California State Board of Pharmacy
1625 N. Market Blvd, N219, Sacramento, CA 95834
Phone: (916) 574-7900
Fax: (916) 574-8618
www.pharmacy.ca.gov

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

To: Board Members

RE: Agenda Item IV: Discussion and Consideration of Draft Reports to the Legislature

- Pursuant to Business and Professions Code Section 4127.2(g)
- Pursuant to Business and Professions Code Section 4129.3

In 2014 following enactment of board-sponsored legislation, the board implemented new requirements for the licensure of sterile compounding pharmacies. One new provision requires board-conducted inspections before licensure or renewal each year of a nonresident sterile compounding pharmacy. This was an unusual activity and responsibility for the board, and included in the enabling legislation was a requirement for the board to prepare a legislative report on its inspection activities out of state.

In 2016, the board sponsored additional provisions to license outsourcing facilities, and to require board-conducted inspections of nonresident outsourcing facilities. This legislation was enacted as part of the board's sunset review process, and required a legislative report by January 1, 2018, seeking responses to similar questions regarding the inspection of nonresident outsourcing facilities.

Copies of the proposed report on nonresident sterile compounding pharmacies and the proposed report on nonresident outsourcing facilities follow this memorandum.

At this Meeting:
During this meeting, the board is asked to review, where desired amend, and approve these reports so they can be finalized and submitted to the Legislature. (Note: because the December 2017 Board Meeting was initially cancelled due to lack of quorum. a draft report was provided to the chairs of the Assembly Business and Professions Committee and Senate Business, Professions and Economic Development Committee until the board could meet, discuss and approve the reports.)

The questions the board was directed to respond to are:

1. *A detailed description of board activities related to the inspection and licensure of nonresident pharmacies (or outsourcing facilities).*
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.*

   Or in the case of outsourcing facilities:

   Whether fee revenue collected pursuant to subdivision (x) of Section 4400 and travel cost reimbursements collected pursuant to subdivision (c) of Section 4129.2 provide revenue in

an amount sufficient to support the board's activities related to the inspection and licensure of nonresident outsourcing facilities.

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.*

   Or in the case of outsourcing facilities:

   The status of proposed changes to federal law that are under serious consideration and that would govern outsourcing facilities and compounding pharmacies, including, but not limited to, legislation pending before Congress, administrative rules, regulations or orders under consideration by the FDA 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.*

   Or in the case of outsourcing facilities:

   If applicable, recommended modifications to the board's statutory duties related to nonresident outsourcing facilities as a result of changes to federal law or any additional modifications necessary to protect the health and safety of the public.

Attachments

California State Board of Pharmacy
1625 N. Market Blvd, N219, Sacramento, CA 95834
Phone: (916) 574-7900
Fax: (916) 574-8618
www.pharmacy.ca.gov

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

December 26, 2017

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

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

RE: Board Mandated Reports to the Legislature, Due January 1, 2018

Dear Senator Hill and Assembly Member Low:

On or before January 1, 2018, the Board of Pharmacy is required to submit two reports to the Legislature on its nonresident inspections of sterile compounding facilities and outsourcing facilities. These reports are required by:

- California Business and Professions Code section 4127.2 (for nonresident sterile compounding pharmacies); and
- California Business and Professions Code section 4129.3 (for nonresident outsourcing facilities).

This letter accompanies draft copies of the two mandated reports.

I am releasing draft copies of the two reports to you at this time because the board has been unable to meet as a board to review, discuss and approve the documents. A board meeting scheduled for December 12, 2017, where the reports were agendized for discussion was cancelled at the last minute because of an unfortunate loss of quorum. A new board meeting has been scheduled for January 11, 2018, at which time the two reports will be discussed and reviewed. Our intent is to submit the completed and board-approved reports shortly thereafter to your committees and to other individuals and agencies on the mandated report distribution list.

Should you have questions or need additional information about these reports, please to not hesitate to contact me at (916) 574-7911.

Season's greetings to you, your families and your staff.

Sincerely,

Virginia Herold

VIRGINIA HEROLD
Executive Officer

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

Governor Edmund G. Brown Jr.

