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

In the Matter of the Statement of Issues Against: **B BRAUN OF AMERICA INC., DBA CENTRAL ADMIXTURE PHARMACY SERVICES INC.** **Applicant for Renewal of Nonresident Outsourcing Facility Permit** Respondent.	Case No. 7917 **STATEMENT OF ISSUES**

PARTIES

1. Anne Sodergren (Complainant) brings this Statement of Issues solely in her official capacity as the Executive Officer of the Board of Pharmacy (Board), Department of Consumer Affairs.

2. On or about October 2, 2019, the Board issued Nonresident Outsourcing Facility Permit number NSF 130 to B Braun of America Inc., dba Central Admixture Pharmacy Services Inc. (Respondent). The Nonresident Outsourcing Facility Permit was in full force and effect at all times relevant to the charges brought herein and will expire on October 1, 2024, unless renewed.

Prior to its expiration, Respondent applied for the renewal of Nonresident Outsourcing Facility Permit number NSF 130. On or about August 28, 2024, Respondent's application for renewal was denied.

3. On or about August 30, 2024, the Board received Respondent's timely appeal of the Board's denial of Respondent's renewal of its Nonresident Outsourcing Facility Permit number NSF 130.

JURISDICTION

4. This Statement of Issues 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. Code section 4300 states, in pertinent part:

> (a) Every license issued may be suspended or revoked.
>
> …
>
> (c) The board may refuse a license to any applicant guilty of unprofessional conduct.
>
> …
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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. Code section 4300.1 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.

STATUTORY PROVISIONS

7. Code section 4022 states, in pertinent part:

> "Dangerous drug" or "dangerous device" means any drug or device unsafe for self-use in humans or animals, and includes the following:
>
> (a) Any drug that bears the legend: "Caution: federal law prohibits dispensing without prescription," "Rx only," or words of similar import.

(b) Any device that bears the statement: "Caution: federal law restricts this device to sale by or on the order of a ," "Rx only," or words of similar import, the blank to be filled in with the designation of the practitioner licensed to use or order use of the device.

(c) Any other drug or device that by federal or state law can be lawfully dispensed only on prescription or furnished pursuant to Section 4006.

8. Code section 4035 states:

"Person" includes, but is not limited to, firm, association, partnership, corporation, limited liability company, state governmental agency, trust, or political subdivision.

9. Code section 4129 states, in pertinent part:

(a) A facility registered as an outsourcing facility with the federal Food and Drug Administration (FDA) shall be concurrently licensed with the board as an outsourcing facility if it compounds sterile medication or nonsterile medication for nonpatient-specific distribution within or into California.

…

(c) The board may adopt regulations in accordance with the Administrative Procedure Act (Chapter 3.5 (commencing with Section 11340) of Part 1 of Division 3 of Title 2 of the Government Code) to establish policies, guidelines, and procedures to implement this article.

…

(e) An outsourcing facility licensed by the board dispensing patient-specific compounded preparations pursuant to a prescription for an individual patient shall not be required to be licensed as a pharmacy, but shall otherwise comply with the same requirements of a pharmacy.

10. Code section 4129.2 states:

(a) An outsourcing facility that is licensed with the federal Food and Drug Administration (FDA) as an outsourcing facility and has an address outside of this state but in the United States of America is a nonresident outsourcing facility. A nonresident outsourcing facility shall not compound sterile drug products or nonsterile drug products for distribution or use into this state without an outsourcing license issued by the board pursuant to this section. The license shall be renewed annually and shall not be transferable.

(b) A nonresident outsourcing facility shall compound all sterile products and nonsterile products to be distributed or used in this state in compliance with regulations of the board and with federal current good manufacturing practices applicable to outsourcing facilities.

(c) A license for a nonresident outsourcing facility shall not be issued or renewed until the location is inspected by the board and found in compliance with this article and any regulations adopted by the board. The nonresident outsourcing facility shall reimburse the board for all actual and necessary costs incurred by the

board in conducting an inspection of the nonresident outsourcing facility at least once annually pursuant to subdivision (x) of Section 4400.

(d) A license for a nonresident outsourcing facility shall not be issued or renewed until the board:

(1) Prior to inspection, reviews a current copy of the nonresident outsourcing facility's policies and procedures for sterile compounding and nonsterile compounding.

