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	03/18/2013 - 04/16/2013* FEI NUMBER 3010087152

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Dr. Kristi A. Kubosh, PharmD., RPh, President, Pharmacist In Charge

FIRM NAME	STREET ADDRESS
NuVision Pharmacy, Inc.	4001 McEwen Road Suite 110
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Dallas, TX 75244	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

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

Specifically,

A. Your firm does not have procedures to prevent microbiological contaimination of injectable drug products, including procedures for the validation of asceptic processes. For example:

a. Media Fills require operators to aseptically fill (b) [redacted] in the ISO 5 clean room. (b) (4) [redacted] are designated as positive controls and (b) [redacted] are used to simulate the process. Your media fill process is deficient in that:

1. Media fills do not simulate aseptic processing operations or reflect worst case processing conditions including:
   - All vial sizes used in routine fill operations are not evaluated;
   - The maximum lot size of (b) vials has not been simulated. For example (b), 10ml vials of Methylcobalamin, Lot N11062012@11 were filled on 11/8/12;
   - Do not include all interventions and (b) (4) [redacted];
   - The aseptic assembly of equipment (e.g., at start-up, during processing) was not included.
2. Investigations are not conducted to determine the root cause and identification of microbial organisms in one or more of the test vials or lack of growth in the control vials. For example:

Operator	Date	Incubation Temp	Length of Incubation	Vial growth observed	Firm's Conclusion

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(b)	1/11/13	RT	14 days	4	Pass
(b)	10/15/12	RT	14 days	4, 5	Pass
(b)	9/18/12	RT	17 days	Control Vial 2&3 no growth	Pass

In addition, the date the media fill vials were removed from incubation and examined were not documented; therefore, there is no assurance the vials were incubated for the entire 14-day period.

b. Your firm failed to validate (b) (4), which are used to sterilize injectable drug products and (b) (4) used to sterilize equipment. According to your (b) (4) operator, drug products are processed using the "liquid" cycle which utilizes a (b) (4) sterilization time (b) (4) SOP 6.023.2, entitled (b) (4) Efficiency Validation", date January 2013 describes the process for using the biological indicators, (b) indicators and (b) strips which are used to routinely monitor the performance of the (b) (4) The (b) (4) operator stated on a monthly basis one strip is placed in an (b) (4) bag and processed with a full load of product and equipment. (b) indicators are included in the first product and equipment load each processing day. The SOP does not define the frequency these monitoring devices should be used. During the review of records provided during the inspection which documented the use of biological and (b) indicators, I observed the following:

(b) (4) ID	BI Spore Strip Date of last test	(b) (4) Indicator date of last test
(b) (4) (product)	No monitoring performed in August 2012	No Documentation
(b) (4) (product)	No monitoring performed in August 2012	No Documentation
(b) (4) (equipment)	No monitoring performed in August 2012	No Documentation

Examples of injectable drug products which are (b) (4) sterilized include:

- Vitamin A, 10mL;
- DHEA, 10mL;
- Vitamin D3, 10mL;
- Vitamin K2, 30mL;
- Olive Oil for Testosterone Injection;
- Curcumin, 10mL;

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- DMSO, 50mL.

For example the following injectable drug products were processed in the (b) (4) :

- Curcumin 10ML, 5MG/ML INJ, Lot Number N10182012@12
- Vitamin K2 10ML (Menaquinone) 10MG/ML INJ, Lot Number N10152012@19
- Silymarin Extract 80%, 30ML 50MG/ML Injectable, Lot Number N103032012@4
- DMSO 50ML 99% INJ, Lot Number N05102012@4

c. Your firm failed to validate the (b) (4) used for the sterilization of injectable drug products. In addition, only the (b) (4) are certified for bacterial retention. For example the following (b) are available for use during aseptic filtration processes:

(b) (4)

The following drug products were processed using (b) (4) :

- Methycobalamin, 30 ml 1mg/mL, Lot N01232013@4; Baxa 50mm
- Curcumin 10ML, 5mg/mL INJ, Lot Number N02142013@8; DMSO Safe Teflon
- Pancreas 10ML 2 mg/mL N01162013@2; Zap Cap
- Ascorbic Acid 100ML, 500 mg/mL, Lot N01222013@3; Supor Capsule
- Methylcobalamin 30ml, 1 mg/mL; Lot N03182013@3; Fast Cap

