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	09/14/2015 - 10/09/2015* FEI NUMBER 3010087152

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Ashley M. Downing, Co-owner

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

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. Review of multiple failing sterility test results and associated documentation noted that in all cases, the investigations were either absent, incomplete, or inadequate. Examples include:

i. On 9/2/14 your firm's contract laboratory reported that Procaine 1% injectable in 50 mL vials lot N05082014@23 consisting of (b)(4) vials with BUD 11/7/14 had initial failing sterility results at day 11. The organism *Afipia felis* was subsequently identified. No investigation was performed. This lot had previously passed sterility testing per CoA dated 5/28/14 and was distributed, for example, (b)(4) vials on 7/21/14.

ii. On 8/26/14, your firm's contract laboratory reported that Methylsulfonylmethane (MSM) 200 mg/mL injectable in 30 mL vials lot N04012014@9 consisting of (b)(4) vials with BUD 10/15/14 had initial failing sterility results at day 4. The organism *Bacillus oleronius* was subsequently identified. No investigation was performed. This lot had previously passed sterility testing per CoA dated 5/1/14 and was distributed, for example, (b)(4) vials on 5/22/14.

iii. Your contract laboratory's CoA dated 8/21/14 states that Cyanocobalamin 1 mg/mL injectable in 30 mL vials lot N05022014@17 consisting of (b)(4) vials with BUD 11/12/14 failed sterility testing with the organism *Afipia felis* recovered. No initial investigation was performed. Your additional investigation dated 6/26/15 is inadequate in that no root cause, process, or product impact was identified. This lot had previously passed sterility testing per CoA dated 6/3/14 and was distributed, for example, (b)(4) vials on 7/15/14.

iv. Your firm's contract laboratory CoA dated 7/23/14 states that Taurine 50 mg/mL injectable in 30 mL vials lot 06252014@4 consisting of (b)(4) vials with BUD 12/22/14 failed sterility testing with *Oceanobacillus caeni* recovered. Your initial investigation dated 7/15/14 is incomplete as it only states the method of sterilization, the organism identified, and the materials used. Your additional investigation dated 6/26/15 is inadequate in that no root cause, process, or product impact was identified.

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v. On 7/21/14 your firm was notified by your contract laboratory that Selenium 40 mcg/mL injectable in 30 mL vials lot 07092014@16 consisting of (b)(4) vials with BUD 1/5/15 failed sterility testing. Organism identification as *Bacillus thermoamylovorans* was reported on 8/1/14. Your initial investigation dated 7/21/15 is incomplete. Your additional investigation dated 6/26/15 is inadequate in that no root cause, process, or product impact was identified.

vi. Your contract laboratory CoA dated 7/23/14 states that Collagenase 1000U/mL injectable in 5 mL vials lot 05212014@19 consisting of (b)(4) vials with BUD 12/18/14 failed sterility testing with *Pseudomonas aeruginosa* recovered. No investigation was performed.

vii. On 6/3/14 your firm was notified by your contract laboratory that Folic Acid 10 mg/mL injectable in 30 mL vials lot 05282014@1 consisting of (b)(4) vials with BUD 11/242/14 failed sterility testing. Organism identification as *Micrococcus luteus* was reported on 6/19/14. Your initial investigation with no date is incomplete. Your additional investigation dated 6/26/15 is inadequate in that no root cause or process impact was identified.

B. Your firm did not provide adequate investigations for the following three failed media fills.

i. High Risk Media Fill Test lot (b) (4) consisting of (b)(4) vials performed by technician (b)(6) on (b) (4). The contract lab CoA states "Positive vials found in batch" without reference to how many. No organism identification was performed. You stated this media fill was invalidated but did not provide adequate supporting documentation.

ii. High Risk Media Fill Test lot (b) (4) consisting of (b)(4) vials performed by technician (b)(6) on (b) (4) resulted in one turbid vial containing *Staphylococcus epidermis*. You stated that this media fill was invalidated due to an (b) (4) but did not provide adequate supporting documentation.

iii. Lyophilization High Risk Media Fill Test lot (b) (4) consisting of (b)(4) vials performed by technician (b)(6) on (b) (4) resulted in one turbid vial containing *Brevibacillus parabrevis*. This was technician (b)(6)'s first lyophilization media fill which was a failure. However, review of batch record documentation reveals that technician (b)(6) has previously processed multiple lyophilization drug product batches, including Sermorelin/GHRP-6/GHRP-2 with 3/3/3mg in 10 mL vials lot 07222015@7 which was filtered and (b) (4) (b) (4) by (b)(6) on 7/22/15.

