DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
US Customhouse, Rm 900 2nd & Chestnut St Philadelphia, PA 19106 (215) 597-4390 Fax:(215) 597-0875 Industry Information: www.fda.gov/oc/industry	05/11/2015 - 05/29/2015* FEI NUMBER 3010680515

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Kyle Y. Flanigan, CEO

FIRM NAME	STREET ADDRESS
US Specialty Formulations LLC	116 Research Dr
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Bethlehem, PA 18015-4731	503B Pharmaceutical Outsourcing Facility

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

Written records are not always made of investigations into unexplained discrepancies.

Specifically,

a). You perform visual inspections prior to a acceptance quality limit (AQL) inspection for product release. Vials found to have defects are removed from the batch during the visual inspections [redacted] (b) (4). You have not established any limits for the number or type of defects found during the visual inspections which would cause an investigation to be initiated.

The following is a summary of product lots which were found to have critical defects on initial visual inspections:

1. Dexamethasone Acetate 16mg/mL (10mL Vial for Injection)
   a. Lot #01RG0407A), (b) visual inspections were performed (b) (4) (b) (4) (b) (4). The (b) (4) inspection on 4/7/15 found no defects. The (b) (4) visual inspection on 4/17/15 found 2 of (b) (4) vials with "aggregates".
   b. Lot #01RG0224A - 2 of (b) (4) vials with black/brown particles and 1 vials with "particle aggregates".
   c. Lot 01RG0409A - 2 of (b) (4) vials with white particles and 1 with crimp defect.
   d. Lot 01RG0129A - 2 of (b) (4) vials with black/brown particles.

   Note: The (b) (4) of Dexamethasone listed above [redacted] (b) (4)

2. 72% Glycerol 100mL Vial for Injection (Lot #01RG0204A)
   a. 4 of (b) (4) vials found to contain white fibers.

None of these critical defects observed during visual inspections initiated further investigation or corrective action. All of the above lots were approved for release and distributed.

b.) When the action limit (>(b) (4) particles/cubic ft.) for non-viable particle counts are exceeded, during production of sterile

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drug products in the ISO 5 area, a deviation investigation is not initiated.

For example, during production of a sterile drug product, Pyridoxine HCL 100mg/mL vials (Lot #01RG0311A), the non-viable particle counts exceeded the action limit of greater than (b) (4) particles per cubic foot for 17 minutes with recorded levels as high as 78,300 particles per cubic foot in the ISO 5 area. There was no investigation or action initiated in response to this deviation.

Additionally, when limits for non-viable counts are exceeded there is no documentation of actions taken such as halting production and performing a wipe down with (b) (4)

OBSERVATION 2

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically,

The following applies to all lots of sterile drug products manufactured and released to date:

a.) You have not conducted any monitoring of personnel as part of your environmental monitoring program.

b.) Your environmental monitoring program has not identified the species of any of the micro-organisms found to date.

For example, the environmental monitoring results for Pyridoxine HCL 100mg/mL (Lot #01RG0311A) was found to have counts of 3 CFU/plate and 2 CFU/plate for the left and right isolator gloves, respectively. However, the test results only differentiated them to be either gram positive spore forming or gram positive non-spore forming.

c.) Your release criteria for all sterile drug products does not include specifications for the results of environmental or personnel monitoring conducted during the production of sterile drug products.

Using your current product release specifications, sterile drug products can be released without consideration for the results of environmental and personnel monitoring.

OBSERVATION 3

Protective apparel is not worn as necessary to protect drug products from contamination.

Specifically,
a) Not all gowning is received sterile or sterilized on site. For example, dedicated shoes are reused and not sterilized on a routine basis. No sterile booties are used to cover the dedicated shoes. Also, goggles are not received sterile and are reused without being resterilized with each wear. The SOP# FC-005 titled Gowning Requirements for Production Areas does not require sterile gowning components to be worn during production.