B. Your firm's procedures designed to prevent microbial contaimination of injectable drug products have not been established. For example:

a. Your firm performs aseptic filling of injectable drug products Sermorelin/GHRP-6 and HCG 5K Lyophilized 5000 units Powder in an ISO 5 hood, the sterile (b) (4) products in partially stoppered vials are transferred out of the ISO 5 work area uncovered and exposed to an ISO 7 conditions prior to being placed in the lyophilizer. In addition, the lyophilizer is not sterilized prior to processing

injectable drug products. For example the following lots of injectable drug product were lyophilized and distributed by your firm:

- Sermorelin/GHRP-6; Lot N10172012@11
- HCG 5K Lyophilized 5000 U Powder; Lot N01292013@15

b. Your firm uses (b) (4) which are not labeled as sterile and pyrogen free to (b) (4) r injectable drug products including Curcumin and Pancreas Inj. prior to (b) (4) the product through a (b) (4) . You have not provided data to demonstrate the (b) (4) are non-shedding and do not impact the quality, safety and purity of the drug products. For example:

- Curcumin 10 ml 5 mg/ml Inj. Lot N02142013@8
- Pancreas 10 mL 2mg/ml INJ, Lot N01162013@2

C. You have not conducted smoke studies performed under dynamic conditions to ensure the flow pattern of filtered air in the ISO Class 5 area do not adversely impact the quality of injectable drug products.

OBSERVATION 2

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. Your firm received a complaint for 1 vial of Methylcobalamin 1mg/ml 30 mL, lot N01232012@4 on 1/31/13. The complaint reported 6 patients that received injections for the same via complained of fever, flu-like symptoms, chills and soreness at the injection site. As a result of the complaint, your firm initiated a recall in an attempt to retrieve unused product from the affected lot. The complaint vial was returned to your firm and tested for endotoxin, no sterility testing was conducted. Your investigation did not include additional sterility testing of the complaint sample or a retain sample. In addition, the investigation did not extend to other batches or identify the root cause of the complaint.

b. Potency failures reported for Vitamin D and combination injectable drug products such as M.I.C Injection, M.I.C/SuperB/L-Carnitine, Vitamin B Complex Methycobalamin are not supported by data to substantiate the firm's

decision to release future batches of product without performing potency testing. Potency failures were attributed to the inability of the method to adequately detect the components in the drug product; however, no investigation was performed to determine of the root cause for the failure and subsequent batches of product were released without testing including:

- Vitamin D3, N01092013@7
- MIC Injection, Lot N02042013@20
- MIC/MB-12/B6, Lot N02182013@8

Furthermore, a formal procedure for handling out of specification tests results or non-conforming tests has not been established. The firm has a procedure in place for "Skip Batch Potency Testing", which includes provisions for the evaluation of a compound not meeting expected parameters, but only requires a review of the formula and compounding technique. In addition, a root cause determination is not required by the policy to ensure adequacy of corrective/preventive actions or full documentation of such activities.

c. According to the contract laboratory summary report provided during the inspection, between April 2012 and March 2013, there were approximately 110 confirmed potency failures for injectable drug products processed by your firm. No investigation has been performed to determine the root cause of the failures or the impact of the failure on other batches of drug product processed by your firm. The following undistributed lots of injectable drug products are representative of failed potency testing:

Product	Lot number	Result (Specification (b) (4))
Vitamin D3	N07202012@4	212%
Chromium	N07062012@1	118%
EDTA Disodium	N03042013@3	117%
Vitamin D3	N11302012@10	0%
Prolotherapy Solution 12.5/1%	N12172012@1	Procaine 24.3% Dextrose 117%
Procaine Buffered	N01032013@13	79.5%
Vitamin D3	N11142012@1	Not detected

d. Your firm has not investigated the source or composition of fibers identified in injectable drug products which have been aseptically filled. During the time period of 9/14/12 to 3/26/13; approximately 80 lots were documented on the (b) (4) Problem vial and count difference log from IV lab to labeling" as having vials which contained fibers and/or

particles.