C. Review of facilities and equipment related incidents and associated documentation noted that in all cases, the investigations were either absent, incomplete, or inadequate. Examples include:

i. A (b)(4) test on 9/22/14 failed for (b) (4) (b) (4) Your firm's investigation was inadequate as no root cause analysis was performed, but only products (b) (4) (b) (4) (b)(4) (b) (4) (b)(4) on (b) (4) were considered affected, including Hyaluronic Acid 20 mg/mL in 10 mL vials lot 09102014@4 (b) (4) on (b) (4) and Resveratrol 10 mg/mL in 5 mL vials lot 07092014@13 (b) (4) on (b) (4) These lots were considered acceptable by your firm based on finished product sterility results. No other batches were identified in your investigation.

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ii. A (b) (4) test on 11/3/14 failed for (b) (4) (b) (4) (b) (4)). Your firm's investigation was inadequate as no root cause for the failure was identified, but only the supplies (e.g. vials, stoppers, etc.) (b) (4) since the date of the previous passing test were deemed affected. (b) (4) tests are only (b) (4) and there is no assurance that routine (b) (4) for sterilizing containers, closures, and equipment are not affected.

iii. A (b) (4) test on 3/3/15 failed for (b) (4) (b) (4) (b) (4)). Your firm's investigation was inadequate as no root cause for the failure was identified and the conclusion states that the failure "appears to be an isolated incident".

iv. On 9/16/15, your firm's calibration service provider reported that (b) (4) (b) (4) (b) (4)) failed calibration with as-found values of (b) (4) when (b) (4) (b) (4) No investigation into this discrepancy was initiated until I notified your firm of this failure on 10/5/15. The investigation is currently in-process. This (b) (4) was last calibrated on 9/3/14 and is used to sterilize items such as vials, stoppers, wipes, etc. for use in aseptic processing operations.

v. Your firm did not document an investigation, including product impact and appropriate CAPA, pertaining to a smoke study failure observed approximately (b) (4) by your contract service provider where the (b) (4) .

D. Review of out-of-specification (OOS) chemical or physical related test results and associated documentation noted that in all cases, the investigation was either absent, incomplete, or inadequate. Examples include:

i. An OOS potency result of 86.79% (specification (b) (4) - (b) (4) %) was reported by your contract laboratory on approximately 4/1/15 for Procaine 1% injectable in 50 mL vials lot 03232015@3 consisting of (b) (4) vials with BUD 9/19/15 which is sterile filtered and (b) (4) . This lot was a stability study lot. Your investigation was inadequate, in part, as no root cause was identified and it did not extend to all previously produced batches of Procaine 1% which were not tested for potency, including lot 01202015@8. Your corrective and preventative action was to (b) (4)

ii. USP specifications for Procaine Hydrochloride Injection states an assay specification of 95.0-105.0%. Procaine 2% injectable lot 04242015@16 yielded (b) (4) vials which were distributed although test results reported a potency of 106.12% on 6/3/15. No investigation was performed.

iii. An OOS potency result of 94.84% (specification (b) (4) - (b) (4) %) was obtained for the (b) (4) time-point for stability testing of Pyridoxine 100 mg/mL injectable in 30 mL vials lot 03232015@6. No investigation was performed.

iv. On 9/1/15 an OOS potency result of 38.6% (specification (b) (4) - (b) (4) %) was reported for the methylcobalamin component of MICMLTRNDPPC injectable in 10 mL vials lot 07202015@23. No investigation was performed. Previously produced batches of this product without potency testing include 04242015@14 which was distributed on 6/1/15.

v. Your contract laboratory reported an OOS for subvisible particle testing on approximately 4/27/15 for L-Glutathione

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200 mg/mL injectable in 50 mL vials lot 03232015@3. No investigation was performed.

vi. Your contract laboratory reported an OOS for subvisible particle testing on approximately 4/2/15 that Procaine 1% lot 03232015@3. No investigation was performed.

vii. Your contract laboratory reported on approximately 6/25/15 that Hydroxocobalamin 1 mg/mL buffered lot 061920115@9 failed potency testing with a result of 82.84% (specification (b) (4) - (b) (4) %). No investigation was performed.

