DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214) 253-5200 Fax:(214) 253-5314 Industry Information: www.fda.gov/oc/industry	06/03/2014 - 07/16/2014* FEI NUMBER 3010087152

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Kristi A. Kubosh, Pharm. D., R.Ph., Pharmacist in Charge

FIRM NAME	STREET ADDRESS
Downing Labs, LLC	4001 McEwen Rd Suite 110
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Dallas, TX 75244-5020	Producer of Sterile Drug Products

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 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. SOP #9.040 entitled, "Sterility Testing of a Finished Preparation" (Effective date: 6/2012) documents that an investigation should be conducted in the event that contamination is observed.

My review of approximately (b) (4) Logged Formula Worksheets for the period between 4/16/2013 and 6/23/2014 revealed that your firm had sterility or endotoxin failures for 22 different lots of drug product. In each case, the investigations were either absent or incomplete.

All lots which failed testing for sterility or endotoxin were destroyed with the exception of the following:

- Cyanocobalamin, lot #N04302014@14

Lot #N04302014@14 was originally (b) (4) on 5/2/14. Subsequent testing for sterility failed (Test dated 6/2/14) and the lot was re-sterilized by (b) (4) on 6/3/14. Subsequent testing for endotoxin and sterility met specifications. The lot is currently being held in inventory pending distribution.

- Folic Acid, lot #N04172014@20 (Production date: 4/30/14, BUD: 10/28/14)

Lot #N04172014@20 was (b) (4) on 4/30/14. Subsequent testing for sterility failed as noted on testing record dated 6/2/14. The lot is being held in quarantine pending destruction.

Each batch with the failed result is identified in the following table:

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Producer of Sterile Drug Products

Product	Lot #	Mfd. Date	BUD	Sterility Test Result/Day Positive	Organism(s)	Endotoxin Result/Date	Investigation
HCG 5 K Lyophilized 5000 U Powder Injectable	N05082014@30	5/9/14	12/12/14	Negative	N/A	Failed endotoxin (Result of 150.75EU/vial versus spec of (b) (4) /vial)	Yes
Cyanocobalamin 30 mL Buffered 1 mg/mL Injectable	N04302014@14	5/2/14	11/1/14	Positive/Day 14	*Afipia felis*	<0.05 EU/mL	No
Folic Acid 30 mL 10 mg/mL Injectable	N04172014@20	4/30/14	10/28/14	Positive/Day 12	*Afipia felis*	<5.00 EU/mL	No
HCG 5 K Lyophilized 5000 U Powder Injectable	N04082014@14	4/17/14	10/15/14	Positive/Day 5	*Staphylococcus haemolyticus*	4.50 EU/Vial	Yes
Cyanocobalamin 30 mL Buffered 1 mg/mL Injectable	N03272014@7	3/27/14	9/23/14	Positive/Day 4	*Afipia felis*	<0.05 EU/mL	No
Green Tea (EGCG) 10 mL 10 mg/mL Injectable	N01202014@8	2/10/14	8/9/14	Negative	N/A	Failed endotoxin (Result of 252.64 EU/.ml)	Yes
L-Carnitine 30ml 500mg/ml	N12202013@8	1/29/14	7/28/14	Negative	N/A	Failed endotoxin (Result 476.19EU/ml versus spec of (b) (4) U/ml)	Yes
Terbutaline/ Betamethasone 5 mL 0.05/0.01 mg/mL Injectable	N12202013@4	12/23/13	6/22/14	Positive/Day 10	*Methylobacterium brachiatum*	Not tested	Yes
Procaine 30 mL 10% Inj	N12182013@1	12/19/13	6/18/14	Positive/Day 8	*Propionibacterium acnes*	Not tested	Yes
Methylcobalamin Buffered 30 mL 5 mg/mL Inj	N11042013@1	12/16/13	6/15/14	Positive/Day 5	*Staphylococcus epidermidis*	Not tested	Yes
Magnesium Chloride Hexahydrate 30 mL 200 mg/mL Injectable	N11042013@14	11/14/13	5/13/14	Positive/Day 6	*Staphylococcus epidermidis*	Not tested	Yes
DMPS B-Complex 10ml	N10172013@20	11/6/13	2/1/14	Positive/Day 4	*Bacillus amyloliquefaciens Methylotrophicus*	Not tested	Yes
Ascorbic Acid (Corn) 50 mL 500 mg/mL Injectable	N10172013@19	10/30/13	4/29/14	Positive/Day 13	*Propionibacterium acnes*	Not tested	Yes
Hyaluronidase 10 mL 150 U/mL Injectable	N09042013@14	10/15/13	1/31/14	Positive/Day 4	*Staphylococcus epidermidis*	Not tested	Yes
Dexpanthenol 30 mL 250 mg/mL Injectable	N09032013@14	9/3/13	2/2/14	Positive/Day 3	Not tested	Not tested	Yes
Calcium Gluconate 50 mL 5% Injectable	N08152013@20	8/22/13	2/23/14	Positive/Day 13	*Bacillus fastidiosus, Bacillus simplex, Nocardia nova*	Not tested	Yes

