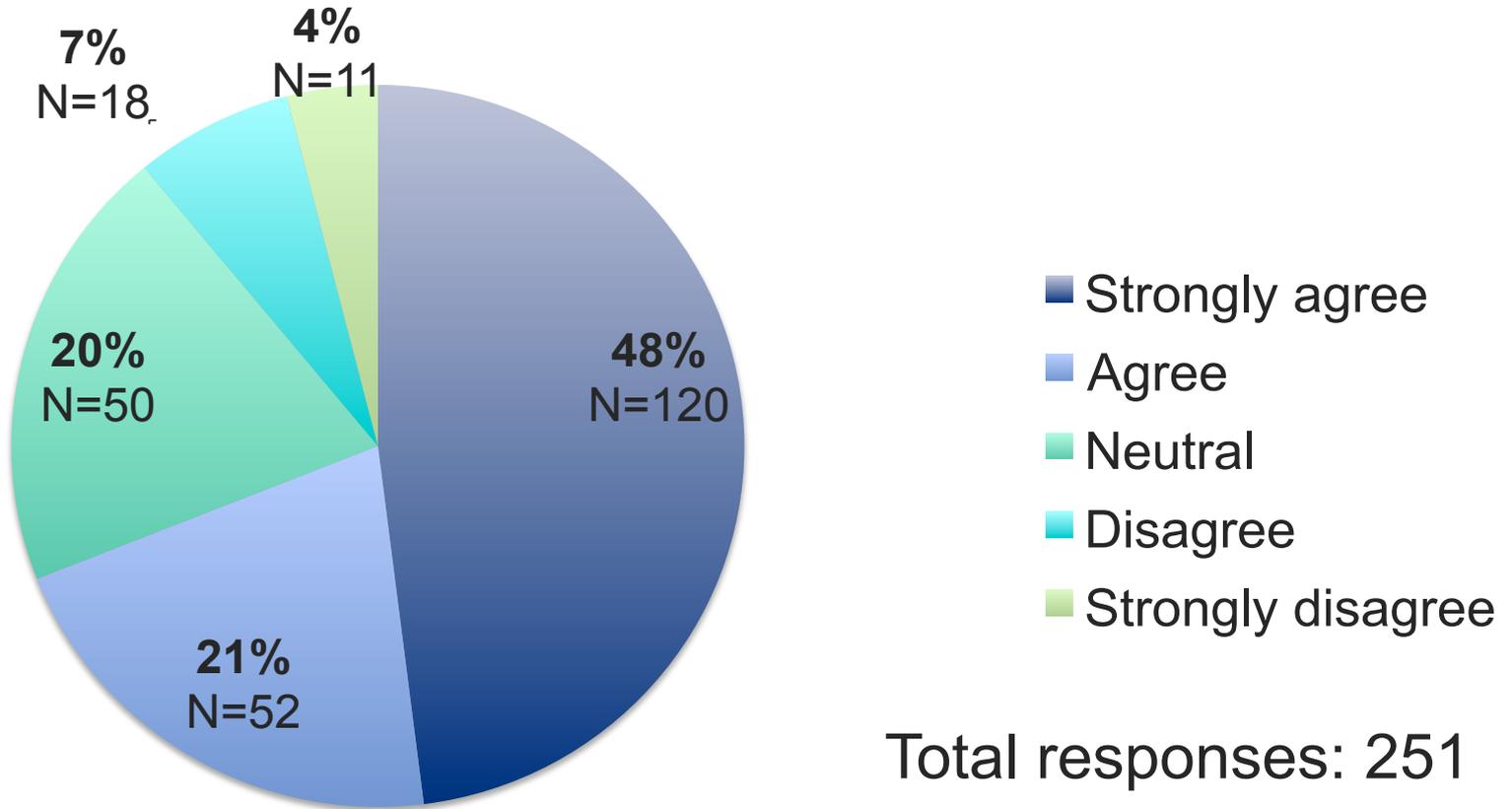


If no, how do you get your prescriptions?

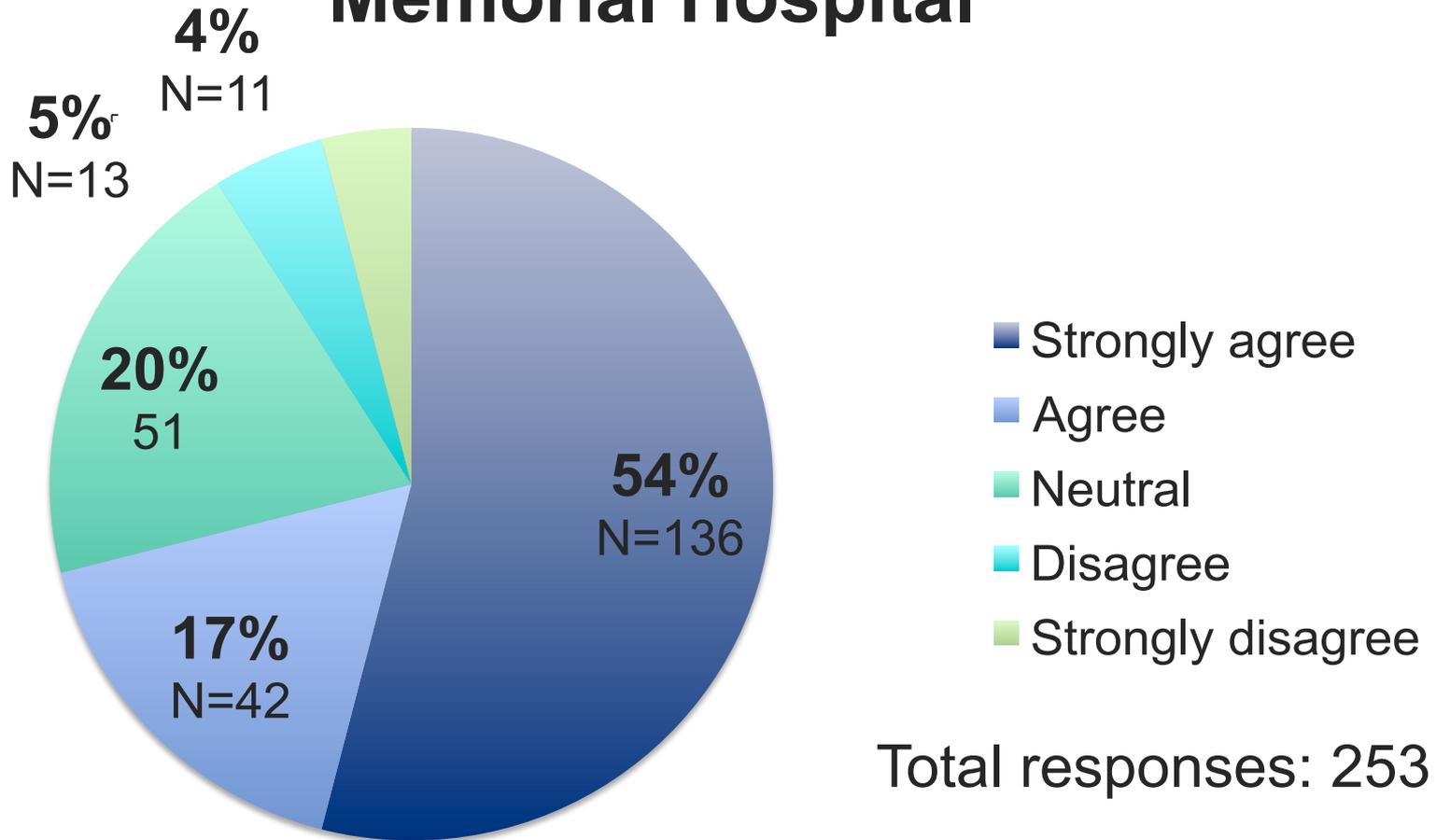


Total responses: 162

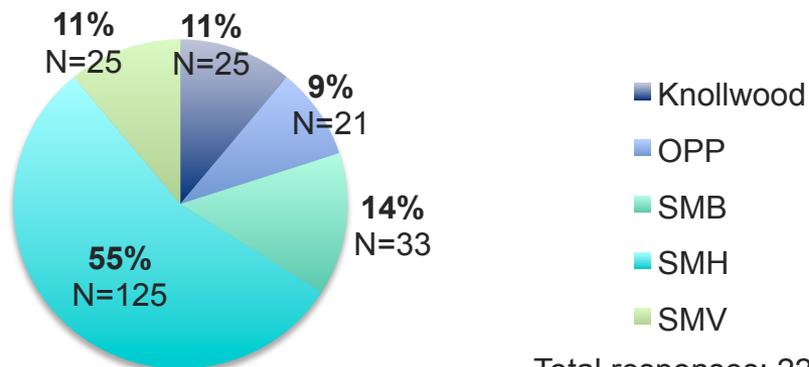
If I had easier access to my prescriptions, I would be more likely to pick up my medications.



I would benefit from being able to pick up prescriptions at Sharp Memorial Hospital



Where is your usual work location?



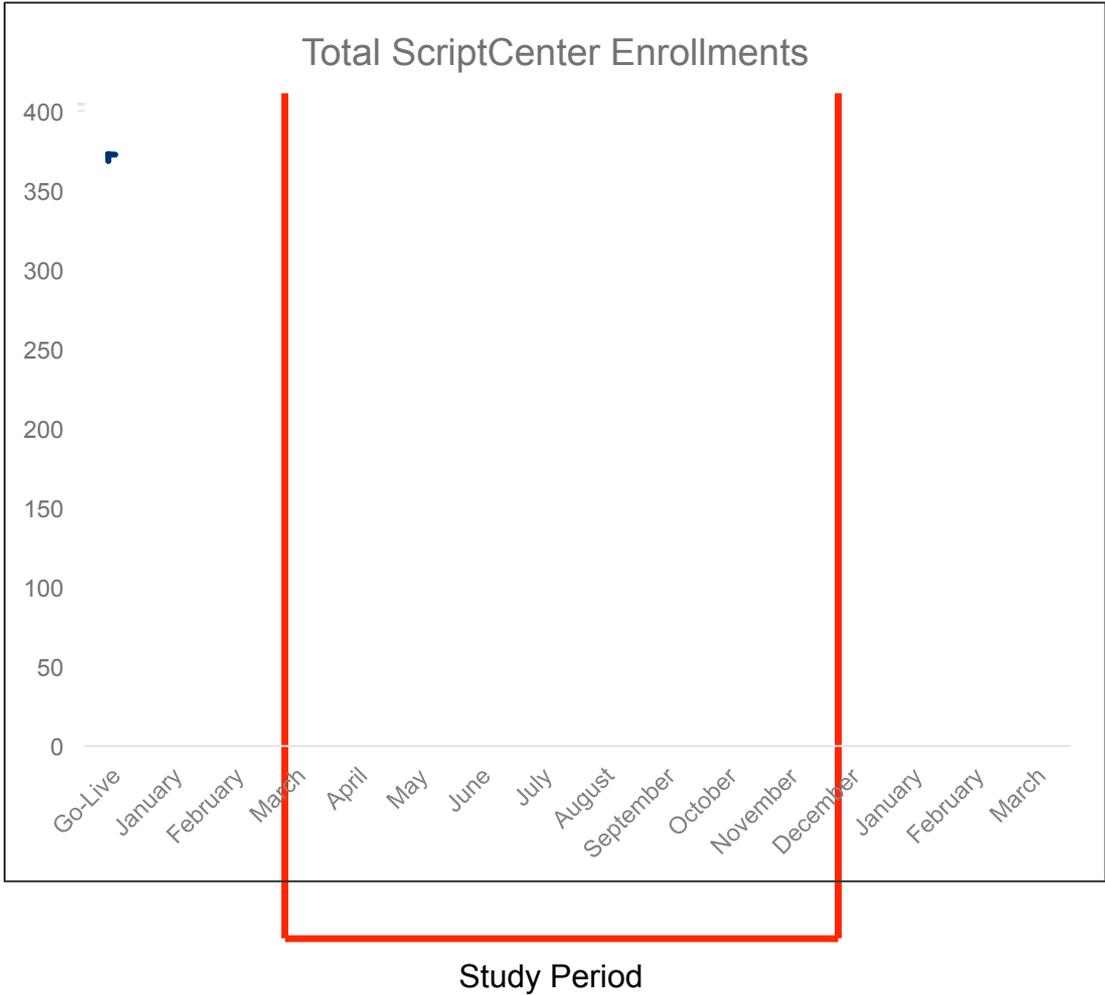
Total responses: 229

- *Greater percentage SMH employees (80%) agreed would be a benefit to pick up at SMH (kiosk location) than employees at other work locations (48% - 66%)*
- *About 40% currently pick up Rx's at SRS Rx – regardless of work location*

Kiosk Operations Data

ScriptCenter Kiosk Activity 1/20/16 through 3/22/17

ENROLLMENT



368 users
(8% Campus Employees)

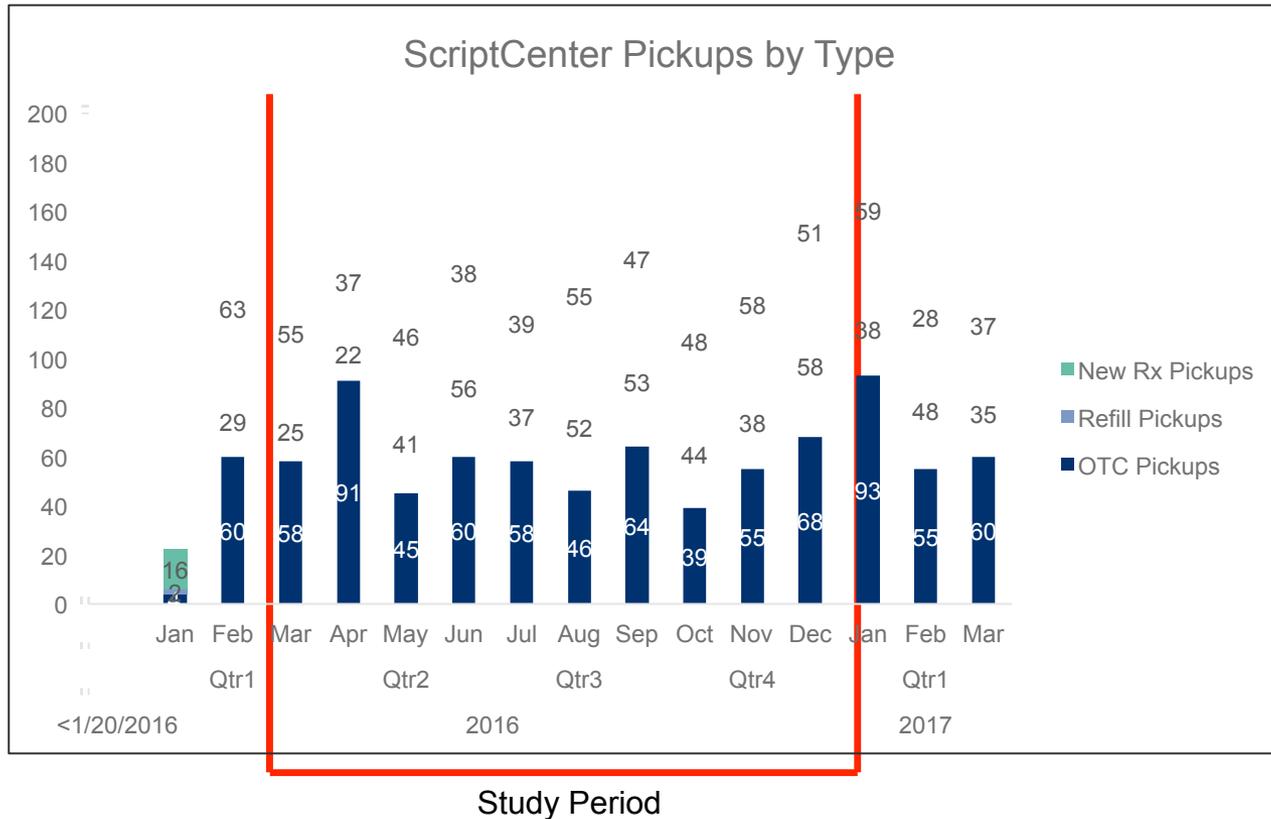
Total Campus Employees
4,820
- Day Shift = 2,592
- PM+ Variable = 2,228

If estimate 2 per household
= 9,640

ScriptCenter Kiosk Activity 1/20/16 through 3/22/16

Pickups by Type

Kiosk Go Live Date: 1/20/16
Study Start: 3/1/16 Study End: 12/31/16

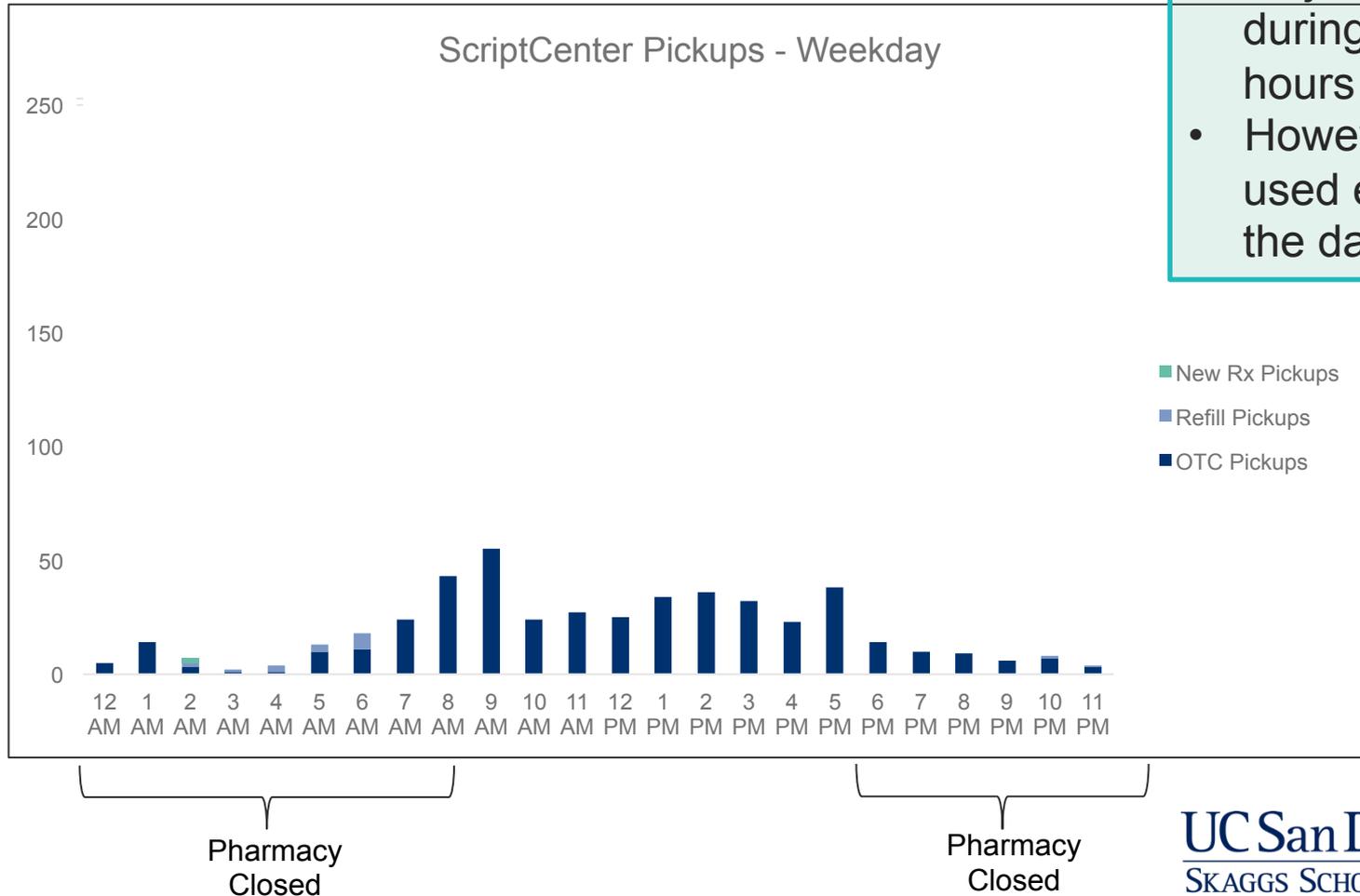


- Fairly evenly divided among
 - New Rxs,
 - Refill Rxs
 - OTCs

368 Users

New prescription # (number) is ScriptCenter tracking method, some may not be "new" to pharmacy or patient

ScriptCenter Kiosk Activity 3/1/16 through 12/31/16 (study period)

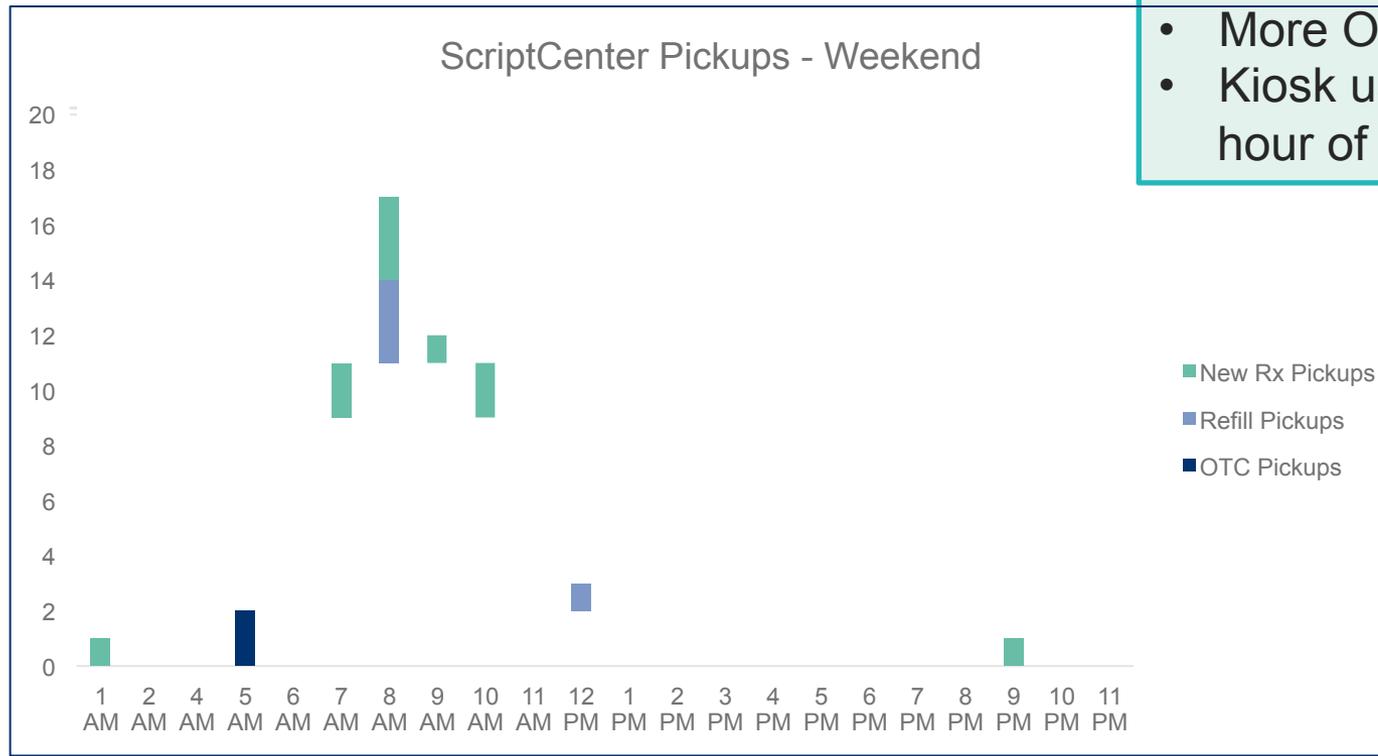


- Majority picked up during pharmacy hours
- However, kiosk used every hour of the day

368 Users

Day Shift = 2,592 PM+ Variable = 2,228

ScriptCenter Kiosk Activity 3/1/16 through 12/31/16 (study period)



- Lower volume on weekend
- More OTCs
- Kiosk used every hour of the day

368 Users

Pharmacy Closed

ScriptCenter Kiosk During vs. After Hours Pickup (*study period*)*

1,484 Total Pickups

1,067 (72%) During pharmacy hours
417 (28%) After pharmacy hours

474 New Rx Pickups

366 (77%) During pharmacy hours
108 (23%) After pharmacy hours

426 Refill Rx Pickups

349 (82%) During pharmacy hours
77 (18%) After pharmacy hours

584 OTC Pickups

352 (60%) During pharmacy hours
232 (40%) After pharmacy hours

- Majority of Rx's (new and refill) picked up during pharmacy hours
- OTC pickups more evenly split

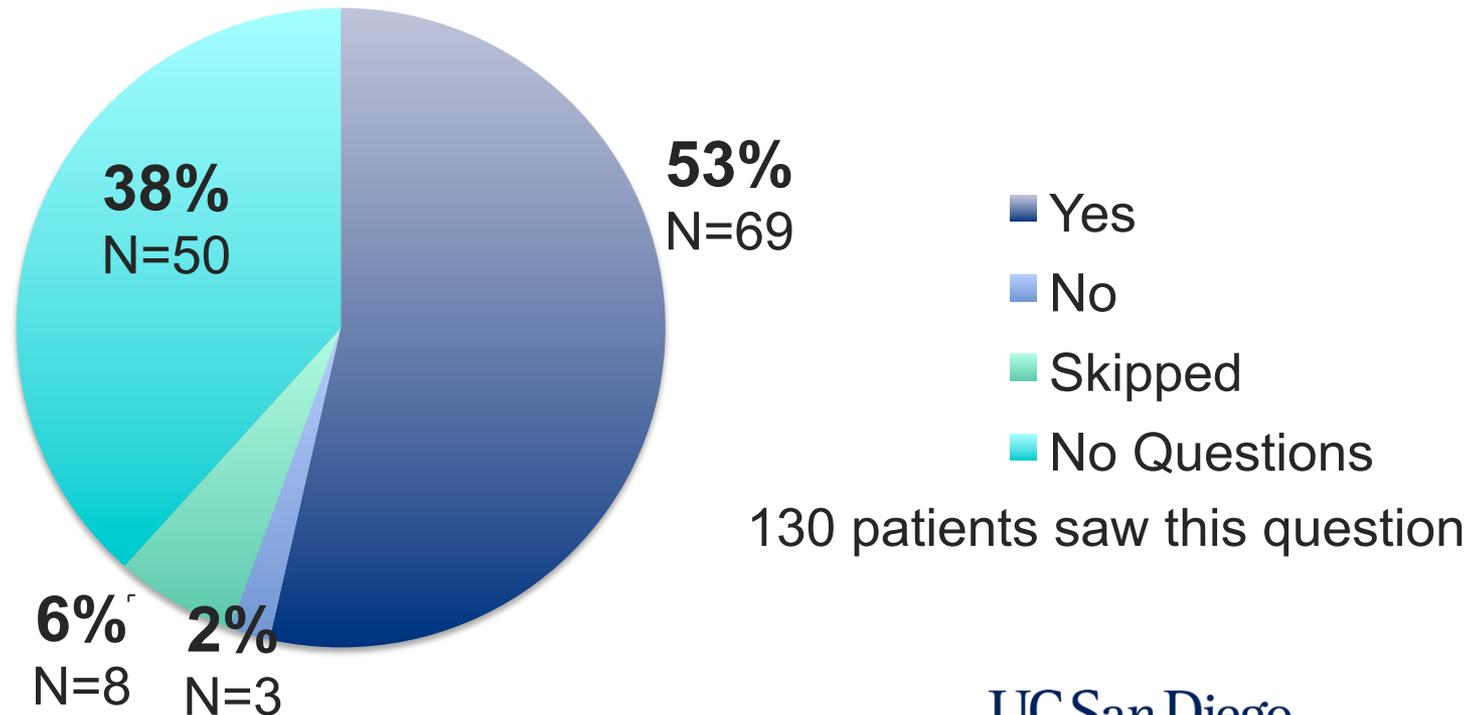
Day Shift: 2,592
PM + Variable: 2,228

368 Users

* Previous updates to Enforcement Committee had included pre-study period. After hours includes weekday & weekend times pharmacy is closed.

