Inspections, Compliance, Enforcement, and Criminal Investigations

Mapa Gmbh 12/31/13

Department of Health and Human Services

Public Health Service
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

December 31, 2013

WARNING LETTER

VIA UNITED PARCEL SERVICE

Mr. Michael Frankenstein
Managing Director
MAPA GmbH
Industriestrasse 21-25
Zeven 27404
Germany

Dear Mr. Frankenstein:

During an inspection of your firm located in Industriestrasse 21-25, Zeven, Germany on September 16 through September 19, 2013, an investigator from the United States Food and Drug Administration (FDA) determined that your firm manufactures breast pumps and latex condoms. 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 a response from Mr. German Frank, Director of Quality Management, dated October 2, 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 this response 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 monitoring and control of process parameters for validated processes to ensure that the specified requirements continue to be met, as required by 21 CFR 820.75(b). For example: your firm's validation reports for **(b)(4)** method used for

testing in-process latex condoms did not document the following:

a. Lot numbers for in-process or finished products for the initial test conducted on June 11, 2011.

b. Lot numbers or original test results for the yearly monitoring test conducted on May 11, 2012.

We reviewed your firm's response and conclude that it is not adequate. The response indicated that your firm intends to complete validation of the **(b)(4)** test equipment by week 43/13 and future monitoring of the test equipment (calibration) will contain the test results. However, your firm failed to provide any evidence of implementation of its corrective actions. Specifically, your firm should submit a copy of any revised procedures, a summary of the validation test results and personnel training records for review.

2. Failure to review and evaluate the process and perform revalidation, where appropriate, when changes or process deviations occur and to document these changes, as required by 21 CFR 820.75(c). For example:

a. A review of your firm's process validation reports for dipping machine **(b)(4)** and **(b)(4)**, used for manufacturing latex condoms, revealed that since 2011 your firm has been using new parameters for the dipping machines and running production batches in accordance with ISO 4704 standards. Your firm's initial process validation was conducted using different parameters and in accordance with the European standard (EN600). However, your firm has not revalidated the dipping process for the new production parameters.

b. A review of your firm's process validation records for sealing machine **(b)(4)**, used for manufacturing latex condoms, revealed that since 2011 your firm has been using new parameters for the sealing machine and running sealing processes in accordance with ISO4704 and ASTM 3492 standards. Your firm's initial process validation was conducted using different parameters and in accordance with EN600. However, your firm has not revalidated the sealing process for the new production parameters.

We reviewed your firm's response and conclude that it is not adequate. The response indicated that your firm intends to complete revalidation of the dipping lines **(b)(4)** and **(b)(4)** and the sealing machine by week 50/13. Your firm's response did not address whether other manufacturing processes will be retrospectively reviewed to address similar deficiencies. Your firm should submit a copy of any revised procedures, a summary of the validation test results and personnel training records for review.

3. 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, during the inspection your firm confirmed that its software program **(b)(4)** version **(b)(4)** released on August 28, 2009, for documenting condom production control tests has not been validated for its intended uses.

We reviewed your firm's response and conclude that it is not adequate. The response indicated that your firm's supplier has validated the **(b)(4)** software and validations will be documented by week 49/13. Your firm should clarify the intended uses of the software. If the software is responsible for calculating data, your firm should validate the software as required by 21 CFR 820.70(i). Your firm should provide evidence of implementation of its corrective actions. Specifically, your firm should provide a copy of its software validation procedures, a summary of the validation test results and personnel training records, if appropriate, for review.

4. Failure to establish and maintain adequate procedures for implementing corrective and preventive action, as required by 21 CFR 820.100(a). For example, review of your firm's Corrective

and Preventive Action procedure, No.V-BQ-013, Rev. 6, revealed the following deficiencies:

a. The procedure does not include the requirements that implementing and recording changes in methods and procedures are needed to correct and prevent identified quality problems.

b. The procedure does not describe how corrective and preventive actions will be verified and/or validated and checked for effectiveness.

c. The procedure does not describe how corrective and preventive actions are analyzed to ensure that all issues related to processes, operations, concessions or quality are detected and corrected effectively.

d. The procedure does not define when appropriate statistical methodology shall be employed to detect recurring quality problems.

e. The procedure does not describe how 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.

We reviewed your firm's response and conclude that it is not adequate. The response indicated that the Corrective and Preventive Action procedure will be revised in accordance with 21 CFR 820.100 by week 43/13. However, your firm failed to provide any evidence of implementation of its corrective actions. Specifically, your firm should submit a copy of its revised procedure and personnel training records, if appropriate, for review.

5. Failure to maintain complaint files and 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 complaint handling procedure, No. V-BQ-012, rev. 11 does not describe how complaints are evaluated to determine whether they represent an event that is reportable under 21 CFR 803, Medical Device Reporting. Additionally, a review of **(b)(4)** complaints related to condom tear, burst and error in shipment revealed that **(b)(4)** of these complaints were evaluated for reportability.

