Reynaldo R. Rodriguez, Jr, District Director
Dallas District Office
4040 North Central Expressway, Suite 300
Dallas, TX 75204

August 6, 2014

Re: FDA 483

Please accept this letter as authorization to post on the US FDA Internet website NuVision Pharmacy's response to the FDA Form 483 Notice of Observations, dated August 6, 2014 as submitted, unredacted but without the attachments. We understand this response will be posted under the FDA Form 483 Notice of Observations for NuVision Pharmacy, issued on July 16, 2014.

This letter and the attached documents are in response to the FDA 483 observations made by FDA investigators Stephen D. Brown and Darla J. Christopher during our FDA inspection from the dates of June 3, 2014 to July 16, 2014. Please note that we are a Class AS pharmacy licensed with the Texas State Board of Pharmacy. We are in compliance with the USP Chapter <797> as well as the laws regulating the practice of pharmacy in the State of Texas. We are not a manufacturer and we are not legally required to follow the FDA 210 and 211 laws which were used as the basis for this inspection. The Compounding Quality Act under section 503B allows a pharmacy to register as an outsourcing facility, but it does not require us to do so. We have been transitioning to dispense only patient specific prescriptions and to no longer dispense prescriptions for office use. As of August 4, 2014 we are only dispensing patient specific prescriptions and our pharmacy will be operating under section 503A. Our pharmacy has already made many changes since 2013 to implement recommendations made by the FDA and to improve our sterile processes and our facility. Although we were not legally obligated to do this, we wanted to take the opportunity to go beyond the requirements of the USP in order to ensure better safety for patients. We have taken into consideration all of the observations made by the FDA and we will make all the necessary changes to correct all of our 483 observations.

NuVision Pharmacy also formally requests that the FDA change their posting of our 483s on the FDA's website. Our pharmacy underwent a change of ownership on January 15, 2014 and we did not receive a pharmacy license under Downing Labs until June 25, 2014. Therefore, it is inaccurate for the FDA to list the 483s from 2013 under Downing Labs, because Downing Labs did not exist at that time and did not own NuVision Pharmacy. These 483s need to be changed back to being listed under NuVision Pharmacy. We also request that our 2014 FDA 483 be listed under the name NuVision Pharmacy because the inspection only covered records dated

from April 1, 2013 to June 3, 2013. During those dates, the pharmacy was only licensed as NuVision Pharmacy and all products were labeled as NuVision Pharmacy.

Sincerely,

Kristi Kubosh, PharmD, RPh
Pharmacist in Charge
NuVision Pharmacy
4001 McEwen Rd, Suite 100
Dallas, TX 75244
Phone: 214-347-4008 ext 102
Fax: 888-839-0241

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 480 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 sterile filtered on 5/2/14. Subsequent testing for sterility failed (Test dated 6/2/14) and the lot was re-sterilized by autoclave 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 sterile filtered 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:

Observation 1.A. Response:

We want to take this opportunity to state that none of the lots with failing sterility or endotoxin results were ever dispensed. We quarantine all CSPs for at least 14 days and until we receive passing sterility and endotoxin results prior to releasing the products to be dispensed. We have changed our sterility investigation documentation form in order to comply with the FDA's requirements for a sterility failure investigation. Please see the attached investigation form. We are also changing developing other documentation forms for endotoxin failures and other out-of-specifications results that will meet the expectations of the FDA.

Timeline: The new sterility failure investigation form is complete. The endotoxin failure investigation form will be completed by September 2014. The remaining out-of-specifications investigation forms and SOPs will be completed by October 2014.

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 480 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 holding each amber vial below a light source against a white/black background. 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

Observation 1. B Response:

We have been following the procedures outlined in the USP <797> for physical inspection of finished CSPs. This procedure is effective for the detection of visible particles and is performed on 100% of our CSPs. In an effort to improve our visual inspection procress, we agree to expand our vial inspection procedures to include detection of subvisible particles using a method outlined in the USP Chapter <788>. We are working with DynaLabs to begin this testing.

We have also attached an email from the supplier of our vials as evidence of our ongoing investigation into identifying the possible sources of the fibers. All vials with any visible particles are destroyed and are not dispensed to patients.

Timeline: We are still in the decision-making phase for the identification of subvisible particles and we have yet to determine our estimated time to implementation.

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

Observation 1.C Response:

We are developing a new investigation form for various out-of-specifications investigations. We are also developing a new SOP for these investigations.

Timeline: We will have this completed by October 2014.

