DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
San Francisco District 1431 Harbor Bay Parkway Alameda, CA 94502-7070 510-337-6700 Industry Information: www.fda.gov/oc/industry	1/20-30/2015
	FEI NUMBER 3011152407

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Hal J. Weaver, Vice President, Operations

FIRM NAME	STREET ADDRESS
AnazaoHealth Corporation	7465 W. Sunset Road, Suite 1200
CITY, STATE AND ZIP CODE	TYPE OF ESTABLISHMENT INSPECTED
Las Vegas, Nevada 89113	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) (WE) OBSERVED

OBSERVATION 1

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

Specifically,

Sterilization (b) (4) were not executed on (b) (4) located in the (b) (4) room, to support the process validation and to ensure that (b) (4) are capable of producing sterile products such as Testosterone 87.5 mg, 100mg, 200mg Pellets.

a. The sterilization (b) (4) for pellets. The firm could not produce documentation on how the (b) (4).

b. On 01/26/2015, the VP of Operations explained that the firm conducted validation studies (VAL-020 and VAL-021) on 11/06/2014, where a mixture of various pellet drug products (e.g.Testosterone and Estradiol pellets) from expired and returned stock was used to test the functionality of the (b) (4) under (b) (4) conditions. The firm did not submit the sample for sterility, endotoxin or potency testing; it only tested to see if (b) (4).

c. This sample used does not represent the characteristics of the actual finished drug pellets nor did it undergo the same compounding steps before the (b) (4) process.

OBSERVATION 2

There is a failure to thoroughly review the failure of a batch or any of its components to meet any of its

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specifications whether or not the batch has been already distributed.

Specifically,

Between September 22, 2014 and January 20, 2015, the following four (4) sterility failures have not been adequately investigated:

i. Testosterone 25 mg Pellet, Lot # 120214-09-KQS-82293
ii. Testosterone 100 mg Pellet, Lot # 120514-04EMMY-82557
iii. Testosterone 200 mg Pellet, Lot # 122014-06KH-83206
iv. Estradiol 10 mg Pellet, Lot # 121114-01SJAFD-82844

The investigation reports for the above mentioned lots, did not contain elements of root cause analysis such as risk assessments, rationale, and scientific justification. The source of the contamination has not been identified.

OBSERVATION 3

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

Specifically,

a. There is no validated expiration date assigned to depyrogenated glass vials and (b) (4) rubber stoppers that are intended for aseptic processing. On 01/21/2015, the firm's management confirmed that it was common practice to keep sterile items for (b) (4). However, the firm has no procedure in place to prevent use beyond expiration. Also, the firm has no documentation to prove sterile container/closure items were not used beyond the (b) (4) expiry.

b. Procedures have not been established for release testing for container and closures (e.g. glass vials, rubber stoppers/caps) to determine whether they meet the criteria for use. There is no documentation to confirm the

quality standards for container and closures.

OBSERVATION 4

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

Specifically,

Although there is analytical data to support the potency of drugs produced, neither its sterility nor endotoxin testing were performed at the labeled shelf life to support the Beyond Use Date dating of the finished product: For example:

In the review of stability studies conducted on 08/13/2013 for MIC w/Cyano & CRCL (Methionine, Inositol, Choline 25/50/50 Cyanocobalamin 1 mg Chromium Chloride 4 mcg), preserved with (b) (4) (Lot (b) (4)), analyzed by (b) (4) , the firm's assigned Beyond Use Date (BUD) exceeded the shortest expiry date of the Bulk Drug Substance. For example, the bulk drug substance Choline Chloride had an expiration date of 06/27/2013. The Beyond Use Date used on the finished product was 07/25/2013.

Your firm did not conduct sterility and endotoxin testing at the labeled shelf life at the (b) (4) time point to support the Beyond Use Date.