(2)(A) Is provided with copies of all federal and state regulatory agency inspection reports, as well as accreditation reports, and certification reports of facilities or equipment of the nonresident outsourcing facility's premises conducted in the prior 12 months.

(B) For purposes of this paragraph, "state" refers to the state in which the nonresident outsourcing facility resides.

(3) Prior to inspection, receives a list of all sterile drug products and nonsterile drug products compounded by the pharmacy as reported to the FDA within the prior 12 months.

(e) A nonresident outsourcing facility licensed pursuant to this section shall provide the board with all of the following:

(1) A copy of any disciplinary or other action taken by another state or the FDA within 10 days of the action.

(2) Notice within 24 hours of any recall notice issued by the nonresident outsourcing facility.

(3) A copy of any complaint it receives involving an outsourcing facility's compounded products from or involving any provider, pharmacy, or patient in California within 72 hours of receipt.

(4) Notice within 24 hours after learning of adverse effects reported or potentially attributable to a nonresident outsourcing facility's products.

11. Code section 4207, subdivision (c) states, in pertinent part:

The board shall deny an application for a license if the applicant does not qualify for the license being sought.

12. Code section 4301 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 includes, but is not limited to, any of the following:

(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.

13. Code section 4302 states, in pertinent part:

The board may deny, suspend, or revoke any license where conditions exist in relation to any person holding 10 percent or more of the ownership interest or where conditions exist in relation to any officer, director, or other person with management or control of the license that would constitute grounds for disciplinary action against a licensee.

14. Code section 4307 states, in pertinent part:

(a) Any person who has been denied a license or whose license has been revoked or is under suspension, or who has failed to renew his or her license while it was under suspension, or who has been a manager, administrator, owner, member, officer, director, associate, partner, or any other person with management or control of any partnership, corporation, trust, firm, or association whose application for a license has been denied or revoked, is under suspension or has been placed on probation, and while acting as the manager, administrator, owner, member, officer, director, associate, partner, or any other person with management or control had knowledge of or knowingly participated in any conduct for which the license was denied, revoked, suspended, or placed on probation, shall be prohibited from serving as a manager, administrator, owner, member, officer, director, associate, partner, or in any other position with management or control of a licensee as follows:

(1) Where a probationary license is issued or where an existing license is placed on probation, this prohibition shall remain in effect for a period not to exceed five years.

(2) Where the license is denied or revoked, the prohibition shall continue until the license is issued or reinstated. . . .

FEDERAL REGULATIONS

15. C.F.R., title 21, section 211.1 states, in pertinent part:

(a) The regulations in this part contain the minimum current good manufacturing practice for preparation of drug products (excluding positron emission tomography drugs) for administration to humans or animals.

16. C.F.R., section 211.22 states:

(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.

(b) Adequate laboratory facilities for the testing and approval (or rejection) of

components, drug product containers, closures, packaging materials, in-process materials, and drug products shall be available to the quality control unit.

(c) The quality control unit shall have the responsibility for approving or rejecting all procedures or specifications impacting on the identity, strength, quality, and purity of the drug product.

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

17. C.F.R., section 211.25 states, in pertinent part:

(a) Each person engaged in the manufacture, processing, packing, or holding of a drug product shall have education, training, and experience, or any combination thereof, to enable that person to perform the assigned functions. Training shall be in the particular operations that the employee performs and in current good manufacturing practice (including the current good manufacturing practice regulations in this chapter and written procedures required by these regulations) as they relate to the employee's functions. Training in current good manufacturing practice shall be conducted by qualified individuals on a continuing basis and with sufficient frequency to assure that employees remain familiar with CGMP requirements applicable to them.

(c) There shall be an adequate number of qualified personnel to perform and supervise the manufacture, processing, packing, or holding of each drug product.

18. C.F.R., section 211.34 states, in pertinent part:

Consultants advising on the manufacture, processing, packing, or holding of drug products shall have sufficient education, training, and experience, or any combination thereof, to advise on the subject for which they are retained. Records shall be maintained stating the name, address, and qualifications of any consultants and the type of service they provide.

19. C.F.R., section 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.

…

(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:

(10) Aseptic processing, which includes as appropriate.

(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.

20. C.F.R., section 211.58 states:

Any building used in the manufacture, processing, packing, or holding of a drug product shall be maintained in a good state of repair.