Alexis Podesta, Secretary Business, Consumer Services and Housing Agency

Dean R. Grafilo, Director, Department of Consumer Affairs

Virginia Herold, Executive Officer, California State Board of Pharmacy

California State Board of Pharmacy

1625 N. Market Blvd, Suite N219

Sacramento, CA 95834

(916) 574-7900

MEMBERS

Amarylis Gutierrez, PharmD, President

Victor Law, R.Ph., Vice President

Allen Schaad, R.Ph., Treasurer

Ryan Brooks

Lavanza Butler, R.Ph.

Amjad Mahmood Khan

Greg Lippe

Valerie Muñoz

Ricardo Sanchez

Deborah Veale, R.Ph.

Stanley Weisser, R.Ph.

Albert Wong, PharmD

VISION

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.

California State Board of Pharmacy
1625 N. Market Blvd, N219, Sacramento, CA 95834
Phone: (916) 574-7900
Fax: (916) 574-8618
www.pharmacy.ca.gov

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

The Honorable Jerry Hill, Chair
Senate Business, Professions and
Economic Development Committee
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,

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 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 questions for the board to respond to:

1. 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 all 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, all 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 two 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.

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: 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.

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 two proposals:

PROPOSAL 1:

Repeal of Health and Safety Code 1250.4 (5). This section concerns non-sterile to sterile compounding, which is the highest risk form of compounding. This proposed repeal identifies specific room requirements to perform such compounding. These requirements now exist in board regulations. Proposed text to do this is provided below:

REFERENCED TITLE 24, PART 2, CHAPTER 12, REGULATIONS

Health and Safety Code Section 1250.4 Compounding Area for Parenteral Solutions.

The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall:

1. In accordance with Federal Standard 209(b), Clean Room and Work Station Requirements, Controlled Environment, as approved by the Commission, Federal Supply Service, General Services Administration meet standards for class 100 HEPA (high efficiency particulate air) filtered air such as laminar air flow hood or clean room.
2. Have non-porous and cleanable surfaces, walls, floors and floor coverings.
3. The pharmacy shall be arranged in such a manner that the laminar-flow hood is located in an area which is exposed to minimal traffic flow, and is separate from any area used for bulk storage of items not related to the compounding of parenteral solution. There shall be sufficient space, well separated from the laminar-flow hood area, for the storage of bulk materials, equipment and waste materials.
4. A sink with hot and cold running water must be within the parenteral solution compounding area or adjacent to it.

~~5. Any pharmacy that compounds sterile injectable products from one or more nonsterile ingredients must compound the medication in one of the following environments:~~

~~5.1 An ISO class laminar airflow hood within an ISO class 7 cleanroom. The cleanroom must have a positive air pressure differential relative to adjacent areas.~~

~~5.2 An ISO class 5 cleanroom.~~

~~5.3 A barrier isolator that provides an ISO class 5 environment for compounding.~~

PROPOSAL 2:

The board also recommends adding 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 Buildings Commission.

CALIFORNIA STATE BOARD OF PHARMACY

BE AWARE AND TAKE CARE: Talk to your pharmacist!

REPORT TO THE LEGISLATURE ON INSPECTIONS OF NONRESIDENT OUTSOURCING FACILITIES

SUBMITTED PURSUANT TO BUSINESS AND PROFESSIONS CODE SECTION 4129.3

JANUARY 1, 2018

STATE OF CALIFORNIA

Governor Edmund G. Brown Jr.

Alexis Podesta, Secretary Business, Consumer Services and Housing Agency

Dean R. Grafilo, Director, Department of Consumer Affairs

Virginia Herold, Executive Officer, California State Board of Pharmacy

California State Board of Pharmacy

1625 N. Market Blvd, Suite N219

Sacramento, CA 95834

(916) 574-7900

MEMBERS

Amarylis Gutierrez, PharmD, President

Victor Law, R.Ph., Vice President

Allen Schaad, R.Ph., Treasurer

Ryan Brooks

Lavanza Butler, R.Ph.