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b) COA's for the following gowning components were reviewed and only the gloves are received sterile. The following gowning components are received nonsterile, are not sterilized on site and are used during the production of sterile drug products in the ISO7, ISO5 areas:
Hair Bouffant nonsterile
Face Mask nonsterile
Safety Glasses nonsterile
Shoes nonsterile

Also gowning currently allows for exposed skin on the forehead while compounding.

OBSERVATION 4

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

Specifically, there are no cleaning studies performed to assure the process used to reduce the bio-burden is effective and the cleaning agents used are sporidial. There is no disinfection study to assure (b) (4) and (b) (4) are effective against microbes, bacterial and spores. Cleaning SOP # PR-003, sections 3.1.5 and 3.2.2 instructs to allow the (b) (4) to remain on the ISO5, ISO7 and ISO8 surfaces for (b) (4). However, (b) (4) product claims requires a dwell time, on surfaces, undiluted for at least (b) (4) to be sporicidal.
The following products are (b) (4)
Pyridoxine Hydrochloride
Ascorbic Acid
Glutathione
Methylcobalamin
Carnitine and Leucine

OBSERVATION 5

Buildings used in the manufacture, processing, packing, or holding of a drug product do not have the suitable location to facilitate cleaning, maintenance, and proper operations.

Specifically, additionally, gowning occurs in a non-classified office area. During the inspection we observed booties, hair nets, and gloves were stored in the office area. Also, right and left booties are placed on employees shoes prior to crossing over the gowning bench.

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OBSERVATION 6

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

Specifically,

The media used in media fills is not qualified, in that, no growth promotion.testing has been conducted on the media.

You have not conducted pH testing on the media and there is no procedure that outlines how media will be qualified or challenged.

OBSERVATION 7

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established.

Specifically, all lots of sterile (b) (4) drug product produced prior to 5/8/15 failed to receive (b) (4) to determine (b) (4) used in production.

OBSERVATION 8

Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the final specifications prior to release.

Specifically,

a.) Your sampling plan allows for potency results to be reported as the (b) (4) (b) (4) (b) (4). You have not established acceptance criteria for the results of each individual test or for the standard deviation of the test results. Therefore, your current practice allows for the release of sterile drug products despite individual potency test results being sub-potent or super-potent compared to the potency release specification of the finished drug product.

For example, potency sample #(b) of Dexamethasone Acetate 16mg/mL Lot #01RG0224A was found to have an active ingredient concentration of 17.0 mg/mL. Potency sample #(b) of the same batch was tested and found to have a concentration of 14.9mg/mL. Your release specification for potency of Dexamethasone is (b) (4) mg/mL. Within this batch you received potency test results that were both above and below the release specification range.

Dexamethasone Acetate Lot #01RG0224A was approved for release and distributed.

b.) You have not conducted testing of the preservative content or determined the effectiveness of the preservatives in your products such as Pyridoxine HCL 100mg/mL vials which contain the preservative (b) (4)

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OBSERVATION 9

Each batch of drug product purporting to be sterile and pyrogen-free is not laboratory tested to determine conformance to such requirements.

Specifically,

Incident and Deviation Report #IDR15-007 states that on 4/13/15 the positive control for endotoxin testing did not pass spike recovery for Dexamethasone Acetate 16mg/mL vials Lot #01RG0409A.

You deviated from your normal endotoxin testing procedure, which uses (b) (4), and "spiked" a sample of the finished product with endotoxin in order to run a positive control. The "spiked" sample failed for "sample rxn time cv" and failed for "test suitability".

Dexamethasone Acetate Lot #01RG0409A, was released for distribution on 4/14/15 without having been tested with a successful positive control for Endotoxin.

Additionally, the investigation states that the lot of Dexamethasone should be re-tested with (b) (4) as part of the investigation. At the initiation of the inspection, endotoxin testing was not performed using (b) (4) and the investigation was open.