THIS IS A REPEAT OBSERVATION

OBSERVATION 2

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

Specifically,

A. Your firm's media fill program does not adequately simulate worse case processing conditions under which drug products are routinely processed. For example:
- Drug products L-Glutathione 200 mg/mL injectable in 50 mL vials lot 06262015@9 and DMAE 100 mg/mL injectable in 30 mL vials lot 07162015@6 required (b) (4) per your batch records. This requires the use of (b) (4) , including the use of (b) (4) (b) (4) not simulated in any media fills.
- Your firm's lyophilization media fills do not include an appropriately simulated (b) (4) Media fill vials are (b) (4) (b) (4) and then (b) (4) for drug products includes (b) (4) (b) (4) . Lyophilized products include Sermorelin/GHRP-6/GHRP-2 with 3/3/3mg in 10 mL vials lot 07222015@7 (b) (4) and HCG 5,000U Lyophilized Powder injectable in 10 mL vials lot 07092015@7 (b) (4)

B. The (b) (4) used by your firm for sterilization of components, equipment, and finished drug products are inadequate for their intended use. (b) (4) (b) (4) are used for (b) (4) of sterile injectable drug products while (b) (4) (b) (4) are used for sterilizing components, equipment, and materials such as vials, stoppers, crimps, wipes, and (b) (4) . The summary reports for the installation, operation, and performance qualifications (IQ/OQ/PQ) performed by your contractor for (b) (4) (b) (4) states in the conclusion: "Performance Exception: The ability to properly document each (b) (4) as required by the FDA is absent on this device due to the lack of an adequate (b) (4) . The (b) (4) , (b) (4) do not adequately (b) (4) (b) (4) , which is a violation of GMP and FDA guidelines. In the event of a (b) (4) to ensure that (b) (4) (b) (4) , (b) (4) (b) (4)

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For example, calibration performed on (b) (4) (b) (4) (b) (4)) on 10/7/14 recorded passing as-found results for (b) (4) (b) (4) (b) (4) instrumentation. However, previously on 9/22/14, a (b) (4) test run in this (b) (4) had failed. No root cause of this failure was identified. Note that no instrumentation adjustments were made during the calibration and the (b) (4) has remained the same.

Additionally, the following deficiencies were noted:

i. For all (b) (4) used to sterilize drug products, containers, closures, and other items, no (b) (4) such as (b) (4) (b) (4) are documented in the (b) (4) log or within the batch records.
ii. The (b) (4) are all located in an unclassified room and SOP EQP 3.6 states to (b) (4) to allow the (b) (4) and (b) (4) before removing.
iii. SOP EQP 3.7 allows an (b) (4) to be (b) (4) for a (b) (4) if the (b) (4) with no requirement for an investigation. There is no data to support the impact of this (b) (4) on product quality characteristics such as potency.
iv. The water used to (b) (4) (b) (4) is not suitable for product contact surfaces such as vials and stoppers. For example, no endotoxin testing of this water is performed. There is no (b) (4) (b) (4) and (b) (4) (b) (4) (b) (4) .
v. In the absence of documented (b) (4) no (b) (4) is used with each sterilized (b) (4) (b) (4) .

Products and materials sterilized within these (b) (4) include:

- DMSO 99% injectable in 50 mL vials lot 06242015@6 (b) (4) on 6/29/15 in (b) (4)
- Hyaluronic Acid X-Link 20 mg/mL injectable in 10 mL vials lot 04132015@2 (b) (4) on 4/13/15 in (b) (4)
- Procaine 2% injectable lot 07212015@12 (b) (4) in (b) (4) (b) (4) .
- Stoppers from lot (b) (4) were (b) (4) in (b) (4) on 4/14/15 and used in L-Tyrosine lot 04202015@12 (b) (4) (b) (4)
- Stoppers from lot (b) (4) were (b) (4) in (b) (4) (b) (4) and used in Phosphatidylcholine/DCA lot 06052015@13 on 6/6/15.

C. **Aseptic practices and techniques observed at your facility during aseptic processing of sterile drug products are inadequate. On 9/17/15 during processing of Thiamine HCl 100 mg/mL in 30 mL vials lot 09162015@7, the following was observed:**

i. The operator's gloved fingers were observed to block first air over open vials during vial filling and stoppering.
ii. The operator used (b) (6) gloved fingers to (b) (4) filled vials.
iii. The operator was observed to rest (b) (6) gowned arms on the ISO 5 work surface during filling.

