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BEFORE THE
BOARD OF PHARMACY
DEPARTMENT OF CONSUMER AFFAIRS
STATE OF CALIFORNIA

In the Matter of the Accusation Against: **CANTRELL DRUG COMPANY** **7321 Cantrell Road, Suite 300-400** **Little Rock, AR 72207** **Non-Resident Pharmacy Permit No. NRP 1071** **Non-Resident Sterile Compounding Permit No. NSC 99637** Respondent.	Case No. 6279 **A C C U S A T I O N**

Complainant Virginia Herold ("Complainant") alleges:

PARTIES

1. Complainant brings this Accusation solely in her official capacity as the Executive Officer of the Board of Pharmacy, Department of Consumer Affairs ("Board").

2. On or about October 7, 2010, the Board of Pharmacy issued Non-Resident Pharmacy Permit Number NRP 1071 to Cantrell Drug Company ("Respondent"). The Non-Resident Pharmacy Permit was in full force and effect at all times relevant to the charges brought herein and will expire on October 1, 2018, unless renewed.

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3. On or about November 3, 2010, the Board of Pharmacy issued Non-Resident Sterile Compounding Permit Number NSC 99637 to Respondent. The Non-Resident Sterile Compounding Permit was in full force and effect at all times relevant to the charges brought herein and expired on October 1, 2017, and has not been renewed.

JURISDICTION

4. This Accusation is brought before the Board, under the authority of the following laws. All section references are to the Business and Professions Code ("Code") unless otherwise indicated.

5. Section 4300 of the Code states in pertinent part:

> (a) Every license issued may be suspended or revoked.
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> (b) The board shall discipline the holder of any license issued by the board, whose default has been entered or whose case has been heard by the board and found guilty, by any of the following methods:
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> (1) Suspending judgment.
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> (2) Placing him or her upon probation.
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> (3) Suspending his or her right to practice for a period not exceeding one year.
>
> (4) Revoking his or her license.
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> (5) Taking any other action in relation to disciplining him or her as the board in its discretion may deem proper.
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> . . .
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> (e) The proceedings under this article shall be conducted in accordance with Chapter 5 (commencing with Section 11500) of Part 1 of Division 3 of the Government Code, and the board shall have all the powers granted therein. The action shall be final, except that the propriety of the action is subject to review by the superior court pursuant to Section 1094.5 of the Code of Civil Procedure.

6. Section 4300.1 of the Code states:

> The expiration, cancellation, forfeiture, or suspension of a board-issued license by operation of law or by order or decision of the board or a court of law, the placement of a license on a retired status, or the voluntary surrender of a license by a licensee shall not deprive the board of jurisdiction to commence or proceed with any investigation of, or action or disciplinary proceeding against, the licensee or to render a decision suspending or revoking the license.

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7. Section 4301 of the Code states in pertinent part:

The board shall take action against any holder of a license who is guilty of unprofessional conduct or whose license has been issued by mistake. Unprofessional conduct shall include, but is not limited to, any of the following:

. . .

(c) Gross negligence.

. . .

(j) The violation of any of the statutes of this state, of any other state, or of the United States regulating controlled substances and dangerous drugs.

. . .

(o) Violating or attempting to violate, directly or indirectly, or assisting in or abetting the violation of or conspiring to violate any provision or term of this chapter or of the applicable federal and state laws and regulations governing pharmacy, including regulations established by the board or by any other state or federal regulatory agency.

UNITED STATES CODE

8. United States Code, title 21, section 353b, states:

(a) In general. Sections 502(f)(1), 505, and 582 [*21 USCS §§ 352(f)(1), 355,* and *360eee-1*] shall not apply to a drug compounded by or under the direct supervision of a licensed pharmacist in a facility that elects to register as an outsourcing facility if each of the following conditions is met:

(1) Registration and reporting. The drug is compounded in an outsourcing facility that is in compliance with the requirements of subsection (b).

(2) Bulk drug substances. The drug is compounded in an outsourcing facility that does not compound using bulk drug substances (as defined in *section 207.3(a)(4) of title 21, Code of Federal* Regulations (or any successor regulation)), unless--

(A)

(i) the bulk drug substance appears on a list established by the Secretary identifying bulk drug substances for which there is a clinical need, by-

(I) publishing a notice in the Federal Register proposing bulk drug substances to be included on the list, including the rationale for such proposal;

(II) providing a period of not less than 60 calendar days for comment on the notice; and

(III) publishing a notice in the Federal

Register designating bulk drug substances for inclusion on the list; or

(ii) the drug compounded from such bulk drug substance appears on the drug shortage list in effect under section 506E [*21 USCS § 356e*] at the time of compounding, distribution, and dispensing;

(B) if an applicable monograph exists under the United States Pharmacopeia, the National Formulary, or another compendium or pharmacopeia recognized by the Secretary for purposes of this paragraph, the bulk drug substances each comply with the monograph;

(C) the bulk drug substances are each manufactured by an establishment that is registered under section 510 [*21 USCS § 360*] (including a foreign establishment that is registered under section 510(i)) [*21 USCS § 360(i)*]; and

(D) the bulk drug substances are each accompanied by a valid certificate of analysis.

