DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
19701 Fairchild Irvine, CA 92612-2445 (949)608-2900 Fax: (949)608-4417	6/13/2017-6/29/2017* FEI NUMBER 3012228279

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Nayan Patel , President and Pharmacist-in-Charge

FIRM NAME	STREET ADDRESS
Auro Pharmacies Inc	511 S Harbor Blvd Ste F
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
La Habra, CA 90631-9375	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 I OBSERVED:

OBSERVATION 1

The responsibilities and procedures applicable to the quality control unit are not fully followed.

Specifically, the quality control unit does not take full responsibility in ensuring that sterile drug products prepared by your firm meet all the required specifications before release and that the firm's operations follow established standard operating procedures or approved documents. For example,

A. Methylcobalamin 1 mg/mL injection lot 170214@1 was tested at a contract lab, (b) (4), with active ingredient assay result of (b) (4)% which failed the specification of (b) (4) %. Even through the associated investigation memo (OOS 00010) concluded that the lot was placed into quarantine and subsequently destroyed, the batch record was approved on 5/2/2017 for release and the product batch was distributed to customers.

B. Methylcobalamin 1 mg/mL injection lot 170310@1 was tested at a contract lab, (b) (4), with active ingredient assay result of (b) (4)% which failed the specification of (b) (4) %. No OOS investigation was generated. The batch record was approved on 3/30/2017 for release and the product batch was distributed to customers.

C. According to your firm's PIC, DMSO 99.9% Infusion product is required by your firm to be (b) (4) sterilized via (b) (4) . For (b) (4) lots of DMSO product prepared in 2017 (170210@1, 170322@2, and 170504@2), although the lots were (b) (4) , none of the associated batch records contained (b) (4) forms. These batch records were approved by QA and the product lots were released without verifying the product sterilization status.

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D. The (b) (4) forms and (b) (4) forms associated with the sterilization of (b) (4) and various parts required for the preparation of Ascorbic Acid 500 mg/mL injection product lot 170511@3 were included in the batch record but were not approved. However, the batch record for this lot was approved and the product lot was released by QA.

E. The instructions in the master formulation documents are not aligned with the actual manufacturing practices documented in the batch records. The product batch records were approved by your firm's quality unit without identifying such discrepancies. For example,
1. The DMSO 99.9% Infusion product master formulation sheet MF-SC-01.1049.01, effective 8-Feb-17, instructs to (b) (4) The drug product preparation does not use this type of (b) (4). Instead, a (b) (4) is used.
2. The DMSO 99.9% Infusion product master formulation sheet does not require (b) (4) sterilization. In practice, the finished product is (b) (4).
3. The Aminosyn 10% injection product master formulation sheet MF-SC-01.1148.01, effective 5-May-17, requires the use of (b) (4) for (b) (4) In practice (b) (4) preparation as per your firm's Pharmacist-in-Charge.

F. Personnel engaged in drug product preparation and supporting activities lack adequate training. For example,
1. There is no training record established for anyone involved in the receiving inspection of materials under SOP-GC-01.3000.01 Receiving and Inspection, effective 12-Dec-16.
2. There is no training record for anyone involved in product labeling operation that is governed by SOP-SC-01.1159.01 Labeling of Finished Product, effective 6-December-16.
3. There is no training record for operators performing the vial and stopper washing operation.
4. There is no training record established for operators performing 100% visual check of the unlabeled product vials.

G. SOP-SC-01.1100.01 Document Numbering System, effective 29-Jul-16, requires the use of document change request (DCR) form FR-SC-02-1100.01 for creating new documents or revising existing documents and such DCR shall be reviewed and approved by QA. None of the firm's SOPs initiation or revision used such DCR form.

H. SOP-SC-01.1145.01 Recall Policy Procedure, effective 29-Jul-16, requires the use of a (b) (4) log to identify dispensed product. No such (b) (4) logs are used by the firm.

OBSERVATION 2

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

Specifically, the test methods used to release your firm's sterile drug products are either not validated or verified for their intended use. For example,

A. Your firm's sterile drug products are sent to a contract lab, (b) (4), for assay test. According to (b) (4) certificate of analysis, most of the assay test procedures are not validated. Your firm used the test results from these non-validated procedures to release drug products.

B. The Methylcobalamin 1 mg/mL injection product lot 170214@1 failed assay test at (b) (4) with a non-validated HPLC procedure (OOS-00010). Your firm retested the product lot in-house with an (b) (4) instrument and released the product lot based on the passing results. This (b) (4) in-house test method was not established and not validated.