D. Smoke studies did not appropriately simulate dynamic processing conditions to evaluate air flow patterns in the ISO 5 workspace and adjacent ISO 7 areas. For example, your firm's smoke study dated (b) (4) of routine aseptic processing simulated (b) (4) On 9/17/15, (b) (4) operators were observed working in close proximity at the ISO 5 workspace during filtration and stoppering operations. Additionally, your firm's smoke studies did not examine the boundaries of the ISO 5 and ISO 7 spaces for potential backflow under dynamic conditions.

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OBSERVATION 3

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

Specifically,

A. **Despite your firm's (b) (4) use of sporicidal disinfectants, a variety of spore forming bacteria are routinely recovered from your environmental and personnel monitoring within the aseptic processing areas. For example:**

Date of Spore Former Recovery	Location(s) Recovered	Organism(s)
6/19/15	(b) (4)	*Bacillus subtilis*
6/23/15		*Bacillus aryabhattai*
7/6/15		*Bacillus amyloliquefaciens* *Bacillus simplex* *& Bacillus marisflavi*
7/7/15		*Bacillus circulans*
7/8/15		*Bacillus circulans* *Bacillus flexus* *Bacillus circulans* *Bacillus circulans* *& Bacillus amyloliquefaciens*
7/14/15		*Bacillus cereus* *Bacillus pumilus* *Nocardiopsis dassonvillei*
7/15/15		*Bacillus altitudinis* *& Bacillus gibsonii*
7/17/15		*Bacillus altitudinis* *Bacillus marisflavi*
7/21/15		*Bacillus pumilus*
7/29/15		*Streptomyces levis*
7/31/15		*Bacillus sp.*
8/7/15		*Terribacillus saccharophilus* *& Terribacillus goriensis* *Bacillus circulans* *Bacillus cereus*

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8/12/15	(b) (4)	*Paenibacillus xylanexedens* *Bacillus oceanisediminis*
8/13/15		*Paenibacillus dongdonensis* *& Fictibacillus nanhaiensis* *& Bacillus hunanensis*

B. Non-sterile disinfectants are routinely used by your employees during cleaning of aseptic processing areas, including the critical ISO 5 work area and ISO 7 buffer room. For example, prior to production of Thiamine HCl 100 mg/mL in 30 mL vials lot 09162015@7 on 9/17/15, I observed technician (b) (6) disinfecting the ISO 5 area interior walls followed by the aseptic processing work surfaces using the same mop head sprayed with (b) (4) Solution lot (b) (4). This bottle of (b) (4) was (b) (4) and consists of (b) (4) (b) (4) (b) (4). Additional non-sterile disinfectants (b) (4) include (b) (4) (b) (4) Solution lot (b) (4) which consists of (b) (4) (b) (4) (b) (4).

C. Your firm has not conducted disinfectant efficacy studies to demonstrate that the disinfectants and application methods (e.g. spray, wipe, mop, aerosol, etc.) used to clean the walls, ceilings, work surfaces, and other items in the ISO 5 and ISO 7 areas can sufficiently reduce bioburden. Disinfectants used by your firm include:

- (b) (4)
- Sanosil HaloMist (hydrogen peroxide and silver nitrate)

Additionally, no data was provided to demonstrate that all disinfectants are suitable for use through expiry once opened or (b) (4). For example (b) (4) Solution lot (b) (4) was (b) (4) and given a (b) (4) day expiry within the filled spray bottle.

OBSERVATION 4

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

Specifically,

The results of environmental, personnel, and surface monitoring are not investigated adequately.

Multiple instances were noted where your firm failed to consider significant adverse environmental and personnel monitoring results during the batch release process. For example:

i. On 8/7/15, you aseptically filtered Phosphatidylcholine/DCA 50 mL 10/4.75% lot 07302015@7 with BUD 2/5/16 and Magnesium Sulfate 50 mL 50% Injectable lot 08062015@1 with BUD 2/5/16. Environmental monitoring and personnel

monitoring on 8/7/15 recovered multiple organisms from multiple locations within the clean room suite and from fingertip sampling from multiple operators.