(3) Ingredients (other than bulk drug substances) If any ingredients (other than bulk drug substances) are used in compounding the drug, such ingredients comply with the standards of the applicable United States Pharmacopeia or National Formulary monograph, if such monograph exists, or of another compendium or pharmacopeia recognized by the Secretary for purposes of this paragraph if any.

(4) Drugs withdrawn or removed because unsafe or not effective. The drug does not appear on a list published by the Secretary of drugs that have been withdrawn or removed from the market because such drugs or components of such drugs have been found to be unsafe or not effective.

(5) Essentially a copy of an approved drug. The drug is not essentially a copy of one or more approved drugs.

(6) Drugs presenting demonstrable difficulties for compounding. The drug—

(A) is not identified (directly or as part of a category of drugs) on a list published by the Secretary, through the process described in subsection (c), of drugs or categories of drugs that present demonstrable difficulties for compounding that are reasonably likely to lead to an adverse effect on the safety or effectiveness of the drug or category of drugs, taking into account the risks and benefits to patients; or

(B) is compounded in accordance with all applicable conditions identified on the list described in subparagraph (A) as conditions that are necessary to prevent the drug or category of drugs from presenting the demonstrable difficulties described in subparagraph (A).

(7) Elements to assure safe use. In the case of a drug that is

compounded from a drug that is the subject of a risk evaluation and mitigation strategy approved with elements to assure safe use pursuant to section 505-1 [*21 USCS § 355-1*], or from a bulk drug substance that is a component of such drug, the outsourcing facility demonstrates to the Secretary prior to beginning compounding that such facility will utilize controls comparable to the controls applicable under the relevant risk evaluation and mitigation strategy.

(8) Prohibition on wholesaling. The drug will not be sold or transferred by an entity other than the outsourcing facility that compounded such drug. This paragraph does not prohibit administration of a drug in a health care setting or dispensing a drug pursuant to a prescription executed in accordance with section 503(b)(1) [*21 USCS § 353(b)(1)*].

(9) Fees. The drug is compounded in an outsourcing facility that has paid all fees owed by such facility pursuant to section 744K [*21 USCS § 379j-62*].

(10) Labeling of drugs.

(A) Label. The label of the drug includes—

(i) the statement "This is a compounded drug." or a reasonable comparable alternative statement (as specified by the Secretary) that prominently identifies the drug as a compounded drug;

(ii) the name, address, and phone number of the applicable outsourcing facility; and

(iii) with respect to the drug--

(I) the lot or batch number;

(II) the established name of the drug;

(III) the dosage form and strength;

(IV) the statement of quantity or volume, as appropriate;

(V) the date that the drug was compounded;

(VI) the expiration date;

(VII) storage and handling instructions;

(VIII) the National Drug Code number, if available;

(IX) the statement "Not for resale", and, if the drug is dispensed or distributed other than pursuant to a prescription for an individual identified patient, the statement "Office Use Only"; and

(X) subject to subparagraph (B)(i), a list of active and inactive ingredients, identified by established name and the quantity or proportion of each ingredient.

(B) Container. The container from which the individual units of the drug are removed for dispensing or for administration (such as a plastic bag containing individual product syringes) shall include—

(i) the information described under subparagraph (A)(iii)(X), if there is not space on the label for such information;

(ii) the following information to facilitate adverse event reporting: *www.fda.gov/medwatch* and 1-800-FDA-1088 (or any successor Internet Web site or phone number); and

(iii) directions for use, including, as appropriate, dosage and administration.

(C) Additional information. The label and labeling of the drug shall include any other information as determined necessary and specified in regulations promulgated by the Secretary.

(11) Outsourcing facility requirement. The drug is compounded in an outsourcing facility in which the compounding of drugs occurs only in accordance with this section.

(b) Registration of outsourcing facilities and reporting of drugs.

(1) Registration of outsourcing facilities.

(A) Annual registration. Upon electing and in order to become an outsourcing facility, and during the period beginning on October 1 and ending on December 31 of each year thereafter, a facility—

(i) shall register with the Secretary its name, place of business, and unique facility identifier (which shall conform to the requirements for the unique facility identifier established under section 510 [*21 USCS § 360*]), and a point of contact email address; and

(ii) shall indicate whether the outsourcing facility intends to compound a drug that appears on the list in effect under section 506E [*21 USCS § 356e*] during the subsequent calendar year.

(B) Availability of registration for inspection; list.

(i) Registrations. The Secretary shall make available for inspection, to any person so requesting, any

registration filed pursuant to this paragraph.