D. A "Sterilizer Test Report" dated 2/27/14 issued by SPS Medical 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.

Observation 1. D Response:

We did not investigate this spore test failure. We followed the CDC guidelines which state "If spores are not killed in routine spore tests, the sterilizer should immediately be checked for proper use and function and the spore test repeated. If the spore tests remain positive, use of the sterilizer should be discontinued until it is serviced". We checked the autoclave and re-ran the test. We did not use that autoclave until after the repeated test and received passing results. This occurred the first time we repeated the test, so according to the CDC guidelines an investigation was not necessary. In order to be in compliance with the FDA, we will develop an investigation form for spore test failures and a SOP for an investigation procedure.

Timeline: This will be completed by October 2014.

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 nine 20 ml vials (three for positive controls and six 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: 1000 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 three tubes of media used as positive controls with the media fills were not inoculated with a known number/type of organisms. Instead, the three tubes were exposed to the environment (undefined), capped and then incubated for 14 days.

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

Observation 2. A Response:

After our 2013 inspection we revised our media fill procedure. However, our 2014 FDA inspection recommended more ways in which we can improve our media fill procedures to better represent actual worst-case conditions. We will update the SOP for the High-Risk Media Fill to account for these changes. We will also develop a media fill process for our lyophilization procedures.

Timeline: The updated media fill procedures are scheduled to be completed and media fills performed by September 2014.

B) Filter validation

Your firm failed to validate the 0.2 micron filters used for the sterilization of injectable drug products. Some examples of sterile filters utilized by your firm consist of the following:

- Baxa #35
- FastCap
- Steri-Top
- Opti-Cap XL300

- Millex-AP
- Millipak-20
- Millipak-40
- Millipak-60
- Supor Capsule Filter

My review of approximately 480 production records for the period between 4/16/2013 and 6/23/2014 revealed that integrity testing was not documented as being performed on sterilizing filters for approximately 400 lots.

Observation 2.B Response:

All of the filters we use are already validated by the filter's manufacturer and come with a Certificate of Analysis. In order to comply with the recommendations made by the FDA, we are currently working on developing a procedure to validate all of our filters in-house. We will also improve documentation procedures for recording the integrity test results of our sterile filters.

Time Line: We have already implemented a better documentation chart on the production logs. The estimated date of completion for the filter validations has yet to be determined.

D) Autoclave Sterilization

Your firm failed to validate the steam autoclave cycle (121C for 30 minutes) used to sterilize injectable drug products and drug product components such as vials and stoppers.

Your firm currently uses the following four autoclaves for the sterilization of drug products and components:

- MagnaClave Model MC (#A6-5065): Vials/stoppers
- MagnaClave Model MC (#A6-5643): Vials/stoppers
- Delta Q (#AD-13910): Drug products
- Delta Q (#AF-005432): Drug products

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 glass beakers for the mixing of drug products which are rinsed and autoclaved before use. The rinse water does not meet the USP standards for Purified Water and is not tested to ensure the absence of endotoxins.

Observation 2. D Response:

We would like to state for the record that we do use biological indicators in every load that we autoclave and we have never had a failed biological indicator. We also perform the weekly spore testing on the autoclaves are required. In order to comply with the FDA's requirements for equipment validation we have contracted with Bio Metrix to have all 4 autoclaves, our dry-heat oven, the lyophilizer, and our incubator validated. Please see the attached quote and proposal from Bio Metrix. This is scheduled to start in August 2014. We have installed a dry-heat oven to depyrogenate all glassware and we will revise our procedure to make sure that our rinse water meets the USP and FDA standards.

Timeline: This is scheduled to be completed by September 2014.

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 60 lots of injectable drug products of which at least 10 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 2.E Response:

A deep cleaning was performed after construction and we agree to improve our documentation of construction and post construction cleaning procedures. We will develop an SOP for this.

Timeline: The SOP will be completed by September 2014 and the improved documentation procedures will be initiated the next time we make changes to our sterile compounding area.

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 six months when the rooms are being re-certified by your outside contractor.

Observation 3.A Response:

Currently the USP <797> only requires viable air sampling to be performed every six months for high-risk sterile compounding. However, we agree to develop a procedure to increase the frequency for performance of viable air sampling to beyond what is required by the USP. We will use a SAMPL'AIR machine to perform this testing and we will revise our SOPs to reflect this.