Location	Result	Organism(s)
(b) (4)	1 cfu	*Penicillium corylophilum*
	TNTC	*Penicillium corylophilum* *Bacillus cereus*
	1 cfu	*Penicillium corylophilum*
	1 cfu	*Terribacillus sp.*
	1 cfu	*Cladosporium sp.*
	5 cfu	*Massilia timonae* *Bacillus circulans* *Kocuria carniphila*

You failed to thoroughly investigate these results prior to distributing the affected batches. Your preliminary investigation did not correctly identify the batches affected. Your investigation addendum completed after 9/14/15 also did not correctly identify the batches affected.

ii. On 7/6/15, 7/7/15, and 7/8/15, environmental monitoring of the ISO 5 area via settle plates and active air samples resulted in numerous TNTC recoveries for *bacillus circulans*. Your investigation states that the plates were likely contaminated prior to use, but did not address the fact that spore forming organisms were brought into the ISO 5 workspace prior to and during aseptic processing of the following batches.

- Cyanocobalamin 1 mg/mL Buffered in 30 ml vials lot 07062015@5 filled on 7/6/15
- EDTA Sodium 150 mg/mL in 100 mL vials lot 07022015@18 filled on 7/7/15
- Folic Acid 10 mg/mL injectable in 30 mL vials lot 07022015@17 filled on 7/8/15
- Magnesium Sulfate 50 mL vials lot 07072015@12 filled on 7/8/15
- Phosphatidylcholine/DCA 10/4.75% injectable in 50 mL vials lot 06292015@2 filled on 7/8/15.

OBSERVATION 5

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

Specifically,

A. Your firm has no data to support pre-sterilization hold times for sterile injectable drug products and no pre-sterilization bioburden or endotoxin testing is performed. There is no assurance that the sterile filters used are capable of removing this unknown level of bioburden. In all cases, (b) (4) . For example:

- Ascorbic Acid 500 mg/mL injectable in 100 mL vials lot 05052015@9 with (b) (4) vials made. (b) (4) with sterile filtration occurring (b) (4) . This is a preservative free

formulation. Endotoxin results for this batch were 134.99 EU/mL.

- Green Tea (ECGC) 10 mg/mL in 10 mL vials lot 06052015@15. (b) (4) with sterile filtration occurring (b) (4) This is a preservative free formulation. Endotoxin results for this batch were 66.3 EU/mL.
- Phosphatidylcholine/DCA 10/4.75% injectable in 50 mL vials lot 07302015@7 with (b) (4) vials made. (b) (4) with sterile filtration occurring (b) (4) This formulation contains the preservative benzyl alcohol.

Additionally, the number of filters used per batch has not been established based on pre-filtration bioburden testing. For example, on 7/22/15 technician (b) (6) aseptically filtered Procaine 2% injectable in 50 mL vials lot 07212015@12. The technician used (b) (4) (b) (4) for (b) (4) (b) (4) (b) (4) (b) (4) Your firm's technicians indicated that the sterile filters are (b) (4) (b) (4) (b) (4)

B. There are no clean storage hold time limits established for (b) (4) prior to filtration. These (b) (4) are stored with a (b) (4) within the ISO 8 cleanroom support room after depyrogenation and prior to use for all sterile drug products. For example on 7/30/15 (b) (4) were (b) (4) Phosphatidylcholine/DCA 10/4.75% injectable lot 07302015@7 with a BUD of 2/5/16 (b) (4) was previously depyrogenated on 7/22/15 and while (b) (4) and (b) (4) were previously depyrogenated on 7/24/15. (b) (4) (b) (4) is located in an unclassified room and SOP EQP 3.8 states (b) (4) (b) (4) (b) (4) (b) (4) ."

OBSERVATION 6

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

Specifically,

Your firm does not ensure that the contents of each individual (b) (4) are tested for endotoxin content. (b) (4) from (b) (4) of sterile injectable drug products is tested for endotoxins. However, your firm frequently uses (b) (4) and which may have differing endotoxin levels. For example:

- Ascorbic Acid 500 mg/mL injectable in 100 mL vials lot 05052015@9 with (b) (4) vials made. This preservative free batch was (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) Endotoxin results from one vial from this batch were 134.99 EU/mL.
- Phosphatidylcholine/DCA 10/4.75% injectable in 50 mL vials lot 07302015@7 with (b) (4) vials made. This batch with preservative was (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) which were (b) (4) Endotoxin results from one vial were <10.00 EU/mL.

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OBSERVATION 7

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 Green Tea (EGCG) 10 mg/mL injectable product in 10 mL vials does not have a specification for endotoxins and only states "report results". For example:
   - Green Tea (ECGC) lot 06052015@15 with endotoxin results of 66.3 EU/mL.
   - Green Tea (ECGC) lot 08092014@22 with endotoxin results of 94.2 EU/mL.

