Inspections, Compliance, Enforcement, and Criminal Investigations

San Up S.A. 11/25/13

Department of Health and Human Services

Public Health Service
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

WARNING LETTER

November 25, 2013

VIA UNITED PARCEL SERVICE

Jorge Shemi
President
SAN UP S.A.
Ruta 8. No: 2967 (1650) San Martin
Buenos Aires, Argentina

Dear Mr. Shemi:

During an inspection of your firm located in Buenos Aires, Argentina, on July 15, 2013, through July 18, 2013, an investigator from the United States Food and Drug Administration (FDA) determined that your firm manufactures piston and ultrasonic nebulizers. 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 function of the body.

Our inspection revealed that your firm's piston and ultrasonic nebulizer devices are misbranded under section 502(t)(2) of the Act, 21 U.S.C. § 352(t)(2), in that your firm failed or refused to furnish material or information respecting the device that is required by or under section 519 of the Act, 21 U.S.C. § 360i, and 21 CFR Part 803 - Medical Device Reporting. These violations include, but are not limited to, the following:

Failure to develop, maintain, and implement written Medical Device Reporting (MDR) procedures, as required by 21 CFR 803.17. For example, your firm's procedure, "*Sistema de vigilancia,* GC-E-08-22, Revision 3," dated January 28, 2013, describes methods for notification, evaluation, and reporting of adverse event incidents to National Competent Authorities. However, the procedure makes no mention of reporting adverse

events to the U.S. Food and Drug Administration. When asked if there were any other procedures that describe Medical Device Reporting, your firm indicated that there were no other procedures.

U.S. 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 awarding of contracts.

Please notify this office in writing within fifteen business days from the date you receive this letter of the specific steps that 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. Please provide a translation of documentation not in English to facilitate our review.

In addition, FDA has noted nonconformances with regards to section 501(h) of the Act (21 U.S.C. § 351(h)), which are deficiencies within your firm's quality system pertaining to current good manufacturing practice requirements specified in the Quality System regulation found at 21 CFR Part 820. These nonconformities include, but are not limited to, the following:

1. Failure to establish and maintain procedures for implementing corrective and preventive action, as required by 21 CFR 820.100(a). For example:

   a. The name of your firm's Quality Manager and a date of January 28, 2013, were typed on CAPA form NC-PAC #PI-11-13, indicating closure. However, the associated training, which was also a corrective action, was not completed until March 25, 2013.

   b. CAPA form NC-PAC #PI-08-13 was closed by your firm's Quality Manger on January 25, 2013. However, no containment actions were listed in Section 3, of NC-PAC #PI-08-13.

2. Failure to document Corrective and Preventive Action activities and results, as required by 21 CFR 820.100(b). For example, a review of **(b)(4)** CAPA reports revealed that required signatures and/or dates were missing.

3. Failure to establish and maintain procedures for receiving, reviewing, and evaluating complaints by a formally designated unit, as required by 21 CFR 820.198(a). For example, your firm's procedure, "*Sistema de vigilancia,* GC-E-08-22, Revision 03," dated January 22, 2013, does not formally specify a group, unit, or individual that is responsible for reviewing and evaluating each complaint, nor does it mention the evaluation of a complaint to determine if the complaint is reportable as a MDR to FDA.

4. Failure of management with executive responsibility to establish the policy and objectives for, and commitment to, quality, as required by 21 CFR 820.20(a). For example, your firm's "Quality Management System Manual," states that "Top management defines the quality objective and the system to measure them," in order to comply with ISO 13485.2003 requirements. The manual does not include documents, requirements, quality objectives, or policies that were established to comply with the Quality System Regulation for Medical Devices, 21 CFR Part 820.

5. Failure of management with executive responsibility to review the suitability and effectiveness of the quality system at defined intervals and with sufficient frequency according to established procedures to ensure that the quality system satisfies the requirements of this part and the manufacturer's established quality policy and objectives, as required by 21 CFR 820.20(c). For example, Section 3.0, Revision 05, of your firm's "Quality Management System Manual," dated July 2013, states that "Top Management reviews the quality management system at

intervals not exceeding **(b)(4)**." However, management reviews in **(b)(4)** and **(b)(4)** were conducted more than **(b)(4)** apart. The Management Review report for **(b)(4)** was dated **(b)(4)**, and the **(b)(4)** report was dated **(b)(4)**.

6. Failure to establish and maintain procedures to prevent contamination of equipment or product by substances that could reasonably be expected to have an adverse effect on product quality, as required by 21 CFR 820.70(e). For example:

a. There is no procedure to document the activities and cleaning requirements for **(b)(4)** used for in-process testing of nebulizers. The **(b)(4)** for in-process testing of ultrasonic nebulizers. It was observed that these **(b)(4)** were not cleaned and are openly exposed to the manufacturing environment.

b. Your firm's procedure, "*Requerimientos de Condiciones Ambientales y de Limpieza,* GC-E-06-06, Rev. 05, dated December 20, 2012," does not specify the methods, supplies, equipment, or personnel responsible for maintaining and cleaning various areas. During the inspection it was noted that multiple areas of the facility were not cleaned or maintained. Specifically:

i. **(b)(4)**

ii. **(b)(4)**

iii. **(b)(4)**

iv. **(b)(4)**

v. **(b)(4)**

7. Failure to maintain procedures for acceptance of incoming product. Incoming product shall be inspected, tested, or otherwise verified as conforming to specified requirements. Acceptance or rejection shall be documented, as required by 21 CFR 820.80(b). For example, your firm's procedure, "*Recepcion de Insumos y Materiales,* GC-E-07-13, Rev. 6," dated April 15, 2010, indicates that a **(b)(4)** sticker is to be placed on each box of incoming material awaiting inspection. Additionally, the application of a **(b)(4)** sticker indicates approval of incoming material and the application of a **(b)(4)** sticker indicates rejected material. However, during the inspection it was noted that several pallets of incoming material were missing the appropriate incoming material inspection stickers.

8. Failure to validate computer software for its intended use according to an established protocol, as required by 21 CFR 820.70(i). For example, your firm uses **(b)(4)** to generate, store, and disseminate standard operating procedures, forms, and other records. **(b)(4)** is also used by your firm to generate and store Device History Records (DHRs) and other quality system data. During the inspection, your firm indicated that the procedure titled, "*Validacion del software utilizado en el sistema de calidad,* GC-E-07-49, Rev. 00," dated March 14, 2011, states that validation is concentrated on software and documents used in the quality system since there is no software used in your firm's manufacturing equipment. However, your firm could not produce any evidence to demonstrate that the software programs were validated for their intended use.

9. Failure to maintain procedures to ensure that DHRs for each batch, lot, or unit are maintained to demonstrate that the device is manufactured according with the Device Master Record, as required by 21 CFR 820.184. For example, production supervisor approval signatures were not present on form R-E-08-04-02, Rev. 01, which was included in the DHR for an ultrasonic nebulizer, Model 3058, lot numbe **(b)(4)**.

Your firm's response to this letter should be sent to: Food and Drug Administration, Center for Devices and Radiological Health, Office of

Compliance, Field Operations Branch, White Oak Building 66, Rm 2609, 10903 New Hampshire Ave., Silver Spring, MD 20993. Refer to the Unique Identification Number CMS case #: 410642. If you have any questions about the contents of this letter, please contact: Carl Fischer, Ph.D., Chief, General Hospital Devices Branch, at 301-796-5770or by fax at 301-847-8137.

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 yours,
/S/
Steven D. Silverman
Director
Office of Compliance
Center for Devices and
Radiological Health

Page Last Updated: 12/06/2013
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