Time line: Our SOPs for this procedure will be completed by September 2014. We have already ordered the necessary equipment and supplies to begin taking viable air samples in-house in between our required 6 month certification testing performed by AirScan.

B) Surface samples are obtained randomly once per month in the clean room. The areas to be sampled are not identified.

Observation 3.B Response:

We have created a map to document the specific sites for surface sampling. Please see the attached map. We also agree to increase the frequency of this sampling plan to beyond the requirements of the USP <797>.

Timeline: This is completed. We have already taken surface samples using our new map to indicate the specific sampling sites.

C) Routine monitoring for clean room personnel is performed once every six months and there is no monitoring of gowns, arms, face masks or other areas of the technician.

Observation 3.C Response:

Currently, the USP <797> only requires gloved finger-tip sampling to be performed every six months. However, in the interest of improving our environmental monitoring program we will begin monitoring sites on the gowns, face masks, and other areas of the technician. We also agree to increase the frequency of personnel monitoring to beyond the requirements of the USP <797>. We will revise our SOPs to include these changes.

Timeline: This will be completed by September 2014.

D) Growth promotion testing is not performed on incoming prepared media (i.e. Envirotest swabs or "TSA with Lecithin and Polysorbate 80 Media Plates") used for environmental sampling.

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

Observation 3.D Response:

In response to this observation and the recommendations made by the FDA, we have switched to Q.I. Medical to supply all of our media. The media we receive from them will come with Certificates of Analysis as required by the FDA. We will discuss with them how to best perform Growth Promotion Testing on the media.

Timeline: The switch to Q.I. Medical is complete. The estimated time to completion for the growth promotion testing has yet to be determined.

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 pre-filtered with a 1.2 micron filter in the ISO 5 area and then autoclaved. The Pharmacist in Charge told me that the lots were autoclaved 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 autoclaved. The three lots are being held in quarantine pending the completion of testing for sterility and endotoxin.

Observation 4.A Response:

Our most recent certification was performed by AirScan and smoke studies were documented on their report to demonstrate laminarity; however, these smoke studies were not videotaped. We agree to have future smoke studies documented on video as recommended by the FDA.

The product in the lyophilizer was under vacuum at the time of inspection and the machine fully stoppers the vials before they are removed from the machine.

We are waiting for the clear plastic barrier to arrive so that it can be installed. In the meantime, we have installed an opaque plastic curtain in order to maintain the 100% HEPA filter coverage of the ISO 5 area.

Timeline: Video documentation of smoke studies will be completed at the time of the next cleanroom certification. The permanent clear plastic barrier will be installed by September 2014.

B. Your firm checks and documents the differential pressure between the ISO 7 and ISO 8 areas once every workshift. There are no requirements for additional monitoring.

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

Observation 4.B Response:

The current USP <797> requirements are to record the pressure daily. We plan to install a constant pressure monitoring system with an alarm in order to comply with the FDA's recommendations and to further improve our facility to a standard above the requirements of the USP.

Timeline: In progress

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 480 lots manufactured between 4/16/2013 and 6/23/2014 revealed that endotoxin testing had not been performed for approximately 180 of the 480 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 5 Response:

We began endotoxin testing on all CSPs on January 29, 2014.

Timeline: Completed on January 29, 2014

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 autoclaves or lyophilizer used for the processing of injectable drug products. My review of the operators' manuals for the autoclaves and one lyophilizer revealed that specific maintenance is required to ensure optimal operation. Some examples of the recommended maintenance consist of the following:

A. FreeZone 12 Liter Freeze Drying System (Model #7754040)

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:

Observation 6 Response:

We have started a maintenance program and we are currently developing SOPs and log forms to document proper maintenance on all of our equipment.

Timeline: In progress

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 480 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 7 Response:

During the time of our inspection we were in the process of completing method suitability testing for all products. We began submitting samples for method suitability testing in April 2014.

Please see the attached document with the completed dates for this testing. Until this testing is complete for each product, they are being tested using a testing method which is equivalent to the USP <71>.

Timeline: As we continue to make any new products, these will be submitted for method suitability testing in order to have this testing for all CSPs.

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 FreeZone Stoppering Tray Dryer 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
Freeze	24 hours	-40C	-10C (3-4 hrs)→-40C
Primary Drying	20-24 hours	-40C	-40C
Secondary	12 hours	-30C	-30C

	24 hours	-20C	-20C
	8-10 hours	-10C	-10C
	2 hours	0C	0C
	1-2 hours	+25C	+25C

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

Observation 8.A Response:

We agree to validate the different cycles for the lyophilizer. We have contracted with Bio Metrix to have all 4 autoclaves, the dry-heat oven, the lyophilizer, and the incubator validated. This is scheduled to start in August 2014. Please see the attached proposal.