B. Your finished product testing does not including testing for drug product impurities that may be present. For example, the batch record for Procaine 1% injectable lot 06042015@6 states it is (b) (4) . This lot was (b) (4) and is currently on BUD study with an (b) (4) potency result of 104.27%.

C. Your firm has not established specifications or performed testing for your lyophilized products HCG and Sermorelin for characteristics such as water content and reconstitution time.

D. Your firm has not established any specifications or performed any finished product testing for the majority of your non-sterile drug products. For example, no testing for identification, assay, impurities, content uniformity, dissolution, or microbial testing is performed for the following products
   - Ergoloid Mesylates 4.5 mg, (b) (4) capsules lot 04152015@1 bottled and labeled as HYDERGIN-PRO.
   - Phenytoin 25 mg, (b) (4) capsules lot 12082014@25 bottled and labeled as PHEN-PRO
   - Hydrocortisone 5 mg, (b) (4) capsules lot 12082014@21 bottled and labeled as HYDROCORT-PRO

OBSERVATION 8

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

Specifically,

Observation of your firm's smoke study dated (b) (4) revealed what appeared to be (b) (4) around the (b) (4) (b) (4) during simulated dynamic conditions. Your cleanroom certification dated (b) (4) . There is inadequate assurance that (b) (4) are sufficient to minimize ingress of contamination from the ISO 7 area during

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routine operations. The ISO 5 area is separated from the ISO 7 area by vertical plastic panels that extend (b) (4) [redacted]

OBSERVATION 9

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

Specifically,

A. Your firm does not have data to support the beyond-use-dates (BUD) applied to drug products produced and distributed. As of 9/14/15, no stability studies were completed. For example:

- Phosphatidylcholine/DCA 10/4.75% injectable in 50 mL vials lot 07302015@7 with BUD of 2/5/2016 (180 days).
- Ascorbic Acid 500 mg/mL injectable in 100 mL vials lot 05052015@9 with BUD of 11/1/15 (180 days).
- Testosterone Cypionate 200 mg/mL injectable in 10 mL vials lot 07302015@9 with BUD of 1/26/16 (180 days).

B. Your firm does not have data to support that any preservatives such as benzyl alcohol and chlorobutanol added to all preserved sterile injectable drug products remain in adequate quantities through the labeled BUD. For example:

- Phosphatidylcholine/DCA 10/4.75% injectable in 50 mL vials lot 07302015@7 with BUD of 2/5/2016 (180 days) containing benzyl alcohol.
- M.I.C. preserved 25/50/50 mg/mL injectable in ## mL vials, lot 07222015@4 with BUD of 1/18/2016 (180 days) containing benzyl alcohol.
- Vitamin D3 100,000U injectable in 10 mL vials, lot 05042015@9 with BUD 8/11/15 containing chlorobutanol.

THIS IS A REPEAT OBSERVATION

OBSERVATION 10

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. Lyophilization (b) (4) for drug products have not been adequately validated. Your firm uses a (b) (4) (b) (4) for the lyophilization of injectable drug products, including Human Chorionic Gonadotropin (HCG) 5,000 Units Lyophilized Powder in 10 mL vials lot 07092015@7 and Sermorelin/GHRP-6/GHRP-2 in 10 mL vials lot 07222015@7. The Summary Report for the Installation, Operational and Performance Qualification (IQ/OQ/PQ) Protocol for this (b) (4) signed on (b) (4) states "Based on the results of the execution of the protocol and a review of all data and

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4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214) 253-5200 Fax:(214) 253-5314 Industry Information: www.fda.gov/oc/industry	09/14/2015 - 10/09/2015* FEI NUMBER 3010087152
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED TO: Ashley M. Downing, Co-owner	
FIRM NAME Downing Labs, LLC	STREET ADDRESS 4001 McEwen Rd Suite 110
CITY, STATE, ZIP CODE, COUNTRY Dallas, TX 75244-5020	TYPE ESTABLISHMENT INSPECTED Outsourcing Facility

excursion, Biometrix concludes that the performance of the [redacted] System as tested [redacted] The [redacted] and [redacted] with [redacted] For example, at the [redacted], actual measurements within the [redacted] ranged from [redacted] to [redacted]. There is no [redacted]

Batch record documentation states the following:

Step	HCG	Sermorelin
[redacted]		

Batches produced using the [redacted] include:

- Human Chorionic Gonadotropin (HCG) 5,000 Units lot 05192015@9 lyophilized [redacted].
- Sermorelin/GHRP-6/GHRP-2 lot 06192015@2 lyophilized [redacted]
- Human Chorionic Gonadotropin (HCG) 5,000 Units lot 07092015@7 lyophilized [redacted]

B. No process performance qualification activities have been performed for the following drug products produced by your firm assure they are of appropriate quality. For example, no in-process testing is performed to support blend uniformity or content uniformity.