21. C.F.R., section 211.68 states, in pertinent part:

(a) Automatic, mechanical, or electronic equipment or other types of equipment, including computers, or related systems that will perform a function satisfactorily, may be used in the manufacture, processing, packing, and holding of a drug product. If such equipment is so used, it shall be routinely calibrated, inspected, or checked according to a written program designed to assure proper performance. Written records of those calibration checks and inspections shall be maintained.

(b) Appropriate controls shall be exercised over computer or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel. Input to and output from the computer or related system of formulas or other records or data shall be checked for accuracy. The degree and frequency of input/output verification shall be based on the complexity and reliability of the computer or related system. A backup file of data entered into the computer or related system shall be maintained except where certain data, such as calculations performed in connection with laboratory analysis, are eliminated by computerization or other automated processes. In such instances a written record of the program shall be maintained along with appropriate validation data. Hard copy or alternative systems, such as duplicates, tapes, or microfilm, designed to assure that backup data are exact and complete and that it is secure from alteration, inadvertent erasures, or loss shall be maintained.

22. C.F.R., section 211.160 states, in pertinent part:

(b) Laboratory controls shall include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity. Laboratory controls shall include:

(1) Determination of conformity to applicable written specifications for the acceptance of each lot within each shipment of components, drug product containers, closures, and labeling used in the manufacture, processing, packing, or holding of drug products. The specifications shall include a description of the sampling and testing procedures used. Samples shall be representative and adequately identified. Such procedures shall also require appropriate retesting of any component, drug product container, or closure that is subject to deterioration.

(2) Determination of conformance to written specifications and a description of sampling and testing procedures for in-process materials. Such samples shall be representative and properly identified.

(3) Determination of conformance to written descriptions of sampling procedures and appropriate specifications for drug products. Such samples shall be representative and properly identified.

(4) The calibration of instruments, apparatus, gauges, and recording devices at suitable intervals in accordance with an established written program containing specific directions, schedules, limits for accuracy and precision, and provisions for remedial action in the event accuracy and/or precision limits are not met. Instruments, apparatus, gauges, and recording devices not meeting established specifications shall not be used.

23. C.F.R., section 211.166 states, in pertinent part:

(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.

DEFINITIONS

24. **Federal current Good Manufacturing Practices (cGMP)** require the implementation of systems to assure proper design, monitoring, and control of manufacturing processes and facilities for the compounding of non-patient specific, large batches of sterile products which are riskier to compound, than small batches of patient-specific sterile products.

25. **ISO-Class 5 Environment** is an atmospheric environment that has less than 100 particles >0.5 microns or larger per cubic foot in compliance with the ISO/TC209 International Cleanroom Standards.

FACTUAL ALLEGATIONS

26. Respondent is a nonresident outsourcing facility that compounds non-patient specific, large batches of sterile drug products for dispensing to patients in healthcare facilities or

institutions. Pharmacy law requires outsourcers such as Respondent to compound their sterile drug products in compliance with federal current Good Manufacturing Practices (cGMP) applicable to outsourcing facilities. The Board inspects outsourcing facilities, such as Respondent, annually to determine if they are compounding sterile drug products in accordance with cGMP and investigates complaints filed against them.

27. On July 22 through 24, 2024, Inspector J.K.F. and Inspector M.V. conducted an annual outsourcing renewal inspection at Respondent's facility in Phoenix, Arizona. The Board's inspectors were assisted by various employees of Respondent. The inspectors walked through the facility, communicated with employees, and requested and received records.

28. Board inspectors found violations of pharmacy law and non-compliance with cGMP.

FIRST CAUSE FOR DENIAL OF APPLICATION

(Design and Construction Features)

29. Respondent's application is subject to denial under sections 4300, subdivision (c), 4129.2, subdivision (c), and 4207, subdivision (c), on the grounds of unprofessional conduct as defined by Code section 4301, subdivision (o), in conjunction with C.F.R., title 21, section 211.42, subdivision (c)(10)(v), in that it violated pharmacy law, federal cGMP, and failed to follow required procedures. The facts and circumstances of this violation arose from the inspection described above in paragraphs 26 through 28, and as follows: Respondent failed to follow procedure SOP-CAPS- 4000750 Cleaning Requirements PHX rev 16.0. Section 7.12.5 states "*Bucket systems (including the wheels), cleaning tools, and mop handles shall be inspected at this time for functionality and defects. Any equipment that shows signs of rust or damage must immediately be removed from service and replaced*." Upon onsite inspection it was observed that several mop and bucket systems were in a poor state of repair including rust, degradation, filth, and/or shedding material on caster wheels. Cleaning tools were also observed to be in a poor state of repair with significant discoloration and apparent degradation and/or filth.