Amjad Mahmood Khan

Greg Lippe

Valerie Muñoz

Ricardo Sanchez

Deborah Veale, R.Ph.

Stanley Weisser, R.Ph.

Albert Wong, PharmD

VISION

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.

California State Board of Pharmacy
1625 N. Market Blvd, N219, Sacramento, CA 95834
Phone: (916) 574-7900
Fax: (916) 574-8618
www.pharmacy.ca.gov

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

The Honorable Jerry Hill, Chair
Senate Business, Professions and
Economic Development Committee
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 4129.3 on the board's regulation of out-of-state outsourcing facilities that are licensed to compound and ship sterile and other compounded medications into California.

In 2016, SB 1193 (Hill, Chapter 484) 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. These new licensure requirements took effect January 1, 2017, which affect both in-state and nonresident facilities licensed with the FDA as outsourcing facilities and performing sterile and other compounding services in or into California.

The board began issuing its first outsourcing facility licenses in June 2017, following the training of staff for the entirely new program. The legislation requires annual board inspections before issuance or renewal of outsourcing facilities doing business within or into California, and requires compliance with federal current good manufacturing practices, which is a body of standards with which the board did not have experience enforcing because they pertain to drug manufacturers generally.

This report details the board's activities and efforts to meet its public protection mandate for patients of these sterile compounded medications where the medication has been prepared by out-of-state FDA registered outsourcing facilities. It addresses four questions which the board has been directed to answer.

There is a companion report to respond to the board's regulation of compounding activities by nonresident sterile compounding pharmacies, which are licensed under Article 7.5 of Chapter 9, Division 2 of the California Business and Professions Code. Whereas outsourcing facilities typically compound large quantities of medication at one time and not pursuant to a patient-specific prescription, pharmacies generally compound pursuant to a patient-specific prescription, and in smaller quantities.

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

Sincerely,

Amarylis C. Gutierrez, PharmD
President, Board of Pharmacy

MESSAGE SUMMARY

Pursuant to California Business and Professions Code section 4129.3, the board provides the following responses to the four questions asked of the board in the statute that are directed to be discussed in this report regarding its regulation on nonresident outsourcing facilities.

OVERVIEW AND BACKGROUND

By January 1, 2018, the California State Board of Pharmacy shall provide a report to the Legislature regarding the regulation of nonresident outsourcing facilities.

Per Business and Professions Code Section 4129.3, the board shall address the following:

1. A detailed description of board activities related to the inspection and licensure of nonresident outsourcing facilities.
2. Whether fee revenue collected pursuant to subdivision (x) of Section 4400 and travel cost reimbursements collected pursuant to subdivision (c) of Section 4129.2 provide revenue in an amount sufficient to support the board's activities related to the inspection and licensure of nonresident outsourcing facilities.
3. The status of proposed changes to federal law that are under serious consideration and that would govern outsourcing facilities and compounding pharmacies, including, but not limited to, legislation pending before Congress, administrative rules, regulations or orders under consideration by the FDA 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 outsourcing facilities as a result of changes to federal law or any additional modifications necessary to protect the health and safety of the public.

This report summarizes the board's efforts to regulate nonresident outsourcing facilities. Outsourcing facilities are generally large-scale production facilities that compound large quantities of medications and at the federal level, are registered with the FDA. Federal law created in November 2013 defines an outsourcing facility as a facility at one location that is engaged in the compounding of sterile and other drugs, that has elected to register as an outsourcing facility, and complies with all the requirements of federal law under federal Food, Drug and Cosmetic Act section 503B.

Drugs compounded by an outsourcing facility can qualify for exemptions from the FDA drug-approval requirements and the requirement to label products with adequate directions for use, but not from current good manufacturing practice (cGMP) requirements. CGMPs are more rigorous than the compounding requirements for sterile compounding pharmacies. Patients in multiple locations and in multiple states can receive these compounded medications. Outsourcing facilities serve an important function in that they can produce necessary medications that may be in short supply, which is an ongoing problem facing health care providers.

