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320 S. Polk, Suite 100
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April 25, 2013

RE: FDA Disclosure of Warning Letter Response on FDA's Web Site

Dear Ms. Pickworth:

On behalf of IV Solutions of Lubbock, I authorize the United States Food and Drug Administration (FDA) to publicly disclose the information described below on FDA's web site. I understand that the information that is disclosed may contain confidential commercial or financial information or trade secrets within the meaning of 18 U.S.C. § 1905, 21 U.S.C. § 331(j), and 5 U.S.C. § 552(b)(4) that is exempt from public disclosure under those statutory provisions and/or relevant FDA regulations. I agree to hold FDA harmless for any injury caused by FDA's sharing the information with the public.

Information to be disclosed: IV Solutions of Lubbock's letter dated April 2, 2013 which responds to FDA's Form 483 dated March 20, 2013.

Authorization is given to FDA to disclose the above-mentioned information which may include confidential commercial or financial or trade secret information. As indicated by my signature, I am authorized to provide this consent on behalf of IV Solutions of Lubbock and my full name, title, address, telephone number, and facsimile number is set out below for verification.

Sincerely,

Carl Birdsong

Carl Birdsong
President
Phone: (806) 324-5481
Fax: (806) 351-5495

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April 2, 2013

Mr. Ricky Rodriguez, District Director
FDA Field Office, Dallas District
4040 North Central Expressway, Suite 300
Dallas, TX 75204

Via Fax (214) 253-5314
and Overnight Delivery

Attn: Paul C. Mouris, Investigator
Scott T. Ballard, Investigator
Ricky Rodriguez, District Director

Re: FDA 483, IVSolutions of Lubbock

Dear District Director Rodriguez and Investigators Mouris and Ballard,

On March 18-20, 2013 the FDA field office conducted an inspection of our pharmacy located at 3706 20th Street, Suite A in Lubbock, TX. At the conclusion of the inspection we received an FDA Form 483 indicating seven observations.

This letter is in response to the FDA Form 483. We respectfully request that this response, excluding the attached SOPs, be posted on the FDA's website with the Form 483 and be included any time the FDA provides a copy of the IVSolutions of Lubbock's FDA Form 483 to anyone outside the FDA.

We would like to ensure this 483 is viewed in the proper context. The observations noted on the 483 are all requirements imposed on drug manufacturers under the Current Good Manufacturing Practices (CGMPs) for Finished Pharmaceuticals contained in 21 CFR Part 211, and further explained in the FDA's Industry Guidance on CGMPs for Sterile Drug Products Produced by Aseptic Processing. IVSolutions of Lubbock is not licensed as a manufacturer and does not engage in drug manufacturing. IVSolutions of Lubbock is licensed by the Texas State Board of Pharmacy as a Class A Community pharmacy and is subject to its jurisdiction. IVSolutions engages in traditional retail prescription drug dispensing, as well as pharmacy compounding of sterile products. All medications are issued to patients based on a patient-specific prescription, including all compounded medications.

For these reasons, IVSolutions disputes the measurement of its operations against drug manufacturing CGMP requirements. In 2008, the 5th Circuit Court of Appeals in *Medical Center Pharmacy v. Mukasey*, 536 F. 3d 383 (5th Cir. 2008), upheld the remaining provisions of Section 503A of the FDA Modernization Act (FDAMA) [21 U.S.C. §353a] after severing those provisions related to advertising restrictions. The FDA has previously stated that it will follow the Fifth Circuit's decision within the Fifth Circuit.

21 USC §353a(a) states:

(a) In general

Sections 351 (a)(2)(B), 352 (f)(1), and 355 of this title shall not apply to a drug product if the drug product is compounded for an identified individual patient based on the unsolicited receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient, if the drug product meets the requirements of this section, and if the compounding—

(1) is by—

(A) a licensed pharmacist in a State licensed pharmacy or a Federal facility, or

(B) a licensed physician,

on the prescription order for such individual patient made by a licensed physician or other licensed practitioner authorized by State law to prescribe drugs; or

(2)

(A) is by a licensed pharmacist or licensed physician in limited quantities before the receipt of a valid prescription order for such individual patient; and

(B) is based on a history of the licensed pharmacist or licensed physician receiving valid prescription orders for the compounding of the drug product, which orders have been generated solely within an established relationship between—

(i) the licensed pharmacist or licensed physician; and

(ii)

(I) such individual patient for whom the prescription order will be provided; or

(II) the physician or other licensed practitioner who will write such prescription order.

21 USC §351 (a)(2)(B) states:

A drug or device shall be deemed to be adulterated if it is a drug and the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this chapter as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess.