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SECOND CAUSE FOR DENIAL OF APPLICATION

(Responsibilities of Quality Control Unit)

30. Respondent's application is subject to denial under sections 4300, subdivision (c), 4129.2, subdivision (c), and 4207, subdivision (c), on the grounds of unprofessional conduct as defined by Code section 4301, subdivision (o), in conjunction with C.F.R., title 21, section 211.22, subdivision (c), in that it violated pharmacy law, federal cGMP, and failed to follow required procedures, when it failed to maintain adequate oversight and control of the change control process. The facts and circumstances of this violation arose from the inspection described above in paragraphs 26 through 28, and as follows: Due dates are not followed and extensions to due dates are not performed in a timely manner with adequate justification. For example, CCR-4000268 was opened on May 26, 2024, with a due date of November 30, 2023. An extension was requested on or about January 24, 2024, for a January 31, 2024, due date. The actual completion of the change control was on February 23, 2024. Review of the change control log for 2024 indicates there were 52 change control requests initiated and only 5 change controls opened in 2024 have been completed. The staffing including the quality control unit responsible for the execution and oversight of the change control process is inadequate and not commensurate to the needs required for change and/or remediation.

THIRD CAUSE FOR DENIAL OF APPLICATION

(Inadequate Visual Inspection Program)

31. Respondent's application is subject to denial under sections 4300, subdivision (c), 4129.2, subdivision (c), and 4207, subdivision (c), on the grounds of unprofessional conduct as defined by Code section 4301, subdivision (o), in conjunction with C.F.R., title 21, section 211.25, subdivision (a), in that it violated pharmacy law, federal cGMP, and failed to follow required procedures when it failed to comply with personnel qualifications. The facts and circumstances of this violation arose from the inspection described above in paragraphs 26 through 28, and as follows: During inspection it was observed the visual inspection program was inadequate. Specifically, operators are required to identify turbidity per SOP-CAPS-4000688. Operators are not directly challenged on their ability to identify turbidity within the challenge

defect kits. The current procedure does not require operators to undergo an examination of color blindness. There are inadequate assurance operators can decipher a color change in solution as required. The challenge kits have not been validated and do not have adequate documentation such as the specific content and specific size of defects created. The procedure requires there to be a range of defect sizes from 300um to 3000um. Review of laboratory notebook pages related to the creation of defects required all defects to be 3000um. Similarly, documentation of the creation of other defect types were not available at the time of inspection. There is no supporting documentation that the intended particle sizes are represented in the defect kits. There is not a current understanding of the limit of detection of a qualified operator and/or the probability of detection as specific sizes and defect types. The visual inspection program places no sensitivity to extrinsic particulates or other defects which would otherwise be and should be considered critical in the 100% visual inspection process. For example, a unit found with extrinsic particulates which suggests the presence of filth, sterility assurance issues, or other cGMP violations would not always require an investigation if subsequent Acceptable Quality Level (AQL) and release testing met acceptance criteria.

FOURTH CAUSE FOR DENIAL OF APPLICATION

(Inadequate Environmental Monitoring)

32. Respondent's application is subject to denial under sections 4300, subdivision (c), 4129.2, subdivision (c), and 4207, subdivision (c), on the grounds of unprofessional conduct as defined by Code section 4301, subdivision (o), in conjunction with C.F.R., title 21, section 211.25, subdivision (a), in that it violated pharmacy law, federal cGMP, and failed to follow required procedures when it failed to comply with appropriate environmental monitoring. The facts and circumstances of this violation arose from the inspection described above in paragraphs 26 through 28, and as follows: During inspection, the quality control unit was observed performing environmental monitoring and failed to follow the procedure SOP-CAPS-4000582 rev 29.0. Specifically, section 6.5.3 states in part: "*To sample surfaces using a contact plate, gently touch the area with the agar surface and roll the plate across the surface to be sampled. ...immediately after sampling with the contact plate, the samples area is thoroughly wiped with a*

clean room wipe soaked in 70% IPA or sterile 70% IPA presaturated wipe." The quality control unit took a surface sample of the computer monitor for hood F-3 and failed to sanitize the area after sampling.