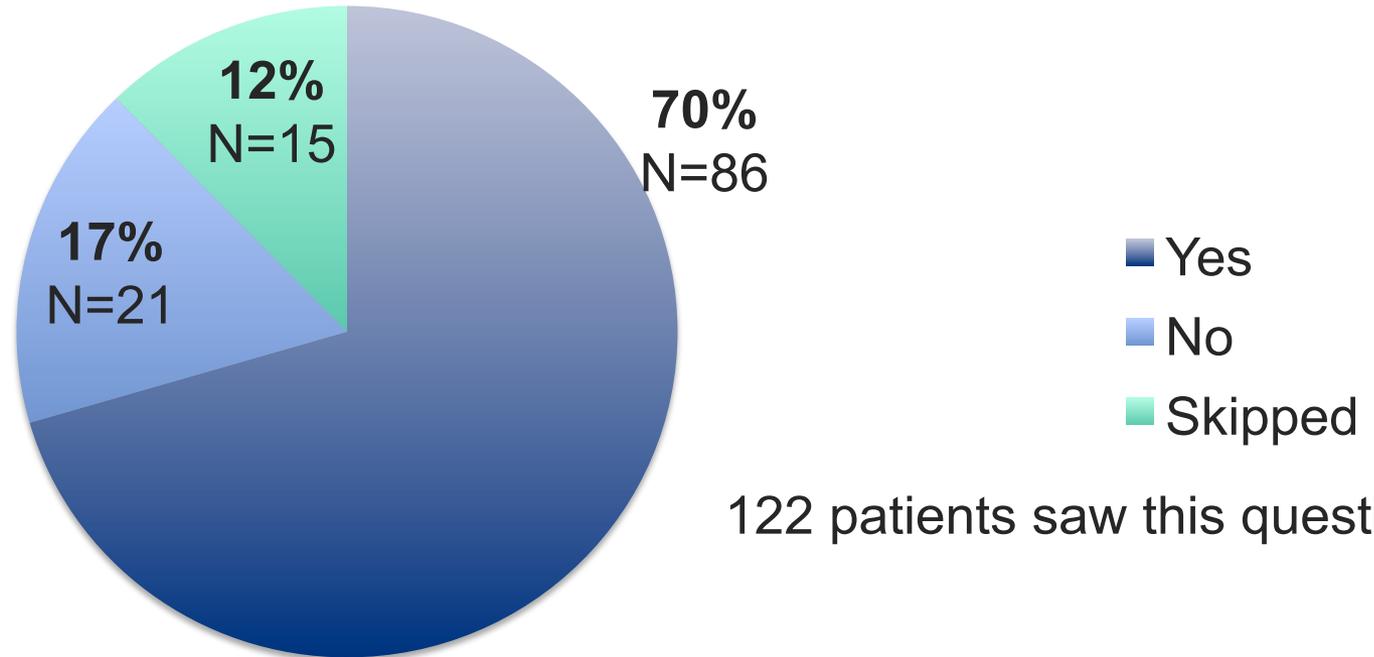
Post-Kiosk Use Satisfaction Survey

Do you feel your questions were answered regarding the prescriptions you picked up today?



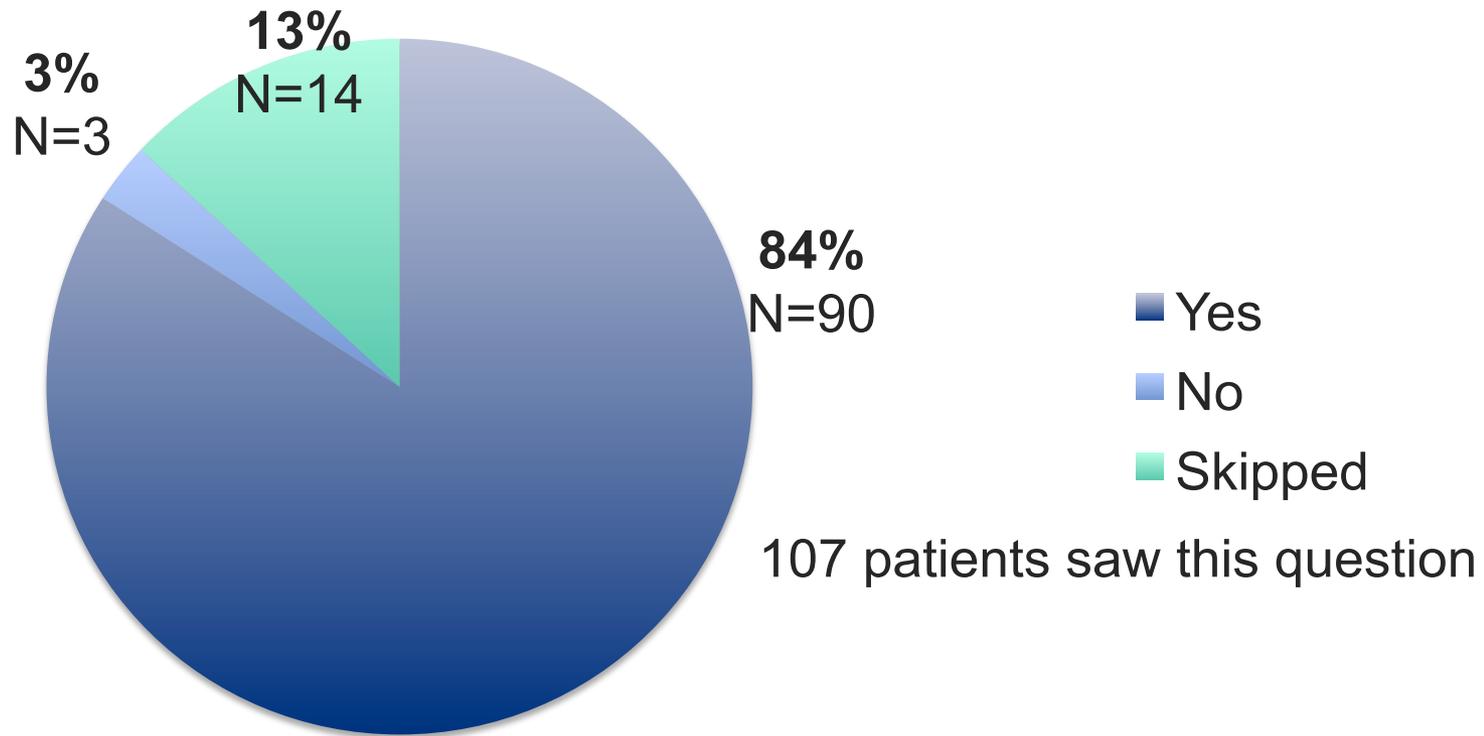
Percentages do not add to 100% due to rounding error

If you have questions for a pharmacist regarding the prescriptions you picked up today, do you know where to call?

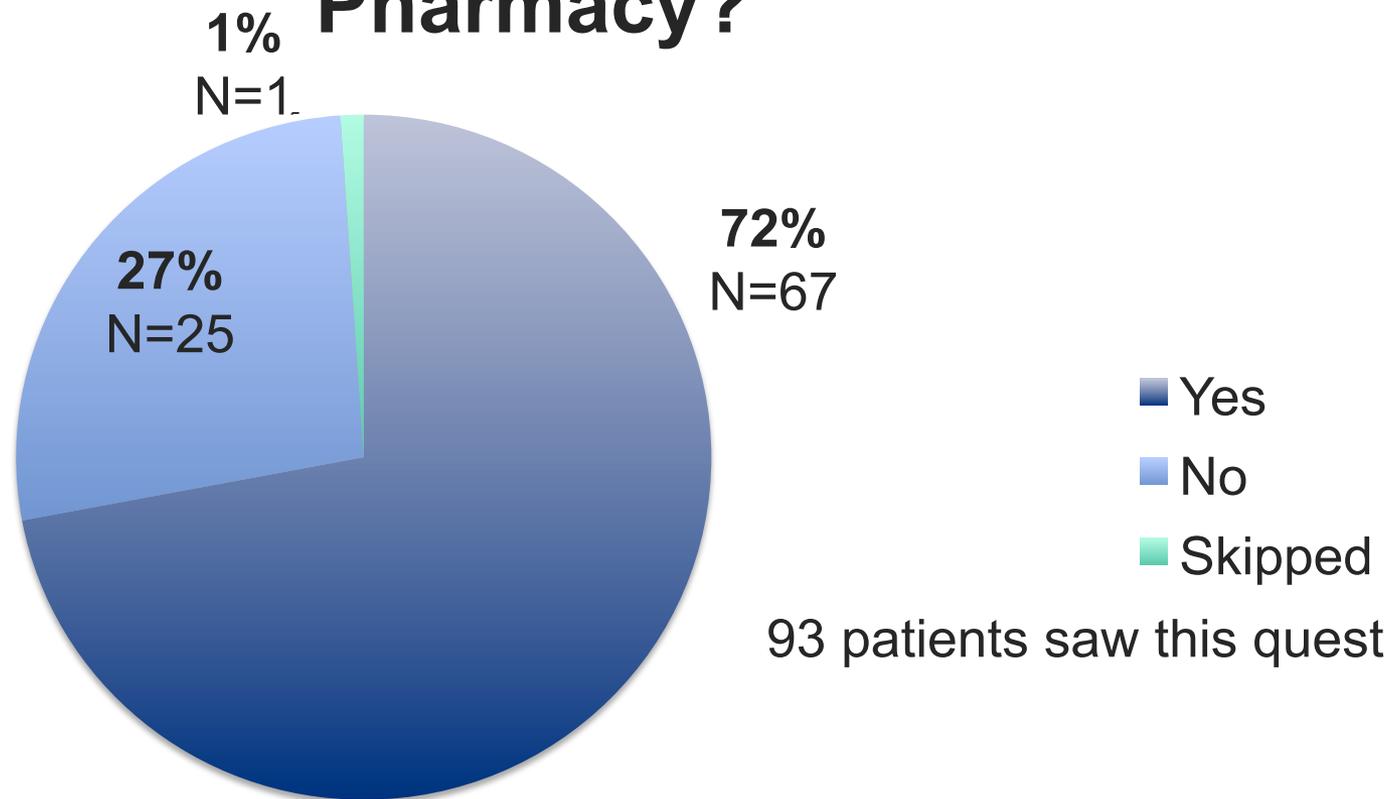


Percentages do not add to 100% due to rounding error

Is the convenience of after-hours prescription pick-up an important reason to use this pharmacy?



Is ScriptCenter a main reason for you to use the Sharp Rees Stealy Pharmacy?



93 patients saw this question

Regular Counter vs. Kiosk

RTS Rate: Regular Counter vs. Kiosk

	Total Rx Filled	Total Rx Picked Up	Total Rx RTS	Mean* Monthly RTS (%)
Regular Counter (6 months prior)	4,924	4,668	256	5.2 ± 1.2
Regular Counter (study period)	7,015	6,643	372	5.3 ± 1.3
Kiosk**	943	893	50	5.0 ± 3.9

No significant difference in mean RTS at Kiosk vs. Regular Counter
(p = 0.942 6 months prior, p = 0.834 study period)

Regular Counter = Employees and Dependents only to “match” group using Kiosk

* Monthly mean over 10 month study period or 6 month pre-study

** 1 Kiosk patient had 3 RTS for 2 and 4 RTS for 1 of 10 months,

1 Kiosk patient had 1 RTS for 4 and 4 RTS for 2 of 10 months

Time Verify to Pick up: Regular Counter vs Kiosk

	Days (Mean ± SD)	Hours (Mean ± SD)	Range
Regular Counter	1.8 ± 0.2	42.2 ± 3.9	15 sec to 28.9 days
Kiosk	3.0 ± 0.6	71.5 ± 14.5	7 min to 17.6 days

Mean time to pick up was greater at Kiosk vs. Regular Counter
(p <0.001)

Differences by Therapeutic Categories

Antibiotics

Antifungals

Antivirals

Antiparasitics

Contraceptives*

Antidiabetics

Cardiovascular Agents

Antihyperlipidemics*

Cough & Cold Products

Respiratory Products

Antidepressants*

Anticoagulants

*Dermatologic Agents**

Diagnostic Aids*

*Other Class**

Time to Pick Up: Kiosk mean greater (range 1.4 to 4.9 days)

** RTS %: Kiosk rate greater (range 0.3 to 10.1 percentage points)*

Data in appendix slides.

Patient Consultations: Counter vs. Kiosk

	Counter (sample)	Kiosk
Number of consultation logs	151	169
n(%) consultations patient had:		
• no more questions	100 (66.2%)	137 (81.1%)
• more questions	51 (33.8%)	32 (18.9%)
Average number questions if patient had more questions	1.1 (56 Q's/51 logs)	1.1 (35 Q's/32 logs)

Percentage consultations with *no more questions* greater at Kiosk vs. Regular Counter ($p = 0.002$)

A sampling of counseling sessions at the Regular Counter was conducted. Logs completed during 3 one week periods (May, June, December 2016)

Types of Patient Questions

- Kiosk Operations
- General Pharmacy Operations
- Drug Related (including cost)

Question Type	Regular counter	Kiosk
Kiosk Operations	0 (0%)	5 (15%)
General Pharmacy	0 (0%)	4 (12%)
Drug Related	44 (100%)	24 (73%)

Based on examination of “Types of Questions” appendix slides. Number of questions lower than on “Patient Consultations: Counter vs. Kiosk” slide since appendices did not report duplicates and pharmacist did not always specify type of question.

Consultations: Initiation, Conduct & Duration

Consult initiated by*	Regular counter	Kiosk
Pharmacist	151 (100%)	144 (85.7%)
Patient	0 (0%)	24 (14.3%)

Kiosk patients received text message: asked to call back for counseling

Consult conducted	Regular counter	Kiosk
Counter	151 (100%)	1 (0.6%)
Phone	0 (0%)	168 (99.4%)

All but one Kiosk consultation conducted via phone

Consult duration	Regular counter	Kiosk
Mean (SD)	3.5 ± 2.1	2.6 ± 1.7
Range	1-10 min	1-10 min

Mean consult duration shorter at Kiosk vs Regular Counter (p =0.009)

* Pharmacist includes Pharmacy Intern

Missing data = 0 Counter and 1 at Kiosk: Pharmacist did not record.

Consultations: Day of Week and Time of Day Kiosk & Regular Counter Combined

Day	Mon	Tues	Wed	Thurs	Fri	Sat	Sun	Total
# Consults	60	66	62	66	66	0	0	320
% of Total	18.8%	20.6%	19.4%	20.6%	20.6%	0%	0%	

All consultations were performed on weekdays.

Only 3 consultations performed after hours
(all for new prescriptions)

Pharmacist counseling available 24/7

Pharmacist Assessments

- Ability to build therapeutic relationship with patient
- Ability to establish a management plan with patient
- Ability to negotiate “safety netting” strategies with patient

Scale

Not Able		Partially Able		Fully Able		Not Applicable
0	1	2	3	4		5

Ability to build therapeutic relationship with patient

Not Able		Partially Able		Fully Able
0	1	2	3	4

Score	Counter		Kiosk	
	Number	Percent	Number	Percent
0	0	0.0%	1	1.0%
1	1	0.7%	0	0.0%
2	4	2.8%	4	4.1%
3	79	56.0%	41	41.8%
4	57	40.4%	52	53.1%

Very similar ability to build therapeutic relationship.

N/A: Counter n=10, Kiosk n=71
 Percentages may not add to 100% due to rounding error

Ability to establish a management plan with patient

Not Able		Partially Able		Fully Able
0	1	2	3	4

Score	Counter		Kiosk	
	Number	Percent	Number	Percent
0	0	0.0%	2	3.6%
1	0	0.0%	1	1.8%
2	2	1.5%	3	5.4%
3	77	57.0%	31	55.4%
4	56	41.5%	19	33.9%

Very similar ability to establish management plan.

N/A: Counter n=16, Kiosk n=113
 Percentages may not add to 100% due to rounding error

Ability negotiate “safety netting” strategies with patient

Not Able		Partially Able		Fully Able
0	1	2	3	4

Score	Counter		Kiosk	
	Number	Percent	Number	Percent
0	0	0.0%	2	2.8%
1	0	0.0%	2	2.8%
2	2	1.5%	3	4.2%
3	71	54.6%	38	53.5%
4	57	43.8%	26	36.6%

Very similar ability to negotiate “safety netting”.

N/A: Counter n=21, Kiosk n=98
 Percentages may not add to 100% due to rounding error

Conclusions

Majority of employees surveyed agreed

- More likely pick up medications if had easier access
- Would benefit from being able to pick up at work

Kiosk usage

- Fairly evenly divided among New, Refill and OTCs
- Majority RxS (new & refill) picked up during pharmacy hours
 - However, kiosk used every hour of the day

Majority Kiosk users agreed

- Questions were answered regarding prescriptions
- If had questions knew how to call pharmacist

Conclusions (continued)

Kiosk vs. Regular Counter

- No significant difference in mean RTS
- Mean time to pick up was about one day greater at Kiosk
- Percentage consultations with *no more questions* greater at Kiosk
- No appreciable difference in pharmacists' assessment of their ability to counsel

Next Steps

- Q2 2017 Report Results to Board
 - April 18th, 2017 Enforcement Committee
 - May 3-4th, 2017 Board
- Continue Kiosk operation until regulation
1713 revised



Questions?

UC San Diego
SKAGGS SCHOOL OF PHARMACY
AND PHARMACEUTICAL SCIENCES

Appendices

Pre-Kiosk Sharp Employee Survey

Subject:

Employee Prescription Delivery Service: Tell Us Your Thoughts!

Body of E-mail:

Sharp Rees-Stealy pharmacies are developing a way to deliver new and refill prescriptions for Sharp Metropolitan Medical Campus employees. The prescriptions would be available for convenient pick-up, any time or day at Sharp Memorial Hospital. Tell us your thoughts on this service by answering [a one-minute survey](#).

RTS: regular counter vs kiosk, by therapeutic class

Raw counts (not means due to small numbers)	COUNTER (study period)			KIOSK		
	Therapeutic Class	Total Rx	Total RTS	RTS Rate (%)	Total Rx	Total RTS
Antibiotics	343	16	4.7	25	0	0
Antifungals	49	1	2.0	8	0	0
Antivirals	87	3	3.4	11	0	0
Antiparasitics	8	3	37.5	3	0	0
Contraceptives	148	5	3.4	42	4	9.5
Antidiabetics	582	34	5.8	72	4	5.6
Cardiovascular Agents	282	36	12.8	153	4	2.6
Antihyperlipidemics	495	20	4.0	66	3	4.5
Cough & Cold Products	100	8	8.0	15	0	0
Respiratory Products	211	19	9.0	47	1	2.1
Antidepressants	423	16	3.8	73	3	4.1
Anticoagulants	98	1	1.0	2	0	0
Dermatological Agents	277	22	7.9	24	3	12.5
Diagnostic Aids	201	15	7.5	17	3	17.6
Other class	3711	173	4.7	385	25	6.5

Time from verify to pick up: regular counter vs kiosk, by therapeutic class

Therapeutic Class	REGULAR COUNTER		KIOSK	
	Days	Hours	Days	Hours
Antibiotics*	1.1 ± 0.4	27.2 ± 9.1	4.0 ± 3.2	96.2 ± 77.2
Antifungals*	0.9 ± 1.2	20.6 ± 28.1	3.2 ± 2.4	77.6 ± 57.6
Antivirals	1.3 ± 1.1	32.0 ± 26.7	3.5 ± 3.6	83.9 ± 86.0
Antiparasitics	0.6 ± 0.3	14.1 ± 8.1	4.7 (one Rx)	113.8 (one Rx)
Contraceptives	1.8 ± 0.6	44.0 ± 14.8	2.6 ± 1.7	62.1 ± 40.7
Antidiabetics	1.8 ± 0.5	42.7 ± 11.8	2.2 ± 1.4	52.5 ± 33.4
Cardiovascular Agents*	1.8 ± 0.3	43.4 ± 6.0	3.2 ± 1.2	77.2 ± 28.9
Antihyperlipidemics	1.9 ± 0.4	45.1 ± 10.5	2.4 ± 1.0	57.6 ± 23.3
Cough & Cold Products	1.7 ± 0.6	40.4 ± 15.6	2.7 ± 2.7	63.8 ± 65.9
Respiratory Products*	1.6 ± 0.8	38.9 ± 19.5	3.2 ± 2.1	75.7 ± 51.0
Antidepressants	2.3 ± 0.6	56.7 ± 15.3	2.5 ± 0.9	60.6 ± 22.7
Anticoagulants*	1.7 ± 0.9	40.8 ± 21.9	6.6 ± 2.1	157.9 ± 50.1
Dermatological Agents*	2.2 ± 0.7	52.5 ± 17.7	4.9 ± 3.6	118.5 ± 85.8
Diagnostic Aids	3.0 ± 1.9	71.9 ± 45.9	2.6 ± 3.4	61.3 ± 81.5
Other class*	1.7 ± 0.2	40.3 ± 5.2	3.2 ± 2.1	74.6 ± 14.7

Counseling Log

Patient has: <small>(write in number)</small> _____ New RA _____ Refill RA	<u>Introduction</u> (Build a Relationship)	<u>Action</u> (Incorporate Patient's Understanding)	<u>Closing</u> (Safety Net Strategy)
Call day & time:	1. Introduce self Yes or No 2. Explain role of pharmacist Yes or No	1. What med is for: Yes or No 2. How to take med: Yes or No	1. What to do if patient had difficulties following the plan RA or No 2. Future appointment or contact provided: Yes or No
Call duration:	3. Confirm patient ID Yes or No 4. Discuss consult purpose: Yes or No	<ul style="list-style-type: none"> • Time of day Yes or No • Length of therapy Yes or No • Missed dose Yes or No 	3. Opportunity to ask additional questions: Yes or No
Consult: <small>(check one)</small> ___ Counter for regular patient ___ Phone for regular patient ___ Phone for walk patient	<ul style="list-style-type: none"> • Structure Yes or No • Desired length Yes or No 5. Has the patient previously talked with a pharmacist about this/these medication(s)? Yes or No	3. What to expect: Yes or No <ul style="list-style-type: none"> • Efficacy Yes or No • DDI Yes or No • S/E Yes or No 	PHARMACIST ASK PATIENT Do you have any more questions about your medication(s) I haven't answered yet? check No/Yes and write in number) _____ No _____ Yes Write in Number of Questions _____
Consult Initiated by: <small>(check one)</small> Pharmacist Patient	6. Invite patient to discuss: Yes or No <ul style="list-style-type: none"> • Medication concerns Yes or No • Health related concerns Yes or No 	4. Invite patient to teach back: Yes or No <ul style="list-style-type: none"> • Patient understands Yes or No • Questions answered Yes or No 5. Lifestyle and prevention: Yes or No, N/A <ul style="list-style-type: none"> • Additional information Yes or No, N/A • Referral Yes or No, N/A 	What questions did the patient have?
Pharmacist-Assessment	Ability to <u>build therapeutic relationship</u> with patient RA Not Able Partially Able Fully Able 0 1 2 3 4	Ability to <u>establish a management plan</u> with patient RA Not Able Partially Able Fully Able 0 1 2 3 4	Ability to <u>negotiate "safety netting" strategies</u> with patient RA Not Able Partially Able Fully Able 0 1 2 3 4

ScriptCenter Kiosk Consultations *(study period)*

	Total prescriptions with a new Rx #, pharmacist released for pick up at ScriptCenter	New Rx's Requiring Counseling (including transferred) Counseling Provided	New Rx's Not Requiring Counseling <small>(due to Sharp re-write with no changes)</small> Counseling Not Required
March	49	28	21
April	37	17	20
May	41	28	13
June	42	22	20
July	45	32	13
August	63	33	30
September	55	23	32
October	49	16	33
November	59	38	21
December	58	18	40

- New prescription # (number) is ScriptCenter tracking method, some may not be “new” to pharmacy or patient.
- Pharmacist released Rx after required counseling provided.
- Total Rx’s released may not match number of pick-ups per month on previous slides due to pick-up occurring in month following release.

Month	Types of Questions Asked at Kiosk
March	<ul style="list-style-type: none"> • Where do I pick up the medication? • How does the kiosk work? • Do I have additional refills on my medications? • Are you going to call me every time moving forward?
April	<ul style="list-style-type: none"> • Whether she can start taking it today as she is already on her period?
May	<ul style="list-style-type: none"> • Can I use both medications at the same time?
June	<ul style="list-style-type: none"> • Can you check to see if I have more refills than what the doctor charted? • Should I take all my meds with food?
July	<ul style="list-style-type: none"> • N/A
August	<ul style="list-style-type: none"> • I'm switching from Januvia, is it cheaper? • Can I take 2 doses of the antibiotic today? • Does it cause nervousness? • How/when to take food? • First time using the kiosk. Can you explain how to pay? • Is it the right prep my doctor ordered?

Month	Types of Questions Asked at Kiosk
September	<ul style="list-style-type: none"> • How many Rx's do I have? • Is it safe to take while pregnant? • Is it ok to take with Humira? • When should I start this medicine?
October	<ul style="list-style-type: none"> • Checking with increased dose of medication • Is it the same dose as my old medication? • Is it ok to take with probiotics?
November	<ul style="list-style-type: none"> • How many days supply is the antibiotic? • Can I have 3 months supply at a time? • What is my copay? • Will it interfere with my BP meds? • Can I get my other Rx's refilled?
December	<ul style="list-style-type: none"> • Do I have another pain medication to pick up? • Did my doctor authorize my birth control pills? • Do I need a prescription for ibuprofen 800 mg? • Did my doctor prescribe glucometer/strips/lancets? • Does the the kiosk have refrigeration? • Which one is the antibiotic? Is it a high dose? • How can I get my Rx transferred to you?

Month	Types of Questions Asked at Counter
May	<ul style="list-style-type: none"> • Hydration question • Patient is having surgery and wants to know start date (patient will call MD to double check) • Are side effects similar to prednisone? • MD stated that it is ok to use in both eyes. Is it ok? • What are the side effects? • Can I take this medication with food? • When to take the drug? • Is there a DDI between Venlafaxine and Ventolin? • Applying inside the anal area? Direction on label said not to apply inside anal area. Patient said he was told to apply inside anal area and will call and confirm with doctor. • Can I still take my morning high BP medication? • Patient needs to reschedule colonoscopy due to lack of diet education prior to procedure. • What food is ok to eat while on medication? • What other strengths does Zolpidem come in?

A sampling of counseling sessions at the Regular Counter was conducted. Logs completed during 3 one week periods (May, June, December 2016)

Month	Types of Questions Asked at Counter
June	<ul style="list-style-type: none"> • When can I eat? • Reschedule Colonoscopy due to misinformation about diet restrictions • Does it have to be taken in the morning? • Does Simvastatin need to be stopped prior to colonoscopy? • Can I take it with Naproxen? • Can I still take my Calcium MVI before colonoscopy? • Can I still take my BP/DM meds before colonoscopy? • Can I take the medication with food? • Can I take my Blood pressure meds on the day of the colonoscopy? • How do I dispose of this if I am not taking it? • Do I need to stop my high cholesterol medications prior to colonoscopy?

A sampling of counseling sessions at the Regular Counter was conducted. Logs completed during 3 one week periods (May, June, December 2016)

Month	Types of Questions Asked at Counter
December	<ul style="list-style-type: none"> • Do I have another pain medication to pick up? • How to prepare medication? When to take medication? • Swish or gargle? If throat pain. • BP meds? • Is this medication refrigerated? Should this med be swallow or put on tongue? • Can this medication be taken with yogurt or probiotics? • Is it ok with breast feeding? • Does he have to take it with food? • Does it taste bad? • Can he take this medication now, before driving? • What do I do If I get nausea? • Should this be taken with food? • Is this med administered the same as Lantus? • Can I take the first two at once? • How much do I apply? Does it have to be refrigerated? • What time of day should I take it? • Can I suck on a lozenge while preparing for colonoscopy? • Does pt have to get up in the middle of the night to take the prescription? • Does it interact with Percocet? • Can I drink it all at once?