C. Your firm has conducted sterility, endotoxin, and particulate tests in-house to release the sterile drug products since May 2017. None of these test methods used in-house have been validated or verified.

OBSERVATION 3

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

Specifically, the gowning is not appropriate for the sterile filtration operation inside the clean room (b) (4). For example,

A. On 6/13/2017 during a walk through inspection, (b) (4) operators were observed with partially exposed skin inside the ISO 7 clean room (b) (4). The facial area around the eyes was not covered. Even though operators used goggles to cover the skin around eyes when working at the ISO 5 LFH, the goggles were put on when operators were inside the ISO 7 room (b) (4). The operators were observed performing aseptic preparation of Magnesium Chloride drug product lot 170613@1 on that day. According to section 3.2.2.11 of SOP-SC-01.1300.02 Gowning and Gowning Certification effective 16-Dec-16, (b) (4) (b) (4)

B. The goggles used by operators during Magnesium Chloride drug product lot 170613@1 aseptic preparation on 6/13/2017 were not sterile. Section 3.2.7 of SOP-SC-01.1300.02 states "(b) (4)

OBSERVATION 4
Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established and followed.

Specifically, your firm's aseptic preparation of drug product is not appropriate. For example,

During a walk through inspection on 6/13/2017, an operator was seen filling Magnesium Chloride drug product lot 170612@1 (b) (4) inside the ISO 5 LFH. The operator (b) (4)

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OBSERVATION 5

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

Specifically,

A. The ISO 5 LFH certification performed in February 2017 did not include active air viable count assessment.

B. The certification of all clean areas including ISO 5 LFHs and ISO 7 rooms performed in February 2017 were performed only at the (b) (4) condition.

C. Your firm does not perform active air monitoring during aseptic processing of drug product.

D. Your firm does not perform growth promotion tests for every batch of media (b) (4) that were prepared in-house for environmental monitoring during sterile drug product preparation to ensure that the media used can support microbial growth. For example, the following batches of (b) (4) media were not tested for growth promotion (b) (4)

1. Lot 170206/20 and lot 170124/21 used for environmental monitoring during the preparation of Methylcobalamin 1 mg/min injection product lot 170214@1. The product lot was released on 5/2/2017.
2. Lot 170503 and lot 170424 used for environmental monitoring during the preparation of Ascorbic Acid 500 mg/mL injection product lot 170511@3. The product lot was released on 5/26/2017.

OBSERVATION 6

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

Specifically, the cleaning practice used in your firm's aseptic filling operation areas is not appropriate. For example,

A. No sporicidal agent is used in the clean rooms other than inside the ISO 5 LFH.

B. The surface of equipment used for aseptic filling process inside ISO 5 LFH, such as peristaltic pump, was never cleaned with sporicidal agent.

C. According to section 3.2 of SOP-SC-01.1305.02 Cleaning of Sterile Compounding Facility effective 9-December-16 "(b) (4) ." There are at least 3 instances shown below where the (b) (4) cleaning on walls and ceilings was not performed. Sterile drug products were prepared during these weeks. No deviation investigation or justification was documented.
   1. The week of 5/08/2017. The cleaning form was approved.
   2. The week of 5/15/2017. The cleaning form was approved.
   3. The week of 5/22/2017. The cleaning form was not approved.

OBSERVATION 7

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

Specifically,

E. Your firm's current environmental monitoring program does not include any viable and non-viable particulate monitoring during aseptic filling of drug product inside ISO 5 LFH.

F. Pressure differentials are monitored (b) (4) in the classified clean rooms. However such pressure differentials are not monitored at the time during aseptic filling of drug products.

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G. Your firm takes (b) (4) from the ISO5 LFH (b) (4) as part of the (b) (4) EM monitoring. No justification is established on why no other surface samples are taken from the inner walls of the ISO5 LFH.

H. Your firm has no justification for the alert and action limits established for environmental monitoring. This deficiency was cited during the last FDA inspection. For example, alert and action limits for settling plates used during aseptic filling of drug product in ISO 5 LFH are set incorrectly at (b)(4) CFU/Plate and (b)(CFU/Plate respectively. During the following drug product preparations, the settling plates showed results that exceeded the required limit of (b) (4) CFU per plate.
   1. 3 CFUs were detected from settling plate for Ascorbic Acid 500 mg/mL injection product lot 170511@2 prepared in ISO 5 LFH (b) (4).
   2. 1 CFU was detected from settling plate for Magnesium Chloride 200 mg/mL injection product lot 170518@1 prepared in ISO 5 LFH (b) (4).