(ii) List. The Secretary shall make available on the public Internet Web site of the Food and Drug Administration a list of the name of each facility registered under this subsection as an outsourcing facility, the State in which each such facility is located, whether the facility compounds from bulk drug substances, and whether any such compounding from bulk drug substances is for sterile or nonsterile drugs.

(2) Drug reporting by outsourcing facilities.

(A) In general. Upon initially registering as an outsourcing facility, once during the month of June of each year, and once during the month of December of each year, each outsourcing facility that registers with the Secretary under paragraph (1) shall submit to the Secretary a report—

(i) identifying the drugs compounded by such outsourcing facility during the previous 6-month period; and

(ii) with respect to each drug identified under clause (i), providing the active ingredient, the source of such active ingredient, the National Drug Code number of the source drug or bulk active ingredient, if available, the strength of the active ingredient per unit, the dosage form and route of administration, the package description, the number of individual units produced, and the National Drug Code number of the final product, if assigned.

(B) Form. Each report under subparagraph (A) shall be prepared in such form and manner as the Secretary may prescribe by regulation or guidance.

(C) Confidentiality. Reports submitted under this paragraph shall be exempt from inspection under paragraph (1)(B)(i), unless the Secretary finds that such an exemption would be inconsistent with the protection of the public health.

(3) Electronic registration and reporting. Registrations and drug reporting under this subsection (including the submission of updated information) shall be submitted to the Secretary by electronic means unless the Secretary grants a request for waiver of such requirement because use of electronic means is not reasonable for the person requesting waiver.

(4) Risk-based inspection frequency.

(A) In general. Outsourcing facilities—

(i) shall be subject to inspection pursuant to section 704 [*21 USCS § 374*]; and

(ii) shall not be eligible for the exemption under section 704(a)(2)(A) [*21 USCS § 374(a)(2)(A)*].

(B) Risk-based schedule. The Secretary, acting through one or more officers or employees duly designated by the Secretary, shall inspect outsourcing facilities in accordance with a risk-based schedule established by the Secretary.

(C) Risk factors. In establishing the risk-based schedule, the Secretary shall inspect outsourcing facilities according to the known safety risks of such outsourcing facilities, which shall be based on the following factors:

(i) The compliance history of the outsourcing facility.

(ii) The record, history, and nature of recalls linked to the outsourcing facility.

(iii) The inherent risk of the drugs compounded at the outsourcing facility.

(iv) The inspection frequency and history of the outsourcing facility, including whether the outsourcing facility has been inspected pursuant to section 704 [*21 USCS § 374*] within the last 4 years.

(v) Whether the outsourcing facility has registered under this paragraph as an entity that intends to compound a drug that appears on the list in effect under section 506E [*21 USCS § 356e*].

(vi) Any other criteria deemed necessary and appropriate by the Secretary for purposes of allocating inspection resources.

(5) Adverse event reporting. Outsourcing facilities shall submit adverse event reports to the Secretary in accordance with the content and format requirements established through guidance or regulation under *section 310.305 of title 21, Code of Federal R*egulations (or any successor regulations).

(c) Regulations.

(1) In general. The Secretary shall implement the list described in subsection (a)(6) through regulations.

(2) Advisory committee on compounding. Before issuing regulations to implement subsection (a)(6), the Secretary shall convene and consult an advisory committee on compounding. The advisory committee shall include representatives from the National Association of Boards of Pharmacy, the United States Pharmacopeia, pharmacists with current experience and expertise in compounding, physicians with background and knowledge in compounding, and patient and public health advocacy organizations.

(3) Interim list.

(A) In general. Before the effective date of the regulations finalized to implement subsection (a)(6), the Secretary may designate drugs, categories of drugs, or conditions as described such subsection by—

(i) publishing a notice of such substances, drugs, categories of drugs, or conditions proposed for designation, including the rationale for such designation, in the Federal Register;

(ii) providing a period of not less than 60 calendar days for comment on the notice; and

(iii) publishing a notice in the Federal Register designating such drugs, categories of drugs, or conditions.

(B) Sunset of notice. Any notice provided under subparagraph (A) shall not be effective after the earlier of—

(i) the date that is 5 years after the date of enactment of the Compounding Quality Act [enacted Nov. 27, 2013]; or

(ii) the effective date of the final regulations issued to implement subsection (a)(6).

(4) Updates. The Secretary shall review, and update as necessary, the regulations containing the lists of drugs, categories of drugs, or conditions described in subsection (a)(6) regularly, but not less than once every 4 years. Nothing in the previous sentence prohibits submissions to the Secretary, before or during any 4-year period described in such sentence, requesting updates to such lists.

(d) Definitions. In this section:

(1) The term "compounding" includes the combining, admixing, mixing, diluting, pooling, reconstituting, or otherwise altering of a drug or bulk drug substance to create a drug.

