DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
6th & Kipling St. (P.O. Box 25087) Denver, CO 80225-0087 (303)236-3000 Fax:(303)236-3100	6/20/2016-6/29/2016* FEI NUMBER 3011752429

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Mr. William O. Richardson , CEO

FIRM NAME	STREET ADDRESS
Isomeric Pharmacy Solutions, LLC	2401 S. Foothill Drive, Suite D
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Salt Lake City, UT 84109-1479	503B 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 WE OBSERVED:

OBSERVATION 1

Written records of investigations into unexplained discrepancies and the failure of a batch or any of its components to meet specifications do not include the conclusions and follow-up.

Specifically,

A) Investigation into your MedWatch adverse drug event (Complaint EN-16001) did not include an evaluation of non-viable particle monitoring during the production time period associated with the product in question. During the production of triamcinolone 40mg/mL, Lot No. 12072015@10, there was a non-viable particle excursion in the (b) (4) room directly outside the (b) (4) when the product was compounded.

B) No investigation was conducted when two finished product HCG lots failed potency specifications in April 2016. HCG lots 02081 and 03003 failed your internal potency specification of (b) (4) with results of 111.8% and 118.3%, respectively. These products were later released and distributed to customers because, according to deviation reports (DVN-16040123 and DVN-16040128), both products meet USP potency specifications of 80-125%. The potency specification and the production process remains unchanged.

C) Investigations were inadequate to mitigate future recurrence when three lots of betamethasone acetate/betamethasone sodium phosphate 7mg/mL injection (Beta combo) failed in-process appearance specification for (b) (4) Beta combo non-conformances occurring on 2/15/16, 3/7/16, and 3/25/16 (Lot Numbers respectively: 01020, 02020, and 02070) all failed appearance specification and were discarded prior to completion of batch. The root causes identified on 2/15/16 were: (b) (4)

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(b) (4) . No corrective and preventative actions were implemented. Failures continued on 3/7/16 and 3/25/16. Later in May 2016, two complaints concerning the same Beta combo (b) (4) (b) (4) issues occurred in doctor's offices in Florida and New York.

a. Complaint EN-160002, 5/6/16, Beta Combo (no lot number documented): A doctor reported that he thought there were (b) (4) in the betamethasone combo injectable.

b. Complaint EN-160004, 5/18/16, Beta Combo (no lot reported or documented): on a sticky note attached to the record the following was noted: "Complaint for Beta molecule size too big? Vials caps breaking off. Dr. had to stop injection."

D) No investigations were conducted to mitigate future recurrence when six methylprednisolone/lidocaine (MP40) 40/10mg/mL (involving Lot Numbers 03045 and 03046) customer complaints commenced on May 19, 2016. Doctors' office concerns included: "clumping issues" and "sticking to the vial." Review of the two batch records discovered that both batches had been sterilized using a (b) (4) when the prescribed sterilization (b) (4) Complaints reviewed from customers, with no investigation, include:

a. Complaint EN-160005, 5/23/16, (MP40 lot number was not recorded) – "they are unable to fully mix the vial. The vial/product is stuck to the bottom. After shaking vigorously it is still clumpy. Unable to draw up in a 20 gauge needle."
b. Complaint EN-160006, 5/23/16, MP40, Lot Numbers: 03045, 03046 – "the office received two lots of MP40 where the product was not mixing and stuck to the bottom of the vial."
c. Complaint EN-16007, (no date documented), MP40, Part No (b) (4) Lot No. 03045 – "Lot #3045 10 vials * cloudy/clumpy 2 open vials ¾ is coming off when shaking."
d. Complaint EN-16008, (no date documented), Methylprednisolone 40/10 mg/mL, Part No. (b) (4), Lot No. 03045 – "10 vials of MP40. Clumpy, sticking to vial. Lot 3045. Same issue as mentioned by other offices."

e. Complaint EN-16009 (no date documented), MP40, Part No. (b) (4) Lot No. 03045, "clumping issues Lot #03045."

f. Complaint EN-160003, 5/19/16, Methylprednisolone/lidocaine 40/10mg/mL "the powder and liquid are not mixed well…they shook the vial but it has no results. All of the vials. Clinic wants all 20 vails replaced ASAP."