OBSERAVATION 5

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

Specifically,

The following observations pertain to the gowning of operators we observed, during the aseptic processing of the following injectable drug products compounded in the ISO 7/ISO 5 Cleanroom ((b) (4) on 01/20/2015:

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i.) MIC w/Cyano 25/50/50/1 mg/ml #250 Lot 012015-1TS-84471 / 30 ml (b) (4) sterilized);
ii.) Testosterone Cyp 200 mg/ml 10 ml #250 Lot 012015-2MC-84477 ((b) (4) sterilized);
iii.) Testosterone Cyp 200 mg/ml 10 ml #250 Lot 012015-3JDS-84483 ((b) (4) sterilized).

a. On 01/22/2015, the Supervisory Pharmacist stated that compounding operators wear the same clothes worn from home (street clothes), underneath their non-sterile gowns. Additionally, we confirmed that non-sterile gowns are worn by operators in the clean room while performing aseptic compounding manipulations in the ISO 5 hoods.

b. On 01/20/2015, the Supervisory Pharmacist stated that goggles used by operators are purchased sterile. They are re-used after being sprayed with (b) (4) and wiped with a a non-sterile wipe. There is no assurance that the goggles have been adequately sterilized after re-use. On 01/20/2015, we observed that non-sterile goggles are used in ISO 5 hoods while performing aseptic compounding operations.

c. On 01/20/2015, we observed operators wearing non-sterile goggles and non-sterile gowns leaning with their upper bodies over the work surfaces inside ISO 5 hoods. The operators were in the process of capping open product vials in the ISO 5 hoods. After capping, they are crimped (sealed) and finished for dispensing.

OBSERVATION 6

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

Specifically,

SOP 501.060, entitled, "General Aseptic Technique", made effective 10/21/2014, Rev 1.0 established requirements for using aseptic technique in any area to minimize contamination. We observed the following:

a. According to SOP 509.100, entitled "Garbing, Antiseptic Hand Cleansing & Donning of Sterile Gloves", made effective 1/14/2015, section 9.5.13 states "check for proper gowning, e.g. skin are not exposed." On 01/20/2015, we observed an operator working in the ISO 5 hood with bare skin exposed around (b) forehead area.

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b. According to SOP 501.060, entitled, "General Aseptic Technique", made effective 10/21/2014, section 9.2.1 states "leaning over the work area over open containers." 01/20/2015, we observed an operator leaning there (b) (4) upper body over the work area inside the ISO 5 hood.

c. On 1/20/2015, we observed that non-sterile wipes were sprayed with (b) (4) and were used to disinfect work surfaces inside the ISO 5 hoods prior to each batch and throughout the sterile compounding operation. Non-sterile items brought into the ISO 5 areas can contaminate the aseptic compounding operations.

d. According to SOP 501.060, section 9.4.5 states "any bottles, vials, or containers should be wiped down with (b) (4) prior to placement in the hood to prevent possible contamination." On 01/20/2015, we observed an operator open and pour a bag of (b) (4) rubber stoppers directly on to the corner surface of an ISO 5 hood, touching the plexi glass side, as well as the back grille side of the ISO 5 hood. These stoppers were seen in various arrangements including bottom side up and down and on their sides.

i. On 01/20/2015, the Supervisory Pharmacist confirmed that the ISO 5 surface was cleaned the morning of 01/20/2015. We observed on 01/20/2015, that the surface in the ISO 5 hood was not re-cleaned before the stoppers were poured onto the surface. Furthermore, the ISO 5 hoods were cleaned with non-sterile wipes that were sprayed with (b) (4).

e. According to SOP 501.060, Section 9.1.1 states (b) (4) ." On 01/20/2015, we observed an operator use sterile forceps that were used to repeatedly pick up sterile rubber stoppers. The same forceps were placed back on the compounding work surface, without disinfecting the surface first; thus possibly contaminating the forceps. Additionally, we observed the operator use the same forceps, to pick up each sterile rubber stopper by the split (a product contact surface), instead of by the rim (a non-product contact surface).

f. According to SOP 501.060, Section 9.4.6 states (b) (4) ." On 01/20/2015, we observed operators spray gloves with (b) (4) inside the ISO 5 hood, holding hands up to the HEPA air briefly, and proceeded with compounding activities. We observed that the sprayed gloves were not allowed to fully air-dry.