(2) The term "essentially a copy of an approved drug" means—

(A) a drug that is identical or nearly identical to an approved drug, or a marketed drug not subject to section 503(b) [*21 USCS § 353(b)*] and not subject to approval in an application submitted under section 505 [*21 USCS § 355*], unless, in the case of an approved drug, the drug appears on the drug shortage list in effect under section 506E [*21 USCS § 356e*] at the time of compounding, distribution, and dispensing; or

(B) a drug, a component of which is a bulk drug substance that is a component of an approved drug or a marketed drug that is not subject to section 503(b) [*21 USCS § 353(b)*] and not subject to approval in an application submitted under section 505 [*21 USCS § 355*], unless there is a change that produces for an

individual patient a clinical difference, as determined by the prescribing practitioner, between the compounded drug and the comparable approved drug.

(3) The term "approved drug" means a drug that is approved under section 505 [*21 USCS § 355*] and does not appear on the list described in subsection (a)(4) of drugs that have been withdrawn or removed from the market because such drugs or components of such drugs have been found to be unsafe or not effective.

(4) (A) The term "outsourcing facility" means a facility at one geographic location or address that—

(i) is engaged in the compounding of sterile drugs;

(ii) has elected to register as an outsourcing facility; and

(iii) complies with all of the requirements of this section.

(B) An outsourcing facility is not required to be a licensed pharmacy.

(C) An outsourcing facility may or may not obtain prescriptions for identified individual patients.

(5) The term "sterile drug" means a drug that is intended for parenteral administration, an ophthalmic or oral inhalation drug in aqueous format, or a drug that is required to be sterile under Federal or State law". (*sic*)

(d) (*sic*) Obligation to pay fees. Payment of the fee under section 744K [*21 USCS § 379j-62*], as described in subsection (a)(9), shall not relieve an outsourcing facility that is licensed as a pharmacy in any State that requires pharmacy licensing fees of its obligation to pay such State fees.

CODE OF FEDERAL REGULATIONS

9. Code of Federal Regulations, title 21, part 211.22, states in pertinent part:

(a) There shall be a quality control unit that shall have the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging material, labeling, and drug products, and the authority to review production records to assure that no errors have occurred or, if errors have occurred, that they have been fully investigated. The quality control unit shall be responsible for approving or rejecting drug products manufactured, processed, packed, or held under contract by another company.

. . .

(d) The responsibilities and procedures applicable to the quality control unit shall be in writing; such written procedures shall be followed

10. Code of Federal Regulations, title 21, part 211.42, states in pertinent part:

(a) Any building or buildings used in the manufacture, processing, packing, or holding of a drug product shall be of suitable size, construction and location to facilitate cleaning, maintenance, and proper operations.

(b) Any such building shall have adequate space for the orderly placement of equipment and materials to prevent mixups between different components, drug product containers, closures, labeling, in-process materials, or drug products, and to prevent contamination. The flow of components, drug product containers, closures, labeling, in-process materials, and drug products through the building or buildings shall be designed to prevent contamination.

(c) Operations shall be performed within specifically defined areas of adequate size. There shall be separate or defined areas or such other control systems for the firm's operations as are necessary to prevent contamination or mixups during the course of the following procedures:

(1) Receipt, identification, storage, and withholding from use of components, drug product containers, closures, and labeling, pending the appropriate sampling, testing, or examination by the quality control unit before release for manufacturing or packaging;

(2) Holding rejected components, drug product containers, closures, and labeling before disposition;

(3) Storage of released components, drug product containers, closures, and labeling;

(4) Storage of in-process materials;

(5) Manufacturing and processing operations;

(6) Packaging and labeling operations;

(7) Quarantine storage before release of drug products;

(8) Storage of drug products after release;

(9) Control and laboratory operations;

(10) Aseptic processing, which includes as appropriate:

(i) Floors, walls, and ceilings of smooth, hard surfaces that are easily cleanable;

(ii) Temperature and humidity controls;

(iii) An air supply filtered through high-efficiency particulate air filters under positive pressure, regardless of whether flow is laminar or nonlaminar;

(iv) A system for monitoring environmental conditions;

(v) A system for cleaning and disinfecting the room and

equipment to produce aseptic conditions;

(vi) A system for maintaining any equipment used to control the aseptic conditions.

11. Code of Federal Regulations, title 21, part 211.113, states:

(a) Appropriate written procedures, designed to prevent objectionable microorganisms in drug products not required to be sterile, shall be established and followed.

(b) Appropriate written procedures, designed to prevent microbiological contamination of drug products purporting to be sterile, shall be established and followed. Such procedures shall include validation of all aseptic and sterilization processes.

12. Code of Federal Regulations, title 21, part 211.125, states in pertinent part:

(a) Strict control shall be exercised over labeling issued for use in drug product labeling operations.

