U.S. Department of Health & Human Services

U.S. Food and Drug Administration

Inspections, Compliance, Enforcement, and Criminal Investigations

Health Robotics Srl 3/14/11

Department of Health and Human Services

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

MAR 14 2011

WARNING LETTER

VIA UNITED PARCEL SERVICE

Werner Rainer
Chief Executive Officer
Health Robotics Srl
Via Altmann 9/A
39100 Bolzano, Italy

Dear Mr. Rainer:

During an inspection of your firm located in Trieste, Italyon November 8, 2010, through November 12, 2010, an investigator from the United States Food and Drug Administration (FDA) determined that your firm manufactures pharmacy compounding systems - the CytoCare system and i.v.STATION system. 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 are intended 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 (CGMP) requirements of the Quality System (QS) regulation found at Title 21, Code of Federal Regulations (C.F.R.), Part 820. We received a response from Mr. Fabio Fioravanti dated December 3, 2010, concerning our investigator's observations noted on the Form FDA 483, List of Inspectional Observations that was issued to you. 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 adequate procedures for validating device design, as required by 21 CFR 820.30(g).

For example: your firm's Design Control procedure (D R&D 33.00) and the Design and Development Planning procedure (P R&D 01.01) require documentation of validation in the design history file (DHF), however, there was no evidence of design validation during a complete review of the i.v.STATION's DHF.

We reviewed your response dated December 3, 2010, and conclude that it is not adequate because there was no evidence of R&D personnel retraining. Your firm only provided a retraining request. Furthermore, evidence of implementing the revised internal audit procedures to identify procedural deficiencies was not submitted to FDA. Lastly, your firm's retrospective review and update of all DHFs was not scheduled for completion until February 2011.

Additionally, documentation of all software validation results for the i.v.STATION was not completed per your firm's Design Control, (D R&D 33.00) and the Design and Development Planning (P R&D 01.01) procedures. For the **(b)(4)** software validation test, the output is to verify that the procedure was completed correctly and that the "bag contains the requested volume of the drug." The test completion date and the volume of the drug were not recorded. Additionally, successful completion of the **(b)(4)** software validation test is to verify "that the syringe contains the required volume of drug." The completion date and the volume of the drug in the syringe

were not recorded, per procedure, for this test as well.

We reviewed your response dated December 3, 2010, and conclude that it is not adequate because retraining documentation for the R&D personnel, scheduled for completion on December 20, 2010, was not provided. Furthermore the revised test report format which includes fields for documenting test results/acceptance criteria was not submitted to FDA. Lastly, repeated software validation under the revised procedure (which should be submitted to FDA) was not scheduled for completion until January 2011.

2. Failure to establish and maintain adequate procedures for verifying the device design, as required by 21 CFR 820.30(f).

For example: the DHF for the i.v.STATION failed to include documentation of design input and that all design outputs met design inputs as directed in your firm's Design Control procedure (D R&D 33). Furthermore, documentation of verification test results, identified in the test plan, was not located in the DHF. The only verification documentation found in the i.v.STATION's DHF was a test of syringe output accuracy, and evaluation of the air flow in the i.v.STATION cabinet. The syringe output test did not have acceptance criteria listed. The product specification calls for accuracy of +/- **(b)(4)** % from **(b)(4)** mL; however a test result of - **(b)(4)** % for a **(b)(4)** mL fill did not contain an explanation of failing to meet specifications. Additionally, there was no acceptance criteria listed for the evaluation of air flow, and the testing did not demonstrate laminar flow or a determination of air quality in the chamber, even though the specification calls for an **(b)(4)** level air quality.

We reviewed your response dated December 3, 2010, and conclude that it is not adequate because your firm only provided the revised design control procedure, with the traceability matrix for input/output verification. Evidence of corrective action implementation was not submitted to FDA. Additionally, your firm's planned retrospective review of all DHFs was not scheduled for completion until February 2011.

3. Failure to establish and maintain adequate procedures for implementing corrective and preventive action, as required by 21 CFR 820.100(a).

For example: the Improvement/Corrective and Preventive Actions procedure (D ZM 03.01) does not describe the frequency of collecting data and trending information to ensure the corrective action is initiated. There is also no documentation to ensure quality data source information is being analyzed. Additionally, four out of **(b)(4)** corrective actions lacked the following information:

- CAPA20100814 was opened in response to a report involving **(b)(4)** liter bag failure with the CytoCare system. The CAPA form was not completed appropriately as described in your firm's CAPA procedure (D QM 03.01). Only "Section I – Description" and the proposed corrective action of Section III was filled out on the form. The CAPA form, among other things, did not document: results of the root cause investigation, status of the corrective action, and the appropriate signatures and dates for various stages of the investigative process.

- CAPA20100806 was opened in response to a report involving **(b)(4)** mL syringes breaking in the CytoCare system when removed from the dosing monitor. The CAPA form was not completed appropriately as described in your firm's CAPA procedure (D QM 03.01). Only "Section I – Description" and the proposed corrective action field of Section III was filled out. The CAPA form, among other things, did not document: results of the root cause investigation, status of the corrective action, and the appropriate signatures and dates for various stages of the investigative process.