A sampling of counseling sessions at the Regular Counter was conducted. Logs completed during 3 one week periods (May, June, December 2016)

Attachment 2

State Board of Pharmacy- Enforcement Committee
 Review- Pharmacy Automation Technology

Background: Multiple pharmacy automation vendors provided presentations at the February 17, 2017 Board meeting. These vendors provided an overview of existing technology, and dispensing/restocking workflow for their respective products. Each vendor also requested modification of existing pharmacy law to accommodate use of their technology. The Enforcement Committee was asked to review these requests and provide recommendations to the full Board of any changes needed to the law to enable technology that is believed to be safe, accurate, minimizes ability for drug diversion, and improves patient access.

In an effort to provide a framework for this discussion, a table was prepared that outlines the various technologies presented (so far) as well as policy discussion items for each.

CATEGORY 1: Medication dispensing technology that is accessed by Nursing at the remote site to obtain medications that are then administered to the patient at the remote site. Examples of remote sites include skilled nursing facilities and correctional settings.

Category I Technology	Description	Medication dispensing	Replenishment of medications	Transport of Medication	Who performs replenishment	Policy discussion items
A1	Automated Dispensing Cabinets- hosted by pharmacy not physically located at remote site	Nurse at remote site	Host Pharmacy replenishes medication in unit dose packets. Stock levels and reports are accessed from the pharmacy location to facilitate replenishment	Sealed tamper-proof sealed plastic container with a chip that identifies the canister. Container will not allow placement into technology if tampered with.	Various workflows described: Nurse at remote site Pharmacist physically places into ADC Pharmacy technician, under pharmacist supervision, physically places into ADC	<ul style="list-style-type: none"> Is the medication stored in the remote site ADC part of the pharmacy inventory? If the licensed clinic owns the ADC, what role does pharmacy play in restocking? Who should be allowed to place the sealed tamper-proof plastic container into the ADC? Is Nursing allowed to place the tamper-proof canister into the ADC after receipt from the pharmacy? If controlled drugs are supplied, does this require a DEA 222 form for each restock? Should the remote site be licensed?
A2	Automated Dispensing Cabinets- hosted by pharmacy not	Nurse at remote site	Host Pharmacy replenishes medication in unit dose packets. Stock levels and reports	Sealed medication delivery bags are utilized to transport medication	Various workflows described: Nurse at remote site Pharmacist	<p>Same as A1 above, plus:</p> <ul style="list-style-type: none"> Are there concerns for drug diversion due to less than secure transport workflow? How will pharmacy be assured that all medication arrived at location?

	physically located at remote site		are accessed from the pharmacy location to facilitate replenishment	from pharmacy to remote site. May or may not have tamper proof seal; no plastic container. Remote site replenishment involves placement of individual doses into ADC cell manually (no canister with chip)	physically places into ADC Pharmacy technician, under pharmacist supervision, physically places into ADC	
B1	Medication Canisters with patient-specific packaging that is performed at the remote site	Nurse at remote site-typically in 24-hour patient-specific plastic packets for oral solids	Host pharmacy replenishes drug-specific oral solid canisters that are placed into the device at the remote site. Stock levels and reports are accessed from the pharmacy location to facilitate replenishment	Sealed tamper-proof sealed plastic container with a chip that identifies the canister. Container will not allow placement into technology if tampered with.	Nurse physically places the drug-specific oral solid canister into the device.	<ul style="list-style-type: none"> • Is the medication stored at the remote site part of the pharmacy inventory? If the licensed clinic owns the technology, what role does pharmacy play in restocking? • Who should be allowed to place the sealed tamper-proof plastic container into the device? Is Nursing allowed to place the tamper-proof canister into the device after receipt from the pharmacy? • If controlled drugs are supplied, does this require a DEA 222 form for each restock? • Should the remote site be licensed?

CATEGORY 2: Medication dispensing technology that is accessed by healthcare providers in order to provide the patient at the remote site to access medications for at home self-administration

Category I Technology	Description	Medication dispensing	Replenishment of medications	Transport of Medication	Who performs replenishment	Policy discussion items
A1	Robot that dispenses medication through	Staff at remote site. Robot labels the patient	Host Pharmacy replenishes medication in drug specific	Various	Staff at remote site	<ul style="list-style-type: none"> • Is the medication stored in the remote site part of the pharmacy inventory? If the licensed clinic owns the technology, what role does pharmacy play in restocking? • Who should be allowed to place the containers into the

	direct real-time link with pharmacist	medication containers per information input by remote pharmacist.	containers. Stock levels and reports are accessed from the pharmacy location to facilitate replenishment			<p>technology? Is Nursing allowed to place the medication after receipt from the pharmacy?</p> <ul style="list-style-type: none"> • Some vendors cited the use of a wholesaler to replenish the inventory in the automated device. Should the board allow wholesalers to receive and restock medication on behalf of a pharmacy? • If controlled drugs are supplied, does this require a DEA 222 form for each restock? • Should the remote site be licensed? • How is patient counseling performed? Is the patient interaction conducive to patient teaching (screen size, technology, etc.) Is patient counseling always provided (some state only upon patient request) • Does the label meet state label requirements? • How is drug diversion detected if transport does not include tamper-proof sealed canisters? How is drug diversion detected from a wholesaler or other non-pharmacy replenishment?
A2	Robot that dispenses medication through direct real-time link with pharmacist	Staff at remote site. Staff must assemble medication container, and label printed separately and affix the label to the container at remote site	Host Pharmacy replenishes medication in drug specific containers. Stock levels and reports are accessed from the pharmacy location to facilitate replenishment	Various	Staff at remote site	<p>All of the above plus:</p> <ul style="list-style-type: none"> • Are there any patient safety concerns with someone other than a pharmacist affixing a medication label?
B	Technology that dispenses pharmacy-filled medications to facilitate patient access	Performed within the pharmacy	Host pharmacy places filled patient-specific medication bags into technology to facilitate patient pick-up from a remote location.	Pharmacy	Pharmacy	<p>Current pilot ongoing with UCSD; awaiting pilot results.</p> <ul style="list-style-type: none"> • How is patient counseling performed? • How is drug diversion detected? • Should the remote site be licensed?

Attachment 3

Health and Safety Code § 1261.6 Automated Drug Delivery Systems

- (a) (1) For purposes of this section and Section 1261.5, an "automated drug delivery system" means a mechanical system that performs operations or activities, other than compounding or administration, relative to the storage, dispensing, or distribution of drugs. An automated drug delivery system shall 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.
- (2) For purposes of this section, "facility" means a health facility licensed pursuant to subdivision (c), (d), or (k), of Section 1250 that has an automated drug delivery system provided by a pharmacy.
- (3) For purposes of this section, "pharmacy services" means the provision of both routine and emergency drugs and biologicals to meet the needs of the patient, as prescribed by a physician.
- (b) Transaction information shall be made readily available in a written format for review and inspection by individuals authorized by law. These records shall be maintained in the facility for a minimum of three years.
- (c) Individualized and specific access to automated drug delivery systems shall be limited to facility and contract personnel authorized by law to administer drugs.
- (d) (1) The facility and the pharmacy shall develop and implement written policies and procedures to ensure safety, accuracy, accountability, security, patient confidentiality, and maintenance of the quality, potency, and purity of stored drugs. Policies and procedures shall define access to the automated drug delivery system and limits to access to equipment and drugs.
- (2) All policies and procedures shall be maintained at the pharmacy operating the automated drug delivery system and the location where the automated drug delivery system is being used.
- (e) When used as an emergency pharmaceutical supplies container, drugs removed from the automated drug delivery system shall be limited to the following:
 - (1) A new drug order given by a prescriber for a patient of the facility for administration prior to the next scheduled delivery from the pharmacy, or 72 hours, whichever is less. The drugs shall be retrieved only upon authorization by a pharmacist and after the pharmacist has reviewed the prescriber's order and the patient's profile for potential contraindications and adverse drug reactions.
 - (2) Drugs that a prescriber has ordered for a patient on an as-needed basis, if the utilization and retrieval of those drugs are subject to ongoing review by a pharmacist.
 - (3) Drugs designed by the patient care policy committee or pharmaceutical service committee of the facility as emergency drugs or acute onset drugs. These drugs may be retrieved from an automated drug delivery system pursuant to the order of a prescriber for emergency or immediate administration to a patient of the facility. Within 48 hours after retrieval under this paragraph, the case shall be reviewed by a pharmacist.
- (f) When used to provide pharmacy services pursuant to Section 4119.1 of the Business and Professions Code, the automated drug delivery system shall be subject to all of the following requirements:
 - (1) Drugs removed from the automated drug delivery system for administration to a patient shall be in properly labeled units of administration containers or packages.
 - (2) A pharmacist shall review and approve all orders prior to a drug being removed from the automated drug delivery system for administration to a patient. The pharmacist shall review the prescriber's order and the patient's profile for potential contraindications and adverse drug reactions.
 - (3) The pharmacy providing services to the facility pursuant to Section 4119.1 of the Business and Professions Code shall control access to the drugs stored in the automated drug delivery system.
 - (4) Access to the automated drug delivery system shall be controlled and tracked using an identification or password system or biosensor.
 - (5) The automated drug delivery system shall make a complete and accurate record of all transactions that will include all users accessing the system and all drugs added to, or removed from, the system.
 - (6) After the pharmacist reviews the prescriber's order, access by licensed personnel to the automated drug delivery system shall be limited only to drugs ordered by the prescriber and reviewed by the pharmacist and that are specific to the patient. When the prescriber's order requires a dosage variation of the same drug, licensed personnel shall have access to the drug ordered for that scheduled time of administration.
 - (7) (A) Systems that allow licensed personnel to have access to multiple drugs and are not patient specific in their design, shall be allowed under this subdivision if those systems have electronic and mechanical safeguards in place to ensure that the drugs delivered to the patient are specific to that patient. Each

facility using such an automated drug system shall notify the department in writing prior to the utilization of the system. The notification submitted to the department pursuant to this paragraph shall include, but is not limited to, information regarding system design, personnel with system access, and policies and procedures covering staff training, storage, and security, and the facility's administration of these types of systems.

(B) As part of its routine oversight of these facilities, the department shall review a facility's medication training, storage, and security, and its administration procedures related to its use of an automated drug delivery system to ensure that adequate staff training and safeguards are in place to make sure that the drugs delivered are appropriate for the patient. If the department determines that a facility is not in compliance with this section, the department may revoke its authorization to use automated drug delivery systems granted under subparagraph (A).

(C) This paragraph shall remain in effect only until January 1, 2012, unless a later enacted statute is enacted on or before January 1, 2012, deletes or extends that date.

(g) The stocking of an automated drug delivery system shall be performed by a pharmacist. If the automated drug delivery system utilizes removable pockets, cards, drawers, or similar technology, the stocking system may be done outside of the facility and be delivered to the facility if all of the following conditions are met:

(1) The task of placing drugs into the removable pockets, cards, or drawers is performed by a pharmacist or by an intern pharmacist or a pharmacy technician working under the direct supervision of a pharmacist.

(2) The removable pockets, cards, or drawers are transported between the pharmacy and the facility in a secure tamper-evident container.

(3) The facility, in conjunction with the pharmacy, has developed policies and procedures to ensure that the pockets, cards, or drawers are properly placed into the automated drug delivery system.

(h) Review of the drugs contained within, and the operation and maintenance of, the automated drug delivery system shall be done in accordance with law and shall be the responsibility of the pharmacy. The review shall be conducted on a monthly basis by a pharmacist and shall include a physical inspection of the drugs in the automated drug delivery system, an inspection of the automated drug delivery system machine for cleanliness, and a review of all transaction records in order to verify the security and accountability of the system.

(i) Drugs dispensed from an automated drug delivery system that meets the requirements of this section shall not be subject to the labeling requirements of Section 4076 of the Business and Professions Code or Section 111480 of this code if the drugs to be placed into the automated drug delivery system are in unit dose packaging or unit of use and if the information required by Section 4076 of the Business and Professions Code and Section 111480 of this code is readily available at the time of drug administration. For purposes of this section, unit dose packaging includes blister pack cards.

Attachment 4

**Title 16. Board of Pharmacy
Modified Text**

Changes made to the originally proposed language are shown by ~~striketrough~~ for deleted language and underline for added language.

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. Inventory Reconciliation 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:
 - 1) A physical count, not an estimate, of all quantities of 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;
 - 2) A review of all acquisitions and dispositions of Schedule II controlled substances since the last Inventory Reconciliation Report;
 - 3) A comparison of (1) and (2) to determine if there are any variances; and
 - 4) All records used to compile each Inventory Reconciliation Report shall be maintained in the pharmacy or clinic for at least three years in a readily retrievable form.
- d) A pharmacy or clinic shall report in writing identified losses and possible causes, shall be identified in writing and reported to the board and, when appropriate, to the Drug Enforcement Administration within 30 days unless the cause of the loss is theft, diversion, or self-use in which case the report shall be made within 14 days. If the pharmacy or clinic is unable to identify the cause of the loss, further investigation shall be undertaken to identify the cause and security improvements necessary to prevent additional losses of controlled substances.
- e) Likely Possible causes of overages shall be identified in writing and incorporated into the Inventory Reconciliation Report.
- e)f) The Inventory Reconciliation Report shall be dated and signed by the individual(s) performing the inventory, and countersigned by the pharmacist-in-charge or professional director, if a clinic, and be readily retrievable in the pharmacy or clinic for three years. A countersignature is not required if the pharmacist-in-charge or professional director personally completed the inventory reconciliation report.

- ~~f)-g)~~ A new pharmacist-in-charge of a pharmacy shall complete an inventory reconciliation report within 30 days of becoming pharmacist-in-charge as identified in subdivision (c). Whenever possible an outgoing pharmacist-in-charge should complete an inventory reconciliation report as required in subdivision (c).
- ~~g)-h)~~ For inpatient hospital pharmacies, a separate quarterly Inventory Reconciliation Report shall be required for Schedule II controlled substances stored within the pharmacy and for each pharmacy satellite location.
- ~~h)-i)~~ The pharmacist-in-charge of an inpatient hospital pharmacy or of a pharmacy servicing onsite or offsite automated drug delivery systems shall ensure that:
- 1) All controlled substances added to an automated drug delivery system are accounted for;
 - 2) Access to automated drug delivery systems is limited to authorized facility personnel;
 - 3) An ongoing evaluation of discrepancies or unusual access associated with controlled substances is performed; and
 - 4) Confirmed losses of controlled substances are reported to the board; ~~and~~
 - 5) ~~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, 4105.5, 4119.1, and 4332, Business and Professions Code and 1261.6, Health and Safety Code.



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RESOURCES > Title 21 Code of Federal Regulations > Part 1301 > 1301.76

Title 21 Code of Federal Regulations

PART 1301 – REGISTRATION OF MANUFACTURERS, DISTRIBUTORS, AND DISPENSERS OF CONTROLLED SUBSTANCES

SECURITY REQUIREMENTS

§1301.76 Other security controls for practitioners.

(a) The registrant shall not employ, as an agent or employee who has access to controlled substances, any person who has been convicted of a felony offense relating to controlled substances or who, at any time, had an application for registration with the DEA denied, had a DEA registration revoked or has surrendered a DEA registration for cause. For purposes of this subsection, the term "for cause" means a surrender in lieu of, or as a consequence of, any federal or state administrative, civil or criminal action resulting from an investigation of the individual's handling of controlled substances.

(b) The registrant shall notify the Field Division Office of the Administration in his area, in writing, of the theft or significant loss of any controlled substances within one business day of discovery of such loss or theft. The registrant shall also complete, and submit to the Field Division Office in his area, DEA Form 106 regarding the loss or theft. When determining whether a loss is significant, a registrant should consider, among others, the following factors:

- (1) The actual quantity of controlled substances lost in relation to the type of business;
- (2) The specific controlled substances lost;
- (3) Whether the loss of the controlled substances can be associated with access to those controlled substances by specific individuals, or whether the loss can be attributed to unique activities that may take place involving the controlled substances;
- (4) A pattern of losses over a specific time period, whether the losses appear to be random, and the results of efforts taken to resolve the losses; and, if known,
- (5) Whether the specific controlled substances are likely candidates for diversion;
- (6) Local trends and other indicators of the diversion potential of the missing controlled substance.

(c) Whenever the registrant distributes a controlled substance (without being registered as a distributor as permitted in §§1301.13(e)(1), 1307.11, 1317.05, and/or 1317.10 of this chapter), he/she shall comply with the requirements imposed on non-practitioners in §1301.74(a), (b), and (e).

(d) Central fill pharmacies must comply with §1301.74(e) when selecting private, common or contract carriers to transport filled prescriptions to a retail pharmacy for delivery to the ultimate user. When central fill pharmacies contract with private, common or contract carriers to transport filled prescriptions to a retail pharmacy, the central fill pharmacy is responsible for reporting in-transit losses upon discovery of such loss by use of a DEA Form 106. Retail pharmacies must comply with §1301.74(e) when selecting private, common or contract carriers to retrieve filled prescriptions from a central fill pharmacy. When retail pharmacies contract with private, common or contract carriers to retrieve filled prescriptions from a central fill pharmacy, the retail pharmacy is responsible for reporting in-transit losses upon discovery of such loss by use of a DEA Form 106.

[36 FR 7778, Apr. 24, 1971, as amended at 36 FR 18731, Sept. 21, 1971; 37 FR 15919, Aug. 8, 1972. Redesignated at 38 FR 26609, Sept. 24, 1973; 47 FR 41735, Sept. 22, 1982; 56 FR 36728, Aug. 1, 1991; 62 FR 13957, Mar. 24, 1997; 68 FR 37409, June 24, 2003; 70 FR 47097, Aug. 12, 2005; 79 FR 53562, Sept. 9, 2014]

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- DATA Waived Physicians
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- Federal Register Notices
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- NFLIS
- Publications & Manuals
- Questions & Answers
- Significant Guidance Documents
- Synthetic Drugs
- Title 21 Code of Federal Regulations
- Title 21 USC Codified CSA



HOME CONTACT US A-Z SUBJECT INDEX PRIVACY NOTICE WEBSITE ASSISTANCE

REGISTRATION

Applications
Tools
Resources
CMEA Required Training & Self-Certification
Quota Applications

REPORTING

ARCOS
BCM Online
Chemical Import/Export Declarations
CSOS (Controlled Substances Ordering System)
Drug Theft/Loss

RESOURCES

Cases Against Doctors
Chemical Control Program
CMEA (Combat Meth Epidemic Act)
Controlled Substance Schedules
DATA Waived Physicians
Drug Disposal Information

National Take-Back Initiative
NFLIS
Publications & Manuals
Questions & Answers
Significant Guidance Documents
Synthetic Drugs

ABOUT US

Program Description
Customer Service Plan
DEA Forms & Applications
Mailing Addresses
Meetings & Events
What's New

Import/Export
Medical Missions
Registrant Record of Controlled
Substances Destroyed
Quotas
Reports Required by 21 CFR
Submit a Tip to DEA
Year-End Reports

Drug and Chemical Information
E-commerce Initiatives
Federal Agencies & Related Links
Federal Register Notices

Title 21 Code of Federal Regulations
Title 21 USC Codified CSA



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EXCERPT: DRAFT MINUTES OF THE JANUARY 24, 2017 BOARD OF PHARMACY MINUTES

VII. Discussion and Consideration of the Proposed Regulation to Add Title 16 California Code of Regulations (CCR) Section 1715.65, Related to Inventory Reconciliation Report of Controlled Substances

President Gutierrez reported that at the July 2016 Board Meeting, the board approved proposed text to add Section 1715.65 of Title 16 CCR, related to Inventory Reconciliation Reporting. The 45-day comment period began on September 16, 2016 and ended October 31, 2016. She explained that at the December 2016 Board Meeting, the board approved a modified text to address concerns expressed by stakeholders and initiated a 15-day comment period.

President Gutierrez stated that the 15-day comment period began on December 23, 2016 and ended on January 7, 2017. She reported that the board received several comments during the 15-day comment period (the comments were provided in the board meeting materials).

President Gutierrez explained that upon reviewing the comments there is confusion on the language. Specifically in regards to the definition of perpetual inventory and what would constitute a significant loss. She asked that the Enforcement Committee to review the language and focusing on ways to clarify the language.

A representative from Pacific West Pharmacy noted that the regulation will be very cumbersome for pharmacies that dispense large volumes. The board asked him to attend the Enforcement Committee meeting to provide suggestions to improve the language.

The board also discussed the need for the committee to consider what volume of loss needs to be reported to the board. Ms. Herold noted that the law already requires the reporting of *any* loss of controlled substances no matter the volume.

Dr. Gray, from Kaiser, spoke in favor of sending the regulation back to the Enforcement Committee. He added that the DEA developed a report that defines “significant loss.”

Dr. Wong commented that the DEA spends a significant amount of time investigating drug losses even when diversion is not suspected. He added that the board needs to focus on losses that are the result of diversion. Ms. Herold noted that the board often works with the DEA on investigations.

Motion: Return the Regulation to Add Title 16 California Code of Regulations (CCR) Section 1715.65, Related to Inventory Reconciliation Report of Controlled Substances to the Enforcement Committee for further review and clarification.

M/S: Lippe/Law

Support: 10 Oppose: 0 Abstain: 0

Board Member	Support	Oppose	Abstain	Not Present
Brooks				x
Butler	x			
Gutierrez	x			
Law	x			
Lippe	x			
Munoz	x			
Sanchez	x			
Schaad	x			
Veale	x			
Weisser	x			
Wong	x			

A pharmacist noted that in the hospice care setting having a perpetual inventory would be difficult due to the heightened volume of controlled substances used.

Motion: Ask the Enforcement Committee to consider creating thresholds of controlled substance losses for purposes of reporting to the board.

M/S: Weisser/Veale

Support: 10 Oppose: 0 Abstain: 0

Board Member	Support	Oppose	Abstain	Not Present
Brooks				x
Butler	x			
Gutierrez	x			
Law	x			
Lippe	x			
Munoz	x			
Sanchez	x			
Schaad	x			
Veale	x			
Weisser	x			
Wong	x			

Attachment

CURES, Prescription Drug Abuse and Overdose Prevention; What a Pharmacist Needs to Know

Joint Training by the California State Board of Pharmacy, UC San Diego Skaggs School of Pharmacy and U.S. Drug Enforcement Administration



UC San Diego
SKAGGS SCHOOL OF PHARMACY
AND PHARMACEUTICAL SCIENCES



**CALIFORNIA STATE
BOARD OF PHARMACY**

BE AWARE AND TAKE CARE: Talk to your pharmacist!



March 11, 2017

UCSD Skaggs School of Pharmacy
Pharmaceutical Sciences Building, 873
9500 Gilman Drive
(Off Osler Lane at Gilman Drive)
La Jolla, CA 92093

See Attached Map

Pharmacists will be awarded 6 hours of CE credit for attending the session. An additional 1 hour of CE can be earned at the end of the day that meets the requirements of the State's Pharmacist Protocol to Provide Naloxone (for a total of 7 hours CE).

This is a FREE event. Space is limited; pre-registration is strongly encouraged. To register email your full name and license number (if applicable) to registration@dca.ca.gov. If you have questions please contact Laura Hendricks at laura.hendricks@dca.ca.gov or (916) 574-7918.

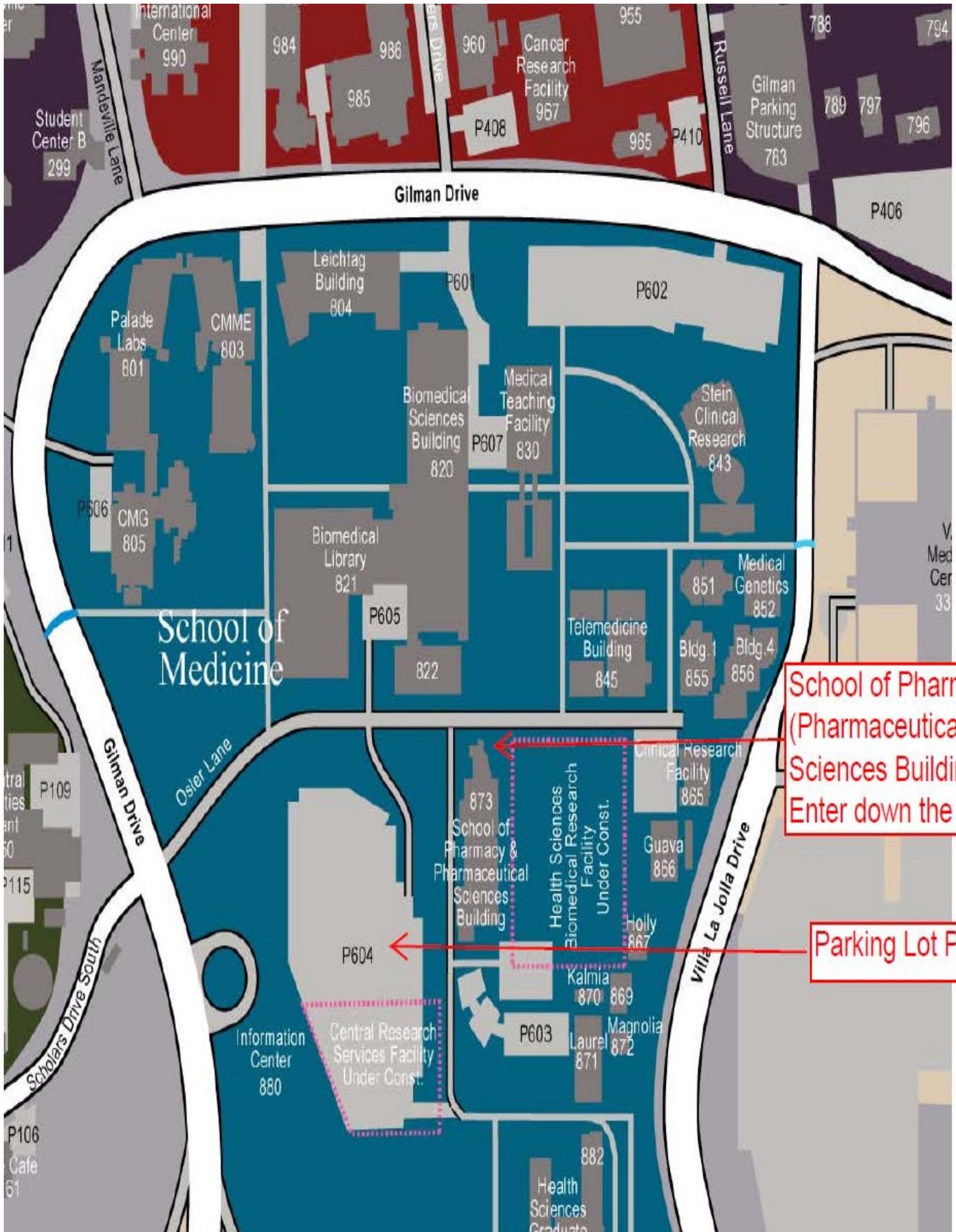
March 11, 2017 Agenda

Space is Limited, Registration Strongly Encouraged -See First Page for Registration Instructions

Location: UCSD Skaggs School of Pharmacy
Pharmaceutical Sciences Building, 873
9500 Gilman Drive
La Jolla, CA 92093

See attached map

- | | |
|--------------------------------|---|
| 7:30 a.m. - 8:15 a.m. | Registration |
| 8:15 a.m. - 8:30 a.m. | Welcoming Remarks
<i>Board of Pharmacy, DEA, UCSD</i> |
| 8:30 a.m. - 10:00 a.m. | Law Enforcement Trends, Drugs of Abuse and Reporting Procedures for Controlled Substances Losses
<i>DEA</i> |
| 10:00 a.m. - 10:15 a.m. | Break |
| 10:15 a.m. - 10:45 p.m. | Preventing Drug Thefts and Diversion from Pharmacies
<i>Board of Pharmacy</i> |
| 10:45 a.m. - 11:45 a.m. | Corresponding Responsibility & Red Flags
<i>Board of Pharmacy</i> |
| 11:45 a.m. - 12:15 p.m. | Drug Take Back Process in California
<i>Board of Pharmacy</i> |
| 12:15 p.m. - 1:15 p.m. | Lunch Break |
| 1:15 p.m. - 1:45 p.m. | California's Prescription Drug Monitoring Program -- CURES
<i>Board of Pharmacy, UCSD</i> |
| 1:45 p.m. - 2:15 p.m. | How to Prepare for Pharmacy Inspections by the Board of Pharmacy
<i>Board of Pharmacy</i> |
| 2:15 p.m. - 2:45 p.m. | How to Prepare for a DEA Inspection and Compliance with the Combat Methamphetamine Enforcement Act
<i>DEA</i> |
| 2:45 p.m. - 3:00 p.m. | Break |
| 3:00 p.m. - 3:30 p.m. | E-Prescribing at UCSD
<i>UCSD</i> |
| 3:30 p.m. - 4:45 p.m. | Training for California Pharmacists to Provide Naloxone Pursuant to the State's Pharmacist Protocol
<i>UCSD</i> |
| 4:45 p.m. | Wrap Up |



School of Medicine

School of Pharmacy
(Pharmaceutical
Sciences Building)
Enter down the stairs

Parking Lot P604

Attachment 6



**Item 1111-001-0767 - Department of Consumer Affairs
Board of Pharmacy
Combatting Prescription Drug Abuse**

As part of its oversight role, the Legislative Analyst's Office (LAO) instructed the California State Board of Pharmacy (Board) to provide a report to the fiscal subcommittees regarding its efforts to combat prescription drug abuse. Specifically, the Board was asked to provide a supplemental report to the 2016-17 Budget and provide information on the following:

1. Narrative description of the preceding year's activities related to combatting prescription drug abuse.
2. Funding and expenses information including the budgeted, allocated and expended money.
3. Number of positions and responsibilities.
4. Number of cases and disposition of cases referred to the Office of the Attorney General (AG) as a result of a case opened from a coroner report.
5. Number of hours spent combating prescription drug abuse, including separately identifying the total number of hours spent reviewing coroners reports and submitting public records requests to obtain the reports.