(b) Labeling materials issued for a batch shall be carefully examined for identity and conformity to the labeling specified in the master or batch production records.

(c) Procedures shall be used to reconcile the quantities of labeling issued, used, and returned, and shall require evaluation of discrepancies found between the quantity of drug product finished and the quantity of labeling issued when such discrepancies are outside narrow preset limits based on historical operating data. Such discrepancies shall be investigated in accordance with § 211.192. Labeling reconciliation is waived for cut or roll labeling if a 100-percent examination for correct labeling is performed in accordance with § 211.122(g)(2).(c) Procedures shall be used to reconcile the quantities of labeling issued, used, and returned, and shall require evaluation of discrepancies found between the quantity of drug product finished and the quantity of labeling issued when such discrepancies are outside narrow preset limits based on historical operating data. Such discrepancies shall be investigated in accordance with § 211.192. Labeling reconciliation is waived for cut or roll labeling if a 100-percent examination for correct labeling is performed in accordance with § 211.122(g)(2). Labeling reconciliation is also waived for 360 [degrees] wraparound labels on portable cryogenic medical gas containers.

(d) All excess labeling bearing lot or control numbers shall be destroyed.

(e) Returned labeling shall be maintained and stored in a manner to prevent mixups and provide proper identification.

(f) Procedures shall be written describing in sufficient detail the control procedures employed for the issuance of labeling; such written procedures shall be followed.

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13. Code of Federal Regulations, title 21, part 211.130, states:

There shall be written procedures designed to assure that correct labels, labeling, and packaging materials are used for drug products; such written procedures shall be followed. These procedures shall incorporate the following features:

(a) Prevention of mixups and cross-contamination by physical or spatial separation from operations on other drug products.

(b) Identification and handling of filled drug product containers that are set aside and held in unlabeled condition for future labeling operations to preclude mislabeling of individual containers, lots, or portions of lots. Identification need not be applied to each individual container but shall be sufficient to determine name, strength, quantity of contents, and lot or control number of each container.

(c) Identification of the drug product with a lot or control number that permits determination of the history of the manufacture and control of the batch.

(d) Examination of packaging and labeling materials for suitability and correctness before packaging operations, and documentation of such examination in the batch production record.

(e) Inspection of the packaging and labeling facilities immediately before use to assure that all drug products have been removed from previous operations. Inspection shall also be made to assure that packaging and labeling materials not suitable for subsequent operations have been removed. Results of inspection shall be documented in the batch production records.

14. Code of Federal Regulations, title 21, part 211.165, states:

(a) For each batch of drug product, there shall be appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient, prior to release. Where sterility and/or pyrogen testing are conducted on specific batches of shortlived radiopharmaceuticals, such batches may be released prior to completion of sterility and/or pyrogen testing, provided such testing is completed as soon as possible.

(b) There shall be appropriate laboratory testing, as necessary, of each batch of drug product required to be free of objectionable microorganisms.

(c) Any sampling and testing plans shall be described in written procedures that shall include the method of sampling and the number of units per batch to be tested; such written procedure shall be followed.

(d) Acceptance criteria for the sampling and testing conducted by the quality control unit shall be adequate to assure that batches of drug products meet each appropriate specification and appropriate statistical quality control criteria as a condition for their approval and release. The statistical quality control criteria shall include appropriate acceptance levels and/or appropriate rejection levels.

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(e) The accuracy, sensitivity, specificity, and reproducibility of test methods employed by the firm shall be established and documented. Such validation and documentation may be accomplished in accordance with § 211.194(a)(2).

(f) Drug products failing to meet established standards or specifications and any other relevant quality control criteria shall be rejected. Reprocessing may be performed. Prior to acceptance and use, reprocessed material must meet appropriate standards, specifications, and any other relevant critieria.

15. Code of Federal Regulations, title 21, part 211.166, states:

(a) There shall be a written testing program designed to assess the stability characteristics of drug products. The results of such stability testing shall be used in determining appropriate storage conditions and expiration dates. The written program shall be followed and shall include:

(1) Sample size and test intervals based on statistical criteria for each attribute examined to assure valid estimates of stability;

(2) Storage conditions for samples retained for testing;

(3) Reliable, meaningful, and specific test methods;

(4) Testing of the drug product in the same container-closure system as that in which the drug product is marketed;

(5) Testing of drug products for reconstitution at the time of dispensing (as directed in the labeling) as well as after they are reconstituted.

(b) An adequate number of batches of each drug product shall be tested to determine an appropriate expiration date and a record of such data shall be maintained. Accelerated studies, combined with basic stability information on the components, drug products, and container-closure system, may be used to support tentative expiration dates provided full shelf life studies are not available and are being conducted. Where data from accelerated studies are used to project a tentative expiration date that is beyond a date supported by actual shelf life studies, there must be stability studies conducted, including drug product testing at appropriate intervals, until the tentative expiration date is verified or the appropriate expiration date determined.