FIFTH CAUSE FOR DENIAL OF APPLICATION

(Inadequate Aseptic Technique)

33. Respondent's application is subject to denial under sections 4300, subdivision (c), 4129.2, subdivision (c), and 4207, subdivision (c), on the grounds of unprofessional conduct as defined by Code section 4301, subdivision (o), in conjunction with C.F.R., title 21, section 211.25, subdivision (a), in that it violated pharmacy law, federal cGMP, and failed to follow required procedures, when it failed to comply with appropriate aseptic technique. The facts and circumstances of this violation arose from the inspection described above in paragraphs 26 through 28, and as follows: During inspection, it was observed that staff failed to follow the procedure SOP-CAPS-4000175 - Aseptic Technique rev 19.5. Specifically, section 9.9 requires: "*Packages of supplies ... shall be sprayed on all sides, with adequate 70% IPA to ensure the entire surface has visible IPA coverage, for entry into the ISO-5 environment...*" Board Inspectors observed operators transfer prefilled IV bags and empty IV bags by spraying the outer containers and failed to ensure adequate Isopropyl Alcohol (IPA) coverage in the location(s) under which their hands held the material. The action of spraying with IPA is inherently not reliable for complete coverage and lacks rationale. Additionally, the operator in hood F-3 on July 22, 2024, during production routinely stored their hand-held scanner in the first 6 inches of the inside edge of the hood. Subsequent aseptic connections were made such as connecting new source IV bags which utilized the scanner, and the operator did not re-sanitize the scanner prior to use with gloved hands and making aseptic connections. Section 9.4 of SOP-CAPS-4000175 rev 19.5 states "*No product or supplies can be stored within the first six inches of the ISO Class 5 work area during aseptic compounding with the exception of one spray bottle of 70% IPA*."

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SIXTH CAUSE FOR DENIAL OF APPLICATION

(Inadequate Automatic, Mechanical, or Electronic Equipment)

34. Respondent's application is subject to denial under sections 4300, subdivision (c), 4129.2, subdivision (c), and 4207, subdivision (c), on the grounds of unprofessional conduct as defined by Code section 4301, subdivision (o), in conjunction with C.F.R., title 21, section 211.68, subdivision (b), in that it violated pharmacy law, federal cGMP, and failed to follow required procedures. The facts and circumstances of this violation arose from the inspection described above in paragraphs 26 through 28, and as follows: During the inspection it was observed that Respondent's computer systems which have the ability to make entries into LANCE (and subsequent electronic batch record (EBR)) do not have adequate user and administrative controls to ensure the reliability and integrity of data generated. Some examples include, but are not limited to:

• Computer date and time settings can be changed without administrative and/or quality control unit oversight. For example, for Lot# 36-268739, the time zone was able to be changed to +3 hours from the local time on the computer and subsequent entries into the EBR during the label verification process by operations did not accurately reflect the actual time of performance. PROT-CAPS-4000174 for the LANCE system completed under change control CCR-4000268 had a documented exception #2 which described circumstances of equivalent inaccuracies in user data "time performed/verified by" which did not result in a durable corrective action.

• Users who log into LANCE may remain logged into the system for an extended timeframe when no action is performed. The system remains unrestricted for 45 minutes and when logged in a user barcode can be printed. The barcode serves as a single sign on option which bypasses the need to enter a username and password to perform restricted actions.

SEVENTH CAUSE FOR DENIAL OF APPLICATION

(Failure to Comply with Design and Construction Features)

35. Respondent's application is subject to denial under sections 4300, subdivision (c), 4129.2, subdivision (c), and 4207, subdivision (c), on the grounds of unprofessional conduct as

defined by Code section 4301, subdivision (o), in conjunction with C.F.R., title 21, section 211.42, subdivision (c)(10)(iii), in that it violated pharmacy law, federal cGMP, and failed to follow required procedures. The facts and circumstances of this violation arose from the inspection described above in paragraphs 26 through 28, and as follows: During the inspection it was observed that Respondent's smoke visualization studies were inadequate. Specifically, the studies performed on January 5, 2024, failed to include at least the following:

• Set up of the Apex compounding unit and associated initial aseptic connections to diluent and API source materials was not simulated in the ISO-5.