We reviewed your firm's response and conclude that it is not adequate. The response indicated that the "complaint management" will be changed by week 44/13. However the response did not address whether the compliant handling procedure will be revised and a retrospective review of all complaints will be conducted for reportability per revised procedure. Your firm failed to provide evidence of implementation of its corrective actions. Your firm should submit a copy of any revised procedures, a summary of its complaint trend analysis and personnel training records, if appropriate, for review.

6. 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). For example, review of your firm's Design Change Procedure, Doc. #V-BK-004, Rev.2, revealed the following deficiencies:

a. The procedure does not define at what stage a re-validation/or re-verification of the change should be conducted when a design change of a device occurs. During the inspection, your firm indicated that the design verification changes occur at the supplier's end; however, this is not stated in the procedure.

b. The procedure does not define steps necessary to document engineering changes of a device. Specifically, a review of your firm's design update document for electrical breast pumps, Doc. No. TD-036, Rev. 3.0 revealed that the design changes implemented for **(b)(4)** versions (**(b)(4)**) of the electrical breast pump were not documented.

c. The procedure does not require a review and approval of design changes prior to transfer into production. Specifically, your firm failed to provide design specifications for **(b)(4)** versions (**(b)(4)** version **(b)(4)**) of the electrical breast pump to its contract manufacturer.

We reviewed your firm's response and conclude that it is not adequate. The response indicated that the procedure for the change management will be revised in accordance with 21 CFR 820.30 by week 52/13. However, the response did not address whether all design files will be retrospectively reviewed to address the similar deficiencies. Specifically, the response did not provide any assurance that the **(b)(4)** version **(b)(4)** electrical breast pumps are manufactured in accordance with the design specifications. Your firm should also provide a copy of its revised design change procedures.

7. 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, your firm confirmed during the inspection that the design reviews for electrical breast pump and latex condoms were not conducted by individuals who do not have direct responsibility for the design of these devices. Additionally, your firm's Device History Files failed to document that independent individuals were selected to review the design.

We reviewed your firm's response and conclude that it is not adequate. The response indicated that the design review procedures will be revised in accordance with the requirements of 21 CFR 820.30 by week 52/13. However, the response did not address whether all design files will be retrospectively reviewed for similar deficiencies. Your firm should provide a copy of its revised design review procedures for review.

8. Failure to establish and maintain procedures to ensure that device history records (DHRs) for each batch, lot, or unit are maintained to demonstrate that the device is manufactured in accordance with the device master record (DMR) and the requirements of 21 CFR 820, as required by 21 CFR 820.184. For example, a review of your firm's DHRs for the finished lots (Lot #s **(b)(4)**, **(b)(4)** and **(b)(4)**) of latex condoms revealed that the DHRs did not contain the following:

a. Production records for washing and drying of in-process condoms.

b. The primary identification label and labeling used for each production lot.

c. Acceptance records demonstrating the devices were manufactured in accordance with DMRs.

We reviewed your firm's response and conclude that it is not adequate. The response indicated that your firm will address the DHR issues to comply with the requirements of 21 CFR 820 by week 45/13 and ensure the device is produced in accordance with the DMR. However, the response did not address whether DHRs for all devices will be retrospectively reviewed to address similar deficiencies. Your firm should provide evidence of its corrective actions, including revised procedures and the results of its retrospective review.

9. Failure to establish procedures for identifying training needs and ensure that all personnel are trained to adequately perform their assigned responsibilities and to document training, as required by 21 CFR 820.25(b). For example, your firm's training procedure V-AP-001-U-E, version 9 does not describe the process of training new employees and current employees on production processes and test methods for manufacturing the latex condoms. At the time of the inspection, your firm did not have training records demonstrating that the operators were adequately trained to perform the activities and tests methods used during production.

We reviewed your firm's response and conclude that it is not adequate. The response indicated that the training procedures will be updated and personnel will be trained per revised procedures by week 46/13. Your firm should provide evidence of its corrective actions for review, including a copy of its revised training procedures and personnel training records . .

Our inspection also revealed that your firm's devices (breast pumps and latex condoms) 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. Significant 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, during the inspection your firm confirmed that it does not have written MDR procedures.

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**.

Your firm's response 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 2622, 10903 New Hampshire Ave., Silver Spring, MD 20993. Refer to CMS case #415564 when replying. If you have any questions about the contents of this letter, please contact: Mr. Daniel Walter, Chief, Foreign Enforcement Branch at 301-796-5587.

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

cc:
Dr. Ralf Holschumacher
Vice President of Technical Operations
Mr. German Frank
Director of Quality Manager
MAPA GmbH
Industriestrasse 21-25
Zeven 27404
Germany

Mr. Eric Johnson
U.S. Agent
728 Booster Boulevard
Reedsburg, Wisconsin

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