(c) For homeopathic drug products, the requirements of this section are as follows:

(1) There shall be a written assessment of stability based at least on testing or examination of the drug product for compatibility of the ingredients, and based on marketing experience with the drug product to indicate that there is no degradation of the product for the normal or expected period of use.

(2) Evaluation of stability shall be based on the same container-closure system in which the drug product is being marketed.

(d) Allergenic extracts that are labeled "No U.S. Standard of Potency" are exempt from the requirements of this section.

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16. Code of Federal Regulations, title 21, part 211.192, states:

All drug product production and control records, including those for packaging and labeling, shall be reviewed and approved by the quality control unit to determine compliance with all established, approved written procedures before a batch is released or distributed. Any unexplained discrepancy (including a percentage of theoretical yield exceeding the maximum or minimum percentages established in master production and control records) or the failure of a batch or any of its components to meet any of its specifications shall be thoroughly investigated, whether or not the batch has already been distributed. The investigation shall extend to other batches of the same drug product and other drug products that may have been associated with the specific failure or discrepancy. A written record of the investigation shall be made and shall include the conclusions and followup.

CALIFORNIA CODE OF REGULATIONS

17. California Code of Regulations, title 16, section 1735.2, states in pertinent part:

(e) A drug preparation shall not be compounded until the pharmacy has first prepared a written master formula document that includes at least the following elements:

(1) Active ingredients to be used.

(2) Equipment to be used.

(3) The maximum allowable beyond use date for the preparation, and the rationale or reference source justifying its determination.

(4) Inactive ingredients to be used.

(5) Specific and essential compounding steps used to prepare the drug.

(6) Quality reviews required at each step in preparation of the drug.

(7) Post-compounding process or procedures required, if any. Instructions for storage and handling of the compounded drug preparation.

. . .

(k) Prior to allowing any drug product preparation to be compounded in a pharmacy, the pharmacist-in-charge shall complete a self-assessment for compounding pharmacies developed by the board (Incorporated by reference is "Community Pharmacy & Hospital Outpatient Pharmacy Compounding Self-Assessment" Form 17M-39 Rev. 02/12.) as required by Section 1715 of Title 16, Division 17, of the California Code of Regulations. That form contains a first section applicable to all compounding, and a second section applicable to sterile injectable compounding. The first section must be completed by the pharmacist-

in-charge before any compounding is performed in the pharmacy. The second section must be completed by the pharmacist-in-charge before any sterile compounding is performed in the pharmacy. The applicable sections of the self-assessment shall subsequently be completed before July 1 of each odd-numbered year, within 30 days of the start date of a new pharmacist-in-charge or change of location, and within 30 days of the issuance of a new pharmacy license. The primary purpose of the self-assessment is to promote compliance through self-examination and education.

18. California Code of Regulations, title 16, section 1751.4, states in pertinent part:

(c) All equipment used in the areas designated for compounding must be made of a material that can be easily cleaned and disinfected.

. . .

(f) Pharmacies preparing sterile compounded preparations require the use of a PEC that provides ISO Class 5 air or better air quality. Certification and testing of primary and secondary engineering controls shall be performed no less than every six months and whenever the device or area designated for compounding is relocated, altered or a service to the facility is performed that would impact the device or area. Certification must be completed by a qualified technician who is familiar with certification methods and procedures in accordance with CETA Certification Guide for Sterile Compounding Facilities (CAG-003-2006-13, Revised May 20, 2015), which is hereby incorporated by reference. Certification records must be retained for at least 3 years. Unidirectional compounding aseptic isolators or compounding aseptic containment isolators may be used outside of an ISO Class 7 cleanroom if the isolator is certified to meet the following criteria:

(1) Particle counts sampled approximately 6-12 inches upstream of the critical exposure site shall maintain ISO Class 5 levels during compounding operations.

(2) Not more than 3520 particles (0.5 um and larger) per cubic meter shall be counted during material transfer, with the particle counter probe located as near to the transfer door as possible without obstructing transfer.

(3) Recovery time to achieve ISO Class 5 air quality shall be documented and internal procedures developed to ensure that adequate recovery time is allowed after material transfer before and during compounding operations.

Compounding aseptic isolators that do not meet the requirements as outlined in this subdivision or are not located within an ISO Class 7 cleanroom may only be used to compound preparations that meet the criteria specified in accordance with subdivision (d) of Section 1751.8 of Title 16, Division 17, of the California Code of Regulations.

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COST RECOVERY

19. Code section 125.3 provides, in pertinent part, that the Board may request the administrative law judge to direct a licentiate found to have committed a violation or violations of the licensing act to pay a sum not to exceed the reasonable costs of the investigation and enforcement of the case, with failure of the licentiate to comply subjecting the license to not being renewed or reinstated. If a case settles, recovery of investigation and enforcement costs may be included in a stipulated settlement.