This report summarizes the Board's efforts to combat prescription drug abuse.

1. Description of the preceding year's activities related to combatting prescription drug abuse.

During the budget process last year, the LAO requested a report be provided with specific information. This request was made on or about May 1, 2016. It was upon this request that the Board began collecting data specific to the report. As such the reporting period is between May 1, 2016 and February 28, 2017, the Board initiated 167 investigations. During this timeframe the Board completed 147 investigations. The investigations substantiated violations of pharmacy law in 82% of the cases, including 66 investigations that resulted in the issuance of a citation, 37 that resulted in the issuance of a letter of admonishment, and 18 that resulted in referral to the AG.

As part of its proactive approach, the Board reviews information from various sources to determine if an investigation may be appropriate. The completed investigations during this reporting period were initiated based on a number of different activities including:

1. Reporting of sales data from wholesalers to pharmacies.
2. CURES data looking for excessive furnishing aggregate volumes by a single pharmacy.
3. CURES data looking for popular prescription drug combinations of abuse.
4. CURES data looking for red flags of prescription drug abuse including clinical irregularities, geographic irregularities, and signs of over prescribing and over dispensing.
5. CURES system alerts identifying anomalies in dispensing data by a single pharmacy.
6. Prescriptions written for medications outside of a practitioner's scope of practice.
7. Review of CURES for reporting compliance.

Summary of Some Investigations

One case completed during this timeframe was initiated after review and analysis of sales reports from a wholesaler. The Board's investigation revealed significant unaccounted for drug shortages

including over 32,000 tablets of hydrocodone/acetaminophen; almost 11,00 tablets of alprazolam; about 8,700 tablets of carisoprodol; and almost 1,500 ml of promethazine/codeine. (The street value for these missing medications is well over \$200,000.) The matter was referred to the AG and the administrative hearing is scheduled for mid-September 2017.

In another case the Board initiated an investigation after review and analysis of CURES data showed red flags. The investigation revealed respondents failed to exercise corresponding responsibility and ignored many of the warning signs a pharmacy should consider prior to dispensing a controlled substance. Specifically, review of the data and investigation found that respondents dispensed prescriptions written by a prescriber whose profile revealed that 98% of the prescriptions were paid for with cash, 96% of the prescriptions written by the prescriber were written for controlled substances and nearly all the patients' prescriptions were for the highest tablet strength of oxycodone. This matter was referred to the AG and the administrative hearing is scheduled for June 2017.

In another case, the Board initiated an investigation after an inspection of a pharmacy revealed violations of pharmacy law including a failure to report to CURES. As part of the investigation, analysis of records and CURES data was completed which revealed that the respondents were dispensing controlled substances pursuant to fraudulent prescriptions and that the pharmacy was negligent in excessively furnishing controlled substances. This matter was referred to the AG. The accusation was on March 18, 2017.

2. Total amount of funding budgeted, allocated, and expended

Reporting Period May 2016 – February 2017	Budgeted**	Expended
Staffing and Operating Expenses	\$1,261,000	\$1,221,223*
AG Costs	N/A	\$167,957
Total	\$1,261,000	\$1,389,180

*FY 2015-16 (May 2016 - June 2016) - \$302,816 salary included

FY 2016-17 (July 2016 - Jan 2017) - \$918,407

** Budget for FY 2016-17

3. Number of positions and their responsibilities

The Board acquired one Supervising Inspector position; five Inspector positions, one Research Program Specialist (RPS) position, and one Associate Governmental Program Analyst (AGPA) position through BCP #1110-27 in Fiscal Year 2014-15. General duties of the positions are detailed below.

Supervising Inspector:

- Reviewing cases for assignment and closure
- Developing investigation plans and assessments
- Conducting investigations and inspections
- Reviewing submitted investigations
- Presiding over citation and fine appeals
- Supervision duties

- Training Prescription Drug Abuse Team inspector staff
- Administrative duties
- Collaborating with other State and Federal Regulatory Agencies

Inspector:

- Reviewing cases and data from the Controlled Substance Utilization Review and Evaluation System (CURES)
- Conducting inspections
- Conducting investigations
- Testifying in Administrative Hearings

RPS:

- Requesting dispensing data from licensees (California Code of Regulations (CCR) section 1782)
- Evaluating information obtained in CCR 1782 reports
- Running CURES reports based on CCR 1782 data
- Evaluating CURES reports for trends
- Developing trend reports for prescription drugs abused
- Presenting findings to the committee and Board
- Performing statistical analysis on CURES
- Running CURES compliance reports
- Serving as a CURES liaison with the Department of Justice (DOJ)

AGPA:

- Requesting data derived from coroner's reports related to drug overdoses *
- Utilizing data from coroner's reports to initiate CURES reports
- Running subsequent CURES reports based on investigations initiated
- Opening investigations relating to prescription drug abuse
- Routing cases relating to prescription drug abuse
- Closing cases relating to prescription drug abuse
- Referring cases to Attorney General's (AG's) Office
- Referring cases to the Enforcement Unit to issue citations and fines

*This task was reassigned from the RPS duties.

4. Number of cases and disposition of those cases referred to the AG for prosecution that were a direct result from findings from a coroner's report.

One of the sources the Board has used to identify pharmacies that may be violating their corresponding responsibility is through review of decedent reports from counties. The Board requests a list of decedents with specific parameters and upon receipt a cursory review of the list is completed to identify if, based on the information, actions by a board licensee could have played a role in the patient's death. In such instances, the Board will generate a patient report from the CURES system to identify what pharmacy or pharmacies the patient used. After the pharmacy report is generated, analysis is completed to assess if the pharmacy data contains any red flags that warrant further review at which point an investigation may be initiated.

No investigations initiated directly from a finding from a coroner's report have been referred to the AG for prosecution. The Board currently has seven investigations pending.

5. Hours Spent Investigation Prescription Drug Abuse

Between May 1, 2016 and February 28, 2017 Board staff spent 6,978.75 hours on efforts to combat prescription drug abuse. The primary time spent is categorized below:

Task	Time
Opening/Routing Investigations	225 hours
Generating CURES Reports	360 hours
Data Analysis (not part of Investigation)	357 hours
Investigations	6036.75 hours

Notes: RPS position vacant from June 2016 until September 2016. AGPA position vacated January 15, 2017. Also, the time reported above does not include any administrative time such as meetings, training, etc.

The number of hours spent submitting a public records act request for coroner report and reviewing the report is two hours during this time period with an additional 187 hours spent generating and reviewing CURES reports for decedents. Based on this review and analysis of pharmacy CURES data, the Board initiated seven investigations during this reporting time period. Below is brief synopsis of allegations of two such investigations:

1. A review of a patient activity report identified a suspect pharmacy. Analysis of the pharmacy's overall dispensing data in CURES for controlled substances determined nearly 50% of the controlled substances were paid for without prescription insurance. A review of the prescribers with the most controlled drugs dispensed revealed three of the top doctors have pending accusations, criminal convictions and/or revoked licenses. The top doctor showed a prescribing pattern of maximum strength opioid and benzodiazepine drugs with no upward titration. It was based on these red flags for potential abuse that the Board initiated an investigation.
2. Review of a patient activity report identified a suspect pharmacy. An examination of pharmacy's CURES data, dispensing data, and prescription documents determined controlled drugs were dispensed earlier than directed by the doctor. This occurred repeatedly and consistently for some patients. For example, with one patient, in aggregate, the pharmacy dispensed 390 days' worth of a controlled drug to the patient over 297 days. In turn, approximately a three month supply surplus was received by the patient. Patients that receive controlled substance drugs ahead of schedule are exposed to the risk of taking higher doses than prescribed. The pharmacy received a citation for violations related to the dispensing of excess controlled drugs.

In addition, the Board sometimes receives information of a patient death from a different source. For example, a pharmacist notified the Board he declined to fill a prescription for an opioid drug based on his professional judgment that the patient was an opiate naïve patient (an opiate naïve patient is one that does not chronically receive opioid analgesics on a daily basis and has not built up a tolerance to opioids). The pharmacist considered the dose to be too high and attempted consultation with the

prescriber. The patient requested the prescription back. CURES data showed the patient filled the prescription a few days later at a different pharmacy. The day after filling the prescription, the patient died. The coroner's report showed mixed drug intoxication including the prescription filled.

Attachment 7



Guidance on Applying for Compliance Delays During Construction In Pharmacies that Compound

Title 16 of the California Code of Regulations (CCR) section 1735.6 (f) states where compliance with California's compounding regulations requires physical construction or alteration to a facility or physical environment, the board may grant a waiver of such compliance for a period of time to permit the required physical changes. See also related provisions in CCR section 1751.4.

Application for any waiver must be made in writing, identify the provisions requiring physical construction or alteration, and provide a timeline for any such changes. The board may grant the waiver for a specified period when, in its discretion, good cause is demonstrated for such waiver.

For hospitals, please see Guidance on Applying for Compliance Delays During Construction in Hospital Pharmacies that Compound, to request an exemption.

Please submit your request via email to: Compounding.waivers@dca.ca.gov

Or mail to: Compounding Construction Waiver Request
 CA State Board of Pharmacy
 1625 N Market Boulevard, Suite N-219
 Sacramento, CA 95834

Please retain a copy of your submitted request and make available for review at the licensed location.

Below is an example of the requested information in a format that you may submit to the board to request a waiver. It is in a fillable PDF format that you can complete online, printout, have signed and then return to the board along with any attachments. This document and form are available at www.pharmacy.ca.gov.

Pharmacy Name:

License Number: PHY/PHE

Please provide sterile compounding licenses associated with the above license: LSC/LSE

Name of the Individual Submitting this Request:

Title:

Email:

Phone Number:

The provisions of the regulation for which a compliance delay for construction is needed:

(Note: CA Code of Regulations section 1735.6(f) requires the identification of code sections requiring physical construction, alteration or improvement that are the reason for the waiver request)

1735.6, list subsections

1751.4 list subsections

Please list if other sections

A description of the physical changes that must be made for compliance *(Attach additional page if necessary):*

Please provide the timeframe for construction to completion:

Have building plans been developed? Yes No

Has a building permit been secured? If yes, please provide number:

Please provide a written description of how the pharmacy will perform compounding while the compliance delay is in effect.

Reviewed by:

Pharmacy Pharmacist-in-Charge _____

Please Print

Signature: _____ Date: _____

Please do not send architectural drawings or structural plans as they will not be reviewed.



Guidance on Applying for Compliance Delays During Construction In Hospital Pharmacies that Compound

Title 16 of the California Code of Regulations (CCR) section 1735.6 (f) states where compliance with California's compounding regulations requires physical construction or alteration to a facility or physical environment, the board may grant a waiver of such compliance for a period of time to permit the required physical changes. See also related provisions in CCR section 1751.4.

Application for any waiver must be made in writing, identify the provisions requiring physical construction or alteration, and provide a timeline for any such changes. The board may grant the waiver for a specified period when, in its discretion, good cause is demonstrated for such waiver.

For non-hospitals, please see [Guidance on Applying for Compliance Delays During Construction in Pharmacies that Compound](#), to request an exemption.

Please submit your request via email to: Compounding.waivers@dca.ca.gov

Or mail to: Compounding Construction Waiver Request
 CA State Board of Pharmacy
 1625 N Market Boulevard, Suite N-219
 Sacramento, CA 95834

Please retain a copy of your submitted request and make available for review at the licensed location.

Below is an example of the requested information in a format that you may submit to the board to request a waiver. It is in a fillable PDF format that you can complete online, printout, have signed and then return to the board along with any attachments. This form is available at www.pharmacy.ca.gov.

Hospital Pharmacy Name:

License Number: HSP/HPE

Provide all sterile compounding license numbers associated with the above license that require modification as part of this request:

LSC LSC LSC LSC LSC LSC

Name of the Individual Submitting this Request:

Title:

Email:

Phone Number:

OSHPD Project Number for this modification (if applicable):

OSHPD Facility Identification (if applicable):

OSHPD Hospital Building Number (if applicable):

Please attach a copy of the Project Completion Timeline, including a specific timeline for construction for EACH compounding pharmacy location that needs modification and is included under this Project Number.

The provisions of the regulation for which a compliance delay for construction is needed:

(Note: CA Code of Regulations section 1735.6(f) requires the identification of code sections requiring physical construction, alteration or improvement that are the reason for the waiver request.)

1735.6, list subsections

1751.4 list subsections

Please list if other sections

Please provide the timeframe for construction to completion:

A description of the physical changes that must be made for compliance (*Attach additional page if necessary*):

Have building plans been developed? Yes No

Has a building permit been secured? If yes, please provide number:

Please provide a written description of how the pharmacy will perform compounding while the compliance delay is in effect. Identify how compounding will take place after 1/1/17 until construction starts, during construction, and the transition into the newly remodeled location. (Please note if a new or temporary location is needed, a new permit may be required with the Board of Pharmacy and notification may be required to the California Department of Public Health. Additionally inspections are likely to be required before the use of any sterile compounding location begins operation. Please plan and communicate accordingly.)

Reviewed by:

Hospital Chief Executive Officer, Hospital Chief Operating Officer or Executive Director:

Please Print Name and Title

Signature: _____ Date: _____

Please do not send architectural drawings or structural plans as they will not be reviewed.

Attachment

Table I.1: The Number of State Pharmacy Regulatory Bodies Reporting That Their Office Has Primary Responsibility for the Oversight of Drug Compounding for Human Use

Type of drug compounder	Number of states (%)		
	Yes	No	No response
Drug compounding by pharmacies and pharmacists	50 (100)	0 (0)	0 (0)
Drug compounding by Food and Drug Administration registered outsourcing facilities	35 (70)	13 (26)	2 (4)
Drug compounding by physicians	7 (14)	41 (82)	2 (4)
Drug compounding by other nonpharmacist health care practitioners (e.g., nurse practitioners, physician assistants)	8 (16)	41 (82)	1 (2)

Source: GAO survey of state pharmacy regulatory bodies, survey question 2. | GAO-17-363SP

Note: GAO surveyed the state pharmacy regulatory bodies in the 50 states, the District of Columbia, Guam, Puerto Rico, and the U.S. Virgin Islands, and all but 4 completed the survey.

Attachment

California Code of Regulations § 1735.2. Compounding Limitations and Requirements; Self-Assessment.

- (a) Except as specified in (b) and (c), no drug 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 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 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” 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 preparation that:
 - (1) 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; 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
 - (4) That the pharmacist has a credible basis for concluding it is a reasonable quantity for office use considering the intended use of the compounded medication and the nature of the prescriber’s practice; and
 - (5) With regard to any individual prescriber to whom the pharmacy furnishes, and with regard to all prescribers to whom the pharmacy furnishes, 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 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.

- (e) A drug preparation shall not be compounded until the pharmacy has first prepared a written master formula document that includes at least the following elements:
- (1) Active ingredients to be used.
 - (2) Equipment to be used.
 - (3) 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) 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.
- (f) Where a pharmacy does not routinely compound a particular drug preparation, the master formula record for that preparation may be recorded on the prescription document itself.
- (g) The pharmacist performing or supervising compounding is responsible for the integrity, potency, quality, and labeled strength of a compounded drug preparation until the beyond use date indicated on the label, so long as label instructions for storage and handling are followed after the preparation is dispensed.
- (h) All chemicals, bulk drug substances, drug products, and other components used for drug compounding shall be stored and used according to compendia and other applicable requirements to maintain their integrity, potency, quality, and labeled strength.
- (i) Every compounded drug preparation shall be given 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.
- (1) For non-sterile compounded drug preparation(s), 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 compounded drug 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
- (4) In addition to the requirements of paragraph three (3), the drugs or compounded drug preparations tested and studied shall be identical 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.
- (j) The pharmacist performing or supervising compounding is responsible for the proper preparation, labeling, storage, and delivery of the compounded drug preparation.
- (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 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 data of receipt by the pharmacy

Erin Shull
1322 S. Ogden Drive, Apt. 8
Los Angeles, CA 90019
erineshull@gmail.com

STATE BOARD OF PHARMACY
2017 APR 10 PM 2:49

April 5, 2017

California State Board of Pharmacy
1625 N. Market Blvd.
Suite N219
Sacramento, CA 95834
Attn: Virginia Harold, Executive Officer

Re: **Negative Impact of New Potency Over Time Testing on Animal Rescue**

Dear Ms. Harold:

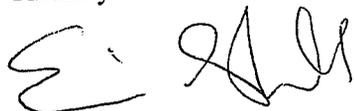
I am writing to voice my concern over the new laws on potency over time testing to valid Beyond Use Dates. I am a volunteer and foster for Kitten Rescue, a 501(c)(3) based in Los Angeles. We rescue young kittens and cats from animal shelters all over Los Angeles, foster them in our homes (and also at our sanctuary), spay and neuter and give them vaccinations and medications in order to get them ready and then adopted out into forever homes. Many of these cats and kittens come to us with medical issues after being on the streets of Los Angeles, and/or from being exposed to diseases and illnesses due to overcrowding at shelters. In order to successfully treat them, it is necessary for us to compound certain medications and administer them in liquid form. Common medications we use would be various antibiotics, prednisilone, gabapentin and budesonide, to name a few.

While it is relatively simple to get a cat to swallow a medication in water, it is not so easy to get them to stomach almond oil. Not only do the cats gag and spit at the taste and consistency (which is what we rescuers and pet owners are trying to avoid by compounding in the first place), but very often, even after shaking the bottle, it does not appear to mix properly, and then we are left wondering if the cats even got the correct dose. It is not financially possible for most animal rescue groups (or individuals) to buy short term quantities of compounded medications that need to be given over longer periods of time, and now that the laws have changed, and we can only get the water mixed compounded medications in much smaller amounts, we are forced to try and medicate our animals with oily medications that cause them to be stressed out, which obviously negatively impacts their health further.

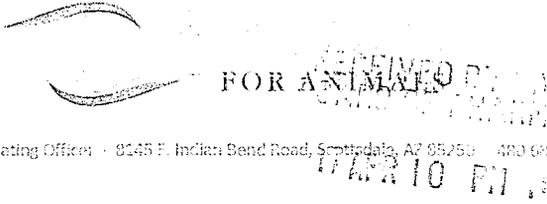
I have been getting medications compounded in a water base for years, keeping them in the fridge for 1-3 months, and have never had any issues with an animal getting sick from the medicine being expired. I have been using the same compounding pharmacy for 8 years, and am willing to sign a waiver accepting this risk, but my pharmacist tells me this isn't even an option, as he cannot afford the liability.

I hope you will document this letter as evidence that this new law is having a very negative and burdensome impact on the animal rescue community and pet owners.

Thank you.

A handwritten signature in black ink, appearing to read 'Erin Shull', written in a cursive style.

Erin Shull



Frank J. Frascotto III, ACHE, BSHM, CRT, Chief Operating Officer - 8145 E. Indian Bend Road, Scottsdale, AZ 85250 - 480.682.1017 - info@eyecareforanimals.com

To: California Board of Pharmacy
Executive Officer
Board Members

April 4, 2017

RE: Newly adopted compounding regulations

Members of the Board,

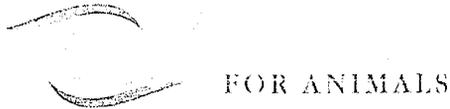
I fully intend to attend the upcoming meeting scheduled for April 18, 2017 in Sacramento, CA. My letter is in hopes of having some points addressed and/or added to the topics of discussion for that meeting.

I am writing you out of pure concern following a myriad of obstacles set forth against the Veterinary community along with my organization, my doctors, and our patients, following recent regulations set into motion by the California Board of Pharmacy. I am of the assumption the information I am providing below may have been an oversight.

I am in a unique position as my experience and knowledge come from a 20-year career within human healthcare as both a licensed clinician and a healthcare administrator. Wishing to exit the constant barrage of federal mandates, insurance pitfalls, and HIPAA related incidents plaguing the environment, I felt it was time for a much-needed change. Much to my surprise, I find myself in the midst of exactly the same environment. At present, I am the Chief Operating Officer of Eye Care for Animals; my primary duty is to ensure the protection of each member of my organization. I accomplish this by monitoring and directing a set of uniform operating procedures established to maintain code requirements and navigate within compliance mandates applicable at each of our 54 locations scattered throughout 16 States. Ten of our locations fall within the State of California.

Eye Care for Animals is the largest Veterinary Ophthalmology organization in the world. Our board certified veterinary ophthalmologists are some of the most highly trained in their profession, and diligently work toward enhancing their skills throughout their medical community to achieve the best patient outcomes on a routine basis. These unique and unbelievably skilled folks are hands down the best in their business; I am truly honored to be permitted represent them and this organization. There are many ophthalmic ailments in animals that require medications that are not commercially produced. We rely on a large number of compounded ophthalmic medications to treat these ailments. These are the exact medications you have now placed under some of the tightest restrictions.

If the regulations we were discussing today were only directed at mixed used compounding pharmacies (both human and veterinary), I would have a slightly easier time understanding and accepting your regulations. However even when specifically addressing VETERINARY ONLY compounding pharmacies who dispense medications ONLY to animal patients for diseases noted only in animals, these regulations still hold true. As written, these pharmacies are required to dispense patient specific prescriptions (eliminating office use = delayed treatment), must limit the amount of the compound they



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make in order to stay under the 503B mandate (decrease in availability = delay in treatment), and now must utilize a beyond use date which many times causes the prescription to expire at the time of arrival/delivery to the patient (failed standard of care).

Our patients are in **danger** of inadequate treatment that can result in loss of vision. Our veterinarians have been forced to utilize sub-standard/over the counter medications to control some diseases that if human's were to experience, we would never subject to the same form of treatment. How is this acceptable?

As the regulation is written, which this Board passed, there is liability placed on the practitioner to verify that the medications being dispensed to the patient have met the sterility and stability standards adopted by this regulation. Regardless of whom I contact, requesting said studies, I am informed, "Studies are proprietary" and would not be shared. How am I to verify compliance without the ability to do so? In the one instance I received a "stability study"; I received a one-page document that was clearly a POTENCY OVER TIME" study which was labeled "Stability Study". How could this possibly meet the requirements of your regulation?

Additionally, with the current constraints in place, even when we are able to acquire sterile and stable compounds, the medication arrives with an expiration date clearly identified to be months in the future however, has a label which states "to be disposed of within xx days per California Board of Pharmacy". Apparently, the compound although stable and sterile in all remaining 49 States is just fine up until it crosses the State lines of California. Not to mention, we are talking about patient's who do not have insurance (people's pets), and the costs for these very medications has tripled, quadrupled, even reached 10-fold in some cases, making treatment more expensive than surgery to remove the affected eye of the patient!

My standard response to our clients calling to complain has been "take your pet to anywhere outside of California, you will easily be able to obtain the care, service, and MEDICATIONS necessary to treat the condition your pet is experiencing". This is truly unacceptable. Our veterinarians care for thousands of pets in California every year.

This letter could continue to over 10 pages in length following the issues, complaints, concerns, and problems, experienced at the hands of our doctors, our clients, my staff, myself, and our patients, should they ever have the ability to speak. To say your adoption of these regulations have placed our patients in jeopardy would truly minimize the situation. I beg of you to modify these regulations in order to permit the veterinary community to once again properly care for their patients.

Respectfully,



Frank J. Frassetto III

Attachment

**Interim Policy on Compounding
Using Bulk Drug Substances
Under Section 503A of the
Federal Food, Drug, and
Cosmetic Act
Guidance for Industry**

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Office of Compliance/OU DLC**

**January 2017
Compounding and Related Documents
Revision 1**

Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act **Guidance for Industry**

Additional copies are available from:
Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
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Silver Spring, MD 20993-0002
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<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
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TABLE OF CONTENTS

I.	INTRODUCTION AND SCOPE	1
II.	BACKGROUND	2
	A. Compounding From Bulk Drug Substances Under Section 503A of the Act.....	2
	B. Efforts to Develop the List of Bulk Drug Substances under Section 503A.....	4
III.	POLICY	9
	A. Compounding from Bulk Drug Substances under Section 503A	9
	B. Substances Not Nominated or Nominated Without Adequate Support	10
	C. Comments about Nominated Bulk Drug Substances.....	10
	APPENDIX: SUMMARY OF POLICY	12

Guidance for Industry¹

Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act

This guidance represents 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 office 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) interim regulatory policy concerning compounding using bulk drug substances under section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act or Act). Section 503A of the FD&C Act includes certain restrictions on the bulk drug substances that can be used in compounding and directs FDA to develop a list of bulk drug substances that can be used in compounding under that section. FDA is developing this list of bulk drug substances (the 503A bulks list), and this guidance describes FDA's interim regulatory policy for licensed pharmacists in State-licensed pharmacies and Federal facilities and for licensed physicians that compound human drug products using bulk drug substances while the list is being developed.^{2,3}

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.

¹ This guidance has been prepared by multiple offices in the Center for Drug Evaluation and Research (CDER), in consultation with the Office of Regulatory Affairs at the Food and Drug Administration.

² This guidance does not apply to drugs compounded from bulk drug substances for use in animals. 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*.

All FDA guidances are available on the FDA guidance web page. FDA updates guidances regularly. To make sure you have the most recent version of a guidance, always consult the guidance web page at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

³ FDA is developing a separate list of bulk drug substances that can be used in compounding under section 503B of the FD&C Act. Because section 503B contains different criteria for that list and provides for a different process for its development, the section 503B bulks list is covered under a separate guidance (see guidance for industry, *Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act*).