IVSolutions of Lubbock understands and respects the FDA's commitment and authority in the regulation of drug manufacturing; however, IVSolutions of Lubbock engages in pharmacy compounding pursuant to a valid prescription issued by a physician. Only one compounded product prepared by IVSolutions is prepared in batch, and it is done in a limited quantity of a 1-2 week supply based on its history of prescription orders for that product. It is compounded in batch in advance so that sterility test results are received prior to dispensing the product. Since IVSolutions is located in the 5th Circuit and it is engaged in pharmacy compounding as specified by 21 USC §353a, the CGMP requirements imposed on drug manufacturers are not applicable to IVSolutions.

IVSolutions of Lubbock practices its compounding in full compliance with Texas State Board of Pharmacy sterile product compounding requirements. In addition, IVSolutions of Lubbock voluntarily goes above the pharmacy requirements imposed by the Texas State Board of Pharmacy and maintains accreditation by the largest and most respected national accreditation agency, the Joint Commission on Accreditation of Healthcare Organizations (Joint Commission). IVSolutions of Lubbock operates in full compliance with USP <797> recommendations on sterile product compounding to ensure the safest possible outcome for our patients, again surpassing regulations set forth by the Texas State Board of Pharmacy. To continue our commitment to continued improvement in pharmacy compounding, IVSolutions of Lubbock has addressed each observation in detail below.

1. **<u>Observation 1</u>: Clothing of personnel engaged in the processing of drug products is not appropriate for the duties they perform.**

IV Solutions of Lubbock disputes this observation on the basis that the CGMP requirements stated in 21 CFR §211.28 are not applicable to its pharmacy compounding operations. IVSolutions of Lubbock complies with the Texas State Board of Pharmacy requirements for protective clothing, which requires that:

> Personnel must don personal protective equipment and perform hand hygiene in an order that proceeds from the dirtiest to the cleanest activities as follows: Activities considered the dirtiest including donning of dedicated shoes or shoe covers, head and facial hair covers (e.g., beard covers in addition to face masks), and face mask/eye shield. Eye shields are optional unless working with irritants like germicidal disinfecting agents. After donning dedicated shoes or shoe covers, head and facial hair covers, and face masks, personnel shall perform a hand hygiene procedure by removing debris from underneath fingernails using a nail cleaner under running warm water followed by viperous hand washing. Personnel shall begin washing arms at the hands and continue washing to elbows for at least 30 seconds with either a plain (non-antimicrobial) soap, or antimicrobial soap, and water while in the anteroom/ante-area. After completion of hand washing, personnel shall don clean non-shedding gowns with sleeves that fit snugly around the wrists. Gloves that form a continuous barrier with the gown shall be the last item donned before compounding begins. Gloves, either those which are sterile or have been disinfected by applying 70% IPA or appropriate disinfectant to all contact surface areas and allowed to dry, that form a continuous barrier with the gown shall be the last item donned before compounding begins. Routine application of 70% IPA shall occur throughout the compounding day and whenever nonsterile surfaces are touched

22 Texas Administrative Code §291.133 (d)(11) (C) (iv).

Further, IVSolutions of Lubbock meets all United State Pharmacopeia <797> requirements for personal protective equipment, which require that:

> Personnel shall don the following PPE in an order that proceeds from those activities considered the dirtiest to those considered the cleanest. Garbing activities considered the dirtiest include donning of dedicated shoes or shoe covers, head and facial hair covers (e.g., beard covers in addition to face masks), and face masks/eye shields. Eye shields are optional unless working with irritants such as germicidal disinfecting agents or when preparing hazardous drugs. ..After completion of hand washing, a nonshedding gown with sleeves that fit snugly around the wrists and enclosed at the neck is donned. Gowns designated for buffer area use shall be worn, and preferably they should be disposable.

USP <797>, Pharmaceutical Compounding – Sterile Preparations, Personnel Cleansing and Garbing.

Corrective Action: IVSolutions of Lubbock SOP-Cleanroom 1, Entering and gowning- clean room, complies with Texas State Board of Pharmacy requirements, as well as, USP <797> requirements. Accordingly, we do not believe corrective action is required for observation 1.

