DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214) 253-5200 Fax:(214) 253-5314 Industry Information: www.fda.gov/oc/industry	01/25/2016 - 02/05/2016* FEI NUMBER 3010836489

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Carlos H. Garcia, Director of Pharmacy (Pharmacist-in-Charge)

FIRM NAME	STREET ADDRESS
I.V. Specialty, Ltd	3200 Steck Ave Ste 330
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Austin, TX 78757-8034	Producer of Sterile Drug Products

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

Aseptic processing areas are deficient regarding systems for maintaining any equipment used to control the aseptic conditions.

Specifically,

1) Your firm has a number of structural deficiencies in classified areas. These are summarized below:
   a. One of the (b) (4) ISO 5 hoods in the ISO 7 cleanroom has a work surface made of wood covered with formica, with visible scratches in the surface. The HEPA cover of the ISO 5 LAF Hood was visibly dirty with apparent white residue and rust. The Pharmacist-in-Charge acknowledged that this surface is not amenable to suitable cleaning.
   b. The ISO 7 cleanroom is outfitted with HEPA filters directly adjacent to returns in the ceiling. The Pharmacist-in-Charge stated (b) (4) (the contractor for room certification) expressed concerns regarding the placement of the HEPA filters adjacent to the returns.
   c. In the ISO 7 cleanroom there are observable gaps between the HEPA filters and the ceilings, as well as between the returns and the ceiling.
   d. The ISO 8 ante room has a ceiling made of fiber board ceiling tiles, like that found in an office space. In portions of the ceiling, tape is used to seal gaps.
   e. There is no mechanism to prohibit wooden doors that access the ISO 8 ante room and the ISO 7 cleanroom from opening simultaneously.

2) The firm contracts (b) (4) to perform room certification: During the certification dated (b) (4) (the latest certification) the following deficiencies were documented:
   a. (b) (4), the maximum microbial count for the ISO 7 cleanroom and ISO 8 ante room exceeded microbial count allowable of (b) (4) for actionable organisms. On (b) (4) (b) (4) performed a (b) (4) and the ISO 8 ante room exceeded microbial count allowable of (b) (4) for actionable organisms. The Pharmacist-in-Charge stated the (b) (4) informed the firm that the bioburden of the ISO 8 ante room would continue to exceed the microbial count allowable due to design flaws.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE	DATE ISSUED
	Massoud Motamed, Investigator Shelby N. Marler, Investigator	02/05/2016

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Date	Location	CFU
(b) (4)	ISO (b) (4)	1 CFU/25cm^2 (fungal counts)
	ISO (b) (4)	17 CFU/m^3 (bacterial counts)
	ISO (b) (4)	34 CFU/m^3 (fungal counts)
	ISO (b) (4)	18 CFU/m^3 (bacterial counts)

b. The ISO 8 ante room failed air changes per hour. The criterion for air changes per hour was ≥ (b) (4) however a recording of 16 air changes per hour was observed.

c. The ISO 8 ante room failed pressure limitations during certification. The criterion for air pressure was ≥ (b) (4) however a recording of 0.015 was observed. This room lacks a HEPA filter.

d. The pressure differential between the ISO 8 ante room and unclassified area was observed at 0.005 inches of water throughout the course of the inspection; this is below the firm's lower threshold of (b) (4) On 02/04/2016, when the door between the ISO 8 ante room and unclassified area was opened, positive pressure from the ISO 8 ante room to the unclassified area was lost.

e. Furthermore, the ISO 8 ante room failed all listed criteria during the certification dated (b) (4), however, was given a final determination of "pass" on the (b) (4) certification by (b) (4). The certification of the classified areas expired on (b) (4), however your firm continued aseptic operation.

3) The firm lacks the following items to assess the acceptability of the air quality

a. There is no evidence that smoke studies were conducted under dynamic conditions within the ISO 5 areas used to prepare sterile drug products. Furthermore, there is no evidence that smoke studies have ever been conducted in the ISO 8, ISO 7, and ISO 5 areas.

b. Pressured differential between the ISO 7 and ISO 5 areas and the unclassified and ISO 8 areas are not actively monitored or recorded to ensure positive pressure is maintained during sterile drug manipulation activities. Furthermore, the pressure gauges between the ISO 8 and ISO 7 areas and the unclassified and ISO 8 areas are not calibrated to ensure accurate pressure readings.

Your Pharmacist-in-Charge stated that the above deficiencies in the certification had neither been addressed or investigated.

REPEAT OBSERVATION FROM FDA 483 ISSUED ON 07/22/2014

OBSERVATION 2

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

Specifically,

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1) Your firm does not conduct sterility and endotoxin testing of finished drug products purporting to be sterile. Your firm produces approximately (b) (4) types of sterile drug products from 08/28/2015 to 01/28/2016. Your Pharmacist-in-Charge stated that (b) (4) is sterility tested (b) (4). Upon further inquiry, it was discovered that your firm (b) (4) conducts sterility tests on approximately (b) (4) of the (b) (4) (b) (4), along with (b) (4).