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II. BACKGROUND

A. Compounding From Bulk Drug Substances Under Section 503A of the Act

Section 503A of the FD&C Act 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 505 (concerning the approval of drugs under new drug applications or abbreviated new drug applications); section 502(f)(1) (concerning the labeling of drugs with adequate directions for use); and section 501(a)(2)(B) (concerning current good manufacturing practice requirements).

One of the conditions that must be met for a compounded drug product to qualify for these exemptions is that a licensed pharmacist, or licensed physician compounds the drug product using bulk drug substances that:

1. Comply with the standards of an applicable United States Pharmacopeia (USP) or National Formulary (NF) monograph, if a monograph exists, and the USP chapter on pharmacy compounding;
2. If such a monograph does not exist, are drug substances that are components of drugs approved by the Secretary; or
3. If such a monograph does not exist and the drug substance is not a component of a drug approved by the Secretary, appears on a list developed by the Secretary through regulations issued by the Secretary under subsection (c) of section 503A.⁴

A bulk drug substance is defined as meaning “the same as active pharmaceutical ingredient as defined in 21 CFR 207.1(b).” See 21 CFR 207.3. Active pharmaceutical ingredient is defined as “any substance that is intended for incorporation into a finished drug product and is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body,” but the term “does not include intermediates used in the synthesis of the substance” (see section 503A(b)(1)(A) and 21 CFR 207.3).^{5,6} FDA has interpreted “an applicable USP or NF

⁴ See Section 503A(b)(1)(A)(i) of the FD&C Act.

⁵ Section 503A references the definition of bulk drug substances in FDA’s drug establishment registration and listing regulations, which was codified at 21 CFR 207.3(a)(4) when section 503A was enacted. On August 31, 2016, FDA published a final rule in the Federal Register to update its registration and listing regulations in Part 207, which made minor changes to the definition of bulk drug substance and moved the definition to 21 CFR 207.3 See 81 FR 169 (August 31, 2016). Under the previous definition, bulk drug substance was defined to mean “any substance that is represented for use in a drug and that, when used in the manufacturing, processing, or packaging of a drug, becomes an active ingredient or a finished dosage form of the drug, but the term does not include intermediates used in the synthesis of such substances.”

⁶ Inactive ingredients are not subject to section 503A(b)(1)(A)(i) or the policies described in this guidance because they are not included within the definition of a bulk drug substance. See 21 CFR 207.3. Pursuant to section 503A(b)(1)(B), inactive ingredients used in compounding must comply with the standards of an applicable United States Pharmacopeia or National Formulary monograph, if a monograph exists, and the USP chapter on pharmacy compounding.

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monograph” to mean an official USP or NF **drug substance** monograph. Accordingly, FDA does not consider USP monographs for dietary supplements to be “applicable” USP or NF monographs within the meaning of section 503A(b)(1)(A)(i)(I).

Under section 503A(c)(1), before developing this list through regulation, FDA must convene and consult an advisory committee on compounding unless FDA determines that the issuance of such regulation before consultation with the advisory committee is necessary to protect the public health. FDA must also consult with USP when promulgating the regulations.⁷ The criteria for determining which bulk drug substances should appear on the section 503A bulks list “shall include historical use, reports in peer reviewed medical literature, or other criteria the Secretary may identify.”⁸

Bulk drug substances used in compounding under section 503A must also meet certain other requirements, including: (1) the bulk drug substance must be manufactured by an establishment registered under section 510 of the FD&C Act and (2) the bulk drug substance must be accompanied by a valid certificate of analysis (COA).⁹

In July 2014, FDA issued a guidance, *Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act*, that states:

Until a bulk drug substances list is published in the *Federal Register* as a final rule, human drug products should be compounded using only bulk drug substances that are components of drugs approved under section 505 of the FD&C Act, or are the subject of USP or NF monographs.¹⁰

FDA has received comments that this policy could be causing unnecessary and inappropriate disruptions in patient care because there are patients receiving drugs compounded with bulk drug substances that are not components of FDA-approved drugs, or the subject of an applicable USP or NF monograph, but that may ultimately be included on the 503A bulks list, and those patients’ care should not be disrupted while the list is under development. After considering this issue, FDA has decided to use this guidance to describe its interim policy concerning compounding with bulk drug substances while the 503A bulks list is being developed. FDA has revised the July 2014 guidance to state:

FDA’s interim policy concerning bulk drug substances that are not components of drugs approved under section 505 of the FD&C Act or that are not the subject of applicable USP or NF monographs can be found in the guidance, *Interim Policy on*

⁷ See section 503A(c)(2) of the FD&C Act.

⁸ See section 503A(c)(2) of the FD&C Act.

⁹ See section 503A(b)(1)(A) of the FD&C Act.

¹⁰ See page 5 of the guidance, *Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act*.

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Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug and Cosmetic Act.

FDA seeks to avoid unnecessary disruption to patient treatment while the Agency considers the bulk drug substances that were nominated with sufficient support to permit FDA to evaluate them and promulgates the regulations required under section 503A. Therefore, as described further below, FDA is issuing this interim guidance stating that it does not intend to take regulatory action for compounding drug products under section 503A using a bulk drug substance when an applicable USP or NF monograph for the substance does not exist and the substance is not a component of an FDA-approved product if, among other conditions, FDA has determined that the nomination for the bulk drug substance included adequate information for FDA to evaluate the substance and at this time, the substance does not appear to present significant safety risks.

B. Efforts to Develop the List of Bulk Drug Substances under Section 503A

1. Section 503A Bulks List — Early History

Section 503A was enacted in 1997 as part of the Food and Drug Administration Modernization Act. In the *Federal Register* of April 7, 1998 (63 FR 17011), FDA invited all interested persons to nominate bulk drug substances for inclusion on the list of bulk drug substances that can be used in compounding under section 503A and received nominations for 41 different drug substances. In November 1998, FDA published a guidance for industry, *Enforcement Policy During Implementation of Section 503A of the Federal Food, Drug, and Cosmetic Act*. In this guidance, FDA announced that it would not normally take regulatory action relating to a drug product that had been compounded with a bulk drug substance that had been nominated for inclusion on the bulk drug substances list on or before November 21, 1999, while the substance was being evaluated, as long as the compounding complied with the other effective requirements in section 503A and did not appear to present a significant safety risk.¹¹

In January 1999, after evaluating the nominated drug substances and consulting with the Pharmacy Compounding Advisory Committee (PCAC) as required by section 503A, FDA published a proposed rule listing 20 drug substances on the section 503A bulks list (64 FR 996, January 7, 1999). The preamble to the proposed rule indicated that 10 of the 41 nominated substances were the subject of a USP or NF monograph, or components of FDA approved drugs and did not need to be considered for inclusion on the list.¹² The proposed rule also described 10 nominated substances that were still under consideration for the bulk drug substances list and stated that one of the substances was withdrawn by its nominator at the first meeting of the PCAC. The PCAC reconvened in May 1999 to discuss bulk drug substances included in the proposed rule, in addition to other bulk drug substances (64 FR 19791; April 22, 1999).

¹¹ The 1998 guidance was withdrawn in the *Federal Register* notice announcing the availability of the draft guidance *Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act*. See 78 FR 72901 (Dec. 4, 2013). The final guidance was published in July 2014.

¹² See 64 FR 996, at 997 (January 7, 1999).

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However, after a 2002 U.S. Supreme Court decision holding that certain provisions of section 503A were unconstitutional,¹³ FDA suspended its efforts to develop the bulk drugs list under section 503A.

Because of the amount of time that had passed between the publication of the proposed rule and the enactment of the 2013 Drug Quality and Security Act, which removed the provisions of the FD&C Act that the U.S. Supreme Court held to be unconstitutional in 2002, FDA felt it was necessary to begin again to develop the section 503A bulk drug substance list. In the December 4, 2013, *Federal Register* (78 FR 72841), FDA published a notice withdrawing the 1999 proposed rule and inviting all interested persons to nominate bulk drug substances for inclusion on a list of bulk drug substances that can be used for compounding under section 503A of the FD&C Act.

2. Current Nominations for the 503A Bulks List

In response to the December 2013, *Federal Register* notice, over 2,000 substances were nominated for the 503A bulks list. However, many of the substances nominated for the 503A list were for substances that can be compounded without being on the list because they are the subject of an applicable USP or NF monograph or are a component of an FDA-approved drug. In addition, many of the nominations were not for substances used in compounding as active ingredients, or did not include sufficient information for FDA to evaluate the nominated substances for inclusion on the list. To improve the efficiency of the process for developing the 503A bulks list, FDA reopened the nomination process in July 2014 (79 FR 37742) and provided more detailed information on what it needs to evaluate nominations for the 503A bulks list. FDA stated that bulk drug substances that were previously nominated would not be considered further unless they were re-nominated with adequate support to permit a meaningful evaluation. Substances that were already eligible for use in compounding or that were not adequately supported would not be evaluated for placement on the 503A bulks list.

In response to this request for nominations, approximately 740 unique substances were nominated. Of the nominated substances:

- Approximately 315 substances are already eligible for use in compounding under section 503A.

These are the subject of an applicable USP or NF monograph or components of an FDA-approved drug product, which can be used in compounding pursuant to sections 503A(b)(1)(A)(i)(I) and (II) and, therefore, can be compounded without being included on the 503A bulks list. To determine if a bulk drug substance is the subject of an applicable USP or NF monograph, see the *USP-NF* available at www.USPNF.com. To determine if a bulk drug substance is a component of an FDA approved drug, see the FDA's *Orange Book*:

¹³ For additional legal history of section 503A, see the guidance *Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act*.

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Approved Drug Products with Therapeutic Equivalence Evaluations, available at <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>.

- At least one¹⁴ of the nominated substances is not a bulk drug substance.

This is a finished drug product that was nominated by its brand name. Finished drug products are not eligible for the 503A bulks list because they do not meet the definition of a bulk drug substance in 21 CFR 207.3.

- At least one of the substances is considered a biological product subject to approval in a biologics license application (BLA) under section 351 of the Public Health Service (PHS) Act when used for the indication proposed in the nomination.

This substance is not eligible for the 503A bulks list because biological products subject to approval in a BLA under section 351 of the PHS Act are not eligible for the exemptions in section 503A of the FD&C Act.¹⁵ No biological products subject to approval in a BLA will be considered for the 503A bulks list.

- At least four of the nominated substances appear on the list published by FDA of substances that have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective (withdrawn or removed list).¹⁶

Such substances cannot be used in compounding under section 503A of the FD&C Act and, therefore, are not eligible for inclusion on the 503A bulks list.

- One of the nominated substances has no currently accepted medical use and is included on Schedule I of the Controlled Substances Act (CSA) (21 U.S.C. § 812(c)).¹⁷

The CSA does not allow possession or distribution of Schedule I substances (21 USC §§ 841(a)(1) and 829), except for research purposes (21 U.S.C. § 823(f)), and these substances will not be considered for the 503A bulk drug substances list at this time. Those desiring to do research on a Schedule I substance can apply to do so under an investigational new drug application (IND).

¹⁴ The over-the-counter finished drug product Maalox was nominated. Maalox is not a bulk drug substance.

¹⁵ The nominated substance is sodium hexachloroplatinate (IV) hexahydrate. See the revised draft guidance, *Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application* for FDA's proposed policies regarding State-licensed pharmacies, Federal facilities, and outsourcing facilities that mix, dilute, or repackage biological products outside the scope of an approved BLA.

¹⁶ See Section 503A(b)(1)(C) of the FD&C Act. See also 21 CFR 216.24. The four substances are: chloroform reagent, cobalt chloride hexahydrate, cobalt gluconate, and phenacetin.

¹⁷ An extract of cannabidiol (CBD) and tetrahydrocannabinol (THC) derived from marijuana (marihuana) was nominated. Marijuana (marihuana) is a Schedule I substance.

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- Of the substances that are not components of an approved drug or the subject of an applicable USP or NF monograph and that are not biological products subject to licensure in a BLA or included on Schedule I of the CSA, and do not appear on the withdrawn or removed list, approximately 350 substances were nominated without sufficient supporting evidence for FDA to evaluate them.
- The remaining substances may be eligible for inclusion on the 503A list and were nominated with sufficient supporting information for FDA to evaluate them. However, FDA has identified significant safety risks relating to the use of some of these bulk drug substances in compounded drug products.

FDA's website identifies the following categories of substances nominated for the 503A bulks list:¹⁸

503A Category 1 – Substances Nominated for the Bulks List Currently Under Evaluation: These substances may be eligible for inclusion on the 503A bulks list, were nominated with sufficient supporting information for FDA to evaluate them, and do not appear on any other list.

503A Category 2 – Substances Nominated for the Bulks List That Raise Significant Safety Risks: These substances were nominated with sufficient supporting information to permit FDA to evaluate them and they may be eligible for inclusion on the 503A bulks list. However, FDA has identified significant safety risks relating to the use of these substances in compounding pending further evaluation, and therefore does not intend to adopt the policy described for the substances in Category 1. If FDA adds a substance to Category 2, it will publish a public communication (e.g., a safety alert) describing the safety risks and will post the communication on FDA's human drug compounding website,¹⁹ advising that the substance has been added to Category 2 and is no longer eligible for the policies that apply to substances in Category 1.

503A Category 3 – Substances Nominated for the Bulks List Without Adequate Support: These substances may be eligible for inclusion on the 503A bulks list, but were

¹⁸ <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467373.pdf>. As discussed in the July 2014 Federal Register notice requesting nominations for the 503A bulks list (79 FR 37742), nominators were to confirm that all substances nominated for the list are active ingredients that meet the definition of a "bulk drug substance." Inclusion of a substance in any of these categories does not reflect a determination by FDA that the substance is a bulk drug substance. Whether a substance is a bulk drug substance subject to the conditions in section 503A(b)(1)(A) depends on whether it meets the definition of a bulk drug substance in 21 CFR 207.3. If the substance is used in a compounded drug as an inactive ingredient, then it does not meet the definition of a bulk drug substance in 21 CFR 207.3, is not subject to the conditions in section 503A(b)(1)(A), and need not appear on the 503A bulks list to be eligible for use in compounding. Instead, when used as an inactive ingredient, the substance is subject to the conditions in section 503A(b)(1)(B), which applies to ingredients other than bulk drug substances used in compounded drugs.

¹⁹ <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/default.htm>. FDA also encourages compounding facilities to subscribe to FDA's list serve to receive updates at: http://service.govdelivery.com/service/subscribe.html?code=USFDA_429.

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nominated with insufficient supporting information for FDA to evaluate them. These substances can be re-nominated with sufficient supporting information through a docket that FDA has established, as discussed below in section III.B.

3. Process for Developing the 503A List

FDA is currently evaluating the substances that were nominated for the 503A bulks list with sufficient information to permit evaluation. FDA is considering a number of factors in prioritizing the order in which it reviews the nominated bulk drug substances, including but not limited to the following:

- Safety concerns about use of the bulk drug substance in compounding
- Whether the bulk drug substance was nominated by multiple parties or identified as necessary by medical professional organizations
- The efficiency with which the evaluation can be completed, based on ease of acquiring the necessary information to conduct the review, available resources, and other logistical issues

FDA may also group some nominated drug substances to facilitate efficient review and discussion. These include drugs that raise similar issues (e.g., vitamins or botanicals) or have been nominated for the treatment of the same condition (e.g., warts).

In conducting its evaluations, FDA reviews the information provided in support of the nomination and other available information to assess each bulk drug substance according to the following four criteria discussed at the PCAC meeting on February 23, 2015:

- The physical and chemical characterization of the substance
- Any safety issues raised by the use of the substance in compounded drug products
- Historical use of the substance in compounded drug products, including information about the medical condition(s) the substance has been used to treat and any references in peer-reviewed medical literature
- The available evidence of effectiveness or lack of effectiveness of a drug product compounded with the substance, if any such evidence exists

In evaluating candidates for the 503A bulks list under these criteria, FDA is using a balancing test. No single one of these criteria is dispositive; rather, FDA is considering each criterion in the context of the others and balancing them, on a substance-by-substance basis, to evaluate whether a particular substance is appropriate for inclusion on the list.

Once the evaluation of a substance is complete, FDA will present the results of its review to the PCAC to obtain its advice on whether to include the substance on the list.²⁰

²⁰ See Section 503A(c)(1) of the FD&C Act.

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Section 503A requires that FDA create the 503A bulks list by regulation in consultation with the USP. To this end, FDA has been periodically meeting with USP and discussing the list. FDA will publish a notice of proposed rulemaking (NPRM) that identifies substances FDA proposes for placement on the 503A bulks list and the substances FDA has evaluated but is not proposing to include on the 503A bulks list. After publication of the NPRM, the public will have an opportunity to comment on the proposed rule. After considering the comments submitted to the docket, FDA will publish a final rule that establishes the 503A bulks list and identifies the substances that were considered and will not be placed on the list. FDA does not intend to evaluate all of the sufficiently supported nominations before publishing the first NPRM. Instead, after FDA has made a decision on whether to propose a group of substances (e.g., 10 substances) it intends to publish an NPRM with respect to that group of substances and continue to prepare the list on a rolling basis.

A final rule will list the substances that FDA has determined can be used in compounding under section 503A and those substances that have been evaluated and not placed on the 503A bulks list, if any.

After a final rule is published, drug products compounded using the substances on the 503A bulks list will be eligible for the section 503A exemptions provided the drug product is compounded in compliance with the other conditions of section 503A. Those substances that have been evaluated and not placed on the 503A bulks list will not qualify for the policies described for the substances in Category 1.

III. POLICY²¹

A. Compounding from Bulk Drug Substances under Section 503A

Under section 503A of the FD&C Act, a bulk drug substance that is not the subject of an applicable USP or NF monograph or is not a component of an FDA-approved drug cannot be used in compounding unless it appears on a list promulgated as a regulation pursuant to section 503A(b)(1)(A)(i)(III) of the FD&C Act. This list will be codified at 21 CFR part 216 subpart E.

However, until a substance has been evaluated and is identified in a final rule as being included or not included on the 503A bulks list, FDA does not intend to take action against a State-licensed pharmacy, Federal facility, or licensed physician compounding a drug product using a bulk drug substance that is not a component of an FDA-approved drug product and that is not the subject of an applicable USP or NF monograph, provided that the following conditions are met:

1. The bulk drug substance appears in 503A Category 1 on FDA's website at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467373.pdf>. A Category 1 substance may be eligible for inclusion on the 503A bulks list, was nominated with sufficient supporting information for FDA to

²¹ See the Appendix for a chart summarizing FDA's interim policy.

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evaluate it and has not been identified by FDA as a substance that presents a significant safety risk in compounding prior to the publication of a final rule.

2. The original manufacturer and all subsequent manufacturers of the bulk drug substance are establishments that are registered under section 510 (including foreign establishments that are registered under section 510(i)) of the FD&C Act);
3. The bulk drug substance is accompanied by a valid COA; and
4. The drug product compounded using the bulk drug substance is compounded in compliance with all other conditions of section 503A of the FD&C Act.

Original manufacturer means the entity that originally produced the bulk drug substance and not a subsequent packer, repacker, labeler, or distributor.

This policy does not apply to a licensed pharmacist in a State-licensed pharmacy or Federal facility, or a licensed physician, that compounds a drug using a bulk drug substance that does not meet each of the above conditions, and the bulk drug substance is not the subject of an applicable USP or NF monograph or a component of an FDA-approved drug.

B. Substances Not Nominated or Nominated Without Adequate Support

As stated above, one of the categories of bulk drug substances FDA has identified on its website is substances nominated for the 503A bulks list that may be eligible for inclusion on the list, but that FDA is unable to evaluate for inclusion on the list at this time because the substances were nominated with insufficient supporting evidence for FDA to evaluate them (503A Category 3). In the *Federal Register* of October 27, 2015, FDA established a docket (October docket) where these substances can be re-nominated with sufficient supporting information or where nominations for substances that were not previously nominated can be submitted.

After a substance is nominated to the October docket,²² FDA will determine whether the nomination is supported with sufficient information to allow FDA to evaluate it. After FDA makes that determination, the nominated substance will be placed in one of the three categories described in section II.B.2 above, and the categorization will be published on the FDA website. Once the category of a substance is published, FDA intends to apply the policy described in Section III.A of this guidance to that substance. FDA generally expects to categorize bulk drug substances nominated to the October docket and to publish updated categories on its website on the first business day of each month. Please note that until substances nominated for the October docket have been categorized, the policy does *not* apply to those substances.

C. Comments about Nominated Bulk Drug Substances

²² This includes re-nominations of substances with sufficient supporting information.

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If you feel that a substance that you nominated does not appear on the appropriate list or category as described in this guidance you can submit your comment to docket number FDA-2015-N-3534. If you have new information on a previously nominated substance that was placed in Category 3, the substance can be re-nominated with the additional information.

A nominator may also submit a comment to the docket requesting withdrawal of any of its nominations. If the party nominating the substance was the sole nominator, FDA will update the categories described in this guidance to reflect the withdrawn nomination.²³ FDA intends to provide notice to the public before removing any nominated substances from Category 1 or Category 2.

Withdrawal of a nomination upon the nominator's request and the resulting updates to the categories described in this guidance, do not reflect a determination by FDA regarding the validity of the nomination or of any reasons given by the nominator for requesting withdrawal. In addition, FDA may continue to evaluate a substance at its discretion even if the nominator submits a comment requesting withdrawal of the nomination.

²³ If multiple parties nominated the same substance, each party that nominated the substance must withdraw its nomination for the nominated substance to be considered withdrawn and for the categories to be updated to reflect that withdrawal.

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APPENDIX: SUMMARY OF POLICY

The following table summarizes the interim policy for bulk drug substances set forth in this guidance:

Category	FDA Policy
<p>The bulk drug substance appears in 503A Category 1 on FDA’s website at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467373.pdf.</p> <p>Such substances may be eligible for inclusion on the 503A bulks list, were nominated with sufficient supporting information for FDA to evaluate them, and do not appear to present a significant safety risk.</p>	<p>FDA does not intend to take action for compounding a drug product from a bulk drug substance in Category 1 that does not meet the conditions of section 503A(b)(1)(A)(i), provided that the bulk drug substance was manufactured by an establishment registered with FDA under section 510 of the FD&C Act and is accompanied by a valid COA from the entity that originally produced the bulk drug substance and provided that the drug compounded from the bulk drug substance is compounded in compliance with the other conditions of section 503A.</p>
<p>The bulk drug substance is a component of an FDA-approved drug and/or the subject of an applicable USP or NF monograph.</p>	<p>The bulk drug substance can be used in compounding under section 503A of the FD&C Act, provided it complies with the standards of the monograph (if one exists) and is compounded in compliance with the other conditions of section 503A.</p>
<p>The bulk drug substance appears on the withdrawn or removed list.</p>	<p>The bulk drug substance cannot be used in compounding under section 503A of the FD&C Act. A drug compounded using the bulk drug substance is subject to regulatory action.</p>
<p>The bulk drug substance appears in 503A Category 2 on FDA’s website at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467373.pdf. The substance has been identified by FDA as presenting a significant safety risk pending further evaluation.</p>	<p>The bulk drug substance cannot be used in compounding under section 503A of the FD&C Act unless and until FDA publishes a final rule authorizing its use under section 503A.</p>
<p>The bulk drug substance is a biological product subject to approval in a BLA.</p>	<p>The bulk drug substance is not eligible for the 503A bulks list. FDA has issued a separate draft guidance document describing the Agency’s proposed policies concerning mixing, diluting, and repackaging biological products subject to approval in a BLA.²⁴</p>
<p>The bulk drug substance appears in 503A Category 3 on FDA’s website at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467373.pdf. The substance may be eligible for inclusion on the 503A bulks list, but was nominated with insufficient supporting information for FDA to evaluate it.</p>	<p>The bulk drug substance cannot be used in compounding under section 503A of the FD&C Act. See section III.B of this guidance for information about re-nominating substances that were previously nominated with insufficient supporting information.</p>

²⁴ See FDA’s revised draft guidance, *Mixing, Diluting, and Repackaging Biological Products Subject to Approval in a Biologics License Application*.