In addition, injectable drug products produced by your firm are filled in amber colored vials. Each vial is 100% inspected using a non-validated method to identify and remove vials containing fibers and/or particulates. For example, an operator was observed inspecting vials using a black and white background however, there is no data to demonstrate particulates and fibers can be adequately identified in amber vials using this process. Products in which vials with fibers were removed and the remaining vials were distributed:

Product	Lot Number	# vials filled	# vials with fibers	% of vials with fibers
Prozolone	N02280013@11	(b) (4)	53 vials	(b)
Procaine 1%	N11302012@4	(b) (4)	65 vials	(b)
Ascorbic Acid	N12102012@1	(b) (4)	52 vials	(b)

OBSERVATION 3

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

Specifically,

a. Your firm has no scientific sterility and potency data to justify the assigned Beyond Use Dates ranging from 180 to 720 days at room temperature for any preserved or preservative free injectable drug products. For example,

Product	Lot#	Allowed BUD	Actual BUD
Methylcobalamin 1 mg/ml 30 mL	N01232013@4	365 days	331 days
DMSO 50mL 99% Inj	N05102012@4	720 days	338 days
DMPS 5 ML 50mg/mL	N01292013@16	365 days	359 days

b. You firm failed to perform any anti-microbial effectiveness testing to determine whether (b) (4), (b) (4) inhibit microbial growth in your injectable drug products through their BUD period. These preservatives are used in the following injectable drug products:

Preservative	Product
(b) (4)	Testosterone
	MIC W/Meth B-12
	M.I.C

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	Methylcobalamin
	Thymus Substance
	S.O.D Preserved
	Lipotocin Plus
	Ferroplex
(b) (4)	Vitamin D3 Preserve
(b) (4)	Methyl B-12/Methyl Folic Acid
	Dextrose 50%

OBSERVATION 4

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

Specifically,

a. Testing for viable and non-viable particulate air monitoring is not performed in the ISO 5 and ISO 7 work areas on each day of injectable drug product production. Currently monitoring is only conducted every (b) (4) by a third-party contractor under static conditions. The most recent testing for viable air monitoring was on 1/4/2013.
During the August 2012 certification, an action level excursion of 18 CFU and 1 CFU of fungus was reported in the ISO 7 area adjacent to the ISO 7 gowning room. The report indicates the 18CFU excursion exceeded the recommended action level; no investigation was conducted.

b. You have not established a written procedure for monitoring of personnel glove testing which includes method for testing and evaluating the gloves of aseptic filling operators or the frequency of glove monitoring. A spreadsheet containing glove test results was provided; however, this record does not include raw data for the incubation dates and incubation temperatures. In addition, no data was available for aseptic fill employees (b) and (b)

OBSERVATION 5

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

Specifically,

a. your firm has not conducted disinfectant effectiveness studies to demonstrate non-sterile disinfectants used to clean the walls, floors, ceiling and work surfaces in the ISO 5 and 7 areas are capable of sufficiently reducing bioburden.

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Currently, your firm utilizes the following non-sterile disinfectants to clean the ISO 5 and ISO 7 areas:

- (b) (4) [redacted]
- (b) [redacted]

Furthermore SOP 5.001, entitled "Cleaning and Disinfection" stated a (b) (4) [redacted] is used to clean the aseptic processing area; you are currently using (b) [redacted] at a (b) [redacted] concentration. In addition, there is no evidence you are rotating disinfectants as required by the procedure.

b. According to the IV Room Cleaning Log for February 2013 no cleaning was performed in the ISO 5 and ISO 7 areas for the time period 1/31-2/20/13. The production log indicates (b) [redacted] lots of injectable drug products were processed during this timeframe. For example:

- Methylcobalamin Buffered, Lot N01232013@4, (b) [redacted] vials were processed on 1/31/13;
- L-Lysine 200mg/ml, lot N02042013@10, (b) [redacted] vials were processes on 2/5/13;
- Cyanocobalamin 1mg/ml, Lot N02112013@8, (b) [redacted] vials were processed on 2/12/13;
- MIC W/MB-12 B6, Lot N02182013@8, (b) [redacted] vials were processed on 2/20/13.

OBSERVATION 6

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

Specifically,

a. Pressure gauges have not been installed in the IV lab to allow for the monitoring of pressure differentials between the ISO 5 and ISO 7 processing areas. Injectable drug products are filled in an ISO 5 area which is separated from the ISO 7 area by a plastic laminar curtain. There is no assurance that the appropriate pressure is maintained in the ISO 5 during accepting processing operations.

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OBSERVATION 7

Each batch of drug product required to be free of objectionable microorganisms is not tested through appropriate laboratory testing.