I. Your firm has not performed trending and periodic evaluation of the environmental monitoring results.

OBSERVATION 8
The flow of drug product containers and closures though the building is not designed to prevent contamination.

Specifically, the vials and stoppers used for your firm's sterile products are not cleaned appropriately before being depyrogenated or sterilized. For example,

A. The vials were washed in a non-classified room (b) (4). On 6/13/2017 during a walk through inspection, the door to room (b) (4) was widely open and employees working inside the room (b) (4) were seen wearing street shoes.

B. According to section 3.1 of SOP-SC-01.1620.01 Vial Washer -(b) (4) effective 22-

August-16, the wash machine requires (b) (4) of air pressure and (b) (4) of (b) (4) at the inlet. However, (b) (4) water was used by your firm to operate the wash machine for vials. Your firm's (b) (4) system has not been operational yet at the time of this inspection. Vials washed by this machine are used for all sterile drug products prepared by your firm.

C. According to your firm's operator, (b) (4) However, the entire vial washing operation was not recorded even though such operation should be documented on the form SOP-FR-02.1620.01 Vial Washer(b) (4) effective 22-Aug-16. There is no evidence that the vials used for drug product filling were washed and rinsed with(b) (4) prior to being (b) (4)

D. According to your firm's operator, (b) (4) There is no documented evidence for such final (b) (4) rinse on washed stoppers. The stoppers are used for all firm's sterile drug products.

OBSERVATION 9

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, your firm's 100% visual inspection of the finished drug product vials is inadequate. For example,

A. There is no written procedure describing the process for 100% visual inspection of filled drug product vials. This deficiency was cited from the last FDA inspection.

B. On 6/13/2017 during a walk through inspection at the product labeling room, an operator was seen performing visual inspection of the filled AminoSyn 10% drug product lot 170523@2 by (b) (4) to inspection. There is no documented training record for this operator on the 100% visual drug product inspection. This deficiency was cited from the last FDA inspection.

C. According to the batch records, your firm did not perform 100% visual inspection of the filled drug product vials. The field for 100% visual inspection of finished drug product vials were either marked N/A or the field is not available from the master batch record. For example, the following drug product batch records showed that the 100% visual inspection of the filled drug product vials were not performed and the batches were released.

- Ascorbic Acid 500 mg/mL injection lot 170505@1 released on 5/23/2017.
- Ascorbic Acid 500 mg/mL injection lot 170511@2 released on 5/26/2017.
- Ascorbic Acid 500 mg/mL injection lot 170511@3 released on 5/26/2017.
- Glutathione 200 mg/mL injection lot 170526@1 released on 6/9/2017.
- DMSO 99.9% infusion lot 170210@1 released on 3/10/2017.

OBSERVATION 10

Written records are not always made of investigations into unexplained discrepancies and the failure of a batch or any of its components to meet specifications.

Specifically, your firm failed to initiate OOS investigations into EM failures associated with drug product preparation or failed to conduct thorough investigations to understand the root causes of some of the product testing result failures. For example,

A. Your firm failed to conduct thorough investigations on the product assay failures associated with the finished products,

1. The assay result of Procaine HCl 10 gm/mL injection product lot 170131@1 was reported as (b) (4)% which exceeded the specification (b) (4) % and the failure result was confirmed by the contract testing lab (b) (4) as shown in OOS report 0003. No detailed manufacturing investigation was carried out to identify the possible root causes. The lot was destroyed.
2. The assay result of Glutamine 30 mg/mL injection product lot 170221@2 was reported as (b) (4)% which failed the specification (b) (4) % as shown in OOS report 0007. No detailed manufacturing investigation was carried out to identify the possible root causes. A theoretical explanation with respect to the moisture content of the API was provided for the

failure. However, such explanation was not justified as all Glutamine 30 mg/mL injection product batches use the same API. The lot was destroyed.

