



**CALIFORNIA STATE
BOARD OF PHARMACY**

BE AWARE AND TAKE CARE: Talk to your pharmacist!

REPORT TO THE LEGISLATURE ON INSPECTIONS OF NONRESIDENT STERILE COMPOUNDING PHARMACIES

SUBMITTED PURSUANT TO BUSINESS AND PROFESSIONS CODE SECTION 4127.2

JANUARY 1, 2018

STATE OF CALIFORNIA

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Healthy Californians through safe, quality pharmacists care.

MISSION

The Board of Pharmacy protects and promotes the health and safety of Californians by pursuing the highest quality of pharmacists care and the appropriate use of pharmaceuticals through education, communication, licensing, legislation, regulation and enforcement.



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

January 18, 2018

The Honorable Jerry Hill, Chair
Senate Committee on Business Economic
Development and Professions
State Capitol
Sacramento, CA 95814

The Honorable Evan Low, Chair
Assembly Committee on Business and Professions
State Capitol
Sacramento, CA 95814

Dear Senator Hill and Assembly Member Low,

The California State Board of Pharmacy is pleased to provide this report to the California Legislature as required by California Business and Professions Code section 4127.2(g) on the board's regulation of out-of-state sterile compounding facilities that are licensed to compound and ship sterile medications into California.

In 2013, SB 294 (Emmerson, Chapter 565) was enacted in part in response to a national public health emergency originating in a Massachusetts pharmacy in 2012 that resulted in serious health consequences to patients across the United States. California's new licensure requirements, which affected both in-state and nonresident pharmacies performing sterile compounding and doing business in California, took effect July 1, 2014. Provisions of this legislation required an increase in the frequency and quality of inspections performed by the board, including annual inspections of all sterile compounding pharmacies in California as well as initiation of board inspections of out-of-state pharmacies that ship sterile preparations into California.

This report details the board's activities and efforts to meet its public protection mandate for patients of these sterile compounded preparations where the medication has been prepared out-of-state.

There is a companion report to respond to the board's regulation of compounding activities by nonresident outsourcing facilities, which are licensed by the board under Article 7.7 of Chapter 9, Division 2 of the California Business and Professions Code. Whereas pharmacies generally compound pursuant to a patient-specific prescription, outsourcing facilities compound larger quantities at one time and not pursuant to a patient-specific prescription.

We appreciate this opportunity to highlight our consumer protection driven activities for Californians and our future priorities in the area of sterile compounding.

Sincerely,

A handwritten signature in black ink, appearing to read "Amarylis C. Gutierrez".

Amarylis C. Gutierrez, PharmD
President, Board of Pharmacy

MESSAGE SUMMARY

The California State Board of Pharmacy is pleased to provide this report to the California Legislature as required by Business and Professions Code section 4127.2 on the board's regulation of sterile compounding pharmacies outside California.

OVERVIEW AND BACKGROUND

“Drug compounding is a long-standing practice wherein a pharmacist ‘combines, mixes or alters ingredients of a drug to create a medication tailored to the needs of an individual patient.’ While the FDA has the authority to enforce applicable federal laws over pharmacies, states remain the principal regulators of pharmacy practice, including pharmacy compounding activity.”*

Compounding encompasses any of the following activities occurring in a licensed pharmacy by or under the supervision of a licensed pharmacist and generally pursuant to a prescription: altering the dosage form or delivery system, altering the strength, combining components or active ingredients or preparing a compounded drug preparation from chemical or bulk drug substances. Due to the inherent risks associated with the compounding of sterile preparations that are administered to a patient generally through injection, inhalation, or by being placed in the eyes, California’s compounding regulations are comprehensive, requiring inspections to be more rigorous and extensive than routine or normal pharmacy compliance inspections. Compounding pharmacies are especially important in producing vital medications that are needed for specific patients, are in short supply or simply not produced by a manufacturer.