2. **Observation 2: Buildings used in the manufacture, processing, packing, or holding of a drug product do not have the suitable construction to facilitate cleaning, maintenance, and proper operations.**

IV Solutions of Lubbock disputes this observation on the basis that the CGMP requirements stated in 21 CFR §211.42 are not applicable to its pharmacy compounding operations. IVSolutions of Lubbock complies with the Texas State Board of Pharmacy requirements for Pharmacies Compounding Sterile Preparations, which requires that:

> The pharmacy shall prepare sterile pharmaceuticals in a primary engineering control device, such as a laminar air flow hood, biological safety cabinet, compounding aseptic isolator, compounding aseptic containment isolator which is capable of maintaining at least ISO Class 5 conditions, during normal activity. The primary engineering control shall be located in the buffer area or room and placed in the buffer area in a manner as to avoid conditions that could adversely affect its operations such as strong air currents from opened doors, personnel traffic, or air streams from the heating, ventilating and air condition system. The primary engineering control shall be certified by an independent contractor according to the International Organization of Standardization (ISO) Classification of Particulate Matter in Room Air (ISO 14644-1) for operational efficiency at least every six months and when it is relocated, in accordance with the manufacture's specifications.

22 Texas Administrative Code §291.133 (d)(5)(A)(ii).

Further, IVSolutions of Lubbock complies with United States Pharmacopeia <797> requirements for Facility Design and Environmental Controls, which require that:

> HEPA-filtered air shall be supplied in critical areas (ISO Class 5) at a velocity sufficient to sweep particles away from the compounding area and maintain unidirectional airflow during operations. Proper design and control prevents turbulence and stagnant air in the critical area. In situ air pattern analysis via smoke studies shall be conducted at the critical area to demonstrate unidirectional airflow and sweeping action over and away from the product under dynamic conditions.

USP <797>, Pharmaceutical Compounding –Facility Design and Environmental Controls.

IVSolutions of Lubbock uses an independent approved contractor, AirScan Tech Incorporated, to perform all hood certifications on a bi-annual basis. AirScan Tech Incorporated indicates a "pass/fail" for the following categories: Intrusion Structural, External Turbulence, Uniform Airflow, Refluxing/Backstreaming and Unit is Positive Pressure. All hood certifications on file indicate a "Pass" for these categories.

In addition to the aforementioned hood certifications, IVSolutions of Lubbock scheduled an immediate In situ air pattern analysis via smoke study though AirScan Tech Incorporated and the results indicated "The airflow was observed to be moving in a unidirectional pattern without any refluxing or noticeable turbulence. Smoke pattern was found to be in compliance with ISO Class 5 environment as stated in USP <797>." These test results were provided to the inspectors.

With regards to the HEPA filter testing, IVSolutions of Lubbock has both the buffer room and anteroom recertified on a biannual basis by an independent contractor, AirScan Tech Incorporated, to ensure our compounding facility is physically designed and environmentally controlled to minimize airborne contamination from contacting critical sites. Routine HEPA Filter testing is not currently recommended by USP <797>.

Corrective Action: IVSolutions of Lubbock has requested that Advanced Testing and Certification, including smoke studies, be performed and documented with future recertifications.

Responsible Individual: J. Heaton

3. **Observation 3: Equipment used in the manufacture, processing, packing or holding of drug products is not of appropriate design to facilitate operations for its intended use and cleaning and maintenance.**

IV Solutions of Lubbock disputes this observation on the basis that the CGMP requirements stated in 21 CFR §211.63 are not applicable to its pharmacy compounding operations. IVSolutions of Lubbock complies with the Texas State Board of Pharmacy requirements for Pharmacies Compounding Sterile Preparations, which requires that:

> A pharmacy that prepares low- and medium-risk preparations shall have a clean room/controlled area for the compounding of sterile preparations that is constructed

> to minimize the opportunities for particulate and microbial contamination. The clean room/controlled area shall have walls, ceilings, floors, fixtures, shelving, counters, and cabinets that are smooth, impervious, free from cracks and crevices (e.g. coved), non-shedding and resistant to damage by disinfectant agents.

22 Texas Administrative Code §291.133 (d)(5)(A)(i)(VI).

Further, IVSolutions of Lubbock complies with United States Pharmacopeia <797> requirements for Facility Design and Environmental Controls, which require that:

> The surfaces of ceilings, walls, floors, fixtures, shelving, counters, and cabinets in the buffer area shall be smooth, impervious, free from cracks and crevices, and non-shedding, thereby promoting cleanability and minimizing spaces in which microorganisms and other contaminants may accumulate. The surfaces shall be resistant to damage by disinfectant agents.

USP <797>, Pharmaceutical Compounding –Facility Design and Environmental Controls.

All direct compounding areas within the ISO Class 5 environment at IVSolutions of Lubbock are composed of stainless steel. The inspector's observation was pertaining to the edges of the table on which the horizontal hood rests, all outside of the ISO Class 5 environment direct compounding areas. The edges of the table are covered in a hard laminate top layer. Both surface materials provide a smooth, cleanable non-shedding surface as recommend by the Texas State Board of Pharmacy as well as the USP <797>.