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

Senate Bill 1193 took effect January 1, 2017. The establishment and regulation of nonresident outsourcing facilities encompassed one set of provisions in this legislation.

Due to the inherent risks associated with compounding sterile drugs, the board is required to perform a preopening and annual inspection of each outsourcing facility as a condition of licensure and renewal.

As of December 1, 2017, there were 73 FDA registered outsourcing facilities across the United States. The board has received 41 applications for outsourcing licenses, 35 of which are nonresident outsourcing facilities. In addition to the mandated inspection the board conducts, board inspectors reference online FDA inspection reports, warning letters, recalls, drug shortage reports, written policies and procedures, as well as lists of medication compounded and shipped into California as part of preparation before initiating an inspection of an outsourcing facility.

The board has inspected 16 outsourcing facilities and issued ten outsourcing licenses since June of 2017. Of the ten licenses issued, two were California outsourcing facilities. With respect to the six remaining facilities where inspections have occurred, information is currently under review by board staff in making the final licensing decision.

Due of the complexity of these manufacturing-like facilities, each nonresident outsourcing inspection the board conducts requires a minimum of three days to inspect, typically two days to travel to and from and utilizes two inspectors.

Currently two full time inspectors and one supervising inspector have been assigned to perform the in-state and nonresident outsourcing inspections. These positions were created in July 2017 with the enactment of the 2017/18 state budget.

The supervising inspector of the team was promoted from the board's sterile compounding inspector staff to oversee the outsourcing program in May 2017. One additional board inspector transitioned to the outsourcing team in June 2017. Finally, a new inspector was hired and assigned to the outsourcing team in October 2017.

There is a heavy training requirement for this team. The supervising inspector has completed four weeks of FDA-provided training on outsourcing facilities and current good manufacturing practices (cGMPs). This will ensure consistency in the board's enforcement of federal outsourcing requirements. The two inspectors who have been assigned to the outsourcing team will attend FDA training on outsourcing and cGMPs as soon as space is available in 2018.

During the first year of implementation, the supervising inspector will accompany and train the inspectors assigned to outsourcing inspections. This training is currently underway. Two additional inspectors who are not specifically assigned to the outsourcing team have completed the four weeks of FDA training for outsourcing and cGMPs. These two staff members will assist the outsourcing team in conducting both in-state and nonresident outsourcing inspections each year.

While the FDA has offered this training to the board without tuition, the board is responsible for travel costs and expenses during training, which is approximately $8,000 per inspector for the four weeks. By the end of 2018, the board projects that five board inspectors will have completed FDA training for outsourcing facilities.

In the future and on an approximately quarterly basis, the board will redirect a few trained inspectors from other board inspection teams to assist in performing outsourcing inspections. While redirecting inspectors requires them to put their other assigned workload on hold to conduct outsourcing inspections, having additional inspectors available to perform these outsourcing inspections will provide the board with greater flexibility to schedule inspections.

Below is data that reports various components about the board's regulation of outsourcers to date.

INSPECTORS	**FY 16-17**	**FY 17-18**
Total Board Inspectors	49	50
Outsourcing Team Inspectors*	1	2
Total Supervising Inspectors**	9	9

*Inspector joined outsourcing team in June of 2017

** Supervising Inspector joined outsourcing team in May of 2017

LICENSING STATISTICS	**FY 16-17**	**FY 17-18**
Nonresident Outsourcing License Applicants	26	9
Licensed Nonresident Outsourcing Facilities	2	6
Outsourcing Inspections Performed Outside of California	2	0

INSPECTIONS	**FY 16-17**	**FY 17-18**
Outsourcing Inspections Performed Outside of California	3	11

Towards mid-2018, the board plans to decrease the supervising inspector's time in the field to allow for more focus on case review, inspection assignments/scheduling, enforcement issues and testimony, training, staff management and development.

If the outsourcing licensee population remains at approximately 40 facilities for both in-state and nonresident outsourcing facilities, the board hopes to redirect the supervising inspector to focus more on supervisorial duties; this may require hiring another inspector to perform the inspection workload.