In 2003 the board began issuing an additional, specialty license to pharmacies that perform sterile compounding. Sterile compounding is a high-risk form of compounding that requires a high level of compounding skills including specific training, specialty equipment, measurements and highly trained and skilled pharmacy staff because the preparation is typically injected, inhaled or placed in the eyes where contaminated products are the most potentially dangerous. The board began licensing sterile compounding pharmacies as a specialty form of pharmacy following the deaths of three patients from contaminated sterile compounding performed by a pharmacy in Northern California in 2001. The ensuing legislation required an additional license from the board with annual inspections, unless the pharmacy was accredited by specific accreditation agencies. This requirement applied to both California and nonresident pharmacies.

In 2012, following a major national health incident resulting in deaths and permanent injuries to more than 700 persons caused by contaminated sterile compounded products made by a pharmacy in Massachusetts, the board sponsored legislation in 2013 to increase its regulation

*National Assessment of State Oversight of Sterile Drug Compounding, the Pew Charitable Trusts, March 2016.

over pharmacies that perform sterile compounding. At the same time, the board initiated a major review of its compounding and sterile compounding regulations, a process that has led today to modified regulation requirements, and ongoing work as the board continues to evaluate and modify current regulations in this area.

Prior to 2014, California law did not authorize the board to perform inspections of nonresident sterile pharmacies, but to instead accept inspections performed by the home state or the accreditation agency.

This report is being prepared pursuant to the requirements enacted in the 2013 California legislation that pertain to regulation and board inspections of nonresident sterile compounding pharmacies. There are four items for the board to respond to:

1. Provide a detailed description of board activities related to the inspection and licensure of nonresident pharmacies.
2. Whether fee revenue collected pursuant to subdivision (v) of Section 4400 and travel cost reimbursements collected pursuant to subdivision (c) of this section provide revenue in an amount sufficient to support the board's activities related to the inspection and licensure of nonresident pharmacies.
3. The status of proposed changes to federal law that are under serious consideration and that would govern compounding pharmacies, including legislation pending before the United States Congress, administrative rules, regulations or orders under consideration by the federal Food and Drug Administration or other appropriate federal agency, and cases pending before the courts.
4. If applicable, recommended modifications to the board's statutory duties related to nonresident pharmacies as a result of changes to federal law or any additional modifications necessary to protect the health and safety of the public.

QUESTION ONE: A DETAILED DESCRIPTION OF BOARD ACTIVITIES RELATED TO THE INSPECTION AND LICENSURE OF NONRESIDENT PHARMACIES.

Throughout 2013, as the nation responded to the New England Compounding Center tragedy, the board began intensive training of all its inspector staff (who are all California licensed pharmacists) to strengthen their knowledge of compounding and sterile compounding. By early 2014, the board had reorganized its pharmacist inspectors to create a sterile compounding team. These inspectors typically had hospital or some compounding experience. However, all board inspectors underwent extensive training to perform compounding inspections.

Beginning in early 2014 to implement the provisions of SB 294, the board’s pharmacy inspectors began inspections of all California pharmacies that it believed compounded sterile preparations, including those that had been exempted from required annual inspections by being accredited. This included inspections of more than 400 hospitals most of which performed sterile compounding and that would require inspections and licensure by July 1, 2014. Inspections of nonresident sterile compounders were initiated in July 2014.

The board gained four inspector positions in 2014-15 to implement SB 294, creating a total inspector staff of 48. Workload remained high throughout 2014/15 for the sterile compounding team, and the board redirected one additional inspector position to the team to adjust workload to staff resources. In 2016, two additional inspectors were redirected to compounding. The board currently has seven compounding inspectors on staff, and one supervising inspector supervising these staff.

Today, all inspectors have been trained in sterile compounding and perform these inspections; however, the compounding team’s inspectors perform most of the annual sterile compounding inspections.