SEE REVERSE OF THIS PAGE

EMPLOYEE(S) SIGNATURE
Stephen D. Brown, Investigator
Darla J. Christopher, Investigator

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Product	Lot #	Mfd. Date	BUD	Sterility Test Result/Day Positive	Organism(s)	Endotoxin Result/Date	Investigation
Riboflavin (R5P) 30 mL 10 mg/mL Inj	N08212013@5	8/21/13	2/17/14	Positive/ Day 5	*Cupriavidus metalliduran*s	Not tested	Yes
TIFM IV Base#2 Concentrate 50 mL SDV Inj	N07122013@14	8/19/13	1/8/14	Positive/Day 7	*Roseomonas mucosa*	Not tested	Yes
L-Glutathione for Inhalation 10 X 4 mL Soln for Neb	N08142013@3	8/14/13	2/10/14	Positive/ Day 3	*Staphylococcus epidermidis*	Not tested	Yes
Ascorbic Acid (Corn) 50 mL 500 mg/mL Injectable	N07172013@26	8/8/13	1/13/14	Positive/Day 12	*Propionibacterium acnes*	Not tested	Yes
Folic Acid 10 mL 5 mg/mL Injectable	N06112013@27	6/11/13	12/8/13	Positive/Day 2	*Delftia acidovrans*	Not tested	Yes
L-Proline 30 mL 50 mg/mL Injectable	N06052013@19	6/5/13	12/2/13	Positive/Day 10	*Corynbacterium afermentans lipophilum*	Not tested	Yes

Some examples where an investigation was absent include the following:

1. Cyanocobalamin 1mg/ml Buffered, lot #N04302014@14 (Production date: 5/2/14, Beyond Use Date: 11/1/14)

Your contract laboratory determined that this lot failed sterility and the contaminating organism was *Afipia felis*. No investigation was performed.

2. Folic Acid 10mg/ml, lot #N04172014@20 (Production date: 4/30/14, Beyond Use Date: 10/28/14)

Your contract laboratory determined that this lot failed sterility and the contaminating organism was *Afipia felis*. No investigation was performed.

3. Cyanocobalamin 1mg/ml Buffered, lot #N03272014@7 (Production date: 3/27/14, Beyond Use Date: 9/23/140

Your contract laboratory determined that this lot failed sterility and the contaminating organism was *Afipia felis*. No investigation was performed.

Some examples where an investigation was incomplete consist of the following:

1. Green Tea (EGCG) 10ml 10mg/ml Injectable, lot #N01202014@8 (Production date: 2/10/14, Beyond Use date: 8/9/14)

Lot #N01202014@8 failed the test for endotoxin with a result of 252.64 EU/ml as documented on a Certificate of Analysis dated 2/26/14 from the contract laboratory.

Your investigation identified the possible root causes as 1) (b) (4) 2) aseptic technique, or endotoxin in the API.

However, your firm's investigation was incomplete in that:

a. The raw material, EGCG, was identified as a possible source of endotoxin contamination but was never tested.

b. (b) (4) was identified as a possible source of the contamination but was not investigated.

c. Aseptic technique was also included as a possible source of the contamination but was not investigated.

d. There was no assessment of (b) (4) (glassware) which have not been validated.

2. L-Carnitine 500mg/ml for Injection, lot #N12202013@8 (Production date: 1/29/14, Beyond Use Date: 7/28/14)

Lot #N12202013@8 failed the test for endotoxin with a result of 476.19 EU/ml as documented on a Certificate of Analysis dated 3/19/14 from the contract laboratory.