Updated February 1, 2017

Bulk Drug Substances Nominated for Use in Compounding Under Section 503A of the Federal Food, Drug, and Cosmetic Act

503A Category 1 – Bulk Drug Substances Under Evaluation

- 7 Keto Dehydroepiandrosterone
- Acetyl L Carnitine/Acetyl-L-carnitine hydrochloride
- Acetyl-D-Glucosamine
- Alanyl-L-Glutamine
- Aloe Vera/ Aloe Vera 200:1 Freeze Dried
- Alpha Lipoic Acid
- Ammonium Tetrathiomolybdate
- Artemisia/Artemisinin
- Astragalus Extract 10:1
- Beta Glucan (1,3/1,4-D)
- Boswellia
- Brilliant Blue
- Bromelain
- Cantharidin
- Capsaicin palmitate
- Cesium Chloride
- Cetyl Myristoleate
- Choline Chloride
- Chondroitin Sulfate
- Chrysin
- Curcumin
- Deoxy-D-Glucose
- Dichloroacetate
- Diindolylmethane
- Dimercapto-1-propanesulfonic acid (DMPS)
- Diphenylcyclopropenone (DPCP)
- EGCg
- Ferric Sub sulfate
-
- Glutaraldehyde
- Glutathione
- Glycoaminoglycans
- Glycolic Acid
- Glycyrrhizin
- Kojic Acid
- L-Citrulline
- Methylcobalamin
- Methylsulfonylmethane (MSM)
- Nettle leaf (*Urtica dioica* subsp. *dioica* leaf)
- Nicotinamide Adenine Dinucleotide (NAD)
- Nicotinamide Adenine Dinucleotide Disodium Reduced (NADH)
- Ornithine Hydrochloride
- Oxitriptan
- Phosphatidylserine
- Piracetam
- Pregnenolone
- Pyridoxal 5-Phosphate Monohydrate
- Pyruvic Acid
- Quercetin/Quercetin Dihydrate
- Quinacrine Hydrochloride (except for intrauterine administration)
- Resveratrol
- Ribose (D)
- Rubidium Chloride
- Silver Protein Mild
- Squaric Acid Dibutyl Ester (aka dibutyl squarate)
- Tea tree oil (*Melaleuca alternifolia* leaf oil)
- Thymol Iodide
- Tranilast
- Trichloroacetic Acid
- Ubiquinol 30% Powder
- Vanadium
- Vasoactive Intestinal Peptide

Updated February 1, 2017

503A Category 2: Bulk Drug Substances that Raise Significant Safety Risks

- Domperidone
- Quinacrine
Hydrochloride for
intrauterine
administration
- Germanium
Sesquioxide

Updated February 1, 2017

503A Category 3: Bulk Drug Substances Nominated Without Adequate Support

- Acetanilide
- Acidophilus Lactobacillus
- Adenosine-5-triphosphate disodium salt
- Alcloxa
- Aldioxa
- Aldosterone
- Alfalfa
- Alfalfa leaves
- Almadrate sulfate
- Aloin
- Alpha Ketoglutaric acid
- Alumina Powder, hydrated
- Aluminum phosphate
- Aminacrine Hydrochloride
- Ammonium bromide
- Ammonium hydroxide
- Anise seed
- Argentyn
- Aromatic powder
- Asafetida
- Asclepias tuberosa
- Asefetida Tincture
- Asparagus
- Aspergillus oryza enzymes
- Barosma
- Beechwood creosote
- Bean
- Betamechlomathasone
- Beta-Nicotinamide Adenine Dinucleotide Disodium Salt Trihydrate
- Bichloroacetic Acid
- Calcium Folate
- Calcium Glycinate
- Carbazochrome
- Carbimazole
- Cedarwood Essential Oil
- Chlorhexidine Diacetate Hydrate
- Choline bitartrate
- Choline magnesium trisalicylate
- Chromium glycinate
- Coenzyme Q10
- Coenzyme Q50
- Copper
- Copper Bisglycinate
- Copper Hydrosol
- Creatine, Monohydrate
- Decylmethylsulfoxide
- Diaminopyridine (3,4-)
- Dichloroacetic acid
- Dimethyl Ketone
- Dimethylaminoethanol Bitartrate
- Dimethylglycine Hydrochloride
- Dinitrochlorobenzene
- Disodium Phosphate
-
- Edetate tetrasodium tetrahydrate
- Gamma Aminobutyric Acid
- GHRP-2
- GHRP-6
- Ginger root powder
- Ginkgo Biloba Standardized Extract
- Gluconic acid calcium salt
- Glycerol Formal
- Glydiazinamide
- Grape seed oil
- Heart-leaf nettle leaf (Urtica chamaedryoides leaf)
- Hyaluronic Acid Sodium Salt
- Hydrazine sulfate
- Indigo Carmine
- Indole-3-carbinol
- Inositol Hexanicotinate
- Iron Glycinate Chelate
- Karaya Gum
-
- L-Carnosine
- Levulose
- L-Histidine Monohydrochloride, Monohydrate
- L-Ornithin Hydrochloride
- Magnesium ascorbate
- Magnesium bisglycinate
- Magnesium bisglycinate dihydrate
- Magnesium glycinate
- Malt
- Malt soup extract
- Maltodextrin
- Manganese Bisglycinate

Updated February 1, 2017

- Manganese citrate
- m-cresol
- Melatonin
- Menfegol
- Meralein sodium
- Merbromin
- Mercufenol chloride
- Mercuric chloride
- Mercuric oxide
- Mercuric salicylate
- Mercuric sulfide
- Mercury
- Mercury oleate
- Mercury sulfide
- Methapyrilene fumarate
- Methoxyphenamine Hydrochloride
- Methoxypolyoxyethyleneglycol 350 laurate
- Methyl nicotinate
- Methpyrilene Hydrochloride
- Milk and molasses
- milk solids, dried
- Molasses
- Molybdenum Glycinate
- Monosodium L-Aspartate
- Mullein
- Mustard oil (alltlishthiocyanate)
- Mycozyme
- Myrrh gum tincture
- Myrrh tincture
- Natural estrogenic hormone
- Nickel-pectin
- Non-Fat Dry Milk
- Nonylphenoxypoly (ethyleneoxy) ethanol iodine
- Nonylphenoxypoly nonoxynol 9
- Noscapine Hydrochloride
- Nutmeg oil
- Nux vomica extract
- Obtundia
- Octyl triazone
- Oil of erigeron
- Organic vegetables
- Orthophosphoric acid
- Ox bile
- Ox bile extract
- Oxyquinoline
- Padimate a
- Pambron
- Pantothenic acid
- Papaya enzymes
- Papaya, natural
- Para-chloromercuriphenol
- Parethoxycaine Hydrochloride
- Parsley
- Passion flower extract
- Pennyroyal Oil
- Pentylenetetrazole
- Peppermint Oil and Sage Oil
- Pepsin
- Peruvian balsam (Myroxylon balsamum var. pereirae balsam)
- Phenacaine Hydrochloride
- Phenindamine Tartrate
- Phenolate sodium
- Phenolphthalein
- Phenoxyacetic acid
- Phenyl salicyate (Salol)
- Phenyl salicylate
- Phenyltoloxamine dihydrogen citrate
- Phenyltoloxamine Hydrochloride
- Phosphate fluoride
- Phosphorated carbohydrate
- Phosphorus
- Phytolacca
- Picrotoxin
- Pimobendan
- Pine tar
- Piperocaine Hydrochloride
- Pipsisewa
- Piracetam dihydrogen citrate
- Piscidia erythrina
- Plantago ovata husks
- Poloxamer-iodine complex
- Polydimethylsiloxane and poloxamer
- Polyols, liquid
- Polyoxeythylene laurate

Updated February 1, 2017

- Potash Lye
- Potassium chlorate
- Potassium ferrocyanide
- Potassium salicylate
- Povidone-vinylacetate copolymers
- Prolase
- Prune concentrate dehydrate
- Prune powder
- Psyllium
- Psyllium hydrophillic mucilloid
- P-T-butyl-m-cresol
- Pyruvic aldehyde
- Pyruvic Aldehyde 40% Aqueous Solution
- Racephpedrine Hydrochloride
- Red petrolatum
- Reosote
- Rhubarb fluid extract
- Rhubarb, Chinese
- Rice pollishings
- Romohydrate
- Sabadilla, alkaloids
- Sage oil
- Salicyl alcohol
- Sanguinaria extract
- Saw palmetto
- Scopolamine aminoxide Hydrobromide
- Sea mineral
- Senecio aureus
- Senna syrup
- Serotonin Hydrochloride
- Sesame Seed
- Shark liver oil
- Short Chain Fatty Acid
- Silver (see also argentyn)
- Silver, colloidal
- Sodium 3, 4-dimethylphenyl-glyoxylate
- Sodium acetylsalicylate
- Sodium aluminum chlorohydroxy lactate
- Sodium aspartate
- Sodium biphosphate
- Sodium bisulfate
- Sodium borate monohydrate
- Sodium caseinate
- Sodium diacetate
- Sodium dichromate
- Sodium dihydrogen phosphate monohydrate
- Sodium nitrate
- Sodium octanoate
- Sodium oleate
- Sodium para-amino benzoate
- Sodium perborate
- Sodium perborate monohydrate
- Sodium phosphate
- Sodium potassium tartrate
- Sols, secondary
- Soy meal
- Soybean protein
- Squill preparations
- Stannous pyrophosphate and zinc citrate
- Stevia Powder Extract
- Strychnine
- Sucros
- Sugars
- Sulferated oils of turpentine
- Sulfobutylether B-Cyclodextrin
- Tannic acid glycerite
- Taraxacum officinale
- Tartrate
- Tetrahydrochloride
- Thenyldiamine Hydrochloride
- Theobromine Sodium Salicylate
- Theophylline calcium salicylate
- Thioctic
- Thiocynoacetate
- Thonzylamine Hydrochloride
-
- Thylene blue
- Tolindate
- Toltrazuril
- Tolu preparations
- Tricalcium phosphate
- Triethanolamine
- Trillium

Updated February 1, 2017

- Triple dye
- Triticum
- Turpentine Oil
- Turpentine, Venice
- Uinolinium bromide
- Ulose
- Uva ursi, extract of
- Valic acid
- Vitamin A acetate
- Vitromersol
- Wheat germ
- Wheat germ (triticum aestivum/vulgare extract)
- White ointment
- Woodruff
- Yeast
- Yeast cell derivative
- Yellow mercuric oxide
- Zinc caprylate
- Zinc citrate
- Zinc phenol sulfonate
- Zinc picolinate
- Zinc propionate
- Zinc sulfide
- Zirconium oxide
- Zyloxin

Attachment

**Interim Policy on Compounding
Using Bulk Drug Substances
Under Section 503B of the
Federal Food, Drug, and
Cosmetic Act
Guidance for Industry**

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Office of Compliance/OU DLC**

**January 2017
Compounding and Related Documents
Revision 1**

Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act

Guidance for Industry

*Additional copies are available from:
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<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>*

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
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**January 2017
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Contains Nonbinding Recommendations

TABLE OF CONTENTS

I.	INTRODUCTION AND SCOPE	1
II.	BACKGROUND	2
A.	Compounding From Bulk Drug Substances Under Section 503B.....	2
B.	Section 503B Bulks List.....	3
III.	POLICY	7
A.	Compounding from Bulk Drug Substances Under Section 503B.....	7
B.	Substances Not Nominated or Nominated Without Adequate Support	8
C.	Comments about Nominated Bulk Drug Substances.....	9
	APPENDIX: SUMMARY OF POLICY	10

Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act Guidance for Industry¹

This guidance represents 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 office 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 the Agency) interim regulatory policy concerning compounding by outsourcing facilities registered under section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act or Act)² using bulk drug substances. Section 503B of the FD&C Act includes certain restrictions on the bulk drug substances that outsourcing facilities can use in compounding and directs FDA to develop a list of bulk drug substances that can be used in compounding under that section. FDA is developing that list of bulk drug substances (the 503B bulks list), and this guidance describes FDA's interim regulatory policy regarding outsourcing facilities that compound human drug products using bulk drug substances while the list is being developed.^{3,4}

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.

¹ This guidance has been prepared by multiple offices in the Center for Drug Evaluation and Research (CDER), in consultation with the Office of Regulatory Affairs at the Food and Drug Administration.

² *Outsourcing facility* refers to a facility that meets the definition of an outsourcing facility under section 503B(d)(4) of the FD&C Act.

³ This guidance does not apply to drugs compounded from bulk drug substances for use in animals. 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*.

All FDA guidances are available on the FDA guidance web page. FDA updates guidances regularly. To make sure you have the most recent version of a guidance, always consult the guidance web page at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

⁴ FDA is also developing a separate list of bulk drug substances that can be used in compounding under section 503A of the FD&C Act. Because section 503A contains different criteria for that list and provides for a different process for its development, the section 503A bulks list is covered under a separate guidance (see guidance for industry, *Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act*).

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II. BACKGROUND

A. Compounding From Bulk Drug Substances Under Section 503B

Section 503B of the FD&C Act describes the conditions that must be satisfied for human drug products compounded by an outsourcing facility to be exempt from the following three sections of the FD&C Act: section 505 (concerning the approval of drugs under new drug applications or abbreviated new drug applications); section 502(f)(1) (concerning the labeling of drugs with adequate directions for use); and section 582 (concerning drug supply chain security requirements).

One of the conditions that must be met for a drug product compounded by an outsourcing facility to qualify for these exemptions is that the outsourcing facility does not compound drug products using a bulk drug substance unless (a) it appears on a list established by the Secretary identifying bulk drug substances for which there is a clinical need, or (b) the drug compounded from such bulk drug substances appears on the drug shortage list in effect under section 506E of the FD&C Act at the time of compounding, distribution, and dispensing. Section 503B(a)(2)(A) of the FD&C Act.

A bulk drug substance is defined as meaning “the same as active pharmaceutical ingredient as defined in 21CFR 207.1(b).” See 21 CFR 207.3. Active pharmaceutical ingredient is defined as “any substance that is intended for incorporation into a finished drug product and is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body,” but the term “does not include intermediates used in the synthesis of the substance” (see section 503B(a)(2) and 21 CFR 207.3).^{5,6}

Bulk drug substances used in compounding under section 503B must also meet certain other requirements, including: (1) if an applicable monograph exists under the United States Pharmacopeia (USP), National Formulary (NF), or another compendium or pharmacopeia recognized by the Secretary for purposes of this paragraph, the bulk drug substance complies with the monograph; (2) the bulk drug substance must be manufactured by an establishment that is registered under section 510 of the FD&C Act; and (3) the bulk drug substance must be accompanied by a valid certificate of analysis (COA). Section 503B(a)(2) of the FD&C Act.

⁵ Section 503B references the definition of bulk drug substance in FDA’s drug establishment registration and listing regulations, which was codified at 21 CFR 207.3(a)(4) at the time section 503B was enacted. On August 31, 2016, FDA published a final rule in the Federal Register to update its registration and listing regulations in Part 207, which made minor changes to the definition of bulk drug substance and moved the definition to 21 CFR 207.3. The definition is also found in 207.1. See 81 FR 169 (August 31, 2016). Under the previous definition, bulk drug substance was defined to mean “any substance that is represented for use in a drug and that, when used in the manufacturing, processing, or packaging of a drug, becomes an active ingredient or a finished dosage form of the drug, but the term does not include intermediates used in the synthesis of such substances.”

⁶ Inactive ingredients are not subject to section 503B(a)(2) or the policies described in this guidance because they are not included within the definition of a bulk drug substance. See 21 CFR 207.3. Pursuant to section 503B(a)(3), inactive ingredients used in compounding must comply with the standards of an applicable United States Pharmacopeia or National Formulary monograph, if a monograph exists.

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B. Section 503B Bulks List

1. Section 503B Bulks List History

Section 503B, added to the FD&C Act by the Drug Quality and Security Act in 2013, requires that FDA create a list of bulk drug substances for which there is a clinical need by publishing a notice in the *Federal Register* proposing bulk drug substances for inclusion on the list, providing a public comment period of 60 calendar days, and then publishing a notice in the *Federal Register* designating bulk drug substances for inclusion on the list. See section 503B(a)(2)(A)(i) of the FD&C Act. In the December 4, 2013, *Federal Register* (78 FR 72838), FDA published a notice inviting all interested persons to nominate bulk drug substances for inclusion on a list of bulk drug substances that can be used for compounding under section 503B of the FD&C Act.

2. Nominations for the 503B Bulks List

In response to the December 2013 *Federal Register* notice, over 2,000 substances were nominated for the 503B bulks list. However, many of the nominations for the 503B bulks list were not for substances used in compounding as active ingredients, or they did not include sufficient information to allow FDA to evaluate the nominated substances for placement on the list. To improve the efficiency of the process for developing the 503B bulks list, FDA reopened the nomination process in July 2014 (79 FR 37747), and provided more detailed information on what it needs to evaluate nominations for the list. FDA stated that bulk drug substances that were previously nominated would not be further considered unless they were re-nominated and those nominations were adequately supported. Substances that were not adequately supported would not be evaluated by FDA to be placed on the 503B bulks list. The notice stated that the following information about clinical need is necessary to provide adequate support for nominations to the 503B bulks list:

- A statement describing the medical condition(s) that the drug product to be compounded with the nominated bulk drug substances is intended to treat;
- A list of FDA-approved drug products, if any, that address the same medical condition;
- If there are any FDA-approved drug products that address the same medical condition, an explanation of why a compounded drug product is necessary;
- If the approved drug product is not suitable for a particular patient population, an estimate of the size of the population that would need a compounded drug product;
- A bibliography of safety and efficacy data for the drug product compounded using the nominated substance, if available, including any relevant peer-reviewed medical literature; and
- If there is an FDA-approved drug product that includes the bulk drug substance nominated, an explanation of why the drug product proposed to be compounded must be compounded from bulk rather than with the FDA-approved drug product.

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In response to this request for nominations, approximately 2,590 unique substances were nominated. Of the nominated substances:

- Approximately 1,740 are biological products (all but one of these⁷ are individual allergenic extracts) subject to approval in a biologics license application (BLA) under section 351 of the Public Health Service (PHS) Act.

These products are not eligible for the 503B bulks list because biological products subject to approval in a BLA under section 351 of the PHS Act are not eligible for the exemptions in section 503B.⁸ No biological products subject to approval in a BLA will be considered for the 503B bulks list.

- At least one⁹ of the nominated substances is not a bulk drug substance.

This is a finished drug product that was nominated by its brand name. Finished drug products are not eligible for the 503B bulks list because they do not meet the definition of a bulk drug substance in 21 CFR 207.3.

- At least one of the nominated substances is a radiopharmaceutical.¹⁰

Compounding of radiopharmaceutical products will be addressed in a separate guidance document.¹¹

- At least five of the nominated substances appear on the list of drugs that have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective (withdrawn or removed list)

Such substances cannot be used in compounding under section 503B of the FD&C Act, and therefore are not eligible for inclusion on the 503B bulks list.¹²

- One of the nominated substances has no currently accepted medical use and is included on Schedule I of the Controlled Substances Act (CSA) (21 U.S.C. § 812(c)).¹³

⁷ The product is sodium hexachloroplatinate (IV) hexahydrate.

⁸ See the draft guidance, *Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application* for FDA's proposed policies regarding State-licensed pharmacies, Federal facilities, and outsourcing facilities that mix, dilute, or repack biological products outside the scope of an approved BLA.

⁹ The over-the-counter finished drug product Maalox was nominated. Maalox is not a bulk drug substance.

¹⁰ The substance is sodium iodide I-131.

¹¹ FDA has published a draft guidance, "Compounding and Repackaging of Radiopharmaceuticals by Outsourcing Facilities," for public comment. That draft guidance proposes the Agency's policy regarding the use of bulk drug substances to compound radiopharmaceuticals under section 503B of the FD&C Act. Once that guidance is final, FDA intends to update this guidance to reflect the policies set forth therein.

¹² See section 503B(a)(4) of the FD&C Act. See also 21 CFR 216.24. The five substances are: chloroform reagent, cobalt chloride hexahydrate, cobalt gluconate, methapyrilene fumarate, and phenacetin.

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The CSA does not allow possession or distribution of Schedule I substances (see 21 U.S.C. §§ 841(a)(1) and 829), except for research purposes (21 U.S.C. § 823(f)), and these substances will not be considered for the 503B bulk drug substances list at this time. Those desiring to do research on a Schedule I substance can apply to do so under an investigational new drug application (IND).

- Of the substances that may be eligible for use in compounding under section 503B, approximately 650 substances were nominated without sufficient supporting evidence for FDA to evaluate them.
- The remaining substances that were nominated for inclusion on the 503B bulks list may be eligible for inclusion on the list and were nominated with sufficient supporting information for FDA to evaluate them. However, FDA has identified significant safety risks relating to the use in compounded drug products of some of these bulk drug substances.

FDA's website identifies the following categories of substances nominated for the 503B bulk drug substances list:¹⁴

503B Category 1 –Substances Nominated for the Bulks List Currently Under Evaluation: These substances may be eligible for inclusion on the 503B bulks list, were nominated with sufficient supporting information for FDA to evaluate them, and do not appear on any other list.

503B Category 2 –Substances Nominated for the Bulks List That Raise Significant Safety Risks: These substances were nominated with sufficient supporting information to permit FDA to evaluate them and they may be eligible for inclusion on the 503B bulks list. However, FDA has identified significant safety risks relating to the use of these substances in compounding pending further evaluation, and therefore does not intend to adopt the policy described for the substances in category 1. If FDA adds a substance to Category 2, it will publish a public communication (e.g. a safety alert) describing the safety risks and will post

¹³ An extract of cannabidiol (CBD) and tetrahydrocannabinol (THC) derived from marijuana (marihuana) was nominated. Marijuana (marihuana) is a Schedule I substance.

¹⁴ <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467374.pdf>. As discussed in the July 2014 Federal Register notice requesting nominations for the 503B bulks list ((79 FR 37747), nominators were to confirm that all substances nominated for the list are active ingredients that meet the definition of a “bulk drug substance.” Inclusion of a substance in any of these categories does not reflect a determination by FDA that the substance is a bulk drug substance. Whether a substance is a bulk drug substance subject to the conditions in section 503B(a)(2) depends on whether it meets the definition of a bulk drug substance in 21 CFR 207.3. If the substance is used in a compounded drug as an inactive ingredient, then it does not meet the definition of a bulk drug substance in 21 CFR 207.3, is not subject to the conditions in section 503B(a)(2), and need not appear on the 503B bulks list to be eligible for use in compounding. Instead, when used as an inactive ingredient, the substance is subject to the conditions in section 503B(a)(3), which applies to ingredients other than bulk drug substances used in compounded drugs

Contains Nonbinding Recommendations

the communication on FDA's human drug compounding website¹⁵ advising that the substance has been added to Category 2 and is no longer eligible for the policies that apply to substances in Category 1.

503B Category 3 –Substances Nominated for the Bulks List Without Adequate

Support: These substances may be eligible for inclusion on the 503B bulks list, but were nominated with insufficient supporting information for FDA to evaluate them. These substances can be re-nominated with sufficient supporting information through a docket that FDA has established, as discussed below in section III.B.

3. Process for Developing the 503B Bulks List

FDA is currently evaluating the bulk drug substances nominated for the 503B bulks list with sufficient supporting information for evaluation. FDA is considering a number of factors in prioritizing the order in which it reviews these nominated bulk drug substances, including but not limited to the following:

- Safety concerns about use of the bulk drug substance in compounding
- Whether the bulk drug substance was nominated by multiple parties or identified as necessary by medical professional organizations
- The efficiency with which the evaluation can be completed, based on ease of acquiring the necessary information to conduct the review, available resources, and other logistical issues

FDA may also group some nominated drug substances to facilitate efficient review and discussion. These include drug substances that raise similar issues (e.g., vitamins or botanicals) or that are nominated for the treatment of the same condition (e.g., warts).

FDA intends to publish a notice in the *Federal Register* that describes its proposed position on each substance it has evaluated along with the rationale for that proposal, for public comment. We note that there is no requirement in section 503B to consult the Pharmacy Compounding Advisory Committee (PCAC) before developing a 503B bulks list, as is required by section 503A(c)(1) for the 503A bulks list. However, after considering public comment on the nominated substances, FDA will determine whether PCAC input on any of the substances would be helpful to the Agency in making its determination, and if so, it will seek PCAC input. Once FDA makes a determination, it will publish in the *Federal Register* a list identifying the bulk drug substances for which it has determined there is a clinical need and FDA's rationale in making that determination. FDA will also publish in the *Federal Register* a list of those substances it considered but found that there is no clinical need to use in compounding and FDA's rationale in making this determination.

¹⁵ <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/default.htm>.

FDA also encourages compounding facilities to subscribe to FDA's list serve to receive updates at: http://service.govdelivery.com/service/subscribe.html?code=USFDA_429.

Contains Nonbinding Recommendations

Once FDA publishes a 503B bulks list in the *Federal Register* that reflects its determination regarding particular bulk drug substances, drug products compounded with substances on the 503B bulks list will be eligible for the 503B exemptions, provided the drug products are compounded in compliance with the other conditions of section 503B.¹⁶ Once FDA has published in the *Federal Register* its decision not to place a particular substance on the 503B bulks list, the policy described in section III of this guidance no longer applies.

FDA intends to evaluate the substances nominated for the 503B list on a rolling basis. FDA will begin by publishing a *Federal Register* notice identifying a group of substances (e.g., 10 substances) that it has considered and whether it proposes the substances for inclusion on the list. Under section 503B, an outsourcing facility may only compound using bulk drug substances that are on FDA's 503B bulks list or that are used to compound drugs that appear on the shortage list in effect under section 506E of the FD&C Act at the time of compounding, distribution, and dispensing. To avoid unnecessary disruption to patient treatment while FDA considers the substances that were nominated with sufficient support to permit FDA to evaluate them, FDA is issuing this guidance stating that at this time it does not intend to take action against an outsourcing facility for failing to compound in accordance with section 503B(a)(2) if certain conditions are met. Those conditions include that the nomination for the relevant bulk drug substance was submitted with adequate information for FDA to evaluate the substance and that FDA has not identified significant safety risks about its use in compounding prior to publication of the *Federal Register* notice identifying those substances FDA has determined will or will not be placed on the 503B bulks list.

III. POLICY¹⁷

A. Compounding from Bulk Drug Substances Under Section 503B

Under section 503B of the FD&C Act, a bulk drug substance cannot be used in compounding unless it is used to compound a drug that appears on the FDA drug shortage list at the time of compounding, distribution, and dispensing, or it appears on the 503B bulks list.

FDA does not intend to take action against an outsourcing facility for compounding a drug product using a bulk drug substance that is not on the 503B bulks list if the drug compounded from the bulk drug substance: (i) appeared on FDA's drug shortage list within 60 days of distribution and dispensing, and (ii) was to fill an order that the outsourcing facility received for the drug while it was on FDA's drug shortage list.¹⁸

¹⁶ See section 503B(a)(11) of the FD&C Act.

¹⁷ See Appendix A for a summary of FDA's interim policy.

¹⁸ An outsourcing facility may not be able to predict when a drug shortage will be resolved, and the facility may have orders for a compounded drug in-house that were in progress when the drug was removed from FDA's drug shortage list (e.g., the outsourcing facility may have compounded a drug while it was in shortage, but the shortage ended while the outsourcing facility awaits the results of sterility testing before release.) This policy provides some regulatory flexibility where an outsourcing facility fills orders that it received while a drug was in shortage. However, this policy does not apply if an outsourcing facility continues to fill orders received after the shortage

Contains Nonbinding Recommendations

In addition, at this time FDA does not intend to take action against an outsourcing facility for compounding a drug using a bulk drug substance that does not appear on the 503B bulks list and that is not used to compound a drug that appears on the FDA drug shortage list at the time of compounding, distribution, and dispensing, provided that the following conditions are met:

1. The bulk drug substance appears on 503B Category 1 on FDA's website at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467374.pdf>. A Category 1 substance may be eligible for inclusion on the 503B bulks list, was nominated for inclusion on the 503B bulks list with adequate supporting information for FDA to evaluate it, and has not been identified by FDA as a substance that appears to present a significant safety risk in compounding before a determination as to whether to place it on the 503B bulks list has been made.
2. The original manufacturer and all subsequent manufacturers of the bulk drug substance are establishments that are registered under section 510 (including foreign establishments that are registered under section 510(i)) of the FD&C Act;
3. The bulk drug substance is accompanied by a valid COA;
4. If the bulk drug substance is the subject of an applicable USP or NF monograph, the bulk drug substance complies with the monograph; and
5. The drug product compounded using the bulk drug substance is compounded in compliance with all other provisions of section 503B of the FD&C Act.

Original manufacturer means the entity that originally produced the bulk drug substance and not a subsequent packer, repacker, labeler, or distributor.

This policy does not apply to an outsourcing facility that compounds a drug using a bulk drug substance that does not meet each of the above conditions and where the bulk drug substance was not used to compound a drug that appears on the FDA drug shortage list at the time of compounding, distribution, and dispensing, or that appeared on the FDA drug shortage list within 60 days of distribution and dispensing.

B. Substances Not Nominated or Nominated Without Adequate Support

As stated above, FDA is providing a list on its website of substances nominated for the 503B bulks list that may be eligible for inclusion on the list, but that FDA is unable to evaluate for inclusion on the list at this time because the substances were nominated with insufficient supporting evidence for FDA to evaluate them (503B Category 3). In the *Federal Register* of October 27, 2015, FDA established a docket (October docket) where these substances can be re-

ends, or if the outsourcing facility continues to fill orders more than 60 days after the drug was removed from FDA's drug shortage list.

Contains Nonbinding Recommendations

nominated with sufficient supporting information or where nominations for substances that were not previously nominated can be submitted.

After a substance is nominated to the October docket,¹⁹ FDA will determine whether the nomination is supported with sufficient information to allow FDA to evaluate it. After FDA makes that determination, the nominated substance will be placed in one of the three categories described in section II.B.2 above, and the categorization will be published on the FDA website. Once the category of a substance is published, FDA intends to apply the policy described in section III.A. of this guidance to that substance. FDA generally expects to categorize bulk drug substances nominated to the October docket and to publish updated categories on its website on the first business day of each month. Please note that until substances nominated for the October docket have been categorized, the policy does *not* apply to those substances.

C. Comments about Nominated Bulk Drug Substances

If you feel that a substance that you nominated does not appear on the appropriate list or category as described in this guidance you can submit your comment to docket number FDA-2015-N-3469. If you have new information on a previously-nominated substance that was placed in Category 3, the substance can be re-nominated with the additional information.

A nominator may also submit a comment to the docket requesting withdrawal of any of its nominations. If the party nominating the substance was the sole nominator, FDA will update the categories described in this guidance to reflect the withdrawn nomination.²⁰ FDA intends to provide notice to the public before removing any nominated substances from Category 1 or Category 2.

Withdrawal of a nomination upon the nominator's request, and resulting updates to the categories described in this guidance, do not reflect a determination by FDA regarding the validity of the nomination or of any reasons given by the nominator for requesting withdrawal. In addition, FDA may continue to evaluate a substance at its discretion even if the nominator submits a comment requesting withdrawal of the nomination.

¹⁹ This includes re-nominations of substances with sufficient supporting information.

²⁰ If multiple parties nominated the same substance, each party that nominated the substance must withdraw its nomination for the nominated substance to be considered withdrawn and for the categories to be updated to reflect that withdrawal.