- Ergoloid Mesylates 4.5 mg, [redacted] capsules lot 04152015@1
- Phenytoin 25 mg, [redacted] capsules lot 12082014@25
- Hydrocortisone 5 mg, [redacted] capsules lot 12082014@21

For example, the Ergoloid Mesylates lot 04152015@1 batch record states that the batch was [redacted] of [redacted]

THIS IS A REPEAT OBSERVATION

OBSERVATION 11

The accuracy, sensitivity, specificity, and reproducibility of test methods have not been established.

Specifically,

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Dallas, TX 75244-5020	Outsourcing Facility

There is no assurance that test methods used for potency testing of your drug products for release and stability are accurate, sensitive, specific, and reproducible as no product and formulation specific method validation activities have been performed. For example, multiple potency test results from your contract laboratory state that the results were generated using a proprietary method and that the method cannot be considered validated unless specificity of the formulation has been performed per USP/ICH guidelines. Product lots and test results with this statement include:

- Procaine 1% injectable lot 06042015@6 in a BUD study with initial potency results of 104.27%. This product is (b) (4) and then (b) (4) .
- Pyridoxine 100 mg/mL injectable lot 03232015@6 in a BUD study with a (b) (4) result of 97.72%
- Testosterone Cypionate 200 mg/mL injectable lot 07302015@9 with a result of 92.94%

OBSERVATION 12

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

The following information is not found on some of your drug product labels, as required by section 503B(a)(10)(A):

A. The statement, "This is a compounded drug".
B. The established name of the drug.
C. The dosage form of the product.
D. A list of inactive ingredients, identified by established name, and the quantity or proportion of each ingredient.

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

- Potassium Chloride (20 mEq/10mL), lot 07312015@12
- EDTA Calcium Disodium, lot 07282015@15
- Thiamine, lot 07282015@8
- Zinc Sulfate (elemental), lot 07272015@9
- L-Carnitine, lot 07272015@4
- Ascorbic Acid, lot 07212015@10
- M.I.C. Injection (preserved), lot 07222015@4
- DMAE, lot 07162015@6
- HCG (lyophilized), lot 07092015@7
- L-Glutathione, lot 06262015@9

OBSERVATION 13

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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Dallas, TX 75244-5020	Outsourcing Facility

Your outsourcing facility has not submitted a report to FDA identifying all products compounded during the six months prior to registration as required by section 503B(b)(2)(A). Specifically, the following products were produced and not identified on the report submitted on 6/30/15..

- Pentoxifylline 20 mg/mL Preserved injectable in 30 mL vials lot 04082014@3 produced on 4/8/15 consisting of (b)(4) vials with a BUD of 10/5/15.
- Marine Water (b) (4) injectable in 100 mL vials lot 01222015@8 produced on 1/23/15 consisting of (b)(4) vials with a BUD of 7/21/15.
- Magnesium Sulfate 50 % injectable in 50 mL vials lot 05112015@4 produced on 5/12/15 consisting of (b)(4) vials with a BUD of 11/10/15.

OBSERVATION 14

Bulk drug substances used by your facility to compound drug products are not each manufactured by an establishment that is registered under section 510. Specifically,

For example:

- (b) (4) lot (b) (4) manufactured by (b) (4) was used in Phosphatidylcholine/DCA (b) (4) injectable lot (b) (4) with a BUD of (b) (4)

*** DATES OF INSPECTION:**
09/14/2015(Mon), 09/15/2015(Tue), 09/16/2015(Wed), 09/17/2015(Thu), 09/18/2015(Fri), 09/21/2015(Mon), 09/22/2015(Tue), 09/24/2015(Thu), 09/30/2015(Wed), 10/01/2015(Thu), 10/02/2015(Fri), 10/05/2015(Mon), 10/06/2015(Tue), 10/08/2015(Thu), 10/09/2015(Fri)

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