Timeline: To be completed by September 2014

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.

Observation 9.A Response:

We would like to note that we have always cleaned the plastic curtain daily during our cleaning procedure and this observation is due to a lack of clarity on the documentation form. We have changed our documentation form to include a check off box for cleaning the plastic curtain. Please see the attached form. For documentation purposes on this form the plastic curtain is referred to as the flap.

Timeline: Completed.

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:

- Sterile 70% Isopropyl Alcohol
- YGeine 206 Sterilant
- Sodium Hypochlorite

Observation 9.B Response:

The cleaning products we are using meet the USP requirements and provide appropriate coverage of organisms. Even though our cleaning program already meets the legal requirements, we are taking this opportunity to make further improvements and go beyond what is required. We have purchased a Sanosil Halo Fogger. This system uses 5% Hydrogen Peroxide and 0.01% Ionic Silver for surface disinfection. We will begin using this as an additional method of disinfection for our cleanroom. We will also be working with Med Effect to validate our disinfection program. Please see the attached invoice.

Timeline: In progress.

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

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

Observation 9.C Response:

The USP <797> requires the use of sterile 70% isopropyl alcohol and non-shedding wipes. It does not require the use of sterile wipes; however, we agree to change our procedure to use sterile, non-shedding wipes as recommended by the FDA. We have already ordered and received these items and we are now using them. We will update our SOPs to reflect this change.

Timeline: Completed.

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 10 Response:

Since our inspection in 2013, we have implemented the use of sterile gowning and gloving which is beyond the requirements of the USP <797>. At the time of our inspection we were still working on a solution to implement the use of sterile goggles. Attached is a service agreement with Prudential Cleanroom Services. They will begin providing all of our sterile gowning and sterile goggles.

Timeline: This will be completed by September 2014.

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 480 lots of drug products manufactured between 4/16/13 and 6/23/14 revealed that your firm produced approximately 225 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.

Observation 11. A Response:

We will develop a written testing program to assess stability. We are working with DynaLabs to develop this program and to begin all necessary testing and documentation.

Timeline: We are working with DynaLabs to determine the time necessary for this to be completed.

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 480 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

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

Observation 11. B Response:

We will begin conducting anti-microbial effectiveness testing on CSPs containing preservatives. We will be working with DynaLabs to develop a program to begin this testing.

Timeline: We are working with DynaLabs to determine the time necessary for this to be completed.

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 480 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.

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

Observation 12 Response:

The USP Chapter <797> does not require potency testing nor does the current Texas Pharmacy Law. However, we have begun potency testing in order to further improve our quality assurance program. We have a plan in place to begin potency testing on all CSPs. We have already started potency testing on all CSPs with active ingredients that can be potency tested by DynaLabs. We are looking for other labs to test active ingredients that DynaLabs does not currently test for.

Timeline: Our estimated completion time is still being determined. It is dependent on locating alternative third party labs to accommodate our needs.

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 0.2 micron filter 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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Observation 13 Response:

We are working to improve documentation on our production logs. We were not documenting this information on our production logs at the time of our 2013 inspection. We began recording this information in May 2013. During the initial transition period, there were some log sheets still missing this data as we continued to work on re-training and re-educating the staff on documentation requirements. We have implemented an additional check off by the pharmacist to make sure all the required information has been documented.

We acknowledge that there were some logs lacking complete information, but the lot listed as an example in this observation was not missing the lot number for the filter. We have attached a copy of the original production log for Lipotocin Lot# N04302014@18 as it was provided to the investigator. The documentation for the 0.2 micron filter used in the sterilization of this lot can be found on the second page and is hand written. It has been highlighted in yellow on this copy for your convenience.

Timeline: The implementation of documentation of the lot numbers of the filters has been completed. We are still working on improving the instructions on the formula sheets for all CSPs.

It is our goal to have corrected or to have started the necessary process to correct all the observations from our 2014 inspection before January 2015. We will take any additional feedback or recommendations from the FDA into consideration as well.

Sincerely,

Kristi Kubosh, PharmD, RPh
Pharmacist in Charge
NuVision Pharmacy
4001 McEwen Rd, Suite 100
Dallas, TX 75244
Phone: 214-347-4008 ext 102
Fax: 888-839-0241