Contains Nonbinding Recommendations

APPENDIX: SUMMARY OF POLICY

The following table summarizes the interim policy for bulk drug substances set forth in this guidance:

Category	FDA Policy
<p>The bulk drug substance is in 503B Category 1 on FDA’s website at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467374.pdf.</p> <p>Such substances may be eligible for inclusion on the 503B bulks list, were nominated with adequate supporting information for FDA to evaluate them, and have not been identified by FDA as presenting significant safety risks.</p>	<p>The bulk drug substance is not on the 503B bulks list. However, pending a determination about whether to put the bulk drug substance on the 503B bulks list, FDA does not intend to take action against an outsourcing facility for compounding a drug product from a bulk drug substance that does not meet the conditions of section 503B(a)(2) provided that the bulk drug substance is manufactured by an establishment registered with FDA under section 510 of the FD&C Act, is accompanied by a valid COA, complies with an applicable USP monograph, if one exists, and provided that the drug compounded from the bulk drug substance is compounded in compliance with the other conditions of section 503B.</p>
<p>The bulk drug substance appears on the withdrawn or removed list.</p>	<p>The bulk drug substance cannot be used in compounding under section 503B of the FD&C Act.</p>
<p>The bulk drug substance is in 503B Category 2 on FDA’s website at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467374.pdf. The substance has been identified by FDA as presenting a significant safety risk in compounding pending further evaluation.</p>	<p>The bulk drug substance is not on the 503B bulks list, and cannot be used for compounding consistent with section 503B(a)(2) unless it is used to compound a drug that appears on FDA’s drug shortage list.</p>
<p>The bulk drug substance is a biological product subject to approval in a BLA.</p>	<p>The bulk drug substance is not eligible for the 503B bulks list. FDA has issued a separate draft guidance document describing the Agency’s proposed policies concerning mixing, diluting, and repackaging biological products subject to approval in a BLA.²¹</p>
<p>The bulk drug substance is a radiopharmaceutical product.</p>	<p>Compounding radiopharmaceuticals will be addressed in a separate guidance document.</p>
<p>The bulk drug substance is in 503B Category 3 on FDA’s website at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467374.pdf. The substance may be eligible for inclusion on the 503B bulks list but was nominated with insufficient supporting information for FDA to evaluate it.</p>	<p>The bulk drug substance is not on the 503B bulks list, and cannot be used for compounding consistent with section 503B(a)(2) unless the bulk drug substance is used to compound a drug that appears on FDA’s drug shortage list. See section III.B of this guidance for information about supplementing inadequately supported nominations.</p>

²¹ See FDA’s revised draft guidance, *Mixing, Diluting, and Repackaging Biological Products Subject to Approval in a Biologics License Application*.

Updated January 13, 2017

Bulk Drug Substances Nominated for Use in Compounding Under Section 503B of the Federal Food, Drug, and Cosmetic Act

503B Category 1 – Bulk Drug Substances Under Evaluation

- 17-alpha-Hydroxyprogesterone
- Acetylcysteine
- Adenosine
- Alpha Lipoic Acid
- Alprostadil
- Aluminum Chloride Hexahydrate
- Aluminum potassium sulfate
- Amitriptyline HCl
- Ascorbic acid
- Aspartic Acid
- Atenolol
- Atropine sulfate/ Atropine sulfate monohydrate
- Baclofen
- Betamethasone Acetate
- Betamethasone Sodium Phosphate
- Biotin
- Bismuth Nitrate Oxide
- Brilliant Blue
- Bromfenac sodium (for ophthalmic use)
- Brompheniramine maleate, USP
- Budesonide
- Bupivacaine Hydrochloride/ Bupivacaine Hydrochloride Monohydrate
- Caffeine
- Calcium Chloride
- Calcium EDTA
- Calcium Gluconate
- Cantharidin
- Caustic Soda (sodium hydroxide)
- Chloroquine Phosphate
- Chlorpheniramine Maleate
- Choline Bitartrate
- Choline Chloride
- Chromium chloride/ Chromium Chloride Hexahydrate
- Citric Acid Anhydrous
- Clindamycin Phosphate
- Clomipramine Hydrochloride
- Clonidine Hydrochloride
- Cyanocobalamin
- Cyclobenzaprine Hydrochloride
- Cyclopentolate
- Dapiprazole HCl
- Dexamethasone Acetate
- Dexamethasone Sodium Phosphate
- Dexpanthenol
- D-glucose
- Diazepam
- Diclofenac Sodium
- Diltiazem Hydrochloride
- Dimercapto-1-propanesulfonic acid (DMPS)
- Diphenylcyclopropenone
- Disulfiram
- Dopamine HCl
- Droperidol
- Edetate Disodium (EDTA)
- Ephedrine Hydrochloride
- Ephedrine sulfate, USP
- Epinephrine
- Epinephrine Bitartrate
- Estradiol Cypionate
- Estradiol
- Estriol
- Ethanol
- Ethyl Aminobenzoate
- Etomidate
- Famotidine
- Fentanyl Citrate
- Flurbiprofen
- Fluticasone Propionate
- Folic Acid
- Formaldehyde
- Furosemide
- Gabapentin
- Gentamicin Sulfate
- Glutamic acid
- Glutamine
- Glutathione
- Glycerin
- Glycopyrrolate/ Glycopyrrolate Bromide
- Heparin sodium

Updated January 13, 2017

- Hyaluronic acid sodium salt
- Hyaluronidase
- Hydralazine HCl
- Hydromorphone Hydrochloride
- Hydroxocobalamin Hydrochloride
- Hydroxyzine HCl
- Imipramine Hydrochloride
- Inositol
- Iodoform
- Itraconazole
- Ketamine Hydrochloride
- Ketoprofen
- Ketorolac Tromethamine
- Labetalol Hydrochloride
- Lansoprazole
- Lidocaine Hydrochloride
- Lincomycin HCl
- Lorazepam
- Magnesium Chloride
- Magnesium Sulfate Heptahydrate
- Malic Acid
- Medroxyprogesterone Acetate
- Meperidine Hydrochloride (a.k.a. Pethidine Hydrochloride)
- Methacholine Chloride
- Methionine/ Methionine (L)
- Methylcobalamin/ Methyl B12
- Methylprednisolone Acetate
- Methylsulfonylmethane (MSM)
- Midazolam Hydrochloride
- Mineral Oil
- Mitomycin
- Monosodium Glutamate
- Morphine Sulfate/ Morphine Sulfate Pentahydrate
- Moxifloxacin hydrochloride
- Nalbuphine HCl
- Naloxone Hydrochloride Dihydrate
- Neomycin sulfate
- Neostigmine Methylsulfate
- Niacin
- Niacinamide
- Nicardipine hydrochloride
- Nifedipine
- Norepinephrine Bitartrate
- Ondansetron HCl
- Ornithine Hydrochloride
- Oxymetazoline HCl
- Oxytocin
- Papaverine
- Phenol
- Phenoxybenzamine Hydrochloride
- Phentolamine Mesylate
- Phenylephrine HCl
- Phytonadione
- Pitcher Plant
- Podophyllum
- Polidocanol
- Polymyxin B Sulfate
- Potassium chloride
- Potassium phosphate/ Potassium Phosphate Dibasic Anhydrous
- Prednisolone
- Prednisolone Acetate
- Procainamide HCl
- Procaine Hydrochloride
- Progesterone
- Promethazine Hydrochloride
- Proparacaine HCl
- Propranolol hydrochloride
- Prostaglandin E1
- Pyridoxal 5-Phosphate Monohydrate
- Remifentanil Hydrochloride
- Riboflavin 5 PO4
- Rocuronium Bromide
- Ropivacaine Hydrochloride
- Salicylic Acid
- Scopolamine hydrobromide
- Sodium Acetate Anhydrous
- Sodium Ascorbate
- Sodium Benzoate
- Sodium Bicarbonate
- Sodium Chloride
- Sodium Citrate
- Sodium Citrate Dihydrate
- Sodium L-Aspartate Monohydrate
- Sodium phosphate/ Sodium Phosphate Monobasic Anhydrous
- Sodium Selenite
- Sodium Tetradecyl Sulfate
- Squaric acid dibutyl ester
- Succinylcholine Chloride Dihydrate
- Sufentanil Citrate
- Sulfan Blue

Updated January 13, 2017

- Taurine
- Testosterone
- Testosterone Propionate
- Tetracaine Hydrochloride
- Tetracycline Hydrochloride
- Thiamine HCl (vitamin B1)
- Thymol iodide
- Tramadol Hydrochloride
- Triamcinolone Acetonide
- Triamcinolone diacetate
- Tromethamine
- Tropicamide
- Trypan Blue
- Vanadium
- Vancomycin Hydrochloride
- Verapamil HCl
- Vitamin A acetate
- Vitamin D3
- Ziconotide
- Zinc Sulfate

Updated January 13, 2017

503B Category 2: Bulk Drug Substances that Raise Significant Safety Risks

- Germanium sesquioxide

Updated January 13, 2017

503B Category 3: Bulk Drug Substances Nominated Without Adequate Support

- 4-Aminopyridine
- 7-Keto Dehydroepiandrosterone, Micronized
- Acacia Gum, Spray-Dried Powder
- Acacia Syrup
- Acesulfame Potassium
- Acetanilide
- Acetic acid
- Acetone
- Acetone Sodium Bisulfite
- Acetyl Hexapeptide-3
- Acidophilus Lactobacillus
- Adenosine-5-triphosphate disodium salt
- Agar
- Alcloxa
- Aldioxa
- Aldosterone
- Alfalfa
- Alfalfa leaves
- Alginic acid
- Aliphatic Polyesters
- Allantoin
- Almadrate sulfate
- Aloin
- Alpha Ketoglutaric acid
- Alumina Powder, hydrated
- Aluminum acetate
- Aluminum chloride
- Aluminum phosphate
- Aluminum sulfate
- Aminacrine HCl
- Aminoacetic acid
- Ammonia solution, strong
- Ammonium Alginate
- Ammonium bromide
- Ammonium chloride
- Ammonium hydroxide
- Amylase
- Anise oil
- Anise seed
- Argentyn
- Arginine
- Aromatic powder
- Asafetida
- Asclepias tuberosa
- Ascrobyl Palmitate
- Asefetida Tincture
- Asparagus
- Aspartame
- Aspergillus oryza enzymes
- Attapulgate
- Azelaic Acid
- Barosma
- Basic Fuchsin
- Beachwood creosote
- Bean
- Benzalkonium Chloride
- Betamechlomathasone
- Beta-Nicotinamide Adenine Dinucleotide Disodium Salt Trihydrate
- Bethanechol
- Bichloroacetic Acid
- Bipeptide Bocosmetic
- Boric Acid
- Bromelain
- Bronopol
- Buffer Solution, pH Buffer Acid
- Butylated Hydroxytoluene
- Butylene Glycol
- Calcium Alginate
- Calcium Folate
- Calcium glycinate
- Capsules, Empty Gelatin Vegetable
- Carbamide
- Carbazochrome
- Carbimazole
- Carbolic Acid
- Carbomer 940
- Caustic Potash
- Cedarwood Essential Oil
- Ceratonia
- Ceresin
- Cetrimide
- Chlorhexidine Diacetate Hydrate
- Choline magnesium trisalicylate
- Chondroitin Sulfate
- Chromic chloride

Updated January 13, 2017

- Chromium glycinate
- Chrysin
- Cidofovir
- Cocoa butter
- Coconut Oil Edible
- Coenzyme Q10
- Coenzyme Q50
- Collagenase
- Colophony
- Copper
- Copper Bisglycinate
- Copper Hydrosol
- Corn Oil
- Corn Starch
- Corn Starch and Pregelatinized Starch
- Cottonseed Oil
- Creatine, Monohydrate
- Cucumber Melon Fragrance
- Cupric Sulfate
- Decyl Oleate
- Decylmethylsulfoxide
- Deoxy-D-Glucose
- Desonide
- Diaminopyridine (3,4-)
- Dichloroacetic Acid
- Difluoroethane
- Diindolymethane
- Dimercaptosuccinic acid
- Dimethyl Ether (aka Methoxymethane)
- Dimethyl Ketone
- Dimethyl Phthalate
- Dimethylacetamide
- Dimethylaminoethanol Bitartrate
- Dimethylaminoethanol Complex
- Dimethylglycine HCl
- Dinitrochlorobenzene
- Diphenhydramine
- Dipropylene Glycol
- Disodium Hydrogen Phosphate
- Disodium Phosphate
- DL-Phenylalanine
- Docosanol
- Dodecyl Gallate
- Domperidone
- Edetate tetrasodium tetrahydrate
- Ethanolamine
- Ethyl Lactate
- Ethylene Vinyl Acetate
- Ferric subsulfate
- Ferric sulfate hydrate
- Ferric sulfate solution
- Folinic acid calcium salt
- Formoterol Fumarate Dihydrate
- Fructose and Pregelatinized Starch
- Gamma Aminobutyric Acid
- GHRP-2
- GHRP-6
- Ginger root powder
- Ginkgo Biloba Standardized Extract
- Gloconic acid calcium salt
- Glutaraldehyde solution
- Glycerol Formal
- Glyceryl Monostearate
- Glyceryl Palmitostearate
- Glycofurol
- Glycolic acid
- Glydiazinamide
- Grape seed oil
- Gum Arabic
- Hectorite
- Heptafluoropropane
- Hexetidine
- Hyaluronidase, salt free
- Hydrazine sulfate
- Hydrochloric Acid
- Hydroxyethylpiperazine Ethane Sulfonic Acid
- Hydroxymethylmethyl Cellulose
- Ichthammol
- ICU Bottom Paste (Maalox)
- Indigo Carmine
- Indole-3-carbinol
- Inositol Hexanicotinate
- Iodochlorhydroxyquin
- Iopanoic Acid
- Iron Glycinate Chelate
- Isopropyl Isostearate
- Kaolin, Colloidal Powder
- Karaya Gum
- Ketoifen Fumarate
- Kojic Acid

Updated January 13, 2017

- Lactose Monohydrate
- Lactose, Monohydrate and Corn Starch
- Lactose, Monohydrate and Microcrystalline Cellulose
- Lactose, Monohydrate and Powdered Cellulose
- Lactose, Spray-Dried
- Lanolin, Hydrous
- L-Aspartic Acid Sodium Salt
- Lavender Oil
- L-Carnitine
- L-Carnosine
- L-Citrulline
- L-Cysteine
- Lecithin Soya Granular
- Lecithin Organogel
- Levomenthol
- Levulose
- L-Histidine Monohydrochloride, Monohydrate
- Lidocaine, Epinephrine, and Tetracaine
- Linoleic Acid
- L-Ornithin HCl
- Loxasperse
- L-Triiodothyronine Sodium
- Lysine
- Magaldrate
- Magnesium
- Magnesium aluminum silicate
- Magnesium ascorbate
- Magnesium bisglycinate
- Magnesium bisglycinate dihydrate
- Magnesium carbonate
- Magnesium citrate
- Magnesium glycinate
- Magnesium hydroxide
- Magnesium oxide
- Magnesium salicylate
- Magnesium stearate
- Magnesium sulfate
- Magnesium trisilicate
- Malt
- Malt soup extract
- Maltodextrin
- Manganese Bisglycinate
- Manganese Chloride
- Manganese citrate
- Mannitol
- Mannitol and sorbitol
- MBK
- m-cresol
- Meclizine HCl
- Medium Cream
- Menfegol
- Menthol
- Menthol/peppermint oil
- Meradimate (menthyl anthranilate)
- Meralein sodium
- Merbromin
- Mercufenol chloride
- Mercuric chloride
- Mercuric oxide
- Mercuric salicylate
- Mercuric sulfide
- Mercury
- Mercury oleate
- Mercury sulfide
- Mercury, ammoniated
- Metaproterenol sulfate
- Methenamine
- Methoxyphenamine HCl
- Methoxypolyoxyethyleneglycol 350 laurate
- Methyl nicotinate
- Methyl salicylate
- Methylbenzethonium chloride
- Methylcellulose
- Methylparaben
- Methypyrilene HCl
- Metoclopramide HCl
- Miconazole nitrate
- Microcrystalline Cellulose
- Milk and molasses
- Milk of sulfur
- milk solids, dried
- Mineral oil and Lanolin Alcohols
- Minerals
- Molasses
- Molybdenum Glycinate
- Mono- and di-glycerides
- Monosodium L-Aspartate
- Monosodium Phosphate
- Mullein

Updated January 13, 2017

- Mustard oil (allitishthiocyanate)
- Mycozyme
- Myrrh
- Myrrh gum tincture
- Myrrh tincture
- N-Acetyl-D-Glucosamine
- Naphazoline HCl
- Natural estrogenic hormone
- Neohesperidine Dihydrochalcone
- Nettle
- Nickel-pectin
- Nicotinamide
- Nicotinic Acid
- Nitromersol
- Non-Fat Dry Milk
- Nonylphenoxypoly (ethyleneoxy) ethanol iodine
- Nonylphenoxypoly nonoxynol 9
- Noscapine
- Noscapine HCl
- Nutmeg oil
- Nux vomica extract
- Nystatin
- Obtundia
- Octinoxate
- Octisalate
- Octocrylene
- Octoxynol 9
- Octyl Gallate
- Octyl triazone
- Oil of erigeron
- Opium powder
- Opium tincture
- Organic vegetables
- Orthophosphoric acid
- Ox bile
- Ox bile extract
- Oxitriptan
- Oxybenzone
- Oxyquinoline
- Oxytetracycline HCl
- Padimate a
- Padimate o
- Pambron
- Pancreatin
- Pancrelipase
- Panthenol
- Pantothenic acid
- Papain
- Papaya enzymes
- Papaya, natural
- Para-chloromercuriphenol
- Paraffin
- Paregoric
- Parethoxycaine HCl
- Parsley
- Passion flower extract
- Patchouli Essential Oil
- Pectin
- Pennyroyal Oil
- Pentylenetetrazole
- Peppermint
- Peppermint Oil
- Peppermint Spirit
- Pepsin
- Peruvian Balsam
- Petrolatum
- Phenacaine HCl
- Phenindamine Tartrate
- Pheniramine Maleate
- Phenobarbital
- Phenolate sodium
- Phenolphthalein
- Phenoxyacetic acid
- Phenyl salicylate
- Phenylalanine
- Phenylephrine bitartrate
- Phenylmercuric Borate
- Phenylmercuric cetate
- Phenylmercuric nitrate
- Phenylpropanolamine bitartrate
- Phenylpropanolamine HCl
- Phenylpropanolamine maleate
- Phenyltoloxamine citrate
- Phenyltoloxamine dihydrogen citrate
- Phenyltoloxamine HCl
- Phosphate fluoride
- Phosphorated carbohydrate
- Phosphoric acid
- Phosphorus
- Phytolacca

Updated January 13, 2017

- Picrotoxin
- Pilocarpine Nitrate
- Pimobendan
- Pine tar
- Pineapple enzymes
- Piperazine citrate
- Piperocaine HCl
- Piperonyl butoxide
- Pipsissewa
- Piracetam
- Piracetam dihydrogen citrate
- Piscidia erythrina
- Plantago ovata husks
- Plantago seed
- Poloxamer
- Poloxamer-iodine complex
- Poly (DL-Lactic Acid)
- Poly(methyl vinyl ether/maleic anhydride)
- Polycarbophil
- Polydimethylsiloxane and poloxamer
- Polyethylene Glycol 1450
- Polyethylene Glycol 300
- Polyethylene Glycol 400
- Polyethylene Glycol 6000
- Polyols, liquid
- Polyoxeethylene laurate
- Polysorbate 20
- Polysorbate 80
- Polyvinyl alcohol
- Potash Lye
- Potassium Acetate
- Potassium bicarbonate
- Potassium bitartrate
- Potassium bromide
- Potassium carbonate
- Potassium chlorate
- Potassium citrate
- Potassium ferrocyanide
- Potassium guaiacolsulfonate
- Potassium hydroxide
- Potassium iodide
- Potassium nitrate
- Potassium salicylate
- Povidone
- Povidone-iodine
- Povidone-vinylacetate copolymers
- Powdered Cellulose
- Pracasil Plus
- Pramoxine HCl
- Precipitated sulfur
- Pregnenolone micronized
- Prolase
- Propionic acid
- Propylene glycol
- Propylhexedrine
- Propylparaben
- Protease
- Protein hydrolysate
- Protirelin
- Prune concentrate dehydrate
- Prune powder
- Pseudoephedrine HCl
- Pseudoephedrine Sulfate
- Psyllium
- Psyllium hydrophilic mucilloid
- Psyllium seed
- P-T-butyl-m-cresol
- Pyranel pamoate
- Pyrethrum extract
- Pyridoxine
- Pyridoxine HCl
- Ppyrilamine maleate
- Pyrithione zinc
- Pyrrolidone
- Pyruvic Aldehyde 40% Aqueous Solution
- Quinine
- Racemethionine
- Racephpedrine HCl
- Raffinose
- Red petrolatum
- Reosote (Creosote?)
- Resorcinol
- Resorcinol monoacetate
- Resveratrol
- Retinoic Acid-All Trans
- Rhubarb fluid extract
- Rhubarb, Chinese
- Rice polishings
- Romohydrate
- Sabadilla, alkaloids

Updated January 13, 2017

- Saccharin
- Sage Oil
- Salicyl alcohol
- Salicylamide
- Salsalate
- Sanguinaria extract
- Saponite
- Saw palmetto
- Scopolamine aminoxide HBr
- Scopolamine HBr
- Sea mineral
- Secretin, human 99%
- Selenium
- Selenium sulfide
- Senecio aureus
- Senna
- Senna fluid extract
- Senna pod concentrate
- Senna syrup
- Sennosides a and b
- Serotonin HCl
- Sesame Oil
- Sesame Seed
- Shark liver oil
- Shea Butter, Organic
- Short Chain Fatty Acid
- Silver Bulk Drug Substance
- Silver nitrate
- Silver protein mild
- Silver, colloidal
- Silver[1] (Canadian_License_Sovereign_)
- Simethicone
- Simplgel 30
- Sincalide
- Skin protectant
- Sodium
- Sodium 3, 4-dimethylphenyl-glyoxylate
- Sodium acetylsalicylate
- Sodium aluminum chlorohydroxy lactate
- Sodium aspartate
- Sodium biphosphate
- Sodium bisulfate
- Sodium borate
- Sodium borate monohydrate
- Sodium bromide
- Sodium caprylate
- Sodium carbonate
- Sodium carboxymethylcellulose
- Sodium caseinate
- Sodium diacetate
- Sodium dichromate
- Sodium dihydrogen phosphate
- Sodium dihydrogen phosphate monohydrate
- Sodium fluoride
- Sodium hyaluronate
- Sodium monofluoro phosphate
- Sodium nitrate
- Sodium octanoate
- Sodium oleate
- Sodium para-amino benzoate
- Sodium perborate
- Sodium perborate monohydrate
- Sodium phosphate dibasic
- Sodium phosphate monobasic
- Sodium potassium tartrate
- Sodium priopionate
- Sodium salicylate
- Sodium sulfide
- Sodium thiosulfate
- Soft Paraffin
- Sols, secondary
- Sorbitol
- Soy meal
- Soybean oil
- Soybean protein
- Splenda
- Squill preparations
- Stannous fluoride
- Stannous pyrophosphate
- Stearyl alcohol
- Stem bromelain
- Stevia Powder Extract
- Strawberry
- Strontium chloride
- Strychnine
- Sublimed sulfur
- Succinylcholine chloride, USP
- Sucrose
- Sugars
- Sulfacetamide sodium

Updated January 13, 2017

- Sulferated oils of turpentine
- Sulfobutylether B-Cyclodextrin
- Sulfur
- Sulisobenzone
- Supposibase-F
- T3 Sodium Dilution
- Talc
- Tannic acid
- Tannic acid glycerite
- Taraxacum officinale
- Tartaric acid
- Tartrate
- Tea Tree Oil
- Teaberry Oil
- Terpin hydrate preparations
- Testosterone cypionate, USP
- Tetrafluoroethane
- Tetrahydrochloride
- Thaumatin
- Thenyldiamine HCl
- Theobromine Sodium Salicylate
- Theophylline calcium salicylate
- Theophylline sodium glycinate
- Theophylline, anhydrous
- Theophylline, USP
- Theophylline compound with ethylenediamine
- Thiamine mononitrate (vitamin B1)
- Thimerosal
- Thiocitic
- Thiocynoacetate
- Thonzylamine HCl
- Threonine
- Thylene blue
- Thymol
- Titanium dioxide
- Tolindate
- Tolnaftate
- Toltrazuril
- Tolu balsam
- Tommy gel
- Topical starch
- Tranilast
- Triacetin
- Tricalcium phosphate
- Tricaprylin
- Trichloroacetic Acid
- Triclocarban
- Triclosan
- Triethanolamine
- Triglycerides
- Trillium
- Trilostane
- Triolein
- Tripelennamine HCl
- Triple dye
- Triprolidine HCl
- Triticum
- Trolamine salicylate (triethanolamine salicylate)
- Tryptophan
- Turpentine Oil
- Turpentine, Venice
- Tyrosine
- Uinolinium bromide
- Ulose
- Undecoylium chlorideiodine complex
- Undecylenic acid
- Urea
- Uva ursi, extract of
- Valic acid
- Valine
- Vitamin A palmitate
- Vitamin E
- Vitromersol
- Water and additives
- Water, purified
- Wax, Anionic Emulsifying
- Wax, white
- Wax, yellow
- Wheat germ
- White ointment
- White petrolatum
- Witch hazel (hamamelis water)
- Witch hazel skin
- Woodruff
- Xanthan gum
- Xylometazoline HCl
- Yeast
- Yeast cell derivative
- Yellow mercuric oxide
- Zinc

Updated January 13, 2017

- Zinc acetate
- Zinc caprylate
- Zinc carbonate
- Zinc chloride
- Zinc citrate
- Zinc oxide
- Zinc phenol sulfonate
- Zinc picolinate
- Zinc propionate
- Zinc pyrithione
- Zinc stearate
- Zinc sulfide
- Zinc undecylenate
- Zirconium oxide
- Zyloxin

Attachment

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#230

Guidance for Industry Compounding Animal Drugs from Bulk Drug Substances

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 Eric Nelson (CVM) at 240-402-5642, or by e-mail at eric.nelson@fda.hhs.gov.

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Veterinary Medicine (CVM)**

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TABLE OF CONTENTS

I. INTRODUCTION AND SCOPE	1
II. BACKGROUND	2
A. Regulatory Framework	2
B. Compounding Animal Drugs	3
III. POLICY	3
APPENDIX A	9

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Guidance for Industry¹ **Compounding Animal Drugs from Bulk Drug Substances**

This draft guidance, when finalized, represents the Food and Drug Administration's (FDA or Agency) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this draft guidance using the contact information on the title page of this guidance.

I. INTRODUCTION AND SCOPE

This draft guidance sets forth the Food and Drug Administration's ("FDA") policy regarding compounding animal drugs from bulk drug substances² by state-licensed pharmacies, licensed veterinarians, and facilities that register with FDA as outsourcing facilities under section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 353b). This guidance reflects FDA's current thinking regarding compounding animal drugs from bulk drug substances and describes the conditions under which FDA generally does not intend to take action for violations of the following sections of the FD&C Act: section 512 (21 U.S.C. 360b), section 501(a)(5) (21 U.S.C. 351(a)(5)), section 502(f)(1) (21 U.S.C. 352 (f)(1)), and, where specified, section 501(a)(2)(B) (21 U.S.C. 351(a)(2)(B)), when a state-licensed pharmacy, licensed veterinarian, or an outsourcing facility³ compounds animal drugs from bulk drug substances.

This draft guidance only addresses the compounding of animal drugs from bulk drug substances. It does not apply to the compounding of animal drugs from approved new animal or new human drugs. Such compounding can be conducted in accordance with the provisions of section 512(a)(4) and (5) of the FD&C Act (21 U.S.C. 360b(a)(4) and (5)) and 21 CFR part 530. In addition, this draft guidance does not address the compounding of drugs intended for use in

¹ This draft guidance has been prepared by the Center for Veterinary Medicine (CVM) in consultation with the Center for Drug Evaluation and Research (CDER) and the Office of Regulatory Affairs (ORA) at the Food and Drug Administration.