E) Negative environmental monitoring trends are not appropriately investigated.

a. For example, Monitoring Event Form (MEF) 16050012, 5/11/16, documents a positive environmental surface sample collected from the door handle located in the (b) (4) (b) (4) 2 CFU's (Allewia sp.) were identified and triggered the firm's "Action Status" for this area. Per SOP 607-02 (Environmental & Personnel Monitoring System), (b) (4) . There is no root cause or corrective action identified (form is blank) and the investigation was closed on the same day it was opened.

b. In MEF 16050017, 5/26/16, a technician was found with (b) (4) growth (Bacillus flexus) after working within the ISO 5 laminar flow hood (LFH). On 5/27/16, the same technician was found again with positive growth, this time on (b) (6), (b) (7) (C) (b) (4) (Penicillium sp.). Per SOP 607-02, " (b) (4) Root cause in both instances was determined to be: "Most Probable Root Cause is Personnel Training." No retraining was documented. The product and/or process was not identified in the MEF.

c. In CAPA-16004, dated 4/14/16, a non-conformance identified six "microbial and fungal grow outs in clean classified areas that exceeded action limits" (3 incidents found in (b) (4) (b) (4) , 2 incidents found in (b) (4) and 2 incidents within

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(b) (4) Floor and Door Handle) beginning 3/15/16. These events were documented as "Serious environmental contamination." Root causes were identified and corrective actions were implemented; however, after two months the investigation remains open and verification of action items has not occurred. Per SOP 1.020 (Deviation – OOS), which governs non-conformances, "unless justification is provided otherwise, corrective actions and investigations should be completed within (b) (4)

OBSERVATION 2

An adequate number of batches of each drug product are not tested to determine an appropriate expiration date.

Specifically,

A) Your firm's beyond use date (BUD) is not based upon completed stability studies. Per drug stability protocol BUD-16007, "(b) (4) ." The following reviewed stability studies did not follow established protocols:

   a. Current BUD for triamcinolone diacetate 40 mg/mL injection is 124 days. This value is based upon (b) (4) from only (b) (4) of triamcinolone submitted for the stability study. The sterility test parameter does not support your 124 day BUD.

   b. Current BUD for betamethasone acetate and sodium phosphate 7 mg/mL injection is 128 days. This value is based upon (b) (4) from (b) (4) of betamethasone submitted for the stability study. The preservative and sterility parameters do not support your 128 day timeframe.

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c. Current BUD for oxytocin 30 units per 500 mL bag solution (commercial/sterile to commercial/sterile) is 62 days. This value is based upon (b) (4) from (b) (4) (b) (4) lots of oxytocin submitted for the stability study. The preservative and sterility parameters do not support your 62 day timeframe.

d. Current BUD for methylprednisolone acetate/lidocaine 40/10 mg/mL is 180 days. This value is based upon (b) (4) for (b) (4) lots of product submitted for the stability study. The (b) (4) submitted (b) (4) failed preservative content at 180 days (Lot No. 06252015@19 = 70.6%; Lot No. 08052015@14 = 69.10%). The 180 day test point was the only preservative content test point for these stability lots.

B) In addition, the ability to retain sterile conditions, a function of the container/closure system, has not been established for any product. Sterility analysis has not been conducted at the end of each expiration/beyond use dating period for each product. Furthermore, per your stability protocols BUD-16001 and BUD-16007, (b) (4) (b) (4) (b) (4) Hence, drug product (b) (4) during each study, not the (b) (4)

OBSERVATION 3

Time limits are not established when appropriate for the completion of each production phase to assure the quality of the drug product.

Specifically,

Your Media Fill (b) (4) Process Qualification (VPQ-017) fails to closely simulate aseptic compounding, to include worst-case activities (E.g. hold times) and conditions that provide a challenge to your firm's most complex production process: (b) (4)

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A) For example, in step 7 of your batch record a (b) (4) process is conducted where the (b) (4) . Your media fills conducted on (b) (4) were held (b) (4) for only (b) (4) , whereas the (b) (4) product (Lot No. (b) (4) QA released on 3/16/16) was held for (b) (4) .

B) In step 10 of your batch record a (b) (4) process occurs, (b) (4) (batch record calls for a (b) (4)). Your media fills conducted on (b) (4) were only (b) (4) whereas the (b) (4) product (Lot No. (b) (4) , QA released on 3/16/16) was (b) (4) . Furthermore, after the media was (b) (4) , whereas Lot No. (b) (4) was (b) (4) environment and then (b) (4) .

C) The total processing time of your media fill was just (b) (4) whereas the total processing time for Lot No. (b) (4) was almost (b) (4) .

OBSERVATION 4
Deviations from written production and process control procedures are not justified.