Corrective Action: Although IVSolutions of Lubbock feels that it is currently in compliance with the Texas State Board of Pharmacy as well as the USP <797>, we feel that with the advancement in technology it is an opportunity to upgrade the non-direct compounding area outside of the ISO Class 5 environment.

Responsible Individual: J. Heaton/C. Birdsong

4. **Observation 4: Aseptic Processing areas are deficient regarding the system for monitoring environmental conditions.**

IV Solutions of Lubbock disputes this observation on the basis that this CGMP requirements stated in 21 CFR §211.42 (c)(10) is not applicable to its pharmacy compounding operations. The Texas State Board of Pharmacy does not require continual viable or non-viable environmental monitoring during a certified compounding technician's shift. IVSolutions of Lubbock complies with the Texas State Board of Pharmacy requirements for Pharmacies Compounding Sterile Preparations, which requires that:

> The clean room/controlled area contain a buffer zone or buffer room designed to maintain at least ISO Class 7 condition. The pharmacy shall prepare sterile pharmaceuticals in a primary engineering control device, such as a laminar air flow hood, biological safety cabinet, compounding aseptic isolator, compounding aseptic

> containment isolator which is capable of maintaining at least ISO Class 5 conditions during normal activity.

22 Texas Administrative Code §291.133 (d)(5)(A)(i)(XI) and (d)(5)(A)(ii).

In addition, IVSolutions of Lubbock complies with United States Pharmacopeia <797> requirements for Viable and Nonviable Environmental Sampling (ES) Testing, which require that:

> Environmental sampling shall occur as part of a comprehensive quality management program and shall occur minimally under any of the following conditions: as part of the commissioning and certification of new facilities and equipment; following any servicing of facilities and equipment; as part of the re-certification of facilities and equipment (i.e., every 6 months); in response to identified problems with end products or staff technique; or in response to issues with CSPs, observed compounding personnel work practices, or patient-related infections (where the CSP is being considered as a potential source of the infection).

USP <797>, Pharmaceutical Compounding –Viable and Nonviable Environmental Sampling (ES) Testing.

IVSolutions of Lubbock meets or exceeds minimum recommended environmental monitoring as described in USP <797>. Surface contact plates and gloved fingertip sampling are conducted randomly within each quarter. This surpasses the minimum recommendations provided by USP <797>. In addition IVSolutions of Lubbock has Airscan Tech Incorporated perform clean room certifications including viable and nonviable air samplings on a biannual basis which satisfies the recommendation provided by USP <797>.

Corrective Action: Although IVSolutions of Lubbock feels that it is currently in compliance with the Texas State Board of Pharmacy as well as the USP <797>, we have redrafted our Standard Operating Procedures – Cleanroom -SOP 8(Attachment 1) to include the frequency of gloved fingertip sampling as well as created a new SOP 13(Attachment 2) to include Surface contact plates sampling procedures, including the frequency of sampling.

Timeline: This was completed on March 28, 2013

Responsible Individual: J. Heaton

5. **Observation 5: Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established, written, and followed.**

IV Solutions of Lubbock disputes this observation on the basis that the CGMP requirements stated in 21 CFR §211.113 are not applicable to its pharmacy compounding operations. IVSolutions of Lubbock complies with the Texas State Board of Pharmacy requirements for Pharmacies Compounding Sterile Preparations, which requires that:

> Media-fill tests procedures for assessing the preparation of specific types of sterile preparations shall be representative of all types of manipulations, products, risk levels, and batch sizes that personnel preparing that type of sterile preparation are likely to encounter.

22 Texas Administrative Code §291.133 (c)(4)(A)(iv).

Further, IVSolutions of Lubbock complies with United States Pharmacopeia <797> requirements for Medium-Risk Level CSPs, Media-Fill Test Procedure, which require that:

> The Media-Fill Test procedure or an equivalent test is performed at least annually under conditions that closely simulate the most challenging or stressful conditions encountered during compounding. Once begun, this test is completed without interruption.

USP <797>, Pharmaceutical Compounding –Medium-Risk Level CSPs, Media-Fill Test Procedure.

IVSolutions of Lubbock has established, written procedures for the Aseptic Technique Validation (Media-Fill Test), which have been followed since the inception of Standard Operating Procedures – Cleanroom - SOP 12 (Attachment 3). This SOP was written to encompass all mixing procedures, equipment and supplies a sterile product technician may encounter. The procedure is extensive and demonstrates a "worst case scenario," that goes far above what our compounding staff are likely to encounter.