Your investigation identified possible root causes as 1) presence of endotoxin or gram negative bacteria in the API, and 2) excessive time between preparation and (b) (4)

Your firm's investigation was incomplete in that:

a. The testing of the raw material, L-Carnitine, which was identified as a possible source of contamination was not conducted.

b. Excessive time between preparation and (b) (4) was identified as a possible cause but was not investigated.

c. The investigation did not include an assessment of (b) (4) (glassware) which have not been validated.

d. The investigation did not extend to all impacted batches. Per your Pharmacist in Charge, the L-Carnitine, lot (b) (4) which was used in L-Carnitine, lot #N12202013@8 was also used in the product, Lipotocin Plus 10 ml for Injection, lot #N01042014@2 (Production date: 1/9/14 Beyond Use Date: 7/8/14) which was sent to consignees.

3. Human Chorionic Gonadotropin 5000IU Lyophilized, lot #N04082014@14 (Production date: 4/17/14, Beyond Use Date: 10/15/14)

Lot #N04082014@14 failed the test for sterility as documented on a Certificate of Analysis issued by the contract laboratory (Organism: *Staphylococcus haemolyticus*).

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Your investigation identified aseptic technique by the technician as the probable root cause but failed to include an evaluation of the following areas:

(b) (4)
Room pressurization
Laminar flow operation
Assessment of container closure
Sanitization procedures (Room, equipment, product containers, etc.)
Evaluation of other lots compounded by the same technician

B. SOP #9.030 entitled, "Particulate Testing for Sterile Preparations" (Date: 1/2013) provides guidance for the evaluation of vials of sterile, injectable drug products for particulates. My review of (b) (4) lots of drug products manufactured between 4/16/2013 and 6/23//2014 revealed that at least 185 lots had fibers or particulates. No investigations have been conducted.

In each case, your firm conducted a 100% inspection by (b) (4) Vials identified as containing fibers and/or particulates were then removed and discarded. However, this method has not been shown effective to detect fibers or particulates in amber vials.

The remaining vials from each lot were then distributed to consignees. Some examples consist of the following:

- Methylcobalamin, lot #N01162014@21
- DMSO, lot #N01082014@1
- Cyanocobalamin, lot #N01062014@11

C. Investigations have not been conducted for sterile, injectable drug products which were rejected due to precipitation or particulates. Some examples consist of the following:

1. Thiamine HCl 30ml 100mg/ml Injectable, lot #N02212014@10 (Production date: 2/25/2014, BUD: 8/24/2014): Particulates
2. M.I.C.A. 126 50ml Preserved 25/50/50/5/50/25 mg/ml Injectable, lot #N12272013@6 (Production date: 1/2/2014, BUD: 7/1/2014): Precipitation

D. A "Sterilizer Test Report" dated 2/27/14 issued by (b) (4) indicated that a gram stain confirmed spore growth in one or more test strips and control strips for a test conducted on 2/19/14. No investigation was conducted.

THIS IS A REPEAT OBSERVATION FROM THE PREVIOUS INSPECTION CONDUCTED BETWEEN 3/18/2013 AND 4/16/2013.

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OBSERVATION 2

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

Specifically,

A) Media Fills

SOP #7.007.3 entitled, "Media Fill for High Risk Compounding " (Date: 4/17/14) documents, in part, that a total of (b) (4) ml vials ((b) (4) for positive controls and (b) (4) for product) will be used to conduct media fills.

1) The media fills were not representative of actual production processes in that:

a. The media fills failed to simulate a lot with the maximum number of vials (i.e. Cyanocobalamin, lot #N04302014@14: (b) (4) vials)
b. The number and type of interventions was not included.
c. The aseptic assembly of equipment (e.g., at start-up, during processing) was not included.

2) The (b) (4) tubes of media used as positive controls with the media fills were not inoculated with a known number/type of organisms. Instead, the (b) (4) tubes were exposed to the environment (undefined), capped and then incubated for (b) (4) days.

3) Media fills for lyophilized products were not conducted (i.e. Human Chorionic Gonadotropin and Sermorelin)

B) (b) (4) validation

Your firm failed to validate the (b) (4) used for the sterilization of injectable drug products. Some examples of (b) (4) utilized by your firm consist of the following:

(b) (4)

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(b) (4)

My review of approximately (b) (4) production records for the period between 4/16/2013 and 6/23/2014 revealed that integrity testing was not documented as being performed on (b) (4) for approximately (b) (4) lots.

