Inspections, Compliance, Enforcement, and Criminal Investigations

Cotton High Tech S.L. (d/ba COHITECH) 1/23/14

Department of Health and Human Services

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

January 23, 2014

WARNING LETTER

VIA UNITED PARCEL SERVICE

Ramon Vendrell-Vila
President
Cotton High Tech S.L. dba CoHiTech
Colonia La Rabeia, s/n
Balsareny, Barcelona
Spain

Dear Mr. Vendrell-Vila:

During an inspection of your firm located in Barcelona, Spain on August 5 through August 8, 2013, an investigator from the United States Food and Drug Administration (FDA) determined that your firm manufactures tampons and menstrual pads. 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.

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 methods 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 your firm's responses, dated August 30, 2013, September 9, 2013, and September 26, 2013, concerning our investigator's observations noted on the Form FDA 483 (FDA 483), List of Inspectional Observations, which was issued to your firm. We address these responses below, in relation to each of the noted violations. These violations 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. Your firm's corrective and preventive action (CAPA) procedure number 1R-2P-52, edition 3, does not specify how returned products will be analyzed to determine if a CAPA is required.

b. Your firm's CAPA number AP002/12 involved **(b)(4)**. However, the CAPA did not consider the need for verifying and/or validating the corrective action to ensure that the change does not adversely affect the finished product.

We reviewed your firm's responses and conclude that they are not adequate. Your response included a revised CAPA procedure 2P-53, edition 4. Your firm's revised CAPA procedure is deficient. Specifically, the procedure does not define or refer to the types and sources of data that should be analyzed to identify existing and potential causes of nonconformity, statistical methodology to be employed for any analysis of such data, the process for disseminating information related to quality problems, and the process for the review of non-conforming products. Additionally, your firm's response did not state whether your firm plans to conduct a retrospective review of all CAPA reports to address the similar deficiencies. Your response indicated that a process validation plan for the sprayer has been drafted and that a validation report will be provided once validation is completed. A summary of your validation report and relevant personnel training documents should be submitted for review.

2. Failure to establish and maintain procedures to ensure that formal documented reviews of the design results are planned and conducted at appropriate stages of the device's design development, as required by 21 CFR 820.30(e). For example, during the inspection, your firm confirmed that design reviews were not documented for Organyc brand tampons. Specifically, your firm had no documentation to assure that its design review team evaluated design inputs, outputs and verification/validation activities for Organyc brand tampons.

We reviewed your firm's responses and conclude that they are not adequate. Your firm has initiated a CAPA document number AC018/13 to address the above deficiencies. As part of this CAPA, your firm revised its Design Review Standard Procedure, 1I-1P-42, edition 1. This procedure is deficient. Specifically, the procedure does not provide or reference the stages at which a design review should be conducted. The procedure does not ensure that participants at each design review include representatives of all functions concerned with the design stage being reviewed and individuals who do not have direct responsibility for the design stage being reviewed, as well as any specialist needed. Your firm's response did not indicate whether it plans to retrospectively review all products for similar deficiencies.

3. Failure to establish and maintain data to ensure that all purchased or otherwise received product and services conform to specified requirements, as required by 21 CFR 820.50. Specifically, your firm failed to establish adequate quality agreements with its suppliers. For example,

a. A review of your Certificate of Conformance for order number **(b)(4)** (Lot **(b)(4)**) revealed that your firm's suppliers were using test methods that were not approved by your firm. Your firm's suppliers also did not comply with pathogen test requirements identified in your firm's technical data sheet for **(b)(4)**. Your firm was not notified of either change by its supplier.

b. A review of the Instructions for Use for the Organyc tampons revealed that tampons were labeled as "bleached without chlorine" and "without artificial pesticides." However, your firm's supplier documentation did not provide evidence of testing conducted in support of such claims.