3. The assay result of Glutathione 200 mg/mL injection lot 170208@1 was reported as (b) (4)% which failed the specification (b) (4) % as shown in OOS report 0008. No detailed manufacturing investigation was carried out to identify the possible root causes. A theoretical explanation with respect to the moisture content of the API was provided for the failure. However, such explanation was not justified as all Glutathione 200 mg/mL injection product batches use the same API. The lot was destroyed.
4. According to OOS report 00010, the assay results of Methylcobalamin 1 mg/mL injection lot170214@1 and the MIC B12 B6 product lot 170204@1 failed specifications as shown below. No manufacturing investigation was conducted to identify the possible root causes. The investigation memo attributed the failure results to the test procedure bias due to the presence (b) (4) . However, no corrective action was taken to address this possible root cause.
   - For Methylcobalamin 1 mg/mL lot 170214@1, the assay result was (b) (4)% against the specification(b) (4)
   - For MIC B12 B6 product lot 170204@1, the assay results are shown below:
     - Methionine (L): (b) (4)% against specification(b) (4) %
     - Pyridoxine HCl (b) (4)% against specification (b) (4) %
     - Methylcobalamin: (b) (4)% against specification (b) (4) %

B. Your firm failed to investigate action level excursion involving environmental monitoring results,

1. The settling plate sampled from ISO 5 LFH (b) (4) on 5/11/2017 showed 3 CFUs during preparation of Ascorbic Acid 500 mg injection product lot 170511@2 by operator (b) (6). The batch was released on 5/26/2017.
2. The settling plate sampled from ISO5 LFH (b) (4) on 5/18/2017 showed 1 CFU during preparation of Magnesium Chloride 200 mg/mL injection product lot 170518@1 by operator (b) (6). The batch was released on 6/2/2017.

3. The microbial surface sample taken for room (b) (4) (ISO 8 (b) (4) ISO 7 room (b) (4) on 4/28/2017 showed TNTC. The following four products were filled on 4/28/2017 and all these four product batches were released.
   - Methylcobalamin 10 mg/mL injection lot 170427@1 released on 5/16/2017.
   - Calcium Chloride 100 mg/mL injection lot 170428@1 released on 5/16/2017.
   - Methyltetrahydrofolate 5 mg/mL injection lot 170427@3 released on 5/16/2017.
   - Phosphatidylcholine 35 mg/mL injection lot 170427@2 released on 5/18/2017.
4. The microbial surface sample take from ISO 5 LFH 0502 in room (b) (4) on 3/1/2017 showed 31 CFUs. Even through no product was prepared in LFH (b) (4) on that day, no OOS investigation was initiated to find root cause.

C. Your firm failed to use the proper OOS investigation form FR-SC-02.1381.01 Out of Specification Monitoring Report effective 13-Dec-16 that is required by the SOP-SC-01.1380.01 Out of Specification Investigations effective 13-Dec-16 to carry out the OOS investigations.

OBSERVATION 11

Investigations of an unexplained discrepancy and a failure of a batch or any of its components to meet any of its specifications did not extend to other batches of the same drug product and other drug products that may have been associated with the specific failure or discrepancy.

Specifically, the investigation documented in NCR-17-0020 for Methylcobalamin 2 mg/mL injection product lot 170501@2 recognized that the assay test procedure for the product used by the contract lab, (b) (4), was not validated. However, the investigation failed to extend the evaluation of assay test procedures used by (b) (4) to your firm's other drug products. It appeared that most of the assay test procedures used by (b) (4) on the firm's finished drug products were not validated as shown on (b) (4) certificate of analyses. No corrective actions have been taken by your firm to address this deficiency at the time of this inspection.

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OBSERVATION 12
Results of stability testing are not used in determining expiration dates.

Specifically, the shelf life of your firm's products is not supported by stability studies. For example,

A. All sterile drug products prepared by your firm are assigned a 6 month shelf life. There is no stability study carried out on each drug product to demonstrate that the products can maintain their identity, strength, quality, and purity at the end of the shelf life.

B. The (b) (4) on-going product stability studies for Ascorbic Acid 500 mg/mL injection with preservative and Glutathione 200 mg/mL injection without preservative are deficient in that
   1. These studies were initiated without approved stability study protocols.
   2. The studies did not follow the written study protocols with respect to storage conditions and test frequency.
   3. The analytical methods used for the stability studies at contract lab, (b) (4), are not validated to demonstrate that they are stability indicating.

OBSERVATION 13
Laboratory controls do not include the establishment of scientifically sound and appropriate specifications, sampling plans and test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality and purity.

Specifically,

A. The preservative content in your sterile drug products was not determined as part of product release testing.

B. You have not demonstrated the effectiveness of the antimicrobial preservative ingredient used in your sterile drug products. According to section 3.2 of SOP-SC-01.1340.01 Antimicrobial Effectiveness Testing, effective 29-Jul-16, (b) (4)

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(b) (4)
(b) (4)

***DATES OF INSPECTION**
6/13/2017(Tue),6/14/2017(Wed),6/15/2017(Thu),6/16/2017(Fri),6/21/2017(Wed),6/22/2017(Thu),6/29/2017(Thu)

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