The board intends to continue to address this workload in future years by periodically using and training non-outsourcing team inspectors to perform outsourcing inspections. However, if workload remains steady at or above 40 facilities, or increases to approach the number of outsourcing facilities operating nationally (currently 73), additional staff resources will be sought. The board anticipates that many of the remaining FDA registered outsourcers will someday apply for licensure in California given the large population here and the potential business opportunities the state offers these facilities. However, the program is too young to make this workload assessment at this time.

If all current FDA-registered outsourcers apply for licensure in California, the board would need a full-time staff of four or more inspectors to handle the workload, in addition to the supervising inspector.

QUESTION TWO: WHETHER FEE REVENUE COLLECTED PURSUANT TO SUBDIVISION (X) OF SECTION 4400 AND TRAVEL COST REIMBURSEMENTS COLLECTED PURSUANT TO SUBDIVISION (C) OF SECTION 4129.2 PROVIDE REVENUE IN AN AMOUNT SUFFICIENT TO SUPPORT THE BOARD'S ACTIVITIES RELATED TO THE INSPECTION AND LICENSURE OF NONRESIDENT OUTSOURCING FACILITIES.

The board is authorized to collect a fee of $2,380 for the initial issuance of an outsourcing facility license. The fee for annual renewal of an outsourcing license is $2,270. The fee is intended to cover the board's costs of inspecting the facility, processing the application, scheduling travel arrangements, processing and tracking reimbursement of the inspection and issuing the license. The fees were set at the level required to perform these duties for sterile compounding pharmacies during the 2015/16 fee audit because there are some comparable requirements between the two licensing categories. However, outsourcing facilities require substantially longer to inspect in part because they typically are substantially larger, produce larger quantities of medication than do sterile compounding pharmacies, and must follow cGMPS which are more expansive standards to regulate against.

The board also charges nonresident outsourcers for the costs of travel to the facility, just as occurs for nonresident sterile compounding pharmacies. These nonresident travel expenses are separate and in addition to the actual license and renewal fees.

The board has conducted 14 nonresident inspections of nonresident outsourcing facilities as of December 2017. All facilities have reimbursed the board for full the travel costs and expenses associated with each inspection.

The licensure fees will be assessed in the future after the board has more data and longer experience regulating outsourcing facilities.

QUESTION THREE: THE STATUS OF PROPOSED CHANGES TO FEDERAL LAW THAT ARE UNDER SERIOUS CONSIDERATION AND THAT WOULD GOVERN OUTSOURCING FACILITIES AND COMPOUNDING PHARMACIES, INCLUDING, BUT NOT LIMITED TO, LEGISLATION PENDING BEFORE CONGRESS, ADMINISTRATIVE RULES, REGULATIONS OR ORDERS UNDER CONSIDERATION BY THE FDA OR OTHER APPROPRIATE FEDERAL AGENCY, AND CASES PENDING BEFORE THE COURTS.

The board continues to work closely on sterile compounding and outsourcing regulation with the FDA. FDA guidance documents are shared with the board and discussed once they are publicly released, but the board is not aware of the timing of any planned future releases. Outsourcing guidance documents generally share the FDA's focus that outsourcers perform large scale compounding, and sterile compounding pharmacies compound pursuant to patient-specific prescriptions, although under federal law outsourcers may compound pursuant to a single patient-specific prescription.

New guidance from the FDA will likely be released sometime in 2018 that would impact how the board inspects outsourcing facilities. At the current time, the board inspects all outsourcing facilities annually and relies in part on the FDA's training for cGPMS as core training. One area where the board does not follow the federal Drug Quality and Security Act's provisions is that the FDA performs outsourcing inspections based upon a risk-based assessment, and some facilities operate for a period of time before the FDA ever conducts an inspection. In California an outsourcing license cannot be issued or renewed until a board inspection has occurred.

Finally, the board is not aware of any proposed changes to cGMPs.

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

The board is unaware of any changes or planned changes to federal law that would affect how the board's inspectors inspect outsourcing facilities. However, the board will continue to work closely with the FDA on regulation of outsourcing facilities and sterile compounding facilities both within and outside California.