OBSERVATION 10

Equipment and utensils are not cleaned and maintained at appropriate intervals to prevent malfunctions and contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically,

Your cleaning and preventative maintenance program (SOP# EQ-0053 - (b) (4) Operation and EQ-0052 - (b) (4) Log Form) of your (b) (4) equipment requires maintenance activities with less frequency than what is recommended by the manufacturer in the equipment operation manual.

For example, the operating manual states that the (b) (4) should be cleaned (b) (4) while your procedure only requires cleaning of the (b) (4) on a (b) (4) basis.

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Cleaning of the (b) (4) is recommended (b) (4) while your procedure only requires cleaning on a (b) (4) basis.

The (b) (4) is used to conduct (b) (4) of sterile drug products and to sterilize product contact equipment used in the production of sterile drug products.

OBSERVATION 11

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

Specifically, you have not established time limits for appropriate phases of production for your sterile drug products.

For example, during observation of the production of Pyridoxine HCl Lot #01RG0520A on 5/20/15 it took approximately (b) hours for the preservative, (b) (4) to (b) (4) and the (b) (4) was anticipated to take approximately (b) (4) hours.

OBSERVATION 12

The labels of your firm's drug products, do not always contain information required in section 503B(a)(10)(A) and (B) of the Act.

Specifically,

The following information is not found on some of your drug product labels (e.g., the labels applied directly to the product):

1. The statement, "This is a compounded drug."
2. The name, address, and phone number of the applicable facility.
3. The dosage form and strength.
4. The statement of quantity or volume, as appropriate.
5. The storage and handling instructions.
6. The inactive ingredients, identified by established name and the quantity or proportion of each ingredient.

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.

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

- Pyridoxine Hydrochloride 100 mg/mL
- Magnesium Sulfate, 500 mg/mL

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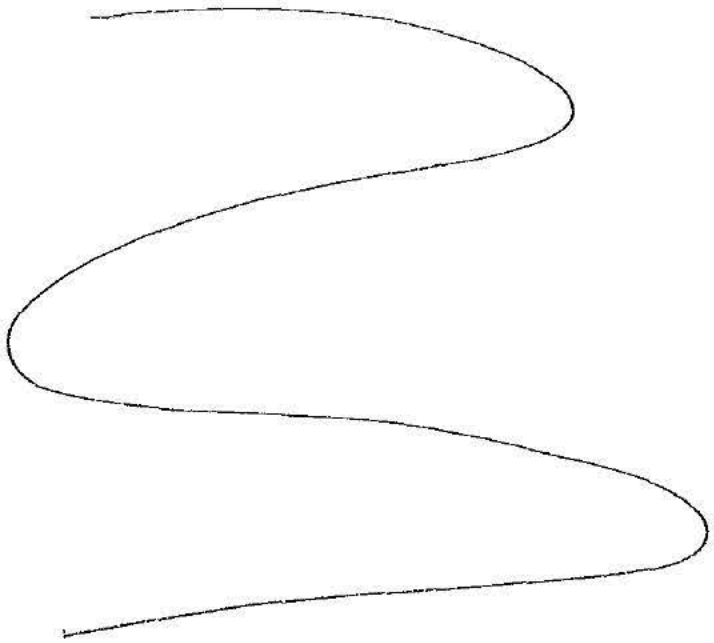
- Ascorbic Acid 500 mg/mL
- Chromic chloride, 4 µg/mL
- Methylcobalamin 5 mg/mL
- Glutathione 200 mg/mL
- Beclomethasone Diproprionate 0.125mg/mL, Oxymetazoline 0.25 mg/mL
- Dexamthasone Acetate 160mg in 10mL

*** DATES OF INSPECTION:**
05/11/2015(Mon), 05/12/2015(Tue), 05/13/2015(Wed), 05/14/2015(Thu), 05/20/2015(Wed), 05/21/2015(Thu), 05/29/2015(Fri)



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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."