DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
One Montvale Avenue Stoneham, MA 02180 (781)587-7500 Fax:(781)587-7556	3/30/2015-4/9/2015*
	FEI NUMBER 3011430551

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. James P. Cangelosi, R.Ph. , President and Owner

FIRM NAME	STREET ADDRESS
Brookfield Medical/Surgical Supply, Inc.	60 Old New Milford Rd, Suite 1B
CITY, STATE, ZIP CODE, COUNTRY Brookfield, CT 06804-2430	TYPE ESTABLISHMENT INSPECTED Outsourcer

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

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.

Specifically,

A. Lot 061914EA Methylprednisolone Acetate PF 80mg/mL (2mL) tested positive for Bacillus circulans and was rejected. Your investigation did not attempt to identify the source of the contamination and determine appropriate corrective actions to prevent recurrence.

B. Your firm rejected two lots of Betamethasone Sodium Phosphate PF 6mg/mL following low potency assay (Lot 120314MB (5mL) at 89.7%, Lot 110314MA (3mL) at 89.01%, specification (b) (4). The following deficiencies were noted with your investigation and corrective actions:

   a. Your investigations did not evaluate for impact to other lots. Lots are released based on potency results from (b) (4).

   b. Your corrective actions to (b) (4) from (b) (4) and to reduce the (b) (4) were inadequate as your firm does not have data and/or studies to assure product specifications/quality/purity can be consistently met with these changes.

   c. Your investigation hypothesized that the (b) (4) could impact potency but you have not systemically evaluated the impact of (b) (4) on Betamethasone Sodium Phosphate, or on Methylprednisolone Acetate and Triamcinolone Acetonide, the latter two of which are drug suspensions. In addition, your firm did not evaluate the impact of (b) (4) on potency on Betamethasone Sodium Phosphate.

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C. Your firm does not have data to support that vials with apparent differences in solids height (for product suspensions where active ingredients settle to the bottom of the vial) do not differ in assay, e.g. for Methylprednisolone Acetate 40mg/mL PF (5mL) Lot 011915EA. This lot was in released status and visually inspected by Investigator on 03/30/15.

D. Your firm does not record the reason for rejected or discarded vials on production records such that these rejects can be investigated where appropriate. For example:
   a. 3 vials of Betamethasone Sodium Phosphate PF Lot 010815 discarded on 01/08/15.
   b. 20 vials of Betamethasone Sodium Phosphate PF Lot 010815 discarded on 02/03/15.

OBSERVATION 2

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile do not include validation of the sterilization process.

Specifically,

A. Your firm has not validated the sterilization process according to a procedure whereby elements such as but not limited to (b) (4) are evaluated. This impacts your three finished drug products (Methylprednisolone Acetate Suspension injection, Triamcinolone Acetonide Suspension injection, and Betamethasone Sodium Phosphate Solution injection), which are (b) (4), preservative free, and assigned a use-by date of 6 months at room temperature.

B. Your firm has not validated the sterilization processes for manufacturing utensils. For example, your firm does not have a validation protocol, or report, or other documentation to demonstrate the following:
   a. (b) (4)
   b. (b) (4).
   c. (b) (4)
   d. That (b) (4) are sufficient to sterilize utensils (e.g. capper, decapper) or

packaging materials (e.g. caps).

C. Your firm has not validated the depyrogenation processes for manufacturing utensils. For example, your firm does not have a validation protocol, report, or other documentation to demonstrate the following:
   a. (b) (4) during your most recent equipment qualification.
   b. (b) (4) performed at initial qualification
   c. That (b) (4) are sufficient to depyrogenate equipment and utensils that are (b) (4)
   d. You do not have a set expiration date on equipment/utensils that have been depyrogenated. You do not label depyrogenated equipment/utensils, or otherwise have a system to assure that depyrogenated stock is used in a first in, first out basis.

OBSERVATION 3
The responsibilities and procedures applicable to the quality control unit are not in writing and fully followed .

Specifically,

Your firm has drafted procedures, none of which have been reviewed and approved by quality. In addition, your firm has not drafted procedures related to the receipt, evaluation, investigation, and/or reporting of complaints and/or adverse drug events, or related to vendor qualification.

OBSERVATION 4
Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established and written and followed .

Specifically,

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The following deficiencies were observed and collectively demonstrate an increased risk of introducing bioburden into drug product intended for (b) (4) sterilization, or an increased risk that bioburden could go undetected:

A. The following personnel and production practices deficiencies were observed:
   a. During production of Betamethasone Lot 040115MA, Investigator observed technician reopening bag of betamethasone to pour betamethasone waste from a (b) (4) previously used to (b) (4) .
   b. Technician was observed on 04/01/15 patting fingers lightly onto (b) (4) plates instead of rolling each digit for personnel monitoring. In addition, monitoring is performed in the (b) (4) rather than at (b) (4) , when the risk for shedding and bioburden is highest.
   c. Pharmacist was observed (b) (4) of all depyrogenated equipment/utensils with (b) (4) and (b) (4) left opened and sitting in ISO 8 air (thereby exposing the previously depyrogenated material to a nonsterile surface) prior to the initiation of production.
   d. The exterior of equipment is wiped with (b) (4) prior to entry into the ISO 8 suite, then with (b) (4) prior to transition from the ISO 8 to ISO 7 suite.
   e. The viable particulate monitor is set up (b) (4) ISO 5 hood
   f. Bottom legs of sterile gown of pharmacist observed to touch the floor during gowning process.
   g. Your firm has not addressed quality impact of (b) (4) ISO 5 vertical flow hood (b) (4) first per the manufacturer's instructions. ISO 5 hood manual instructions state it is recommended the cabinet (b) (4) to ensure cleanliness.

