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	10/5/2020-10/22/2020* FEI NUMBER 3013316698

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Paul G. Kagan, Managing Director

FIRM NAME	STREET ADDRESS
MedisourceRx	10525 Humbolt St
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Los Alamitos, CA 90720-5401	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:

Quality System

OBSERVATION 1

There is a failure to thoroughly review any unexplained discrepancy whether or not the batch has been already distributed.

Specifically, major defects found in 100% visual inspection process from the drug products were not fully investigated. This is a repeat observation.

A. No identification was performed on observed particles from multiple drug product batches. For example,

- Glutathione lot (b) (4) had 1 vial containing unknown particles.
- Glutathione lot (b) (4) had 3 vials containing unknown particles.
- Glutathione lot (b) (4) had 2 vials containing unknown particles.
- Glutathione lot (b) (4) 5 had 2 vials containing unknown particles.
- (b) (4) lot (b) (4) had 2 syringes containing unknown particles.

B. The investigation for media fill lots with particulate counts that exceeded the action limit of (b) (4) % is not adequate. Deviation-20-002 attributed the observed unknown particles to possible aggregate from (b) (4) media. However, such conclusion was not confirmed through additional test or examination. For example,

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	Liming Zhang, Investigator	X Liming Zhang Investigator Signed By: 2001400144 Date Signed: 10-22-2020 06:01:03	10/22/2020

- Syringe media fill lot (b) (4) showed 43 units containing unknown particles (b) (4)% of total units inspected).

- Syringe media fill lot (b) (4) showed 28 units containing unknown particles (b) (4)% of total units inspected).

C. No effort was made to identify the observed particles in media fill vial product lots. For example,

- Vial lot (b) (4) showed 4 vials containing unknown particles.

- Vial lot (b) (4) showed 4 vials containing unknown particles.

- Vial lot (b) (4) showed 1 vial containing unknown particles.

In addition, the (b) (4)% (b) (4)% alert/action limits established for major defects in 100% visual inspection of the drug product and the discontinuation of your (b) (4) inspection in your drug product release requirement are not justified.

Manufacturing System

OBSERVATION 2

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. Not all media fill units from aseptic process simulations carried out in Nov2019 for syringes and Feb2020 for vials were incubated and examined for turbidity. For example,

- Lot (b) (4) : (b) (4) syringes were generated, only (b) (4) syringes were incubated.

- Lot (b) (4) : (b) (4) syringes were generated, only (b) (4) syringes were incubated.

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- Lot (b) (4) : (b) (4) syringes were generated, only (b) (4) syringes were incubated.
- Lot (b) (4) : (b) (4) vials were generated, only (b) (4) vials were incubated.
- Lot (b) (4) : (b) (4) vials were generated, only (b) (4) vials were incubated.
- Lot (b) (4) : (b) (4) vials were generated, only (b) (4) vials were incubated.

B. Not all media fill units were incubated (b) (4) for turbidity evaluation. For example, during (b) (4) competency evaluation for operator (b) (6), (b using media fill lot (b) (4) in June 2020 and operator (b) (6), (b using media fill lot (b) (4) in July 2020, (b) (4) vials and (b) (4) syringes were incubated at (b) (4) °C while (b) (4) vials/(b) (4) syringes were incubated at (b) (4) 5°C. No justification was documented for such practice.

C. Maximum number of operators permitted to be present ISO 7 clean room during aseptic sterile preparation of drug product has not been justified. Your firm allows up to (b) (4) people in ISO7 fill room, which is not supported by media fill studies.

D. There is no (b) (4) bioburden limit established and measured for each lot of sterile drug product produced from non-sterile bulk drug substance.

OBSERVATION 3
Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not written and followed.

Specifically,

A. During (b) (4) and filling process of Glutathione drug product batch (b) (4) on 10/6/2020, the primary operator's arms were observed resting on the ISO5 LAF hood bench. The same operator opened packages of sterile vials and stoppers using a scissor that was placed on the ISO5 LAF bench without wiping it first using sterile (b) (4).

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B. The surface microbial sampling procedure, SOP-LAB-006, does not provide instruction on the specific sampling locations for personnel monitoring. For example, the in-use EM monitoring form, PPC-FRM-002.14, requires primary operator's (b) (4) be sampled, it is not clear which areas of (b) (4) samples shall be taken. On 10/6/2020 after the completion of Glutathione batch (b) (4) filling, it was observed that the (b) (4) of the primary operator's (b) (4) was sampled. There is no justification why the back of the (b) (4) is considered more relevant than the front of the (b) (4) which directly faces the sterile filling operation.

OBSERVATION 4

Written production and process control procedures are not documented at the time of performance.

Specifically,

A. (b) (4) of your firm's drug product requires (b) (4) pump to be set to (b) (4) rpm, the actual speed used during produc(b) (4) was not documented in batch production record.

B. Glutathione injection drug product fill volume test results were not documented in the batch production records.

OBSERVATION 5

The master production and control records are deficient in that they do not include complete manufacturing, control, instructions, testing and specifications.

Specifically,

A. There is no requirement for benzyl alcohol content test as part of Glutathione MDV drug product release specification.

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B. There is no instruction in master batch records for both vial product (b) (4)) and syringe product (b) (4) on how the compounded drug products shall be protected before transferring into ISO 7 clean room for (b) (4) and filling operation.

C. The batch production record review checklist does not include QA evaluation of environmental monitoring test results (i.e. viable and non-viable test).

OBSERVATION 6

Written procedures are not established for the cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing or holding of a drug product.

Specifically, the cleaning procedure for mixing stirrer that is used to compound multiple drug products has not been evaluated to ensure there is no carry over from one API to the other in the mixing process.

Material System

OBSERVATION 7

Establishment of the reliability of the component supplier's report of analyses is deficient in that the test results are not appropriately validated at appropriate intervals.

Specifically, active drug substance supplier qualification does not include verification of all relevant test results against the manufacturer's specifications. For example, the firm only tested assay, microbial counts, and endotoxin level for Glutathione API. No other test results on manufacturer's COA, such as specific optical rotation, related substances, chlorides, sulfates, ammonium, iron, heavy metals, loss on drying, etc., were verified.

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***DATES OF INSPECTION**

10/05/2020(Mon), 10/06/2020(Tue), 10/07/2020(Wed), 10/09/2020(Fri), 10/13/2020(Tue), 10/15/2020(Thu), 10/22/2020(Thu)

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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 judgment, 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."