DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
555 Winderley Place, Suite 200 Maitland, FL 32751 (407)475-4700 Fax:(407)475-4768	5/6/2019-5/16/2019*
	FEI NUMBER 3007488106

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Yan Rotenstein, Pharmacist in Charge & Partial Owner

FIRM NAME	STREET ADDRESS
Synthetopes Inc	216 Earnhardt St
CITY, STATE, ZIP CODE, COUNTRY Conway, SC 29526-8287	TYPE ESTABLISHMENT INSPECTED Producer of Sterile Drugs

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

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

Specifically, your Pharmacist stated that no sterility testing is conducted for the following radiological and nuclear injectable drug products:

a. Dimercaptosuccinic Acid (DMSA) kits, 1.09mg **(b) (4)** , assigned 45 days BUD).

b. Sodium Thiosulfate Anhydrous (Sulfur Colloid) Kits, 1.0mL **(b) (4)** , assigned 45 days BUD).

c. Pentetate Indium Disodium (In-111 DTPA), 3.75mCi (0.50mL) **(b) (4)** and assigned 9 days BUD).

d. Indium Oxyquinoline (In-111 Oxine), 2mCi (1.0mL) (**(b) (4)** and assigned 9 days BUD).

OBSERVATION 2

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	Jessica L Pressley, Investigator	X Jessica L Pressley Investigator Signed By: Jessica L. Pressley -S Date Signed: 05-16-2019 10:56:17	5/16/2019

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

Specifically,

a. Your firm's Pharmacist stated he conducts **(b) (4)** on the **(b) (4)** **(b) (4)** **(b) (4)**, but is unsure of the specific allowable **(b) (4)** requirement, therefore cannot confirm if the **(b) (4)**

This **(b) (4)** is used to render the following nuclear drug injectable products sterile: Pentereotide Kit, 10µg, Mertiatide Kit, 10mL, PYP Kit, 11.9mg, Exametazime Kit, 0.3mg (Sn-HMPAO), DTPA Kit, 10mg, DMSA Kit, 1.09mg, Sulfur Colloid Kit, 2mg and Tetrafosmin Kit, 0.23mg.

b. On 5/7/19, during the aseptic production of Pyrophosphate Kit, lot #050719PYP, Exp:5/1/2020, your Pharmacist was observed prepping the ingredients within the ISO 5-LAFH (prior to aseptic filling), involving **(b) (4)** of a sterile vial, exited the clean room and entered the ISO-8 anteroom, to weigh the bulk drug substances, re-entered the clean room and ISO-5 LAFH and began aseptic filling without changing his gloves.

c. Media fills were not performed that closely simulate aseptic production operations incorporating, as appropriate, worst-case activities and conditions that provide a challenge to aseptic operations. Your firm can produce **(b) (4)** of DTPA, 10mg during routine operations, but your media fill only covers **(b) (4)** and doesn't replicate the entire process, which includes **(b) (4)**.

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OBSERVATION 3

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

Specifically,

a. Your Pharmacist stated that Environmental Monitoring (surface and non-viable air) is performed after cleaning and not after production of drug products within the ISO-5 aseptic processing areas therefore providing unreliable results.

b. On 5/6/19, I observed expired **(b) (4)** (exp.: 4/15/19) being used for surface sampling. **(b) (4)** (exp.: 4/21/19) was used previously on Monday, 4/29/19.

c. Your firm failed to provide sterility assurance of your drug products during the **(b) (4)** **(b) (4)**. On 5/7/19, I observed your firm pouring **(b) (4)** into the **(b) (4)** containing the **(b) (4)** which potentially introduced contamination to the sterile vials prior to the placement into the **(b) (4)** **(b) (4)** within the ISO-5 LAFH). Cleaning of the interior tubing to the **(b) (4)** is not performed. The chamber is only cleaned with **(b) (4)** and your firm has not provided any assurance that this cleaning agent is capable of removing resides from previous **(b) (4)** drug products.

d. Your firm's Pharmacist stated he only uses **(b) (4)** (non-sterile surface disinfectant and decontaminant cleaner) and **(b) (4)** within the ISO 5-LAFH. No sporicidal agent is used.

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e. On 5/7/19, cleaning operations were observed prior to drug production and the Pharmacist was observed spraying the **(b) (4)** and **(b) (4)** onto a non-sterile wipe to clean the ISO 5 LAFH.

f. For the floors, walls and ceilings of the clean room, the firm uses **(b) (4)** (non-sterile neutral disinfectant cleaner) and **(b) (4)** (non-sterile, non-sporicidal disinfectant solution).