D) (b) (4) Sterilization

Your firm failed to validate the (b) (4) used to sterilize injectable drug products and drug product components such as vials and stoppers.

Your firm currently uses the following (b) (4) for the sterilization of drug products and components:

(b) (4)

Some examples of sterile, injectable drug products which were terminally sterilized include the following:

- DMSO 50 mL 99% Injectable, lot #N01082014@1 (Production date: 1/20/2014, Beyond Use Date: 7/19/2014)
- Hyaluronic Acid 10 mL X-Link 10 mg/mL Injectable, lot #N05092014@1 (Production Date: 5/12/2014 Beyond Use Date: 11/1/2014)
- Vitamin A 10 mL 50,000 IU/mL Injectable, lot #N04142014@8 (Production Date: 4/14/2014 Beyond Use Date: 10/11/2014)

In addition, your firm uses (b) (4) of drug products which are (b) (4). The (b) (4) does not meet the USP standards for (b) (4) and is not tested to ensure the absence of endotoxins.

E) Qualification of ISO 5 processing area modifications

Your firm failed to re-qualify the ISO 5 and 7 processing areas after major modifications to the areas. For example, on 4/7/14, your vendor conducted major repairs in the ISO 5 and ISO 7 areas to include the re-positioning of four HEPA filters in the ISO 5 area and re-location of the lyophilizer from the ISO 7 cleanroom to the ISO 5 area. There was no documentation to indicate that cleaning was performed in the controlled areas after the repairs were made.

A re-qualification of the ISO 5 and ISO 7 areas did not occur until 5/21/14. Between 4/7/14 and 6/2/14, your firm

compounded approximately (b)(4) lots of injectable drug products of which at least (b)(4) have been distributed.

Some examples include the following:

- Lidocaine HCl 50ml 1% Injectable, lot #N 05122014@12, (Production date: 5/13/14 Beyond Use Date: 11/11/14)
- Procaine Potassium Buffered 50ml 2% Injectable, lot #N04142014@5 (Production date: 5/13/14, Beyond Use Date: 11/10/14)
- Magnesium Chloride Hexahydrate 50ml 200mg/ml Injectable, lot #N04302014@17 (Production date: 5/12/14 Beyond Use Date: 11/10/14)

THIS IS A REPEAT OBSERVATION FROM THE PREVIOUS INSPECTION CONDUCTED BETWEEN 3/18/2013 AND 4/16/2013.

OBSERVATION 3

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

Specifically, environmental monitoring is not representative of the clean room environment during aseptic processing operations. For example,

A) Viable air sampling is performed in the ISO 5 and ISO 7 areas once every (b) (4) when the rooms are being re-certified by your outside contractor.

B) Surface samples are obtained randomly (b) (4) in the clean room. The areas to be sampled are not identified.

C) Routine monitoring for clean room personnel is performed once every (b) (4) and there is no monitoring of gowns,

arms, face masks or other areas of the technician.

D) Growth promotion testing is not performed on incoming prepared media (i.e. (b) (4) ") used for environmental sampling.

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OBSERVATION 4

Aseptic processing areas are deficient regarding systems for maintaining any equipment used to control the aseptic conditions.

Specifically,

A. There is no assurance that the air quality inside the ISO 5 area is adequately maintained. Currently, the ISO 5 area is separated from the ISO 7 cleanroom by a plastic curtain which descends approximately 30" from the ceiling. The latest cleanroom qualification dated 5/21/14 failed to include documentation to demonstrate that laminarity can be adequately maintained between the ISO 5 and ISO 7 areas.

On 6/3/2014, we observed that the sides of the plastic curtain which enclose the ISO 5 area inside the ISO 7 cleanroom were absent. I was told by management that the sides were removed on 6/2/2014 based on recommendations from the HVAC vendor since they were opaque and needed to be clear. The ISO 5 area was not recertified after this modification.We also observed on 6/3/14 that the product, HCG K Lyophilized 5000 U Powder Injectable, lot #05232014@2, was being processed within the uncertified ISO 5 area.