2) Your firm conducts sterility tests using the (b) (4) method which has the following deficiencies:
Your firm does not conduct finished product testing, but rather uses the (b) (4) method to (b) (4) (b) (4) (b) (4) On, 01/28/2016 we were informed by your operator that sterility tests are conducted on the (b) (4) (b) (4), along with (b) (4) (b) (4). According to your Pharmacist-in-Charge, the (b) (4) method has not been validated to determine equivalence to the USP Membrane Filtration or Direct Inoculation methods. Your firm does not follow the proper procedure for sterility testing using the (b) (4) method (b) (4) which your firm stated was the method used for testing. Precisely, (b) (4) is not (b) (4) and on 01/28/2016 we observed a sterility test (b) (4) (b) (4). Additionally, the (b) (4) incubation at "(b) (4) +/- (b) (4) °C", whereas your firm conducts incubation at (b) (4) - (b) (4) °C.

REPEAT OBSERVATION FROM FDA 483 ISSUED ON 07/22/2014

OBSERVATION 3

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

Specifically,

1) Gowning garments are stored and donned in the ISO 8 ante room and worn during aseptic operations were not sterile, including:
   a. (b) (4) Lab Coat – Item # (b) (4)
   b. (b) (4) Bouffant Cap (hair net) – Item # (b) (4)
   c. (b) (4) Face Mask – Item # (b) (4)
   d. (b) (4) Shoe Covers (b) (4) – Item # (b) (4)

2) During aseptic processing or (b) (4) we observed the pharmacy technician to be operating with exposed hair, ears, neck and forehead. Aseptic processing occurred during this time to produce the following products:

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Date	Rx Number	Product	Container
(b) (4)	(b) (4), (b) (6)	Meropenem 2000 mg/ NS 100ml (HP)	(b) (4)
		Tobramycin 550 mg/ 100 mls (Mylan)	(b) (4)
		Total Parenteral Nutrition 1130 ML	IV Bag
		Total Parenteral Nutrition 1400 ML	IV Bag

3) Throughout the inspection we observed your firms operator enter the ISO 7 ante room and then place exposed ungloved hands into an ISO 5 LAF hood to don sterile gloves.

REPEAT OBSERVATION FROM FDA 483 ISSUED ON 07/22/2014

OBSERVATION 4

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

Specifically,

1) Your cleanroom practices are deficient to prevent product contamination. These are summarized below:

   a. On 01/27/2016, your firm's operator handled the firm's telephone and then continued aseptic operations without changing or disinfecting gloves during the preparation of a sterile TPN pursuant to prescription (b) (4), (b) (6). We observed a similar practice on 01/28/2016.

   b. On 01/27/2016, (b) (4) was sprayed in close proximity to open, uncapped syringes filled with potassium phosphate to be used in a sterile TPN pursuant to prescription (b) (4), (b) (6) in the ISO 5 environment. We observed a similar practice on 01/28/2016.

   c. On 01/27/2016 and 01/28/2016, your firm's (b) (4), (b) (4) for TPNs was visibly soiled with white residue during the filling of TPNs. This equipment was operational in the [redacted] TPN prescriptions (b) (4), (b) (6) and (b) (4), (b) (6).

   d. The (b) (4) was used to (b) (4) (b) (4), (b) (4)) of sterile Meropenem and Tobramycin (prescriptions (b) (4), (b) (6) and (b) (4), (b) (6), respectively) of had visual rust and residue. Furthermore, this equipment was (b) (4) without first sanitizing the equipment.

2) Your firm's media fill is deficient as follows:

   a. Your media fill SOP entitled "ASEPTIC TECHNIQUE VALIDATION - MEDIA FILL PREPARATION" and practice does not represent the most challenging operation. The SOP calls for the use of a (b) (4) during the media fill, however on (b) (4) we observed (b) (4) (b) (4) The (b) (4) were used to (b) (4), (b) (4) (b) (4) (b) (4)

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b. Your firm's SOP calls for a (b) (4) incubation and does not state an incubation temperature, however your Pharmacist-in-Charge stated your firm incubates media fills between (b) (4) and (b) (4) °C. The product insert for the (b) (4) Growth Media from (b) (4) states that incubation should occur (b) (4) - (b) (4) °C for (b) (4) or (b) (4) - (b) (4) °C for (b) (4) (b) (4)

c. The media fill is conducted without positive or negative controls.

REPEAT OBSERVATION FROM FDA 483 ISSUED ON 07/22/2014

OBSERVATION 5

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

Specifically,

On 01/25/2016, we observed cleaning of your ISO 7 cleanroom, ISO 8 ante room, and ISO 5 LAF Hoods, during this time we observed the following deficiencies:

1) The technician used (b) (4) Disinfectant Cleaner (b) (4) (b) (4) in the ISO 8 ante room. This solution was used to clean the ISO 7 cleanroom and ISO 8 ante room floors. Furthermore, the same prepared cleaning solution was used to clean both areas.

