Topspins, Inc. 11/6/14

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Detroit District
300 River Place
Suite 5900
Detroit, MI 48207
Telephone: 313-393-8100
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WARNING LETTER
2015-DET-01

November 6, 2014

VIA UPS

Martin R. Prince, MD
President
Topspins, Inc.
403 Riverview Drive
Ann Arbor, Michigan 48104-1849

Dear Dr. Prince:

During an inspection of your firm located in Ann Arbor, Michigan on August 5, 2014 through August 15, 2014, an investigator from the United States Food and Drug Administration (FDA) determined that your firm is a specification developer and own label distributor of the Smart Set intravenous tubing sets. Under section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act) 21 U.S.C. § 321(h), these products are devices because they are intended for use in the diagnosis of disease or other

conditions or in the cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body.

This inspection revealed that these devices are adulterated within the meaning of section 501(h) of the Act, 21 U.S.C. § 351(h), in that the method, used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with the current good manufacturing practice requirements of the Quality System regulation found at Title 21, Code of Federal Regulations (CFR), Part 820.

We received a response from your firm, dated September 3, 2014, concerning our investigator's observations noted on the Form FDA 483 (FDA 483), List of Inspectional Observations that was issued to your firm. We address this response below, in relation to the noted violations. These violations include, but are not limited to, the following:

1. Failure to establish and maintain procedures to control the design of the device in order to ensure that specified design requirements are met, as required by 21 CFR 820.30. For example:

a. Failure to establish and maintain procedures for the identification, documentation, validation or, where appropriate, verification, review, and approval of design changes before their implementation, as required by 21 CFR 820.30(i). Your firm has made the following design changes to the Smart Set tubing:

1. Version 001.2, in 2003: the initial design of the Smart Set (version 1.2, needle based sideport) was changed to a needleless sideport (version 1.2, needleless sideport);

2. Version 001.4, in 2000: a design change to the Smart Set (version 001.2, needle based sideport) was elimination of the sideport; and

3. Version 001.5, in 2011: a design change to the Smart Set (version 001.4, no sideport), was a two piece connection for the tubing set and solvent bonding of the **(b)(4)** with **(b)(4)**.

Your firm had no raw data in the files to demonstrate design verification studies were performed. There was also no documentation to support why verification was appropriate for these design changes in lieu of design validation. Your "Design Review Procedure" and "Design Process Control Procedure" do not include the requirement to document justification for why verification of a design changes is appropriate in lieu of design validation.

The adequacy of your firm's response cannot be determined at this time. You have

indicated the design process control procedure will be revised; and you will either locate missing raw data or retest with the revised design process control procedure. These are planned actions that we cannot evaluate at this time.

b. Failure to establish and maintain procedures for validating the device design, as required by 21 CFR 820.30(g). Neither of your design control procedures, "Design Review Procedure" and "Design Process Control Procedure" include the following requirements for design validations:

- Defined operating conditions on initial production units, lots or batches or their equivalent.
- Devices conform to defined user needs and intended uses and include testing of production units under actual or simulated conditions;
- Include design risk analysis (where appropriate); and
- Include the results, the identification of the design, methods(s), the date, and the individual(s) performing the validation in the Design History File.

The adequacy of your firm's response cannot be determined at this time. You have indicated you will be making revisions to the design process control procedure. These are planned actions that we cannot evaluate at this time.

2. Failure to establish and maintain procedures that define the responsibility for review and the authority for the disposition of nonconforming product, as required by 21 CFR 820.90(b)(1). For example, your procedure titled "Control of Nonconforming Product 8.3-p" does not require documentation of the evaluation of nonconformance to include a determination of the need for an investigation; notification of the persons or organizations responsible for the nonconformance; and signature of the person authorizing use of nonconforming products, including documented justification for use of nonconforming products.

Smart Set tubing sets (version1.4, lot#CF13L02), received by your firm on March 26, 2014 were found to have a **(b)(4)** of **(b)(4)** which is over the **(b)(4)** specified in the procedure titled "Procedure for Receiving a Shipment of Smart Set Product 7.1a-p". There was no documented evaluation for the need for an investigation and signature of the President authorizing the use of the devices "as is" although the **(b)(4)** were outside the stated specifications.