Specifically,

A) Your justification as to why (b) (4) were not used during (b) (4) sterilization (b) (4) (DEV16010001, 12/30/15; DVN-1603073, 2/29/16) was inadequate. According to SOP 8.010, Sterilization and Depyrogenation, "Validation of (b) (4) sterilization of an object depends (b) (4) Currently your

(b) (4) has not been performance qualified (PQ) as evidenced by draft PQ protocol, VPQ-007.

a. For example in DEV16010001, the justification for disposition of sterilized material without the use of a (b) (4) because they were (b) (4) was (b) (4) has been properly validated and end products (b) (4) undergo end product testing." In addition, the deviation did not identify whether or not sterilized material was actual product or glassware, and no actions were implemented to mitigate future recurrence. This is evidenced by the recurrence of the same issue in DVN-1603073 on 2/29/16;

b. In DVN-1603073, (b) (4) were not included in the sterilization (b) (4) because, "we were (b) (4) could not wait." On 2/11/16, Lot #02112016@2 was produced without a (b) (4) and approved for release because (b) (4) is validated and product was (b) (4) which was sent for testing and passed." No investigation or corrective action was required per deviation. Timeliness is also an issue with this deviation as it was prepared on 2/29/2016 and reviewed by quality assurance on 4/20/16.

OBSERVATION 5

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

Specifically,

A) Your firm's in situ air pattern analysis (smoke studies) are not conducted simulating routine production (i.e. compounding equipment in place and operations ongoing). Dynamic smoke studies filmed on (b) (4) do not reflect the (b) (4)

For example, the (b) (4) and the active air sampler device used in the ISO 5 production area were not observed in the videos.

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Further, the third party (b) (4) l ISO certification conducted (b) (4) was documented as performed under (b) (4) conditions.

This is a repeat observation from the previous FDA inspection conducted August 24th -28th, 2015.

B) The (b) (4) sterilization (b) (4) for product glassware has not been validated, nor has the Performance Qualification (PQ) been conducted. The following finished drug products undergo (b) (4) sterilization (b) (4)) in (b) (4)

(b) (4)

Further, the Tuttenaeur Autoclave sterilization cycle for utensils/equipment (used in production) including: (b) (4) of active air sampler, and (b) (4) has not been validated, nor has Performance Qualification been conducted.

OBSERVATION 6

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

Specifically,

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A) On 6/20/16, sterilized glassware stored on shelving in the (b) (4) Room was found with burnt, brown carbon-like staining/spotting. The glassware is used for processing testosterone prior to (b) (4) sterilization.

B) On 6/20/16, a chemical-type, white staining was observed on the (b) (4) grates (directly in front of HEPA filters) (b) (4) of the ISO 5 laminar flow hoods in the (b) (4) Rooms.

OBSERVATION 7

Separate or defined areas to prevent contamination or mix-ups are deficient regarding operations related to aseptic processing of drug products.

Specifically,

On 6/20/16, a (b) (4) cart was observed transporting processing components (e.g. (b) (4) between unclassified areas and the classified ISO 8 Prep Room. The cart was not cleaned and disinfected prior to entering the ISO 8 area. Additionally, this cart including wheels, are not incorporated in your environmental monitoring program (SOP 607-02), nor in your cleaning procedure (SOP 301-01).

OBSERVATION 8

Employees are not given training in the particular operations they perform as part of their function , current good manufacturing practices and written procedures required by current good manufacturing practice regulations.

Specifically,

There is no training matrix or curriculum established for employees performing sterile compounding operations, including pharmacists and cleanroom operators. Furthermore, your pharmacists are

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(b) (4) ; however, they have not performed process qualifications (I.e. media fills) for any of the sterile products compounded.

OBSERVATION 9

The labels of your outsourcing facility's drug products are deficient.

Specifically,

The labels 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 your drug product labels:

- The statement "Not for Resale."

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

  - Triamcinolone Acetonide/Lidocaine HCl 40/10 mg/mL Injectable Suspension
  - Triamcinolone Diacetate 40 mg/mL Injectable Suspension
  - Methylprednisolone Acetate/Lidocaine HCl 80/10 mg/mL Injectable Suspension
  - Betamethasone Acetate/Betamethasone Sodium Phosphate 7 mg/mL Injectable Suspension
  - Phenylephrine HCl/Tropicamide 2.5%/1% Ophthalmic Solution
  - Testosterone Cypionate/Testosterone Propionate 200/20 mg/mL Injection
  - Cyanocobalamin/Methionine/Inositol/Choline Chloride 1/25/50/50 mg/mL Injection
  - Dexamethasone Sodium Phosphate/Lidocaine HCl 10/10 mg/mL Injectable Solution
  - Methylprednisolone Acetate/Lidocaine HCl 40/10 mg/mL Injectable Suspension

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- A list of inactive ingredients, identified by established name and the quantity or proportion of each ingredient.

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

  - Oxytocin 30 Units added to 500 mL 0.9% Sodium Chloride for Injection USP

***DATES OF INSPECTION**

6/20/2016(Mon),6/21/2016(Tue),6/22/2016(Wed),6/23/2016(Thu),6/24/2016(Fri),6/27/2016(Mon),6/28/2016(Tue),6/29/2016(Wed)

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