² FDA regulations define "bulk drug substance" as "any substance that is represented for use in a drug and that, when used in the manufacturing, processing, or packaging of a drug, becomes an active ingredient or a finished dosage form of the drug, but the term does not include intermediates used in the synthesis of such substances." 21 CFR 207.3(a)(4). "Active ingredient" is defined as "any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or other animals. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect." 21 CFR 210.3(b)(7). Any component other than an active ingredient is an "inactive ingredient." See 21 CFR 210.3(b)(8). Inactive ingredients used in compounded drug products commonly include flavorings, dyes, diluents, or other excipients.

³ "Outsourcing facility" refers to a facility that meets the definition of an outsourcing facility under section 503B(d)(4) of the FD&C Act. See draft guidance for industry *For Entities Considering Whether to Register As Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act*.

<http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm434171.pdf>.

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humans, which is addressed in other guidances.⁴ Further, the draft guidance does not address new animal drugs for investigational use. See 21 CFR part 511.

FDA's guidance documents, including this draft guidance, do not establish legally enforceable responsibilities. Instead, guidances describe FDA'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 FDA guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

A. Regulatory Framework

To be legally marketed, new animal drugs must be approved under section 512 of the FD&C Act, conditionally approved under section 571 of the FD&C Act (21 U.S.C. 360ccc), or included on the Index of Legally Marketed Unapproved New Animal Drugs for Minor Species under section 572 of the FD&C Act (21 U.S.C. 360ccc-1). The FD&C Act does not generally distinguish between compounding and other methods of animal drug manufacturing. Animal drugs that are not approved or indexed are considered "unsafe" under section 512(a)(1) of the FD&C and adulterated under section 501(a)(5) of the FD&C Act.

Although sections 503A (21 U.S.C. 353a) and 503B of the FD&C Act provide certain statutory exemptions for compounded human drugs, these sections do not provide exemptions for drugs compounded for animal use. The compounding of an animal drug from bulk drug substances results in a new animal drug that must comply with the FD&C Act's approval/indexing requirements.⁵ Further, all animal drugs are required to, among other things, be made in accordance with current good manufacturing practice (cGMP) requirements (section 501(a)(2)(B)) of the FD&C Act and 21 CFR parts 210 and 211) and have adequate directions for use (section 502(f)(1) of the FD&C Act).

Sections 512(a)(4) and (5) of the FD&C Act provide a limited exemption from certain requirements for compounded animal drugs made from already approved animal or human drugs. Such use is considered an extralabel use and the FD&C Act provides an exemption from the approval requirements and requirements of section 502(f) of the FD&C Act for extralabel uses that meet the conditions set out in the statute and FDA regulations at 21 CFR part 530. Among other things, these regulations specify that nothing in the regulations should be construed as permitting compounding animal drugs from bulk drug substances.

In 1996, FDA announced the availability of a CPG (section 608.400) entitled, "Compounding of Drugs for Use in Animals" (61 FR 34849, July 3, 1996), to provide guidance to FDA's field and headquarters staff with regard to the compounding of animal drugs by veterinarians and pharmacists. An updated CPG was made available on July 14, 2003 (68 FR 41591). This draft guidance supersedes that CPG, which has now been withdrawn.

⁴ <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm166743.htm>.

⁵ See *Medical Center Pharmacy v. Mukasey*, 536 F.3d 383, 394 (5th Cir. 2008).

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B. Compounding Animal Drugs

Numerous drugs are approved or indexed for use in animals. However, there are many different species of animals with different diseases and conditions for which there are no approved or indexed animal drugs. In some cases, approved human drugs can be used to treat an animal under the extralabel use provisions of the FD&C Act and FDA regulations (sections 512(a)(4) and (a)(5) of FD&C Act and 21 CFR part 530). For example, various chemotherapeutic drugs approved for humans are used to treat cancer in dogs and cats. FDA recognizes that there are circumstances where there is no drug available to treat a particular animal with a particular condition, because either no drug is approved for a specific animal species or no drug is available under the extralabel drug use provisions. In those limited circumstances, an animal drug compounded from bulk drug substances may be an appropriate treatment option.

However, FDA is concerned about the use of animal drugs compounded from bulk drug substances, especially when approved alternatives exist that can be used as labeled or in an extralabel manner consistent with the requirements of FDA's extralabel provisions. Compounded drugs have not undergone premarket FDA review of safety, effectiveness, or manufacturing quality. The unrestricted compounding of animal drugs from bulk drug substances has the potential to compromise food safety, place animals or humans at undue risk from unsafe or ineffective treatment, and undermine the incentives to develop and submit new animal drug applications to FDA containing data and information to demonstrate that the product is safe, effective, properly manufactured, and accurately labeled.

III. POLICY

As discussed above, animal drugs are generally subject to the adulteration, misbranding, and approval provisions of the FD&C Act. Generally, FDA does not intend to take action under sections 512(a), 501(a)(5), 502(f)(1) and 501(a)(2)(B) of the FD&C Act if a state-licensed pharmacy or a licensed veterinarian compounds animal drugs from bulk drug substances in accordance with the conditions described below, and the drug is not otherwise adulterated or misbranded. In addition, FDA generally does not intend to take action under sections 512(a), 501(a)(5), and 502(f)(1) of the FD&C Act if an outsourcing facility compounds animal drugs in accordance with all of the applicable conditions described below, and the drug is not otherwise adulterated or misbranded.

FDA's decision not to take enforcement action depends on its ability to evaluate whether the compounding of animal drugs is in accordance with the conditions below. Therefore, entities compounding animal drugs should keep adequate records to demonstrate that they are compounding such drugs in accordance with all of the applicable conditions described below.

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The conditions referred to above are as follows:

- A. If the animal drug is compounded in a state-licensed pharmacy:
1. The drug is compounded by or under the direct supervision of a licensed pharmacist.
 2. The drug is dispensed after the receipt of a valid prescription from a veterinarian for an individually identified animal patient that comes directly from the prescribing veterinarian or from the patient's owner or caretaker to the compounding pharmacy. A drug may be compounded in advance of receipt of a prescription in a quantity that does not exceed the amount of drug product that the state-licensed pharmacy compounded pursuant to patient-specific prescriptions based on a history of receipt of such patient-specific prescriptions for that drug product over any consecutive 14-day period within the previous 6 months.
 3. The drug is not intended for use in food-producing animals, and the prescription or documentation accompanying the prescription for the drug contains the statement "This patient is not a food-producing animal." For purposes of this draft guidance, all cattle, swine, chicken, turkey, sheep, goats, and non-ornamental fish are always considered to be food-producing animals regardless of whether the specific animal or food from the specific animal is intended to be introduced into the human or animal food chain (e.g., pet pot-bellied pigs and pet chicks are always considered to be food-producing animals). In addition, for purposes of this draft guidance, any other animal designated on the prescription or in documentation accompanying the prescription by the veterinarian as a food-producing animal, regardless of species, is considered to be a food-producing animal (e.g., rabbits, captive elk, captive deer).
 4. If the drug contains a bulk drug substance that is a component of any marketed FDA-approved animal or human drug:
 - a. there is a change between the compounded drug and the comparable FDA-approved animal or human drug made for an individually identified animal patient that produces a clinical difference for that individually identified animal patient, as determined by the veterinarian prescribing the compounded drug for his/her patient under his/her care, and
 - b. the prescription or documentation accompanying the prescription contains a statement that the change between the compounded drug and the FDA-approved drug would produce a clinical difference for the individually identified animal patient. For example, the veterinarian could state that, "Compounded drug X would produce a clinical difference for the individually identified animal patient because the approved drug is too large a dose for the animal and cannot be divided or diluted into the small dose required."
 5. If there is an FDA-approved animal or human drug with the same active ingredient(s), the pharmacy determines that the compounded drug cannot be made from the FDA-approved drug(s), and documents that determination.

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6. The pharmacy receives from the veterinarian (either directly or through the patient's owner or caretaker), in addition to any other information required by state law, the following information, which can be documented on the prescription or documentation accompanying the prescription:
 - a. Identification of the species of animal for which the drug is prescribed; and,
 - b. The statement "There are no FDA-approved animal or human drugs that can be used as labeled or in an extralabel manner under section 512(a)(4) or (5) and 21 CFR part 530 to appropriately treat the disease, symptom, or condition for which this drug is being prescribed."
 7. Any bulk drug substance used to compound the drug is manufactured by an establishment that is registered under section 510 of the FD&C Act (21 U.S.C. 360) (including a foreign establishment that is registered under section 510) and is accompanied by a valid certificate of analysis.
 8. The drug is compounded in accordance with Chapters <795> and <797> of the United States Pharmacopeia and National Formulary (USP—NF)⁶ (e.g., a sterile drug is compounded in an area with air quality that meets or exceeds ISO Class 5 standards (see USP—NF Chapter <797>, Table 1)).
 9. The drug is not sold or transferred by an entity other than the entity that compounded such drug. For purposes of this condition, a sale or transfer does not include administration of a compounded drug by a veterinarian to a patient under his or her care.
 10. Within 15 days of becoming aware of any product defect or serious adverse event associated with animal drugs it compounded from bulk drug substances, the pharmacy reports it to FDA on Form FDA 1932a. Form FDA 1932a can be downloaded at <http://www.fda.gov/downloads/aboutfda/reportsmanualsforms/forms/animaldrugforms/ucm048817.pdf>.
 11. The label of any compounded drug indicates the species of the intended animal patient, the name of the animal patient and the name of the owner or caretaker of the animal patient.
- B. If the animal drug is compounded by a licensed veterinarian:
1. The drug is compounded and dispensed by the veterinarian to treat an individually identified animal patient under his or her care.

⁶ Chapters <795> *Pharmaceutical Compounding—Nonsterile Preparations* and <797> *Pharmaceutical Compounding—Sterile Preparations* can be found in the combined *United States Pharmacopeia and National Formulary (USP-NF)*, available at <http://www.usp.org>.

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2. The drug is not intended for use in food-producing animals as defined in section III.A.3 of this guidance.
 3. If the drug contains a bulk drug substance that is a component of any marketed FDA-approved animal or human drug, there is a change between the compounded drug and the comparable FDA-approved animal or human drug made for an individually identified animal patient that produces a clinical difference for that individually identified animal patient, as determined by the veterinarian prescribing the compounded drug for his/her patient under his/her care.
 4. There are no FDA-approved animal or human drugs that can be used as labeled or in an extralabel manner under sections 512(a)(4) and (5) of the FD&C Act and 21 CFR part 530 to appropriately treat the disease, symptom, or condition for which the drug is being prescribed.
 5. The drug is compounded in accordance with USP—NF Chapters <795> and <797> (e.g., a sterile drug is compounded in an area with air quality that meets or exceeds ISO Class 5 standards (see USP—NF Chapter <797>, Table 1)).
 6. Any bulk drug substance used is manufactured by an establishment that is registered under section 510 of the FD&C Act (21 U.S.C. 360) (including a foreign establishment that is registered under section 360(i)) and is accompanied by a valid certificate of analysis.
 7. The drug is not sold or transferred by the veterinarian compounding the drug. For purposes of this condition, a sale or transfer does not include administration of a compounded drug by the veterinarian to a patient under his or her care, or the dispensing of an animal drug compounded by the veterinarian to the owner or caretaker of an animal under his or her care.
 8. Within 15 days of becoming aware of any product defect or serious adverse event associated with animal drugs the veterinarian compounded from bulk drug substances, he or she reports it to FDA on Form FDA 1932a. Form FDA 1932a can be downloaded at <http://www.fda.gov/downloads/aboutfda/reportsmanualsforms/forms/animaldrugforms/ucm048817.pdf>.
 9. The label of any compounded drug indicates the species of the intended animal patient, the name of the animal patient and the name of the owner or caretaker of the animal patient.
- C. If the animal drug is compounded by an outsourcing facility:
1. The drugs are compounded only from bulk drug substances appearing on Appendix A of this draft guidance.
 2. The drug is compounded by or under the direct supervision of a licensed pharmacist.

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3. The drug is not intended for use in food-producing animals, as defined in Section III.A.3 of this guidance, and the prescription or order, or documentation accompanying the prescription or order, for the drug contains the statement, “This drug will not be dispensed for or administered to food-producing animals.”
4. The drug is compounded in accordance with cGMP requirements.⁷
5. Any bulk drug substance used is manufactured by an establishment that is registered under section 510 of the FD&C Act (21 U.S.C. 360) (including a foreign establishment that is registered under section 360(i)) and is accompanied by a valid certificate of analysis.
6. The drug is not sold or transferred by an entity other than the outsourcing facility that compounded such drug. For purposes of this condition, a sale or transfer does not include administration of a compounded drug by a veterinarian to a patient under his or her care.
7. Within 15 days of becoming aware of any product defect or serious adverse event associated with animal drugs it compounded from bulk drug substances, the outsourcing facility reports it to FDA, on Form FDA1932a. Form FDA 1932a can be downloaded at <http://www.fda.gov/downloads/aboutfda/reportsmanualsforms/forms/animaldrugforms/ucm048817.pdf>.
8. All drugs compounded for animals by an outsourcing facility are included on the report required by section 503B of the FD&C Act to be submitted to the Food and Drug Administration each June and December identifying the drugs made by the outsourcing facility during the previous 6-month period, and providing the active ingredient(s); source of the active ingredient(s); NDC number of the source ingredient(s), if available; strength of the active ingredient(s) per unit; the dosage form and route of administration; the package description; the number of individual units produced; and the NDC number of the final product, if assigned.⁸ The outsourcing facility should identify which reported drugs were intended for animal use.
9. The veterinarian’s prescription or order states that the drug is intended to treat the species and condition(s) for which the substance is listed in Appendix A.

⁷ FDA intends to determine whether this condition is met by evaluating whether the facility complies with FDA regulations applicable to cGMPs for compounding of human drugs by outsourcing facilities. *See, e.g.*, draft guidance for industry, *Current Good Manufacturing Practice—Interim Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act* (July 2014), at

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM403496.pdf>

⁸ FDA has issued a draft guidance for industry, *Electronic Drug Product Reporting for Human Drug Compounding Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act* (November 2014), which prescribes how human drug compounding facilities are to submit drug product reports to FDA. Available at <http://www.fda.gov/downloads/Drugs/NewsEvents/UCM424303.pdf>. Although this guidance addresses reporting of compounded human drug products, outsourcing facilities should follow the same procedure to electronically report the animal drug products they compounded.

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10. The label of the drug includes the following:
 - a. Active ingredient(s).
 - b. Dosage form, strength, and flavoring, if any.
 - c. Directions for use, as provided by the veterinarian prescribing or ordering the drug.
 - d. Quantity or volume, whichever is appropriate.
 - e. The statement “Not for resale.”
 - f. The statement “For use only in [fill in species and any associated condition or limitation listed in Appendix A].”
 - g. The statement “Compounded by [name of outsourcing facility].”
 - h. Lot or batch number of drug.
 - i. Special storage and handling instructions.
 - j. Date the drug was compounded.
 - k. Beyond use date (BUD) of the drug.
 - l. Name of veterinarian prescribing or ordering the drug.
 - m. The address and phone number of the outsourcing facility that compounded the drug.
 - n. Inactive ingredients.
 - o. The statement “Adverse events associated with this compounded drug should be reported to FDA on a Form FDA 1932a.”
 - p. If the drug is compounded pursuant to a patient specific prescription, the species of the animal patient, name of the animal patient, and name of the owner or caretaker of the animal patient.

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APPENDIX A⁹

LIST OF BULK DRUG SUBSTANCES THAT MAY BE USED BY AN OUTSOURCING FACILITY TO COMPOUND DRUGS FOR USE IN ANIMALS

This Appendix, when finalized, will contain a list of bulk drug substances that may be used by facilities registered under section 503B as outsourcing facilities to compound animal drugs pursuant to a prescription from a veterinarian for an individually identified animal patient or pursuant to an order from a licensed veterinarian for veterinarian office use, and in accordance with any specified limitations or conditions.

This list will be developed with public input; the process for nominating bulk drug substances for this list is described in the Federal Register notice soliciting nominations for such bulk drug substances. FDA intends to limit the bulk drug substances in this Appendix to address situations where all of the following criteria are met:

- there is no marketed approved, conditionally approved, or index listed animal drug that can be used as labeled to treat the condition;
- there is no marketed approved animal or human drug that could be used under section 512(a)(4) or (a)(5) and 21 CFR Part 530 (addressing extralabel use of approved animal and human drugs) to treat the condition;
- the drug cannot be compounded from an approved animal or human drug;
- immediate treatment with the compounded drug is necessary to avoid animal suffering or death; and
- FDA has not identified a significant safety concern specific to the use of the bulk drug substance to compound animal drugs (under the listed conditions and limitations).

FDA intends to review the nominated bulk drug substances on a rolling basis and to periodically update this Appendix.

LIST:

⁹ To submit nominations for this list, refer to the Federal Register notice entitled, “List of Bulk Drug Substances That May be Used by an Outsourcing Facility to Compound Drugs for Use in Animals,” published May 19, 2015. After the period for nominations closes, you may petition FDA under 21 CFR 10.30 to add or remove specific listings.

Attachment 13

**California State Board of Pharmacy
Citation and Fine Statistics January
January 1, 2017 - March 31, 2017**

536 Citations were issued this fiscal year

Total dollar amount of fines issued this fiscal year \$504,300.00

***This amount also reflects payment of citations issued prior to July 1, 2009.**

The average number of days from date case is opened until a citation is issued is 209.53

Average number of days from date case is routed to Citation Unit to date citation is issued 29.36

471 citations are closed. The average number of days from date citation is issued to date citation is closed is 147.46

Citation Breakdown by license type

Total Issued	RPH with Fine	RPH no Fine	PHY with Fine	PHY no Fine	PIC with Fine**	PIC no Fine**	TCH with Fine	TCH no Fine
536	235	21	85	90	93	48	50	0

Citation Breakdown by Miscellaneous license type

Wholesalers	Designated Rep	Clinics	Drug Room	Exempt Hosp.	Hosp. Pharmacy	Misc.*	Unlicensed Premises	Unlicensed person
2	0	1	0	4	9	2	12	1

*Intern Pharmacist, Licensed Correctional Facilities, Exempt Pharmacies, Non-Resident Pharmacies, and Vet Retailers

**These numbers are also represented in the RPH columns, but reflect how many RPHs were cited as PICs

Top Ten Violations by license type

Pharmacists	%	Pharmacies	%	Pharmacists In Charge	%
1716 - Variation from prescription	18%	1716 - Variation from prescription	24%	1714(d) - Operational Standards and Security; Pharmacist responsible for pharmacy security	34%
4301(g) - Unprofessional Conduct - Knowingly making or signing any certificate or other document that falsely represents the existence or nonexistence of a state of facts	17%	1714(b) - Operational Standards and Security; pharmacy responsible for pharmacy security	16%	1761(a) - No pharmacist shall compound or dispense any prescription, which contains any significant error or omission...	12%
1761(a) - No pharmacist shall compound or dispense any prescription, which contains any significant error or omission...	15%	4113(d) - Every pharmacy shall notify the board in writing within 30 days of the date of a change in pharmacist-in-charge	14%	11165(d)(2) - Pharmacy shall provide the following information the Department of Justice: prescriber's category of licensure and license number; federal controlled substance registration number ...	11%
4231(d)/1732.5 - Failure to provide documentation substantiating completion of continuing education/Renewal Requirements for Pharmacist	14%	1761(a) - No pharmacist shall compound or dispense any prescription, which contains any significant error or omission...	12%	1716 - Variation from prescription	9%
1714(d) - Operational Standards and Security; Pharmacist responsible for pharmacy security	11%	11164(a)/1761(a) - Prescriptions for schedule II, III, IV, and controlled substance: form and content; record of practitioner dispensing schedule II controlled substance/No pharmacist shall compound o	9%	11164(a)/1761(a) - Prescriptions for schedule II, III, IV, and controlled substance: form and content; record of practitioner dispensing schedule II controlled substance/No pharmacist shall compound o	8%
11164(a)/1761(a) - Prescriptions for schedule II, III, IV, and controlled substance: form and content; record of practitioner dispensing schedule II controlled substance/No pharmacist shall compound o	9%	4305(b) - Disciplinary Grounds: Failure of Pharmacy or Pharmacist to Notify Board of Termination of Pharmacist-in-Charge; Continuing to Operate Without Pharmacist; Operation of a pharmacy for more tha	6%	1735.2(h) - Every compounded drug product shall be given an expiration date...	7%
1761(a)&(b) - No pharmacist shall compound or dispense any prescription, which contains any significant error or omission.../A pharmacist shall not compound or dispense a prescription for a controlled s	4%	4113(a) - Pharmacist-in-Charge: Notification to Board; Responsibilities; Every pharmacy shall designate a pharmacist-in-charge within 30 days in writing of the identity and license number of that phar	6%	4076(a)(4) - Prescription Container - Requirements for Labeling/The name of the prescriber...	6%
11164(a) - Prescriptions for schedule II, III, IV, and controlled substance: form and content; record of practitioner dispensing schedule II controlled substance	4%	4076(a)(4) - Prescription Container - Requirements for Labeling/The name of the prescriber...	5%	4081(a) - Records of Dangerous Drugs and Devices Kept Open for Inspection; Maintenance of Records, Current Inventory	4%
4076(a)(4)/1707.1(a)(1)(B)(2) - Prescription Container - Requirements for Labeling/The name of the prescriber.../Duty to maintain medication profiles; a patient medication profile shall be maintained... f	4%	4081(a)/4105(a)(b)(c) - Records of Dangerous Drugs and Devices Kept Open for Inspection; Maintenance of Records, Current Inventory/Retaining Records of Dangerous Drugs and Devices on Licensed Premises	4%	1761 - Erroneous or uncertain prescriptions	4%
11164 - Prescribing, Filling, Compounding or Dispensing Prescription for Controlled Substance; Requirements	4%	11165(d)(2) - Pharmacy shall provide the following information the Department of Justice: prescriber's category of licensure and license number; federal controlled substance registration number ...	4%	4127.1(a) - A pharmacy shall not compound injectable sterile drug products...unless the pharmacy has obtained a license from the board.	4%

Attachment 14

Board of Pharmacy Enforcement Statistics Fiscal Year 2016/2017

Workload Statistics July-Sept Oct-Dec Jan-Mar Apr-June Total 16/17

Complaints/Investigations

Received	792	659	780		2231
Closed	790	623	956		2369
4301 letters	4	9	8		21
Pending (at the end of quarter)	2441	2459	2241		2241

Cases Assigned & Pending (by Team) at end of quarter*

Compliance / Routine Team	1063	1158	1014		1014
Drug Diversion/Fraud	450	429	456		456
RX Abuse	171	151	172		172
Compounding	126	114	121		121
Probation/PRP	75	79	68		68
Mediation/Enforcement **	252	228	123		123
Criminal Conviction	304	300	287		287

Application Investigations

Received	154	159	80		393
Closed					
Approved	110	71	96		277
Denied	10	15	30		55
Total ***	147	109	161		417
Pending (at the end of quarter)	111	161	86		86

Letter of Admonishment (LOA) / Citation & Fine

LOAs Issued	114	117	139		370
Citations Issued	589	379	537		1505
Total Fines Collected ****	\$447,974.15	\$585,750.00	\$446,932.60		\$1,480,656.75

* This figure includes reports submitted to the supervisor and cases with SI awaiting assignment.

** This figure include reports submitted to the citation and fine unit, AG referral, as well as cases assigned to enf. Staff

*** This figure includes withdrawn applications.

****Fines collected (through 3/31/2017 and reports in previous fiscal year.)

Board of Pharmacy Enforcement Statistics Fiscal Year 2016/2017

Workload Statistics July-Sept Oct-Dec Jan-Mar Apr-June Total 16/17

Administrative Cases (by effective date of decision)

Referred to AG's Office*	105	68	79		252
Accusations Filed	73	56	70		199
Statement of Issues Filed	5	7	7		19
Petitions to Revoke Filed	4	0	3		7
Pending					
Pre-accusation	255	240	218		218
Post Accusation	278	252	241		241
Total*	573	519	490		490

Closed

Revocation					
Pharmacist	4	2	5		11
Intern Pharmacist	1	0	0		1
Pharmacy Technician	37	33	26		96
Designated Representative	0	0	1		1
Wholesaler	0	0	1		1
Sterile Compounding	0	0	1		1
Pharmacy	4	2	2		8

Revocation, stayed; suspension/probation

Pharmacist	1	1	6		8
Intern Pharmacist	0	0	0		0
Pharmacy Technician	0	2	1		3
Designated Representative	0	0	0		0
Wholesaler	0	0	0		0
Sterile Compounding	0	0	0		0
Pharmacy	0	0	1		1

Revocation, stayed; probation

Pharmacist	8	17	10		35
Intern Pharmacist	0	0	0		0
Pharmacy Technician	4	1	5		10
Designated Representative	0	0	0		0
Wholesaler	1	0	0		1
Sterile Compounding	0	0	1		1
Pharmacy	5	10	6		21

Surrender/Voluntary Surrender

Pharmacist	7	8	6		21
Intern Pharmacist	0	1	0		1
Pharmacy Technician	10	10	8		28
Designated Representative	0	0	0		0
Wholesaler	0	0	0		0
Sterile Compounding	0	0	1		1
Pharmacy	3	9	9		21

Board of Pharmacy Enforcement Statistics Fiscal Year 2016/2017

Workload Statistics July-Sept Oct-Dec Jan-Mar Apr-June Total 16/17

Public Reprival/Reprimand

Pharmacist	5	2	6		13
Intern Pharmacist	0	0	0		0
Pharmacy Technician	0	1	2		3
Designated Representative	0	0	0		0
Wholesaler	0	0	0		0
Sterile Compounding	0	0	0		0
Pharmacy	0	1	3		4

Licenses Granted

Pharmacist	0	1	1		2
Intern Pharmacist	0	2	0		2
Pharmacy Technician	1	2	2		5
Designated Representative	1	0	0		1
Wholesaler	0	0	0		0
Sterile Compounding	0	0	0		0
Pharmacy	0	0	0		0

Licenses Denied

Pharmacist	0	0	0		0
Intern Pharmacist	0	0	0		0
Pharmacy Technician	3	4	3		10
Designated Representative	0	0	0		0
Wholesaler	0	0	0		0
Sterile Compounding	0	0	0		0
Pharmacy	0	0	0		0

Cost Recovery Requested**	\$307,270.00	\$620,180.11	\$396,277.52		\$1,323,727.63
Cost Recovery Collected**	\$132,381.11	\$275,441.13	\$299,714.67		\$707,536.91

* This figure includes Citation Appeals

** This figure includes administrative penalties

Immediate Public Protection Sanctions

Interim Suspension Order	0	0	1		1
Automatic Suspension / Based on Conviction	0	0	1		1
Penal Code 23 Restriction	2	3	3		8
Cease & Desist - Sterile Compounding	0	0	1		1

Board of Pharmacy Enforcement Statistics Fiscal Year 2016/2017

Workload Statistics **July-Sept** **Oct-Dec** **Jan-Mar** **Apr-June** **Total 16/17**

Probation Statistics

Licenses on Probation

Pharmacist	176	190	190		190
Intern Pharmacist	3	6	6		6
Pharmacy Technician	37	36	36		36
Designated Representative	1	1	1		1
Pharmacy	54	56	60		60
Sterile Compounding	10	10	12		12
Wholesaler	5	5	5		5
Probation Office Conferences	15	36	31		82
Probation Site Inspections	141	126	151		418
Successful Completion	5	4	12		21
Probationers Referred to AG for non-compliance	0	4	0		4

As part of probation monitoring, the board requires licensees to appear before the supervising inspector at probation office conferences.

These conferences are used as 1) an orientation to probation and the specific requirements of probation at the onset,

2) to address areas of non-compliance when other efforts such as letters have failed, and 3) when a licensee is scheduled to end probation.

As of March 31, 2017.