Specifically, your firm produced and distributed approximately (b) lots of sterile, injectable drug products for the period between April 2012 and March 2013. The sterility testing performed by the contract laboratory consisted of a "Plate Contamination" test which utilizes (b) (4) ; or (b) (4) test. However, your firm provided no data to demonstrate that either method is equivalent to or superior than the USP 71 sterility method.

Sterility testing, as defined under USP 71, was conducted for only 3 lots during the designated time period. Hyaluronic Acid N10162012@5 and L-Tyrosine, Lot N11072012@12 on 12/5/12, Procaine N11302012@4, L-Tyrosine N11072012@12 on 3/15/13. In addition, testing for endotoxin was limited to about only 20 lots.

Examples of the testing for "Plate Contamination" and (b) (4) testing include the following:

- Hyaluronic Acid, Lot N10162012@5 (Plate Contaimination)
- Methycobalamin, Lot N11062012@11 (b) (4)

OBSERVATION 8

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

Specifically, between April 2012 and March 2013, approximately (b) out of (b) lots (approximately 29%) of injectable drug products produced and distributed by your firm were not tested for potency. For example:

- Vitamin D3, Lot N01232013@2
- Methylcobalamin, Lot N02272013@11

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OBSERVATION 9

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. You failed to validate the lyophilization cycles used to process injectable drug products Human Chorionic Gonadotropin Lyophilized 5,000 Units Powder and Sermorelin/GHRP-6. Your firm utilizes a (b) (4) with the following cycle parameters to process these products.

b. Your firm does not maintain procedures and/or specifications for the use of the following sterilization monitoring strips used with the (b) (4) including, Spore test strips, (b) (4) sterilization monitors and (b) (4) Strips.

OBSERVATION 10

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

Specifically,

a. Your firm does not consistently document the name/lot number of the (b) (4) used in the processing of injectable, drug products. For example, MIC N02182013@8 does not include documentation of the type and lot number of the (b) used or the lot numbers of the (b) (4), stoppers and vials used to process the injectable drug product. Formula Worksheets that do not require adequate sterile (b) (4) documentation include:

- Hyaluronic Acid 10ML NON X-Link INJ. 10MG/ML Inj, Formula 1075
- MIC 30ML Preserved INJ, Formula 396
- Lipotocin Plus Inj., Formula 20918

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OBSERVATION 11

The in process control procedures were deficient in that they did not include an examination of the adequacy of mixing to assure uniformity and homogeneity.

Specifically, there is no data to support the extended mix time of (b) (4) for DMPS Lot 01292013@ 16 does not adversely impact the stability of the drug product throughout its BUD. Production records for DMPS Lot 01292013@ 16, instructs the operator to (b) (4) ". Mixing of the batch was initiated on 1/28/13 @ 4:30 PM and completed on 1/31/13 @2:00PM. The lot was not (b) (4) until 1/31/13 @5:00PM. The product is mixed in a clear beaker which is covered with (b) (4) on a countertop. There is no data to assure the (b) (4) cover is capable of preventing oxidation of DMPS during the mixing process.

OBSERVATION 12

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

Specifically, SOP 7.011, entitled "Gowning and Gloving", Approval date April 2012, described your firms procedure for gowning requirements for inside of the ISO 5 curtained barrier area in which the operators whole body is within the curtained ISO 5 fill area. The procedure does not require the use of sterile gowning materials such as masks and gloves. The procedure also does not require operators to wear goggles during aseptic filling of injectable drug products to prevent skin exposure. In addition, the outer gowns worn by the operators do not fully cover employees clothing that is worn outside the facility; the gown only provides coverage to the area between the operators' knees and the feet.

*** DATES OF INSPECTION:**
03/18/2013(Mon), 03/19/2013(Tue), 03/20/2013(Wed), 03/21/2013(Thu), 03/22/2013(Fri), 03/25/2013(Mon), 03/26/2013(Tue), 03/27/2013(Wed), 03/28/2013(Thu), 03/29/2013(Fri), 04/02/2013(Tue), 04/04/2013(Thu), 04/05/2013(Fri), 04/08/2013(Mon), 04/09/2013(Tue), 04/10/2013(Wed), 04/11/2013(Thu), 04/12/2013(Fri), 04/15/2013(Mon), 04/16/2013(Tue)

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