• The smoke visualizations did not simulate common interventions performed frequently during the batch production, such as transfer of materials into the ISO-5 hood, empty IV bags, diluent bags, and commercial drug product used for compounding.

• The preponderance of ISO-5 smoke visualizations did not include adequate supply and/or location of smoke to the critical site of the Apex compounding unit luer supply connection which is eventually used to fill IV bags. The luer connection is staged in a metal slot between fills for which laminar flow was not demonstrated.

• The ISO-5 smoke visualizations did not include the worst case set up. Specifically, the handheld scanner (required per SOP-CAPS-4000062 rev 23.0) and an IPA spray bottle normally kept in the front of the hood was not simulated. Additionally, some studies did not include all equipment normally found in the ISO-5 hood during batch production such as the non-viable particulate counting probe and stand.

EIGHTH CAUSE FOR DENIAL OF APPLICATION

(Inadequate Sterility Testing Procedures)

36. Respondent's application is subject to denial under sections 4300, subdivision (c), 4129.2, subdivision (c), and 4207, subdivision (c), on the grounds of unprofessional conduct as defined by Code section 4301, subdivision (o), in conjunction with C.F.R., title 21, section 211.160, subdivision (b), in that it violated pharmacy law, federal cGMP, and failed to follow required procedures. The facts and circumstances of this violation arose from the inspection described above in paragraphs 26 through 28, and as follows: During the inspection it was

observed the BacT/Alert sterility testing procedures are inadequate. Specifically, the testing procedures include sampling volumes which are inferior to USP <71>. For example, an IV bag of l000mL would normally require a sample volume of l00mL (10% of container volume) per USP <71>, whereas Respondent would require only lmL or 10mL per sample depending on the product for the performance of the sterility test. Additionally, review of the data packet used to support the acceptance of the sterility testing fails to incorporate details of the sample preparation of the product. For example, the sampling date/time, and volumes sampled per container are not documented.

NINTH CAUSE FOR DENIAL OF APPLICATION

(Inadequate Stability Testing Procedures)

37. Respondent's application is subject to denial under sections 4300, subdivision (c), 4129.2, subdivision (c), and 4207, subdivision (c), on the grounds of unprofessional conduct as defined by Code section 4301, subdivision (o), in conjunction with C.F.R., title 21, section 211.166, subdivision (a), in that it violated pharmacy law, federal cGMP, and failed to follow required procedures. The facts and circumstances of this violation arose from the inspection described above in paragraphs 26 through 28, and as follows: During the inspection it was observed the stability program procedure SOP-CAPS-4000617 rev 5.0 was inadequate. The procedure requires the consideration of humidity when performing stability studies. Respondent produces products within semi-permeable containers such as Excel IV bags. The original stability study was reviewed to support NDC -6092- for phenylephrine in Excel bags which did not demonstrate the product could withstand low humidity requirements. The required storage specification for the product was 15-30C and <65% RH. Water/weight loss was not performed during the stability study. At the time of inspection, the historical temperature and humidity for sample storage area(s) was not available to review. Additionally, the orientation of the samples was not documented and there are incomplete assurances the container closure/product relationship was adequately evaluated.

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TENTH CAUSE FOR DENIAL OF APPLICATION

(Inadequate Automatic, Mechanical, or Electronic Equipment)

38. Respondent's application is subject to denial under sections 4300, subdivision (c), 4129.2, subdivision (c), and 4207, subdivision (c), on the grounds of unprofessional conduct as defined by Code section 4301, subdivision (o), in conjunction with C.F.R., title 21, section 211.68, subdivision (a), in that it violated pharmacy law, federal cGMP, and failed to follow required procedures. The facts and circumstances of this violation arose from the inspection described above in paragraphs 26 through 28, and as follows: The quality control unit has inadequate control and oversight of the design, execution, and quality review of validation activities conducted for cGMP processes. Specifically, the Installation, Operational, and Performance Qualification (IOPQ) for the LANCE electronic system under PRO-CAPS-4000174 was found to have incomplete review of issues/exceptions. For example:

• Incomplete tracking of issues/exceptions - Exceptions reported by users are not adequately documented such that a quality review including evaluation of impact could be performed. For example, a user during the PQ phase reported LANCE was displaying inaccurate data for multiple fields. The complete nature of the circumstances was not documented and subsequently not reviewed by the quality control unit prior to approval of the protocol execution and subsequent change control. Only the details of the solution and verification of the solution were documented. The impact of the data integrity problems observed by users was not considered by the quality control unit in the period of risk of October 27, 2023, through October 31, 2023. A risk assessment or similar review of like circumstances were not evaluated.