Board workload associated with licensed sterile compounding pharmacies both within and outside California is provided below:

INSPECTORS	FY 14-15	FY 15-16	FY 16-17
Total Board Inspectors	48	48	49
Sterile Compounding Team Inspectors	4	7	7
Supervising Inspectors	8	8	9

NUMBER OF LICENSED PHARMACIES	FY 14-15	FY 15-16	FY 16-17
California Sterile Compounding Pharmacies	936	917	884
Nonresident Sterile Compounding Pharmacies	91	92	91

As of July 1, 2014, there were 88 licensed nonresident sterile compounding pharmacies.

LICENSING STATISTICS	FY 14-15	FY 15-16	FY 16-17
Nonresident Sterile Compounding License Applicants	22	37	23
Nonresident Change of Ownership Applicants	4	16	7
Nonresident Change of Location Applicants	1	5	7
Nonresident Sterile Compounding Applications Denied	0	2	2

INSPECTIONS PERFORMED	FY 14-15	FY 15-16	FY 16-17
California Sterile Compounding Inspections	964	1047	953
Nonresident Sterile Compounding Inspections	102	99	110
Nonresident Inspections Conducted by Non-compounding Team Members	66	43	19

ENFORCEMENT	FY 14-15	FY 15-16	FY 16-17
Nonresident Sterile Compounding Licenses on Probation	2	2	4
Nonresident Sterile Compounding Licenses Revoked	0	0	0
Nonresident Investigations Completed	6	23	35
Nonresident Sterile Compounding Cease and Desist Orders Issued	1	1	0

In February 2017 as part of a public presentation on the board's sterile compounding activities for the 2016-17 fiscal year, staff reported on California and nonresident sterile compounding inspection data compiled for the previous seven months. The data revealed 50 percent of the licensees received a correction following an inspection for deviations from California or federal requirements, and 5 percent of the licensees received a violation notice as a result of the inspection. Violation notices are indications of violations that are likely to be subject to sanctions such as citations or citations with fines, or in the most serious cases formal discipline.

Top corrections and violations cited upon inspection during the timeframe included:

1. Noncompliance with facility and equipment standards
 - a. not cleaning compliantly
 - b. not cleaning on the required schedule
2. Noncompliance with records of compounding limitations and requirements
 - a. noncompliance with master formula requirements
 - b. noncompliance with beyond use dating assignment
3. Noncompliance with sterile compounding quality assurance and process validation

TRAINING OF BOARD STAFF:

All board inspectors are licensed California pharmacists.

As part of each inspector's onboarding and annual training, every individual completes 40 hours of online training provided by Critical Point, a highly regarded consultant firm for sterile compounding, which inspectors may repeat yearly. This company provides sterile compounding training to pharmacists across the country. Additionally, all compounding team inspectors complete one or a combination of the following:

- an in-person, two-day training through Critical Point,
- a two-day class offered by NABP on compounding,
- a five-day class offered by NABP and the PEW Charitable Trust.

The NABP and Pew Charitable Trust training should be available again to board inspectors in 2018.

In 2017, specialty training was provided to board inspectors through Touro University in Vallejo, California. This was a six-hour training in sterile compounding practices including hands on assessment of garbing and aseptic technique.

In addition, the compounding supervising inspector holds monthly trainings and conference calls with the compounding team and members of other inspection teams who perform sterile compounding inspections. Topics of discussion include but are not limited to current inspection findings, industry trends, practice trends, and review of laws and articles. New inspectors complete a six-hour review and training on the compounding regulations given by the board's compounding supervising inspector.

Additionally prior to or during an inspection, due to the inherent risks associated with compounding sterile drugs, the board's inspectors are mandated to review the following: the pharmacy's policies and procedures to ensure compliance with pharmacy law, inspection reports performed by other agencies at the facility, and the specific sterile preparations compounded in the prior year.

Over the past three years, the sterile compounding inspection team has been understaffed.