STATEMENT OF FACTS

20. Respondent's facility in Little Rock, Arkansas, is a 503b Food and Drug Administration ("FDA") registered outsourcer, compounding non-sterile to sterile single API[1] products and limited non-sterile (i.e. suppositories) for shipment within Arkansas and out-of-state to licensed healthcare facilities.

21. From on or about September 14, 2016, to on or about October 14, 2016, the FDA performed an inspection at Respondent's registered outsourcing facility. Pursuant to that inspection, the FDA made the following observations and found that Respondent did not comply with Code of Federal Regulations, title 21, part 211, and United States Code, title 21, section 353b:

a. OBSERVATION 1: Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room and equipment to produce aseptic conditions. (C.F.R., tit. 21, §211.42(c))

b. OBSERVATION 2: Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established, written and followed. (C.F.R., tit. 21, §§211.165 and 211.113)

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[1] United States Code, title 21, section 379j-41(2) provides that an "API" is an Active Pharmaceutical Ingredient, which is "(A) a substance, or a mixture when the substance is unstable or cannot be transported on its own, intended (i) to be used as a component of a drug; and (ii) to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the human body; or (B) a substance intended for final crystallization, purification, or salt formation, or any combination of those activities, to become a substance or mixture described in subparagraph (A)."

c. OBSERVATION 3: Separate or defined areas to prevent contamination or mix-ups are deficient regarding operations related to aseptic processing of drug products. (C.F.R., tit. 21, §211.42(c))

d. OBSERVATION 4: Test procedures relative to appropriate laboratory testing for sterility and pyrogens are not written and followed. (C.F.R., tit. 21, §211.165)

e. OBSERVATION 5: There is no written testing program designed to assess the stability characteristics of drug products. (C.F.R., tit. 21, §211.166)

f. OBSERVATION 6: Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the identity and strength of each active ingredient prior to release. (C.F.R., tit. 21, §211.165)

g. OBSERVATION 7: Aseptic processing areas are deficient regarding the system for monitoring environmental conditions. (C.F.R., tit. 21, §211.42(c))

h. OBSERVATION 8: Aseptic processing areas are deficient regarding air supply that is filtered through high-efficiency particulate air filters under positive pressure. (C.F.R., tit. 21, §211.42(c))

i. OBSERVATION 9: The building lacks adequate space for the orderly placement of equipment and materials to prevent mix- ups between different components, drug product containers, labeling, inprocess materials and drug products and to prevent contamination. (C.F.R., tit. 21, §211.42(b))

j. OBSERVATION 10: There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed. (C.F.R., tit. 21, §211.192)

k. OBSERVATION 11: The labels of Respondent's outsourcing facility's drug products are deficient. (C.F.R., tit. 21, §§211.125 and 211.130)

22. On or about November 17, 2016, Respondent notified the Board that it was recalling a select number of sterile products due to a lack of sterility assurance.

23. On or about November 18, 2016, Respondent provided the Board with an unredacted version of the FDA's form 483, containing the FDA's observations and required corrective actions from the FDA's inspection that occurred from approximately September 14, 2016, to October 14, 2016, set forth above in paragraph 21 and its subparts. That same day, Respondent also provided the Board with Respondent's redacted response to the FDA's form 483, dated

November 4, 2016. In that response Respondent represented that it had corrected the FDA's Observations, including Observation numbers 1, 2, 7, and 11.

24. On or about November 21, 2016, the FDA posted a MedWatch which stated that Respondent had expanded its recall to all unexpired sterile drugs products within expiry.

25. From on or about June 12, 2017, to on or about June 29, 2017, the FDA performed an inspection at Respondent's registered outsourcing facility. Pursuant to that inspection, the FDA made the following observations and found that Respondent did not comply with Code of Federal Regulations, title 21, part 211, and United States Code, title 21, section 353b:

a. OBSERVATION 1: The quality control unit lacks authority to fully investigate errors that have occurred. (C.F.R., tit. 21, §211.22(a))

b. OBSERVATION 2: The responsibilities and procedures applicable to the quality control unit are not fully followed. (C.F.R., tit. 21, §211.22(d))

c. OBSERVATION 3: Aseptic processing areas are deficient regarding air supply that is filtered through high-efficiency particulate air filters under positive pressure. This was a repeat observation from the FDA inspection that had been conducted on or about October 14, 2016. (C.F.R., tit. 21, §211.42(c))

d. OBSERVATION 4: There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed. (C.F.R., tit. 21, §211.192)

e. OBSERVATION 5: Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not followed. This was a repeat observation from the FDA inspection that had been conducted on or about October 14, 2016. (C.F.R., tit. 21, §211.165)

f. OBSERVATION 6: Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room and equipment to produce aseptic conditions. This was a repeat observation from the FDA inspection that was conducted on or about October 14, 2016. (C.F.R., tit. 21, §211.42(c))

g. OBSERVATION 7: There is no written testing program designed to assess the stability characteristics of drug products. (C.F.R., tit. 21, §211.166)

h. OBSERVATION 8: The labels of Respondent's outsourcing facility's drug products are deficient. This is a repeat observation from the FDA inspection that was conducted on or about October 14, 2016. (C.F.R., tit. 21, §§211.125 and 211.130)

26. On or about July 17, 2017, the Board received FDA form 483, containing the FDA's required corrective actions from the FDA's inspection that occurred from approximately June 12, 2017 to June 29, 2017, which included the FDA's observations set forth above in paragraph 25.