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g. Non-sterile (b) (4) are used to clean the ISO 5 hoods. Additionally, there is a lack of scientific justification for using (b) (4) (sporicidal agent) only (b) (4)

OBSERVATION 7

Aseptic processing areas are deficient in that walls are not smooth and/or hard surfaces that are easily cleanable. Specifically,

On 1/21/2015, we observed (b) (4) protruding approximately five inches from the wall, adjacent to the entrance in each of the following ISO 7 clean rooms:

- Room (b) (4) for the compounding (b) (4) sterile drug products (i.e. testosterone & estradiol pellets)
- Room (b) (4) for the compounding of (b) (4) sterilized drug products (e.g. Injectables)

The (b) (4) appeared to have a brownish color, indicative of rust. It was reported that the (b) (4) are not in use. The (b) (4) pose a contamination risk to the ISO 7 and ISO 5 clean room environments because of their difficulty to clean.

OBSERVATION 8

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

Specifically,

a. Growth promotion was not performed for each lot of (b) (4) for environmental and personnel monitoring. Media should be tested for its ability to support microbial growth. Without media qualification, there is no assurance that (b) (4) media can reliably recover microorganisms from the clean room environment. Similarly, growth promotion was not performed on (b) (4) currently used in Media Fills.

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b. The (b) (4) incubation condition ((b) (4)) of (b) (4) media was not validated. Your firm has not verified that (b) (4) media incubated at the above conditions can reliably recover a wide range of microorganisms (including bacteria and mold) from the compounding environment.

c. SOP 9.110 entitled "Sterile Compounding Process Validation" dated 11/20/2013, is currently used to establish requirements for executing media fills. However, this procedure does not require the preparation of a media fill batch record, which is used to document critical information about the media fill, such as, but not limited to, actual compounding operations, worst-case activities, and operator interventions. Your firm currently documents media fills on Form F-402a entitled "AnazaoHealth Employee Gloved Fingertip Sampling and Media-Fill Results Log", which only documents the results of the media fill and not the actual steps.

d. Personnel monitoring of the operator's gloves are not performed each day that a batch of sterile drug is compounded in the ISO 5 areas. Instead, your firm only monitors gloves of (b) (4)

e. Your firm's SOP 500.050, "Environmental Monitoring of the Sterile Compounding Area", Rev 2.0, effective 01/05/2015 is deficient because it lacks written descriptions and justifications/scientific rationale for why each environmental monitoring location was determined. Additionally, there is no documented scientific rationale for not including (b) (4) monitoring in your firm's ISO-classified clean rooms including the ISO 5 areas where sterile drug products are compounded.

OBSERVATION 9

Bulk drug substances used by your outsourcing facility to compound drug products are not each manufactured by an establishment that is registered under section 510 as required by section 503B(a)(2)(C):

Specifically,

On 01/22/2014, the following bulk drug substance manufacturers were identified as not being registered with the FDA:

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1. (b) (4) (supplier of (b) (4)).
2. (b) (4) (supplier of (b) (4)

These raw ingredients are used in the production of the following finished products:
o Compounded Plaquex 50mg/ml 50 ml
o Phosphatidyl Choline 100.42 mg/ml 50 ml
o PPC Special 50/42 mg/ml 50

OBSERVATION 10

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

Specifically,

The following information is not found on some of your drug product labels:
1. The statement, "This is a compounded drug"
2. The date that the drug was compounded.
3. The statement, "Not For Resale"

Furthermore, the following information is not found on the container labels for some drug products you produce:
1. Information to facilitate adverse event reporting: www.fda.gov/medwatch and 1–800–FDA–1088.

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

- Human Chorionic Gonadotropin 6000 units
- Dexpanthenol 250 mg/mL
- DMFS (PF) 50 mg/mL
- Testosterone Cypionate (Grape Seed Oil) 200 mg/mL
- Pyridoxine (B6) 100 mg/mL

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Additionally, the label for your DMFS (PF) 50 mg/mL drug product does not contain the established name of the drug.

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or

2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgement, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."