CALIFORNIA STATE BOARD OF PHARMACY

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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

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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 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 items asked of the board in the statute that are directed to be discussed in this report regarding the board's regulation of 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's 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.

ITEM 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.

As of December 1, 2017, 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

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.

ITEM 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.

ITEM 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 cGMPs 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.

ITEM 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.