27. On or about July 18, 2017, the Board received a list of products that Respondent shipped into California from January 1, 2017, to July 17, 2017, which included twenty-eight (28) different drugs, and a total of 47,711 units of those drugs.

28. On or about July 25, 2017, the Board received Respondent's reply to the FDA's form 483 for the FDA inspection that occurred in June 2017. In that reply, Respondent stated that it had voluntarily and temporarily ceased production, that it was in the process of recalling all unexpired, sterile products, that it had contracted with third-parties for its microbiology lab, that it had hired a full-time microbiologist, and that it disagreed with the FDA's Observation 3 because at least one of the two sensors for the batches was within range at any given time.

29. On or about July 25, 2017, Respondent notified the Board that it was recalling all unexpired lots of sterile drug products.

30. On or about July 31, 2017, Respondent notified the Board that it had shipped only non-patient-specific products into California.

FIRST CAUSE FOR DISCIPLINE

(Failure to Comply With Statutes and Regulations Re. Dangerous Drugs and Pharmacy Practice)

31. Respondent is subject to disciplinary action under Code sections 4301(j) and (o) in that Respondent violated the statutes of the United States regulating dangerous drugs and pharmacies including United States Code, title 21, section 353b, and Code of Federal Regulations, title 21, sections 211.22(a), 211.22(d), 211.42(b), 211.42(c), 211.113, 211.125, 211.130, 211.165, 211.166, 211.192, as set forth above in paragraphs 20-30.

SECOND CAUSE FOR DISCIPLINE

(Gross Negligence)

32. Respondent is subject to disciplinary action under Code section 4301(c) in that Respondent committed gross negligence by representing to the Board on or about November 18, 2016, that Respondent was in compliance with the statutes and regulations of the United States

regulating dangerous drugs and pharmacy practice, because Respondent had corrected the FDA's observations from its September-October 2016 inspection, including the FDA's Observation numbers 1, 2, 7, and 11, when in fact Respondent was not in compliance with those statutes and observations because Respondent had not corrected those observations, as set forth above in paragraphs 21, 23, and 25.

MATTER IN AGGRAVATION

33. On or about August 9, 2017, Inspector L.P. conducted the annual sterile compounding inspection at Respondent's facilities. Pursuant to that inspection, Inspector L.P. found that Respondent committed the following violations of laws, rules, and regulations of the Board:

a. At the time of inspection, the compounding area buffer cleanroom contained exposed paper and post it notes adjacent to the compounding hoods. (Cal. Code Reg., tit. 16, §1751.4(c))

b. At the time of inspection, the pharmacy had recently moved the primary engineering controls into the secondary engineering control (buffer room) and began production in the space without having retested the secondary engineering controls. (Cal. Code Reg., tit. 16, §1751.4(f))

c. At the time of inspection, the pharmacist in charge had changed more than 30 days from the date of inspection but the new pharmacist in charge had not completed a compounding self-assessment. (Cal. Code Reg., tit. 16, §1735.2(k))

d. At the time of the inspection, the pharmacy master formula did not contain the rationale for the beyond use date assigned to each preparation. (Cal. Code Reg., tit. 16, §1735.2(e)(3))

e. At the time of the inspection, the pharmacy was cleaning ceilings, walls, floors, and doors using a contact time for LPH of 5 minutes when the manufacturer recommended contact time was a minimum of 10 minutes. (Code §4036.5)

PRAYER

WHEREFORE, Complainant requests that a hearing be held on the matters herein alleged, and that following the hearing, the Board of Pharmacy issue a decision:

1. Revoking or suspending Non-Resident Pharmacy Permit Number NRP 1071, issued to Cantrell Drug Company.

2. Revoking or suspending Non-Resident Sterile Compounding Permit Number NSC 99637, issued to Cantrell Drug Company;

3. Ordering Cantrell Drug Company to pay the Board of Pharmacy the reasonable costs of the investigation and enforcement of this case, pursuant to Business and Professions Code section 125.3; and,

4. Taking such other and further action as deemed necessary and proper.

DATED: 1/18/18

VIRGINIA HEROLD
Executive Officer
Board of Pharmacy
Department of Consumer Affairs
State of California
Complainant

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