The adequacy of your firm's response cannot be determined at this time. You have indicated an updated the procedure will be revised by **(b)(4)**. This is a planned action that we cannot evaluate at this time.

3. Failure to establish and maintain procedures to ensure that all purchases or otherwise received product and services conform to specified requirements, as required by 21 CFR 820.50. For example:

a. Your procedure titled “Procedure for Receiving a Shipment of SmartSet Product 7.1 a-p” requires measurement of the **(b)(4)** of the incoming Smart Set tubing set received from your supplier. There are no specifications documented for version 001.5, of the Smart Set tubing, which consists of a short and long piece which would require **(b)(4)** separate **(b)(4)** specifications.

b. Instruction # 11 of the “Procedure for Receiving a Shipment of SmartSet Product 7.1 a-p”, does not specify how to “Verify the functioning of the pinch clamp” for the Smart Set tubing.

The adequacy of your firm’s response cannot be determined at this time. You have indicated an updated procedure will be completed by **(b)(4)**. This is a planned action that we cannot evaluate at this time.

4. Failure to establish and maintain adequate procedures for receiving, reviewing, and evaluating complaints, as required by 21 CFR 820.198(a). For example, your procedure titled “Corrective and Preventive Actions 8.5.2-p” used for complaint handling does not include the evaluation of complaints to determine whether an investigation is necessary and if an investigation is not necessary, the requirement to document the reason and the name of the person making the decision. Also, there was no documentation of evaluation for whether an investigation was necessary for the complaint received on or about January 8, 2010 for the “No Phase Wrap”. During the use of the “No Phase Wrap” there was flame and smoke observed from the sleeves of the patient’s arms where the wraps had been worn to reduce image artifacts during magnetic resonance imaging (MRI).

The adequacy of your firm’s response cannot be determined at this time. You have indicated you are in the process of creating a new Complaint Handling procedure. This is a planned action that we cannot evaluate at this time.

5. Failure to ensure that sampling methods are based on a valid statistical rationale, are adequate for their intended use, and that the sampling plans are reviewed when changes occur, as required by 21 CFR 820.250(b). For example, **(b)(4)** samples were inspected at random from **(b)(4)** different boxes of Smart Set tubing for version 1.4 (**(b)(4)** units) and version 1.5 (**(b)(4)** units) received on March 26, 2014. Your procedures do not include a valid statistical rationale for why **(b)(4)** boxes may be inspected for incoming lots.

The adequacy of your firm’s response cannot be determined at this time. You have indicated you will be making revisions to the sampling schedule and revising the procedure. These are planned actions that we cannot evaluate at this time.

6. Failure to establish and maintain procedures for implementing corrective and

preventive action, as required by 21 CFR 820.100(a). For example, you firm's procedure titled "Corrective and Preventive Actions 8.5.2-p" does not include the following requirements:

- Investigating the cause of nonconformities relating to product, processes, and the quality system;
- Identifying the action(s) needed to correct and prevent recurrence of nonconforming product and other quality problems;
- Verifying or validating the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device;
- Implementing and recording changes in methods and procedures needed to correct and prevent identified quality problems;
- Ensuring that information related to quality problems or nonconforming product is disseminated to those directly responsible for assuring the quality of such product or the prevention of such problems; and
- Documenting all activities required under this section and their results.

The adequacy of your firm's response cannot be determined at this time. You have indicated you will be making revisions to the CAPA procedure. These are planned actions that we cannot evaluate at this time.

Our inspection also revealed that the Smart Set tubing is adulterated under section 501(f)(1)(B) of the Act, 21 U.S.C. § 351(f)(1)(B), because your firm does not have an approved application for premarket approval (PMA) in effect pursuant to section 515(a) of the Act, 21 U.S.C. § 360e(a), or an approved application for an investigational device exemption (IDE) under section 520(g) of the Act, 21 U.S.C. § 360j(g) as described and marketed. The Smart Set Tubing is also misbranded under section 502(o) of the Act 21 U.S.C. § 352(o), because your firm introduced or delivered for introduction into interstate commerce for commercial distribution this device with major changes or modifications to the intended use without submitting a new premarket notification to FDA as required by section 510(k) of the Act, 21 U.S.C. § 360(k), and 21 CFR 807.81(a)(3)(i).