Inspectors from the other inspection teams (compliance, drug diversion and fraud, prescription drug abuse and probation) have been redirected to assist with the sterile compounding inspections on an as-needed basis. However, inspections and investigations that are handled by non-sterile compounding team inspectors reduce the time these inspectors can dedicate to their own workload on their respective teams, but the requirement to inspect these facilities before issuance of renewals creates considerable and mandatory workload that must be handled first.

In fiscal year 2016-17, the board conducted 110 nonresident compounding inspections, 19 of which were conducted by non-compounding team inspectors. This reflects a stabilization in the sterile compounding team as it performed all but 17 percent of the nonresident inspections.

Training is an essential factor for all the board's inspector staff to ensure the consistency of inspections, but ongoing training is critically required for inspectors both on the sterile compounding team and those who perform the sterile compounding inspections on a periodic basis.

QUESTION TWO: WHETHER FEE REVENUE COLLECTED PURSUANT TO SUBDIVISION (v) OF SECTION 4400 AND TRAVEL COST REIMBURSEMENTS COLLECTED PURSUANT TO SUBDIVISION (c) OF THIS SECTION PROVIDE REVENUE IN AN AMOUNT SUFFICIENT TO SUPPORT THE BOARD'S ACTIVITIES RELATED TO THE INSPECTION AND LICENSURE OF NONRESIDENT PHARMACIES.

The board conducted an audit of its fees in 2015-2016 as part of the sunset review process. As a result of this audit, board fees were altered and most were increased in 2016 legislation.

Prior to July of 2017 when the new fees took effect, the initial application fee and annual renewal fees were each \$780 for nonresident sterile compounding pharmacies. Effective July 2017, the fees became \$2,380 for the initial license and annual renewal became \$2,270.

In addition to the annual fees, the board also collects actual travel expenses for the out-of-state travel. The board has conducted over 300 nonresident sterile compounding inspections since 2014. Travel costs and expenses associated with these inspections total approximately \$657,000. Unreimbursed travel expenses are attributed to THREE nonresident facilities of approximately \$7,200 or 1 percent of the total travel costs to the board for all out-of-state travel over the past three years. All three licenses were cancelled for nonpayment of licensure fees.

QUESTION THREE: THE STATUS OF PROPOSED CHANGES TO FEDERAL LAW THAT ARE UNDER SERIOUS CONSIDERATION AND THAT WOULD GOVERN COMPOUNDING PHARMACIES, INCLUDING LEGISLATION PENDING BEFORE THE UNITED STATES CONGRESS, ADMINISTRATIVE RULES, REGULATIONS OR ORDERS UNDER CONSIDERATION BY THE FEDERAL FOOD AND DRUG ADMINISTRATION OR OTHER APPROPRIATE FEDERAL AGENCY, AND CASES PENDING BEFORE THE COURTS.

On November 27, 2013, just months after California enacted SB 294, the federal government enacted the Drug Quality and Security Act as part of a response to the health care tragedy caused by the substandard sterile compounding of the New England Compounding Center. This was the same event that led the California State Board of Pharmacy to sponsor SB 294 in 2013.

Note 2013's DQSA created a new entity called "outsourcing facility" at the federal level to permit large-scale sterile compounding by specialized entities that would operate more like manufacturing plants, be regulated like manufacturers under "current good manufacturing practices," and would not be subject to the new drug approval processes required of manufacturers. The California State Board of Pharmacy sponsored legislation in 2016 to require California licensure of outsourcers to the California Legislature, both those licensed with California as well as those that ship into California. A companion report is being simultaneously developed to respond to similar questions for nonresident outsourcers that are being asked in this report for nonresident sterile compounding pharmacies.

The FDA has developed a series of guidance documents for pharmacies performing sterile compounding to guide the profession to address emergent issues and provide information about what issues are likely to trigger FDA enforcement activities.