ELEVENTH CAUSE FOR DENIAL OF APPLICATION

(Inadequate Personnel Qualifications)

39. Respondent's application is subject to denial under sections 4300, subdivision (c), 4129.2, subdivision (c), and 4207, subdivision (c), on the grounds of unprofessional conduct as defined by Code section 4301, subdivision (o), in conjunction with C.F.R., title 21, section 211.25, subdivision (c), in that it violated pharmacy law, federal cGMP, and failed to follow required procedures. The facts and circumstances of this violation arose from the inspection

described above in paragraphs 26 through 28, and as follows: Respondent's staffing and/or the quality control unit is not robust and not to a level commensurate to the needs and scale of the compounding operations to maintain a state of control. There has been a persistent inability to investigate all deviations, non-conformances, or other events in a timely manner which may impact product quality. Since December 1, 2023, there have been approximately 319 deviations/NQEs entered of which ~ 206 investigations (~65%) are open and ~136 of those investigations (~66%) are identified as past due. The current procedure for NQE's SOP-CAPS-4000693 rev 13.0 does not place requirement or rationale how due dates are created or the necessary requirements for justification of due date extension. For example, NQE-US59-230707-295 was opened on July 7, 2023, with a due date of August 21, 2023, to investigate a customer complaint. The investigation did not receive an extension authorization until July 19, 2024, and remained in a past due status for approximately eleven (11) months.

TWELFTH CAUSE FOR DENIAL OF APPLICATION

(Inadequate Responsibilities of Quality Control Unit)

40. Respondent's application is subject to denial under sections 4300, subdivision (c), 4129.2, subdivision (c), and 4207, subdivision (c), on the grounds of unprofessional conduct as defined by Code section 4301, subdivision (o), in conjunction with C.F.R., title 21, section 211.22, subdivision (d), in that it violated pharmacy law, federal cGMP, and failed to follow required procedures. The facts and circumstances of this violation arose from the inspection described above in paragraphs 26 through 28, and as follows: During the inspection it was observed there is inadequate and untimely review of logbooks used within the facility. Procedure SOP-CAPS-4000743 rev 2.0 requires in part: 6.4.4 – "*Each page must be reviewed, signed by the reviewer and dated, preferably within the same day, or shortly after the last entry on that page*." Some examples include, but is not limited to:

• Logbook 0032 utilized for master batch record issuance - Entries into the logbook from at least June 2019, through October 2019, were not reviewed until July 1, 2024. Entries made on February 28, 2024 (page 57) and April 2, 2024 (page 73) have not been verified and have incomplete documentation such as blank spaces where entries are expected (page 57).

• Logbook 0153 -Accusizer sensor logbook- Entries into the logbook from 2022 and 2023 were not reviewed until May 1, 2024.

• Logbook 0139- BacT temperature verification- Entries into the logbook from December 2023, were not reviewed until March 10, 2024.

• Logbook I - Controlled EM Chamber 112250 (30-35C incubator for media) – Entries into the logbook from November 6, 2023, through November 20, 2023, were not reviewed until July 2, 2024.

THIRTEENTH CAUSE FOR DENIAL OF APPLICATION

(Inadequate Supervision and Control of Contracted Consultants)

41. Respondent's application is subject to denial under sections 4300, subdivision (c), 4129.2, subdivision (c), and 4207, subdivision (c), on the grounds of unprofessional conduct as defined by Code section 4301, subdivision (o), in conjunction with C.F.R., title 21, section 211.34, in that it violated pharmacy law, federal cGMP, and failed to follow required procedures. The facts and circumstances of this violation arose from the inspection described above in paragraphs 26 through 28, and as follows: There is inadequate supervision and control of contracted consultants who participate in cGMP operations which at times include participation in aseptic operations from approximately June 2023, to June, 2024. Specifically, RCA consultant(s) routinely entered the ISO-7 buffer room where aseptic operations occurred without having participated in media fill or process simulations consistent with their duties during routine production. At the time of inspection documentation could not be provided as to which batch(es) the consultant(s) had participation in.