In addition, your firm manufactured the following drug products on 6/19/2014 and 6/23/2014 using the uncertified ISO 5 area:

- AMP Buffered 10ml 25mg/ml Injectable, lot #06192014@3 (Production date: 6/19/14, BUD: 12/16/2014)
- Methylcobalamin Buffered 30ml 1mg/ml Injectable, lot #06172014@14 (Production date: 6/23/14, BUD: 12/21/2014)
- Magnesium Sulfate 50ml 50% Injectable, lot #06132014@9 (Production date: 6/23/14, BUD: 12/21/2014)

Each lot was (b) (4) in the ISO 5 area and then (b) (4) The Pharmacist in Charge told me that the lots were (b) (4) since the firm had identified rationale in literature. In addition, I was told that the ISO 5 area was uncertified and that the firm was only compounding products which could be (b) (4) The three lots are being held in quarantine pending the completion of testing for sterility and endotoxin.

B. Your firm checks and documents the differential pressure between the ISO 7 and ISO 8 areas (b) (4) There are no requirements for additional monitoring.

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OBSERVATION 5

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

Specifically, my review of approximately (b) (4) lots manufactured between 4/16/2013 and 6/23/2014 revealed that endotoxin testing had not been performed for approximately 180 of the (b) (4) lots of injectable drug products distributed. Some examples where testing for endotoxin was not performed consist of the following:

- Taurine 30ml 50mg/ml, lot #N12182013@13 (Production date: 1/22/14, Beyond Use date: 7/21/14)
- Methylcobalamin Buffered 10ml 1mg/ml, lot #N01162014@20 (Production date: 1/23/14 Beyond Use date: 7/22/14)
- Thioctic Acid 30ml 25mg/ml, lot #N12202013@5 (Production date: 1/23/14 Beyond Use date: 7/19/14)

OBSERVATION 6

Equipment and utensils are not 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 firm has never conducted preventive maintenance on the (b) (4) or lyophilizer used for the processing of injectable drug products. My review of the operators' manuals for the (b) (4) and one lyophilizer revealed that specific maintenance is required to ensure optimal operation. Some examples of the recommended maintenance consist of the following:

A. (b) (4)

The lyophilizer is used for the production of two products, HCG 5 K Lyophilized 5000 U Powder Injectable and Sermorelin /GHRP-6/GHRP-2 3/3/3 mg per vial Injectable. Some examples of lots distributed include the following:

- Sermorelin/GHRP-6/GHRP-2 3/3/3 mg per Vial Injectable, lot #N03112014@9 (Production Date: 3/11/2014 Beyond Use Date: 9/7/2014)
- HCG 5 K Lyophilized 5000 U Powder Injectable, lot #N03182014@10 (Production Date: 3/27/2014 Beyond Use Date:

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9/23/2014)

The operating manual recommends the following maintenance:

1. (b) (4)

2. (b) (4)

B. (b) (4)

1.

- (b) (4)

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OBSERVATION 7

Adequate lab facilities for testing and approval or rejection of drug products are not available to the quality control unit.

Specifically, your firm has not authorized your contract laboratory to conduct suitability testing for all drug products tested for sterility as confirmed by management. Review of approximately (b) (4) testing records for the period between 4/16/2013 and 6/23/14 revealed that at least 80% of the records included a statement from the contract laboratory documenting that the sterility test did not meet all the requirements for sampling and/or method suitability specified in USP <71>. Some examples consist of the following:

- L-Glutamine 30ml 30mg/ml Injectable, lot #N05122014@8 (Production date: 5/13/14, Beyond Use Date: 11/11/14)
- Hyaluronic Acid 10ml X-Link 10mg/ml Injectable, lot #N05092014@1 (Production date: 5/12/14 Beyond Use Date: 11/1/14)
- Procaine 50 ml Buffered 1% 10mg/ml Injectable, lot #N05082014@23, (Production date: 5/9/14, Beyond Use Date: 11/7/14)

OBSERVATION 8

There are no written procedures for production and process controls designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess.

Specifically,

A. Your firm utilizes a (b) (4) (b) (4) for the lyophilization of injectable drug products. Your firm has failed to validate the different cycles used for the lyophilization of the drug products, Human Chorionic Gonadotropin Lyophilized 5,000 Units Powder and Sermorelin. Some examples of specific cycle parameters consist of the following:

Freezing	Duration	HCG (Human Chorionic Gonadotropin)	Sermorelin
(b) (4) (b) (4)			(b) (4) (b) (4)

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214) 253-5200 Fax:(214) 253-5314 Industry Information: www.fda.gov/oc/industry	06/03/2014 - 07/16/2014* FEI NUMBER 3010087152

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Kristi A. Kubosh, Pharm. D., R.Ph., Pharmacist in Charge

FIRM NAME	STREET ADDRESS
Downing Labs, LLC	4001 McEwen Rd Suite 110
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Dallas, TX 75244-5020	Producer of Sterile Drug Products

(b) (4) [redacted]

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OBSERVATION 9

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

Specifically,

A. There is no documentation to indicate that the plastic curtain separating the ISO 5 and ISO 7 areas has ever been cleaned or sanitized.