OBSERVATION 4

Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically, on 5/7/19, during the aseptic production of Pyrophosphate Kit, lot #050719PYP, Exp:5/1/2020:

a. Your firm's ISO 5-LAFH was observed to contain visible signs of rust and deterioration of the working surface.

b. A large **(b) (4)** (firm's **(b) (4)**) was observed containing blue piping, stained pvc piping, black inflatable tubing and **(b) (4)** which are difficult to clean and sanitize.

c. Your Pharmacist was observed using a non-sterilized pipet to fill sterile product within the individual product vials (conducted after **(b) (4)**), and non-sterilized **(b) (4)** the vials. The stoppers were **(b) (4)** but the **(b) (4)** minutes), has not been validated and he was uncertain of the date in which the stoppers were **(b) (4)**

OBSERVATION 5

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There is a failure to thoroughly review any unexplained discrepancy and the failure of a batch or any of its components to meet any of its specifications whether or not the batch has been already distributed.

Specifically,

a. Your firm's **(b) (4)** are not validated (**(b) (4)** hours at **(b) (4)** degrees **(b) (4)**) as evidenced by the incomplete **(b) (4)** observed on 5/7/19 for Pyrophosphate Kit, lot #050719PYP, Exp:5/1/2020 (4 out of **(b) (4)** vials remained in a **(b) (4)** state). Your Pharmacist stated this incident has occurred a few times in the past with other drug products and the vials were discarded while the remainder of the lot was shipped. No investigations were ever conducted.

b. On 5/13/19, I observed two colonies (alert level: **(b) (4)** cfu) of growth on the **(b) (4)** (after **(b) (4)** days of incubation at **(b) (4)** degrees Celsius), from the surface sample taken after the completion of the **(b) (4)** for PYP, lot #050719PYP, exp: 5/1/2020. No investigation was conducted.

OBSERVATION 6

Results of stability testing are not used in determining appropriate storage conditions and expiration dates.

Specifically, your firm produces the following preservative free nuclear and radiological drug products containing expiration and BUD dating which are not supported through appropriate stability testing: Pentereotide Kits **(b) (4)** and assigned a 1-year expiration), Mertiatide Kits **(b) (4)** and assigned a 1-year expiration), PYP Kits **(b) (4)** and assigned a 1-year expiration), Exametazime Kits (Sn-HMPAO) **(b) (4)** and assigned a 1-year expiration), DTPA Kits **(b) (4)** and assigned a 1-year expiration), Tetrafosmin Kits **(b) (4)** and assigned a 1-year expiration), DMSA kits

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(b) (4) , assigned 45 days BUD), Sulfur Colloid Kits **(b) (4)** , assigned 45 days BUD), In-111 DTPA, 3.75mCi **(b) (4)** and assigned 9 days BUD) and In-111 Oxine, 2mCi **(b) (4)** and assigned 9 days BUD).

OBSERVATION 7

Testing and release of drug product for distribution do not include appropriate laboratory determination of satisfactory conformance to the final specifications and identity and strength of each active ingredient prior to release.

Specifically, your firm failed to conduct potency testing of each active ingredient within your firm's radiological and nuclear drug products: Pentetreotide Kits (**(b) (4)** and assigned a 1-year expiration), Mertiatide Kits (**(b) (4)** and assigned a 1-year expiration), PYP Kits (**(b) (4)** and assigned a 1-year expiration), Exametazime Kits (Sn-HMPAO) (**(b) (4)** and assigned a 1-year expiration), DTPA Kits (**(b) (4)** and assigned a 1-year expiration), Tetrafosmin Kits (**(b) (4)** and assigned a 1-year expiration), DMSA kits (**(b) (4)** assigned 45 days BUD), Sulfur Colloid Kits (**(b) (4)** assigned 45 days BUD), In-111 DTPA, 3.75mCi (**(b) (4)** and assigned 9 days BUD) and In-111 Oxine, 2mCi (**(b) (4)** and assigned 9 days BUD).

OBSERVATION 8

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

Specifically, on 5/7/19, your firm's Pharmacist was observed donning his non-sterile gown (reusable for one day), non-sterile face mask, sterile boots and bonnet with their bare hands. This same Pharmacist was observed cleaning the ISO-5 LAFH utilizing non-sterile gloves and placing his body, including his head, inside the LAFH.

*DATES OF INSPECTION

5/06/2019(Mon), 5/07/2019(Tue), 5/08/2019(Wed), 5/09/2019(Thu), 5/13/2019(Mon), 5/16/2019(Thu)

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