- CAPA20100914 was opened in response to a customer request to provide a "user friendly trouble shooting manual." The CAPA form was not completed appropriately as described in your firm's CAPA procedure (D QM 03.01). Only "Section I – Description" and the proposed corrective action field of Section III was filled out. The CAPA form, among other things, did not document: results of the root cause investigation, status of the corrective action, and the appropriate signatures and dates for various stages of the investigative process.

- CAPA20100819 was opened to address rust on steel panels of the CytoCare system. The corrective action was to inform the customer, via email, of the rust removal procedure. The CAPA was closed out, but the final effectiveness review did not include documentation on how the corrective action was verified.

We reviewed your response dated December 3, 2010, and conclude that it is not adequate because revision of your firm's CAPA procedure was completed during the review of this inspection on or around December 20, 2010, and was not provided to FDA. Additionally, the evaluation of the revised procedure was not scheduled for completion until January 31, 2011. Lastly, a retrospective review of all CAPAs was not to be completed until January 31, 2011.

4. Failure to establish and maintain adequate procedures for receiving, reviewing, and evaluating complaints by a

formally designated unit, as required by 21 CFR 820.198(a).

For example: your firm only evaluated help desk tickets for the CytoCare system and not the i.v.STATION. Approximately **(b)(4)** help desk tickets pertaining to the i.v.STATION test or installation were not assessed for complaint investigation. Mr. Fabio Fioravanti, Executive VP of Operations and Technical Officer, state that only closed tickets or potential adverse events were elevated for further follow-up. Additionally, all of the CytoCare tickets routed by the help desk for further evaluation were not classified as complaints, even though they meet the definition of a complaint per your firm's complaint handling procedure. Help desk tickets #**(b)(4)** and #**(b)(4)** cited problems with the refrigeration system and waste bin door motor respectively, but were not handled as complaints and, therefore, not investigated.

We reviewed your response dated December 3, 2010, and conclude that it is not adequate because your firm did not provide all of the training records for the employees identified in the new complaint handling retraining request. Only tw of the **(b)(4)** employee training records were provided to FDA. Furthermore, it is difficult to ascertain whether all employees performing help desk duties were retrained because the names of individuals that appear on help desk ticket were not included on the submitted training request. Additionally, corrective actions for complaint handling have only been completed for the three help desk tickets identified as inadequate during the investigation. Lastly, a complete retrospective review for all open and closed tickets will not be completed by your firm until May 2011.

5. Failure to establish and maintain adequate procedures for quality audits and for conducting such audits to assure that the quality system is in compliance with the established quality system requirements and to determin the effectiveness of the quality system, as required by 21 CFR 820.22.

For example, your firm's Internal Audit Guidelines procedure (D QM 02.01) did not describe how all areas of the quality system will be assessed by audits. Furthermore, the audit checklist failed to indicate what quality assurance areas would be covered. The checklist was essentially a recitation of the 21 CFR regulation.

We reviewed your response dated December 3, 2010, and conclude that it is not adequate because the revised internal audit procedure and supporting documents were not scheduled for completion until January 3, 2011. Evidence of corrective action implementation was, therefore, not received during review of the inspection. Additionally, a retraining request for personnel on the new audit procedure was provided to FDA, however, there was no evidence that the training was completed.

A follow up inspection will be required to assure that corrections are adequate. We will contact the appropriate people and request an establishment re-inspection. An FDA trip planner will be in touch with you to arrange a mutually convenient date for this inspection.

You should take prompt action to correct the violations addressed in this letter. Failure to promptly correct these violations may result in regulatory action, which may include detaining your devices without physical examination upon entry into the United States until the corrections are completed. Section 801(a) of the Act (21 U.S.C. § 381(a)). Also, U.S. federal agencies are advised of the issuance of all 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. 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 (15) working days from the date you receive this letter of the specific steps you have taken to correct the noted violations, including an explanation of how you plan to prevent these violations, or similar violations, from occurring again. Include documentation of the corrective action you have taken. I your planned corrections will occur over

time, please include a timetable for implementation of those corrections. If corrective action cannot be completed withi 15 working days, state the reason for the delay and the time within which the corrections will be completed. If the documentation is not in English, please provide a translation to facilitate our review.

Your response should be sent to: Ms. Valerie A. Flournoy, General Hospital and Devices Branch, U.S. Food and Drug Administration, 10903 New Hampshire Avenue, Building 66, Room 3526, Silver Spring, Maryland 20993. If you have any questions about the content of this letter please contact: Mr. Neil A. Mafnas at 301-796-5770 or 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 facility. It is your responsibility to ensure compliance with applicable laws and regulations administered by FDA. The specific violations noted in this letter and in the Inspectional Observations, Form FDA 483 (FDA 483), issued at the closeout of th inspection may be symptomatic of serious problems in your firm's manufacturing and quality assurance systems. You should investigate and determine the causes of the violations, and take prompt
actions to correct the violations and to bring your products into compliance.

Sincerely yours,

/S/

Steven D. Silverman
Director
Office of Compliance
Center for Devices and
Radiological Health

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