There have been six FDA-convened meetings with the state boards of pharmacy of the 50 states since enactment of the DQSA. During these meetings, the FDA shares information about its regulation of sterile compounding and outsourcing, and states are often asked to provide presentations on their activities in this area. California is a leader in the regulation of sterile compounding and now outsourcing, and has provided presentations at the last five national FDA meetings on its activities in this area.

One of the principle differences between how the FDA views outsourcers and sterile compounders are that pharmacies that compound may do so under the federal Food, Drug and Cosmetic Act's exemption for drug approval and specific directions for use by the FDA so long as the compounding is done pursuant to patient-specific prescriptions and very limited advance compounding based on a pharmacy's historical practice where a specific volume is routinely compounded at one time. Large scale compounding not pursuant to a prescription is the realm of outsourcing facilities, where again the facility is not subject to new drug approval processes of the FDA.

The FDA envisions limited or little compounding for pharmacies to compound for prescriber office use, and has proposed development of a memoranda of understanding for dispensing larger quantities of nonpatient specific compounded preparations by pharmacies for shipment across state lines. However, this proposal has been neither refined or finalized since it was proposed several years ago.

The board's regulation of sterile compounding facilities and outsourcing facilities generally follows these guidelines, although current California law allows pharmacies to compound for prescriber office use and allows veterinarians to receive up to a 120 hours supply of pharmacy compounded medication to be provided to veterinary clients for veterinary care.

Another major difference between FDA's and the board's requirements is that California law does not allow pharmacies and outsourcing facilities to be licensed at the same premises. The board believes important pharmacy patient-specific duties could get lost if a pharmacy operates from a conjoined facility with an outsourcer. California's law with respect to outsourcing facilities makes this separation a mandate.

In 2016 the board completed revising and upgrading California's previous compounding regulations following the NECC incident, and these requirements became effective January 1, 2017. Since then the board has spent considerable effort, including during inspections, to educate sterile compounders about the new requirements which often contained provisions specified in the United States Pharmacopeia standards, principally sections 795, 797 and 800. As this report is being prepared, the board is again resuming discussions with the regulated public to further modify the board's compounding requirements to keep them optimally current.

Ongoing review and update of board regulations regarding compounding and sterile compounding will be an ongoing work component for the board. Federal law changes and guidance documents released by the FDA will be part of these ongoing assessments.

QUESTION FOUR: IF APPLICABLE, RECOMMENDED MODIFICATIONS TO THE BOARD'S STATUTORY DUTIES RELATED TO NONRESIDENT PHARMACIES AS A RESULT OF CHANGES TO FEDERAL LAW OR ANY ADDITIONAL MODIFICATIONS NECESSARY TO PROTECT THE HEALTH AND SAFETY OF THE PUBLIC.

The board has modified its regulation requirements with respect to compounding and sterile compounding. Last year, the board sponsored a repeal of an outdated section of law, Business and Professions Code section 4127.7 (SB 510, Stone, Chapter 649, Statutes of 2017).

With respect to statutory requirements still needing adjustment, the board recommends modifications to Business and Professions Code section 4312, subsections (a), (b) and (c) to correct an inadvertent omission leaving sterile compounding pharmacies out of a provision in Pharmacy Law that allows the board to cancel a license if the premises is not active for 120

days. In the interest of public health and safety, the board recommends adding the license type “sterile compounding facility” to this section as follows:

4312. Voiding License of Entity Remaining Closed: Notice; Disposition of Stock; Distribution of Proceeds Where Board Sells Stock.