FOURTEENTH CAUSE FOR DENIAL OF APPLICATION

(Inadequate Building Design and Construction Features)

42. Respondent's application is subject to denial under sections 4300, subdivision (c), 4129.2, subdivision (c), and 4207, subdivision (c), on the grounds of unprofessional conduct as defined by Code section 4301, subdivision (o), in conjunction with C.F.R., title 21, section 211.42, subdivision (a), in that it violated pharmacy law, federal cGMP, and failed to follow required procedures. The facts and circumstances of this violation arose from the inspection

described above in paragraphs 26 through 28, and as follows: During the inspection it was observed SOP-CAPS-4000062 rev 23.0 was not fully followed. Specifically, a leak was found in HEPA filter# 27 for the certification conducted in January 2024, with a leak dimension of 2" x 4" which exceeded the allowable limit of not to exceed 1.5" for lesser dimension. The patch was repaired, but not replaced as required within 30 days of patching. Additionally form FRM-CAPS-4000114 was reviewed and approved by the quality control unit on January 9, 2024, with the smoke study video and report listed as being "in progress." There was no follow up documentation indicating the review and approval by the quality control unit of the smoke studies performed. Review of documentation of FRM-CAPS-4000114 indicated several GDP and/or incomplete sections at the time of approval. Some examples include, but are not limited to:

• Section II- version of SOP-CAPS-4000062 provided to the certifier was not documented.

• Section III- NQE's were marked as "yes", but not listed on the form.

• Section V - Comments section is left as a blank space without N/A.

FIFTEENTH CAUSE FOR DENIAL OF APPLICATION

(Pending Disciplinary Action)

43. Respondent's application is subject to denial under sections 4302 and 4307, due to a pending disciplinary action, First Amended Accusation Number 7634. A true and correct copy of First Amended Accusation Number 7634 is attached as Exhibit A. The facts and circumstances are as follows:

a. Pursuant to Code section 4302, if the First Amended Accusation results in discipline against Respondent, then B Braun of America Inc., dba Central Admixture Pharmacy Services Inc. shall be prohibited from owning 10% or more of any other pharmacy.

b. Pursuant to Code section 4307, if the First Amended Accusation results in discipline against Respondent, then B Braun of America Inc., dba Central Admixture Pharmacy Services Inc. shall be prohibited from owning or managing any pharmacy.

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DISCIPLINE CONSIDERATIONS

44. To determine the degree of discipline, if any, to be imposed on Respondent, Complainant alleges that on or about December 24, 2020, in a prior action, the Board of Pharmacy issued Citation number CI 2019 88388 for violations of Code section 4129.2, subdivision (b) and C.F.R., title 21, section 211.100, subdivision (b), and Health and Safety Code section 111330, and ordered Respondent to pay a $5,000 fine. That Citation is now final and Respondent has paid the fine.

45. To determine the degree of discipline, if any, to be imposed on Respondent, Complainant alleges that on or about June 29, 2021, in a prior action, the Board of Pharmacy issued Citation number CI 2020 88964 for violations of Code section 4129.2, subdivision (b) and C.F.R., title 21, section 211.100, subdivision (b), and ordered Respondent to pay a $1,500 fine. That Citation is now final and Respondent has paid the fine.

46. To determine the degree of discipline, if any, to be imposed on Respondent, Complainant alleges that on or about February 7, 2023, in a prior action, the Board of Pharmacy issued Citation number CI 2021 95546 for violations of Code section 4129.2, subdivision (b) and C.F.R., title 21, section 211.165, subdivision (a), and ordered Respondent to pay a $5,000 fine. That Citation is now final and Respondent has paid the fine.

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. Denying the application of B Braun of America Inc., dba Central Admixture Pharmacy Services, Inc., Central Admixture Pharmacy Services, Inc. for renewal of its Nonresident Outsourcing Facility Permit; and

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

DATED: 9/27/2024

Sodergren, Anne@DCA

Digitally signed by Sodergren, Anne@DCA
Date: 2024.09.27 13:23:17 -07'00'

ANNE SODERGREN
Executive Officer
Board of Pharmacy
Department of Consumer Affairs
State of California
Complainant

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