Corrective Action: Although IVSolutions of Lubbock feels that it is currently in compliance with the Texas State Board of Pharmacy, as well as the USP <797>, we have updated Standard Operating Procedures – Cleanroom -SOP 12 (Attachments 4 & 5) to specify that the Media-Fill Test will be conducted at the end of the employee's shift, as well as allow for the documentation of the total duration of the procedure and the room conditions (i.e. dynamic, rest etc.). A positive control will be incorporated into all Media-Fill Test, as well as surface contact and fingertip sampling.

Timeline: This was completed on March 28, 2013

Responsible Individual: J. Heaton

6. **Observation 6: Equipment for adequate control over air pressure is not provided when appropriate for the manufacture, processing, packing or holding of a drug product.**

IV Solutions of Lubbock disputes this observation on the basis that the CGMP requirements stated in 21 CFR §211.46 are not applicable to its pharmacy compounding operations. IVSolutions of Lubbock complies with the Texas State Board of Pharmacy requirements for Pharmacies Compounding Sterile Preparations.

IVSolutions of Lubbock does comply with United States Pharmacopeia <797> requirements for Pressure Differential Monitoring, which require that:

> A pressure gauge or velocity meter shall be installed to monitor the pressure differential or airflow between the buffer area and the ante-area and the general environment outside the compounding area. The results shall be reviewed and documented on a log at least every work shift (minimum frequency shall be at least daily) or by a continuous recording device. The pressure between the ISO Class 7 and the general pharmacy area shall not be less than 5 Pa (0.02 inch water column).

USP <797>, Pharmaceutical Compounding – Pressure Differential Monitoring.

IVSolutions of Lubbock has pressure gauges installed to monitor both the buffer area and anteroom area to ensure a recommended positive pressure is maintained throughout the compounding process. This ensures our compliance with the recommendation provided by USP <797>.

Corrective Action: Although IVSolutions of Lubbock feels that it is currently in compliance with the Texas State Board of Pharmacy as well as the USP <797>, we feel that with the advancement in technology and the critical objective the positive pressure differential serves in the compounding process, it will be an opportunity to install a continual pressure monitoring device or alarm to ensure employees are alerted if the buffer or anterooms inadvertently fall out of the approved range.

Responsible Individual: J. Heaton/C. Birdsong

7. **Observation 7: Reserve samples for drug products are not retained for one year after the expiration date of the drug product.**

IV Solutions of Lubbock disputes this observation on the basis that the CGMP requirements stated in 21 CFR §211.170 are not applicable to its pharmacy compounding operations. IVSolutions of Lubbock complies with the Texas State Board of Pharmacy requirements for Pharmacies Compounding Sterile Preparations, which requires that:

> Beyond-use dates for compounded sterile preparations shall be assigned based on professional experience, which shall include careful interpretation of appropriate information sources for the same or similar formulations. Beyond-use dates for compounded sterile preparations that are prepared strictly in accordance with manufacturers' product labeling must be those specified in that labeling, or from appropriate literature sources or direct testing.

22 Texas Administrative Code §291.133 (d)(5)(G)(ii).

Further, IVSolutions of Lubbock complies with United States Pharmacopeia <797> requirements for Finished Preparation Release Checks and Tests, which require that:

> Finished CSPs are individually inspected in accordance with written procedures after compounding. If not distributed promptly, these CSPs are individually inspected just prior to leaving the storage area. Those CSPs that are not immediately distributed are stored in an appropriate location as described in the written procedures. Immediately after compounding, and as a condition of release, each CSP unit, where possible, should be inspected against lighted white or black background or both for evidence of visible particulates or other foreign matter. Prerelease inspection also includes container-closure integrity and any other apparent visual defect.

USP <797>, Pharmaceutical Compounding – Finished Preparation Release Checks and Tests.

All compounded sterile product prepared in anticipation of a patient order are immediately quarantined and sterility tested according to USP <71>, as well as tested for the potency to ensure accuracy. There is no requirement by the Texas State Board of Pharmacy or recommendation in USP <797> related to holding product past its established expiration date if less than one year. Our compounded sterile products have a beyond-use-date of less than one year and we question the value of retaining product past its beyond-use-date.

Corrective Action: IVSolutions of Lubbock complies with Texas State Board of Pharmacy requirements, as well as USP <797> requirements, in relation to a compounded sterile product prepared in anticipation of a patient order. Accordingly, we do not believe corrective action is required for observation 7.

Carl Birdsong

Carl Birdsong, R.Ph.
President
IVSolutions of Lubbock