2) The technician used a single non-sterile mop head and non-dedicated mop to clean first the ISO 7 cleanroom and then the ISO 8 ante room. The mop heads are stored under the sink with cleaning chemicals in the ISO 8 ante room in open packaging.

3) The technician used non-sterile wipes with sterile (b) (4) to clean the ISO 5 hoods and table surfaces of the ISO 7 cleanroom. One wipe sprayed with (b) (4) was used to clean several surfaces (e.g. the top, the pole and one wall) of the ISO 5 hood before changing to a new wipe. The wipe was not folded or turned to ensure a clean surface of the wipe was used.

4) The firm stated that they use a Sporicidal (b) (4) ((b) (4)), however we noted that the sporicidal that was in use expired in 9/2014. The expired cleaning product was last used approximately (b) (4) to perform the (b) (4) sporicidal cleaning.

5) (b) (4) and a (b) (4) are used in cleaning of the ISO 5 areas.

6) Materials such as IV bags and syringes, stored in the warehouse area are not sterilized / disinfected prior to entry into the ISO 8 ante room for transport into the ISO 7 cleanroom. Subsequently, these materials are introduced into the ISO 5 LAF hood. On 01/27/2016, your technician said that materials are not wiped or sterilized prior to bringing them into the ISO 7 cleanroom.

SEE REVERSE OF THIS PAGE	EMPLOYEE(S) SIGNATURE Massoud Motamed, Investigator Shelby N. Marler, Investigator	DATE ISSUED 02/05/2016

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Furthermore, after completion of cleaning we observed that the HEPA cover of the ISO 5 LAF Hoods, the metal carts, and the cleanroom area was visibly dirty with apparent white residue and rust. The HEPA cover of the ISO 5 LAF hood was not cleaned during this cleaning.

REPEAT OBSERVATION FROM FDA 483 ISSUED ON 07/22/2014

OBSERVATION 6

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

Specifically,

1) The Pharmacist-in-Charge stated that your firm does not conduct Environmental Monitoring (EM), but rather relies on the EM conducted by (b) (4) (the third party contractor which certifies the classified areas) (b) (4) (b) (4).
2) The Pharmacist-in-Charge stated that your firm does not conduct viable or non-viable monitoring in the ISO 5 environment during aseptic processing.
3) Your firm conducts personnel monitoring (b) (4) per your SOP entitled "Gloved Fingertip Testing" and not daily after production. Additionally, (b) (4) plates are to be incubated at (b)(4) +/- (b)(4) °C per your SOP; however the incubator temperature regularly fluctuates between (b)(4) - (b)(4) °C. This method has not been validated and is conducted without applicable positive or negative controls.

OBSERVATION 7

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

Specifically,

Your firm has no documentation of investigations, deviations, or complaints; however, during our review and observations we found evidence that these items have occurred.

For example,

1) On 01/27/2016 the Pharmacist in-Charge (PIC) stated that on occasion leaks are found in IV bags, which should have been an investigation according to SOP 105-A entitled "Quality Control - (b) (4) " and this was confirmed by the PIC.
2) On 01/28/2016 the operator stated that in the past (as recent as 1 year ago) your firm has found particles in vials of solutions used to produce sterile drug products. Your firm has no documented investigation of these occurrences.

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	Massoud Motamed, Investigator Shelby N. Marler, Investigator	02/05/2016

3) Your firm receives complaints during patient visits or phone interviews by nurses/ nutritionist. These complaints are recorded in the patient files, but not on a formal complaint list. These complaints are not fully investigated to determine if the drug product is the cause of the complaint or to assess product impact. Furthermore, your firm has no SOP pertaining to the handling of complaints.

The following are examples of select complaints found in patient files:

Date	Product	Complaint on Progress Notes
09/15/2015	TPN for (b) (6)	Weight Gain since initiation of TPN
01/06/2016	TPN for	Losing weight with Nausea and Vomiting
08/13/2015	TPN for	Weight Gain
05/24/2013	TPN for	Nausea
05/31/2013	TPN for	Nausea
04/05/2013	TPN for	Nausea
03/08/2013	TPN for	Nausea

OBSERVATION 8

Routine calibration of automatic, mechanical, and electronic equipment is not performed according to a written program designed to assure proper performance.

Specifically,

1) Your firm uses a (b) (4) WEIGHT (serial number: (b) (4)) for the (b) (4) calibration of the (b) (4) (b) (4) for TPNs, per provided calibration records this weight is out of calibration as of 09Dec2015.
2) Your firm does not calibrate the incubator thermometer to a national standard.
3) Your firm does not calibrate the magnehelic gauges between the classified areas to a national standard. These gauges were installed on 08/20/2014 and per your pharmacist the gauges have not be calibrated since installation.

REPEAT OBSERVATION FROM FDA 483 ISSUED ON 07/22/2014

*** DATES OF INSPECTION:**
01/25/2016(Mon), 01/26/2016(Tue), 01/27/2016(Wed), 01/28/2016(Thu), 02/04/2016(Thu), 02/05/2016(Fri)

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."