Specifically, the Smart Set tubing, cleared under K972663 with the following indications: to assist in the administration of fluids into a patient's vascular system during a Magnetic Resonance Imaging (MRI) or Magnetic Resonance Angiography (MRA) examination. However, your firm's promotion of the device provides evidence that the device is intended for running an IV bag through the Smart Set tubing, which would constitute a major change or modification to its intended use, for which your firm lacks clearance or approval.

As indicated above, the Smart Set tubing cleared under K972663 is for hand injection of fluids. Administering fluids from an IV bag through the Smart Set tubing is a new

method of operation.

The Smart Set tubing is also misbranded under section 502(o) the Act, 21 U.S.C. § 352(o), because you did not notify the agency of your intent to introduce the device into commercial distribution in that a notice or other information respecting the modification to the device was not provided to the FDA as required by section 510(k), 21 U.S.C. § 360(k), and 21 C.F.R. 807.81(a)(3)(i). Specifically, you have modified the Smart Set tubing cleared under K972663 by making significant device modifications in design, method of operation, materials. These changes include:

- Removal of the tubing side port that was present in K972663.
- Addition of a needleless sideport.
- Addition of an adaptor that can be used on the Smart Set tubing or another tubing.
- Administering fluids from an IV bag trough the Smart Set tubing is a new method of operation.
- Four (4) different devices under the name “Smart Set” on the Topspins website, when only one device was cleared in K972663.
- Addition of new materials, for example the needleless valve material **(b)(4)**.

The multiple device modifications and addition of new material could significantly affect the safety or effectiveness of the device.

Therefore, changes in the intended use and device modifications made to the Smart Set tubing require the submission of a new 510(k).

For a device requiring premarket approval, the notification required by section 510(k) of the Act, 21 U.S.C. § 360(k), is deemed satisfied when a PMA is pending before the agency. [21 CFR 807.81(b)]. The kind of information that your firm needs to submit in order to obtain approval or clearance for the device is described on the Internet at http://www.fda.gov/MedicalDevices/DevicRegulationandGuidance/HowtoMarketYourDevice/default FDA will evaluate the information that your firm submits and decide whether the product may be legally marketed.

Your firm should take prompt action to correct the violations addressed in this letter. Failure to promptly correct these violations may result in regulatory action being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction, and civil money penalties. Also, federal agencies may be advised of the issuance of Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, premarket approval applications for Class III devices to which the Quality System regulation violations are reasonably related will not be approved until the violations have been corrected. Requests for Certificates to Foreign Governments will not be granted until the violations related to the subject devices have been corrected.

Please notify this office in writing within fifteen business days from the date you receive this letter of the specific steps your firm has taken to correct the noted violations, as well as an explanation of how your firm plans to prevent these violations, or similar violations, from occurring again. Include documentation of the corrections and/or corrective actions (which must address systemic problems) that your firm has taken. If your firm's planned corrections and/or corrective actions will occur over time, please include a timetable for implementation of those activities. If corrections and/or corrective actions cannot be completed within fifteen business days, state the reason for the delay and the time within which these activities will be completed. Your firm's response should be comprehensive and address all violations included in this Warning Letter.

Your firm's response should be sent to: Catherine V. Quinlan, Compliance Officer, Food and Drug Administration at 300 River Place, Suite 5900, Detroit, MI 48207. If you have any questions about the contents of this letter, please contact Ms. Quinlan at (313)393-8153.

Finally, you should know that this letter is not intended to be an all-inclusive list of the violations at your firm's facility. It is your firm's responsibility to ensure compliance with applicable laws and regulations administered by FDA. The specific violations noted in this letter and in the Inspectional Observations, FDA 483, issued at the close of the inspection may be symptomatic of serious problems in your firm's manufacturing and quality management systems. Your firm should investigate and determine the causes of the violations, and take prompt actions to correct the violations and bring the products into compliance.

Sincerely,
/S/
Art O. Czabaniuk
District Director
Detroit District Office