- (a) The board may cancel the license of a wholesaler, third-party logistics provider, pharmacy, veterinary food-animal drug retailer, sterile compounding facility, or outsourcing facility if the licensed premises remain closed, as defined in subdivision (e), other than by order of the board. For good cause shown, the board may cancel a license after a shorter period of closure. To cancel a license pursuant to this subdivision, the board shall make a diligent, good faith effort to give notice by personal service on the licensee. If a written objection is not received within 10 days after personal service is made or a diligent, good faith effort to give notice by personal service on the licensee has failed, the board may cancel the license without the necessity of a hearing. If the licensee files a written objection, the board shall file an accusation based on the licensee remaining closed. Proceedings shall be conducted in accordance with Chapter 5 (commencing with Section 11500) of Part 1 of Division 3 of Title 2 of the Government Code, and the board shall have all the powers granted in that chapter.
- (b) If the license of a wholesaler, third-party logistics provider, pharmacy, veterinary food-animal drug retailer, sterile compounding facility, or outsourcing facility is canceled pursuant to subdivision (a) or revoked pursuant to Article 19 (commencing with Section 4300), or a wholesaler, third-party logistics provider, pharmacy, veterinary food-animal drug retailer, or outsourcing facility notifies the board of its intent to remain closed or to discontinue business, the licensee shall, within 10 days thereafter, arrange for the transfer of all dangerous drugs and controlled substances or dangerous devices to another licensee authorized to possess the dangerous drugs and controlled substances or dangerous devices. The licensee transferring the dangerous drugs and controlled substances or dangerous devices shall immediately confirm in writing to the board that the transfer has taken place.
- (c) If a wholesaler, third-party logistics provider, pharmacy, veterinary food-animal drug retailer, sterile compounding facility, or outsourcing facility fails to comply with subdivision (b), the board may seek and obtain an order from the superior court in the county in which the wholesaler, third-party logistics provider, pharmacy, veterinary food-animal drug retailer, or outsourcing facility is located, authorizing the board to enter the wholesaler, third-party logistics provider, pharmacy, veterinary food-animal drug retailer, or outsourcing facility and inventory and store, transfer, sell, or arrange for the sale of, all dangerous drugs and controlled substances and dangerous devices found in the wholesaler, third-party logistics provider, pharmacy, veterinary food-animal drug retailer, sterile compounding facility, or outsourcing facility.
- (d) If the board sells or arranges for the sale of any dangerous drugs, controlled substances, or dangerous devices pursuant to subdivision (c), the board may retain from the proceeds of the sale an amount equal to the cost to the board of obtaining and

enforcing an order issued pursuant to subdivision (c), including the cost of disposing of the dangerous drugs, controlled substances, or dangerous devices. The remaining proceeds, if any, shall be returned to the licensee from whose premises the dangerous drugs or controlled substances or dangerous devices were removed.

- (1) The licensee shall be notified of his or her right to the remaining proceeds by personal service or by certified mail, postage prepaid.
 - (2) If a statute or regulation requires the licensee to file with the board his or her address, and any change of address, the notice required by this subdivision may be sent by certified mail, postage prepaid, to the latest address on file with the board and service of notice in this manner shall be deemed completed on the 10th day after the mailing.
 - (3) If the licensee is notified as provided in this subdivision, and the licensee fails to contact the board for the remaining proceeds within 30 calendar days after personal service has been made or service by certified mail, postage prepaid, is deemed completed, the remaining proceeds shall be deposited by the board into the Pharmacy Board Contingent Fund. These deposits shall be deemed to have been received pursuant to Chapter 7 (commencing with Section 1500) of Title 10 of Part 3 of the Code of Civil Procedure and shall be subject to claim or other disposition as provided in that chapter.
- (e) For the purposes of this section, “closed” means not engaged in the ordinary activity for which a license has been issued for at least one day each calendar week during any 120-day period.
- (f) Nothing in this section shall be construed as requiring a pharmacy to be open seven days a week.

In the coming months, as the board convenes public discussions with stakeholders, additional statutory requirements may be identified that need modification. These will be brought forward as part of the board’s legislative program.

There will also be work done on building standards requirements in the Office of Statewide Health Planning’s purview for health systems sterile compounding facilities as well as in the regulations of the California Building Commission.