B. Your firm has not conducted disinfectant effectiveness studies to demonstrate that the disinfectants used to clean the walls, floors, ceilings, and work surfaces in the ISO 5 and ISO 7 areas can sufficiently reduce bioburden. Currently, your firm utilizes the following disinfectants in the ISO 5 and ISO 7 areas:

(b) (4) [redacted]

C. Your firm uses non-sterile wipes in the ISO 5 and ISO 7 areas for the cleaning and sanitization of surfaces.

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	Stephen D. Brown, Investigator Darla J. Christopher, Investigator	07/16/2014

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OBSERVATION 10

Clothing of personnel engaged in the manufacturing of drug products is not appropriate for the duties they perform.

Specifically, the goggles used by technicians in the ISO-5 clean room are not sterile and are not disinfected prior to use.

THIS IS A REPEAT OBSERVATION FROM THE PREVIOUS INSPECTION CONDUCTED BETWEEN 3/18/2013 AND 4/16/2013.

OBSERVATION 11

There is no written testing program designed to assess the stability characteristics of drug products.

Specifically,

A) Your firm has no documentation to justify the Beyond Use Date of injectable drug products of 180 days. My review of approximately (b) (4) lots of drug products manufactured between 4/16/13 and 6/23/14 revealed that your firm produced approximately (b) (4) different sterile, injectable drug products with Beyond Use Dates (BUDs) up to 180 days, to include preserved and preservative free drug product units which are intended for single use but not labeled accordingly. For example,

- Phosphatidylcholine 50ml, 5/2.5% Injectable, lot #N05092014@8, BUD 180 days.
- Lipotocin 10 ml Injectable, lot #N04302014@8, BUD 180 days.

B) Your firm has not conducted anti-microbial effectiveness testing to determine whether Benzyl Alcohol, Methylparaben, or Benzalkonium Chloride effectively inhibit microbial growth in sterile injectable drug products through BUD. My review of approximately (b) (4) lots of sterile drug products for the period between 4/16/2013 and 6/23/2014 revealed that your firm manufactured drug products containing these preservatives with BUDs of 180 days. For example,

- B12 3ml (Hydroxo 12.5mg/ml + Cyano 12.5mg/ml) 25mg/ml Injectable, lot #N05082014@22 (BUD: 180 days) Contains: Benzyl Alcohol
- Biotin 30 ml (Preserved) 10mg/ml Injectable, lot #N01282014@10 (BUD 180 days) Contains: Methylparaben
- Acetyl-L-Carnosine Eye Drop 15ml Modified 5% Ophthalmic, lot #N03282014@7 (BUD 180 days) Contains: Benzalkonium Chloride

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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TO: Kristi A. Kubosh, Pharm. D., R.Ph., Pharmacist in Charge

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OBSERVATION 12

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.

Specifically, your firm has not conducted potency testing for any drug products manufactured and distributed. My review of approximately (b) (4) lots of sterile drug products manufactured between 4/16/2013 and 6/23/2014 revealed that potency testing had not been conducted for any lots.

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OBSERVATION 13

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

Specifically, your firm does not consistently document the model/lot number of the (b) (4) used in the sterilization of injectable drug products. For example, Lipotocin 10ml for Injection, lot #N04302014@18 (Production date: 5/5/14, Beyond Use Date: 11/3/14).

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*** DATES OF INSPECTION:**
06/03/2014(Tue), 06/04/2014(Wed), 06/05/2014(Thu), 06/06/2014(Fri), 06/10/2014(Tue), 06/11/2014(Wed), 06/12/2014(Thu), 06/13/2014(Fri), 06/17/2014(Tue), 06/18/2014(Wed), 06/19/2014(Thu), 06/20/2014(Fri), 06/24/2014(Tue), 06/25/2014(Wed), 06/26/2014(Thu), 07/02/2014(Wed), 07/03/2014(Thu), 07/14/2014(Mon), 07/15/2014(Tue), 07/16/2014(Wed)

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