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B. The following deficiencies were noted with your cleanroom facility as a whole:
   a. Smoke studies do not indicate vertical laminarity of air flow from your ISO 5 vertical flow hood.
   b. Doors to the ISO 7 and ISO 8 rooms were observed not to shut completely. Door to the ISO 7 was observed to be partially open during production of Betamethasone Lot 040115MA.
   c. Your firm has not identified the normal microbial flora of your facility.
   d. Pressure differentials are recorded (b) (4) and not sufficient to assure that pressure differentials are maintained during production.
   e. Pressure gauges used to measure the pressure differentials are not calibrated.
   f. Yellowing of borders on the edges of the HEPAs in ISO 5, 7, 8 and yellowing bleeding into HEPA filter in ISO 8 was observed on 03/30/15.
   g. The ISO 5 hood has uncovered spiral compact fluorescent light bulbs that are difficult to clean.

C. Your firm does not have data to demonstrate that your (b) (4) can detect microbial contamination in the presence of residual disinfectants.

OBSERVATION 5

Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room and equipment to produce aseptic conditions.

Specifically,

A. The ISO 5 environment is cleaned with (b) (4) and (b) (4) neither of which are recognized sporicidal agents.

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B. Due to facility design, the ISO 7 ceiling and walls and exterior of the ISO 5 vertical flow hood are cleaned (b) (4) [redacted] of the ISO 5. As observed on 04/01/15, staff does not change their gloves (b) (4) [redacted] ISO 5.
C. The far wall, which is blocked by the ISO 5 hood, is cleaned every (b) (4) [redacted]. Your firm lacks adequate data to support this cleaning infrequency.

OBSERVATION 6

Time limits are not established when appropriate for the completion of each production phase to assure the quality of the drug product.

Specifically, your firm:

A. Has not established approved presterilization hold times.
B. Does not have data to support presterilization hold times.
C. Has not systematically recorded times on production records start and stop times such that presterilization hold times can be determined.

OBSERVATION 7

Master production and control records lack complete manufacturing and control instructions .

Specifically,

Your production records do not include all instructions necessary for manufacturing such as an acceptance range for yield whereby an investigation would be initiated if a lot yield fell outside of those ranges.

OBSERVATION 8

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Laboratory controls do not include the establishment of scientifically sound and appropriate specifications, sampling plans and test procedures, designed to assure that drug products conform to appropriate standards of identity, strength, quality and purity.

Specifically,

A. Your firm has not approved finished product specifications for any of your three drug products: Methylprednisolone, Triamcinolone, or Betamethasone.
B. Your firm has not performed endotoxin method suitability to determine whether or not the endotoxin signal is inhibited or enhanced for drug product solutions (Betamethasone Sodium Phosphate) or suspensions (Methylprednisolone Acetate and Triamcinolone Acetonide).
C. Your firm's contract laboratory does not verify pH is within (b) (4) as required by the manufacturer. This impacts all products at your facility, including Methylprednisolone Acetate, for which you do not measure pH during production, and which is permitted to range from 3.0-7.0 per USP monograph.
D. Your firm does not have adequate justification or rationale for a sample size of (b) (4) for potency and endotoxin testing for product suspensions where batch sizes range from approximately (b) (4) vials.
E. Your firm does not perform growth promotion testing for each lot of media received to date.
F. Your firm incubates (b) (4) environmental monitoring plates in a room under ambient conditions and not in an incubator, where temperature is not monitored daily and where deviation from USP specified limits have been noted.

OBSERVATION 9

The labels and containers of your outsourcing facility's drug products do not include information required by section 503B(a)(10)(A) and (B).

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The following information is not found on some of your drug product labels:

1. The statement, "This is a compounded drug."
2. The phone number of the applicable outsourcing facility.
3. The date that the drug was compounded.

Furthermore, the following information is not found on the container labels for some drug products you produce:

1. Information to facilitate adverse event reporting: www.fda.gov/medwatch and 1–800–FDA–1088.
2. Directions for use, including, as appropriate, dosage and administration.

Examples of drug product labels that do not contain this information include:

- Betamethasone Sodium Phosphate
- Methylprednisolone Acetate Suspension
- Triamcinolone Acetonide Suspension

***DATES OF INSPECTION**
3/30/2015(Mon),3/31/2015(Tue),4/01/2015(Wed),4/09/2015(Thu)

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgement, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."