We reviewed your firm's responses and conclude that they are not adequate. Your response indicated that your firm has initiated CAPA document number AC024 to address the above

deficiencies. As part of this CAPA, your firm has revised its purchasing control procedure, 1P-43, edition 3, to include the requirements for the supplier to notify your firm of any changes made to the product or service. Your firm's response did not state whether your firm has evaluated the unapproved changes to determine whether the changes may affect the quality of your firm's finished product, nor did it indicate any plans for supplier audits. Your firm's response also did not indicate whether your firm has conducted or plans to conduct a review of all existing supplier agreements for similar deficiencies. Additionally, your firm's response indicated that personnel training was conducted; however, training records were not submitted for review.

4. Failure to establish and maintain acceptance procedures, where appropriate, to ensure that specified requirements for in-process product are met, as required by 21 CFR 820.80(c). For example, a review of your firm's in-process testing procedures revealed the following deficiencies:

a. The environmental control procedure, 1P-33, edition 1, requires **(b)(4)** microbiological testing of the tampon production area. However, the procedure does not define test limits or acceptable criteria for the test.

b. Your firm's Syngina Test procedure, 181-1P-44, edition 1, for testing tampon absorbency capacity has not been updated to reflect current practice. Specifically, the procedure does not include the following information:

i. Instructions to verify prior to use that condoms used for this test had a tensile strength between 17 Mega pascals (MPa) and 30 MPa.
ii. Results for the absorbency for the production run, lot, or batch should be rounded off to nearest **(b)(4)** gram.
iii. The use of condoms for this test must be changed after **(b)(4)** tests or **(b)(4)**.
iv. To set the infusion needle at a rate of **(b)(4)** millimeters per hour.

We reviewed your firm's response and conclude that it is not adequate. Your response indicated that your firm has initiated CAPA document number AC023/13 to address the above deficiencies. As part of the CAPA activities your firm has revised its Environmental Control procedure. Your firm's revised procedure fails to set test limits and instead noted that a trend will be followed in order to establish the test limits. It is not clear how your firm intends to ensure adequate environmental controls while it awaits the trend analysis. Additionally, your response did not indicate how your firm plans to conduct the trend analysis and provide justification for methodologies appropriate for establishing test limits. Your firm's response did not address whether all microbiological testing currently in use would be retrospectively reviewed to address similar deficiencies.

Additionally, your response indicated that your firm's revised Syngina Test procedure, 18I-1P-44, edition 2, has been revised to address the above deficiencies. However, your firm's response did not address whether your firm plans retrospectively review all Syngina test records to ensure that the test parameters were within the specification limits. Further, your firm's response did not indicate whether your firm plans to conduct a review of all existing test methods to ensure that appropriate test limits and acceptance criteria are being utilized. Your firm's response indicated that personnel training were conducted; however, no training documents were submitted for review.

5. Failure to validate computer software for its intended use according to an established protocol when computers or automated data processing systems are used as part of production or the quality system, as required by 21 CFR 820.70(i). For example, as per CAPA report number AP_009/13 your firm implemented a **(b)(4)** to conduct quality control functions such as, but not limited to, verifying menstrual pad shape, size, and missing parts. However, your firm was unable to demonstrate that the **(b)(4)** was validated for its intended use.

We reviewed your firm's responses and conclude that they are not adequate. Your firm's response

indicated that your firm has initiated CAPA number AC016/13 to address the above deficiencies. As part of the CAPA, your firm has revised its Process Validation procedure, 8P-44, edition 00. Your firm's revised procedure is deficient in that it does not reference the process that your firm follows in order to determine whether a process requires validation. Your firm's response did not indicate whether your firm plans to conduct a retrospective review of existing **(b)(4)** for similar deficiencies. Your firm's response indicated that personnel training was conducted; however, training documents were not submitted for review.

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. Your firm's Environmental Control Procedure, 1P-33, edition 1, does not include requirements for excluding non-biological contamination such as foreign particles or debris. During the inspection, the FDA investigator observed a **(b)(4)**. Additionally, your firm's tampon assembly line is **(b)(4)** that did not include a barrier to ensure that, if the **(b)(4)** broke, the **(b)(4)** would not fall into the tampon's absorbent pad.

b. Your firm's procedure does not contain sufficient controls to reduce or eliminate contamination by production personnel. Specifically, production personnel are not required to wear gloves when directly contacting cotton at the cotton loosening station. This cotton is used to assemble all tampons.

c. Your firm's current facility layout is not conducive to contamination control. Specifically,

i. There are no hand washing stations or disinfectant station installed inside the gown up room. Wash rooms are located only in the restrooms. This practice increases the risk of contamination in the production line.
ii. The facility floor plan allows employees to enter the production area directly from the street without utilizing the gown up room.

We reviewed your firm's responses and conclude that they are not adequate. Your firm's response indicated that your firm has initiated CAPA number AC020/13 to address the above deficiencies. Your firm plans to implement a new work instruction for gowning and hand washing. Your firm has also identified an improved layout to better manage the workflow and to improve contamination control. However, your firm's response did not indicate whether your firm plans to conduct a retrospective review of existing processes and procedures to ensure they incorporate appropriate contamination control measures. Your firm's response indicated that personnel training was conducted; however, training documents were not submitted for review.

7. Failure to establish and maintain adequate procedures to control labeling activities, as required by 21 CFR 820.120. For example, your firm's Labeling Control procedure, 2P-44, edition 2, includes a requirement to review and approve master drawings for cartons and product labels for tampons against specifications outlined per Checklist IR-2P-44. However, neither the procedure nor the checklist include that the labeling needs to ensure that all instructions and information (statistics and warning signs) related to Toxic Shock Syndrome were displayed.

We reviewed your firm's responses and conclude that they are not adequate. Your firm's response indicated that your firm initiated CAPA number AC017/13 to address the above deficiencies. Your firm revised Labeling Procedure number 2P-4, edition 3, to include the requirements of 21 CFR Part 801.430. However, your firm's response did not indicate whether your firm plans to conduct a retrospective review of existing labeling to ensure it meets all applicable regulatory requirements. Your firm's response indicated that personnel training was conducted; however, training records were not submitted for review.

8. Failure to maintain device master records (DMRs) and to ensure that each DMR is prepared

and approved in accordance with 21 CFR 820.40, as required by 21 CFR 820.181. For example, your firm's DMR did not include quality assurance specifications, including acceptance criteria for microbiological tests conducted per SOP 1P33 and the Syngina Test for tampon absorbency conducted per SOP 181-1P-44.

We reviewed your firm's response and conclude that they are not adequate. Your firm's response indicated that your firm has initiated CAPA number AC023/13 to address the above deficiencies. Your firm has revised the Syngina Test procedure 1P-33. However, your firm's response did not indicate whether your firm plans to conduct a retrospective review of existing DMR records to ensure they include accurate device, production, process, quality assurance procedure, and packaging and labeling specifications. Your firm's response indicated that personnel training was conducted; however, training records were not submitted for review.

Our inspection also revealed that your firm's tampons are misbranded under sections 502(a) of the Act, 21 U.S.C. § 352(a), because your firm's labeling fails to reveal material facts, *i.e.*, required warning statements for menstrual tampons. with respect to the consequences that may result from failing to include the. Your firm's device is further misbranded under sections 502(f) of the Act, 21 U.S.C. § 352(f), in that the labeling fails to provide adequate directions for use. The violations include, but are not limited to, the following:

Failure to establish and maintain adequate user labeling for menstrual tampons, as required by 21 CFR 801.430. For example, your firm's package insert for Organyc Tampons is deficient. Specifically, the package insert does not meet the following requirements:

a. The package insert states that a "sudden, high fever (39^0 or higher)" is one of the warning signs of Toxic Shock Syndrome (TSS). However, the requirement under this section states, "sudden fever (usually 102 deg. or more)" is one of warning signs of TSS.

b. The package insert does not state, "the estimated incidence of TSS of 1 to 17 per 100,000 menstruating women and girls per year." Your firm should revise the package insert to include this information.

c. The package insert does not state that there is a risk of death from contracting TSS. Your firm should revise the package insert to include this information.

A follow up inspection will be required to assure that corrections and/or corrective actions are adequate.

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 award of contracts. Additionally, premarket approval applications for Class III devices to which the Quality System regulation deviations are reasonably related will not be approved until the violations 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, including 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 action (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. Please provide a translation of documentation not in English to facilitate our review.

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/
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Director
Office of Compliance
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cc.
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