



Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

JUN 24 2003

WARNING LETTER

FEDERAL EXPRESS

Mr. Bernd Zimmer
President
Zimmer Elektromedizin GmbH
Junkerstrasse 9
D-89231 Neu-Ulm
GERMANY

Dear Mr. Zimmer:

During an inspection of your firm in Neu-Ulm, Germany on March 10, 2003, through March 13, 2003, investigators acting on behalf of the United States Food and Drug Administration (FDA) determined that your firm manufactures the Cryo 5 skin cooling system and the Disposable Therapy Electrode. These products are medical devices under a United States law, the Federal Food, Drug, and Cosmetic Act (the Act), 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 a function of the body (Section 201(h) of the Act, 21 U.S.C. § 321(h)).

Our records do not show that there is marketing clearance or approval in effect for the Cryo 5 skin cooling system device that you are offering for sale in this country, as required by section 510(k) of the Act (21 U.S.C. § 360(k)). The identification of the product as a reusable cold pack in our device listing records (listing number A 723694) appears to be based on a letter from FDA dated May 2, 1995, in which a similar device, the MATRIX Criojet, was found to be substantially equivalent to a reusable cold pack, which is a class I device that is exempt from the Section 510(k) premarket notification requirement (21 CFR 890.5700). The User Manual for the Cryo 5 states that the product is indicated for "skin cooling for medical purposes." According to other product literature, the Cryo 5 is a "skin cooling system designed for superficial laser skin procedures." The literature also states, "Cold air -32°C skin cooling significantly reduces pain and discomfort for superficial laser applications, while protecting the tissues from possible thermal damage and allowing a higher fluence for increased efficiency."

The Cryo 5, when intended for use as a stand alone device for superficial laser skin procedures, is not exempt from the Section 510(k) premarket notification requirement because it is intended

for a use different from the intended use of a legally marketed device in the generic cold pack device category (21 CFR 890.5700) as per 21 CFR 890.9. Cooling devices intended for use with lasers are considered accessories to lasers, and hence, are class II devices requiring premarket notification. 21 CFR 878.4810. Although the Cryo 5 was cleared in K013864, it was only cleared for use with the Nidek laser system. A new premarket notification must be submitted in order to market the Cryo 5 for use as a stand alone device with a laser system (21 CFR 807.81(a)(3)(ii)).

The law requires that manufacturers of medical devices obtain marketing clearance for their products from FDA before they may offer them for sale. This helps to protect the public health by ensuring that new medical devices are shown to be either safe and effective or substantially equivalent to other devices already legally marketed in this country. The kind of information you need to submit in order to obtain this clearance is described in FDA regulations at Title 21 Code of Federal Regulations, Part 807. You may also find the requirements at www.fda.gov/cdrh/devadvice/3122.html. After you have submitted this information, FDA will evaluate it and decide whether your devices may be legally marketed in this country.

Because your products do not have marketing clearance or approval from FDA, they are in violation of the law. In legal terms, your products are adulterated under Section 501(f)(1)(B) (21 U.S.C. § 351(f)(1)(B)) and misbranded under section 502(o) of the Act (21 U.S.C. § 352(o)). These products are adulterated under the Act because you did not obtain premarket approval based on information developed by you that shows your devices are safe and effective. These products are misbranded under the Act because you did not submit information that shows that your devices are substantially equivalent to other legally marketed predicate devices. (For products that require the submission and approval of a premarket approval application (PMA), the notification required by section 510(k) of the Act is deemed to be satisfied when a PMA is pending before the agency, 21 CFR 807.81(b), but marketing may not begin until premarket approval is granted.)

Our inspection revealed that your other medical devices, the Disposable Therapy Electrodes, 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, packaging, storage, or installation are not in conformity with Current Good Manufacturing Practice (CGMP) requirements, which are set forth in FDA's Quality System (QS) regulation, in Title 21, Code of Federal Regulations (CFR), Part 820, as listed below:

1. Failure to validate with a high degree of assurance a process where the results can not be fully verified by subsequent inspection and test, as required by 21 CFR 820.75(a). For example:
 - a. The packaging sealing process was not validated.
 - b. The ability of the mixing process to ensure that the concentration of free acryl acid remains within the specified limits was not validated.

We acknowledge receipt of your response dated April 7, 2003. In your response you state that the above processes are being validated and that the validation will be completed before June 11, 2003. In order to determine the adequacy of your response, please submit a copy of the final validation report translated into English when it is completed.

2. Failure to establish and maintain process control procedures that describe the process controls necessary to ensure conformance to specifications, as required by 21 CFR 820.70(a). For example:
 - a. The Device Master Record and the specifications/procedures for mixing the gel do not adequately define the mixing parameters.
 - b. There are no established procedures for the pre-process set-up operations or shut-down operations for the production of the electrodes.

In your response of April 7, 2003, you state that the gel mixing process is being validated.

This response is not adequate. Please submit the specifications or procedures (translated into English) for the gel mixing process to demonstrate that the mixing parameters have been clearly defined in any relevant specifications or procedures per the results of the validation. Confirm that the mixing parameters are documented in the Device Master Record.

In your response of April 7, 2003, you state that instructions for the preparation and operation of the Electrode Production System and error procedures have been documented.

This response may be adequate. However, to confirm the adequacy of the response, please submit English translations of the "Operating Instructions for the Disposable Electrode Production System," Version 4 (dated March 31, 2003) and the "Operating Instructions for the Disposable Electrode Machinery Operation" (dated April 3, 2003). A description of how the machine is intended to operate would also be helpful for our review.

3. Failure to adequately establish and maintain procedures for implementing corrective and preventive action to include investigating the cause of nonconformities and identifying actions needed to correct and prevent recurrence, as required by 21 CFR 820.100(a)(2) and 21 CFR 820.100(a)(3). For example, the firm failed to maintain adequate documentation of investigations of nonconformities and complaints or to document the reason for not performing an investigation that was the result of a complaint. Specifically, inspection of two complaints and two reported incidents revealed that the causes of the

nonconformities and the actions needed to prevent recurrence were not documented.

In your response dated April 7, 2003, you state that corrective and preventative measures will be documented on the “Error Report Form” and that SOP 932 has been modified to reflect this change.

The response may be adequate. In order to confirm the adequacy of this response, please submit English translations of the “Error Report Form” and SOP 932, “Corrective Measures,” Version 3 (dated March 21, 2003). Also, describe the difference between an incident report and a complaint and explain whether or not there are differences in the procedures for handling incident reports and complaints. Submit English translations of the procedures related to complaints and incident reports for our review.

4. Failure to establish and maintain procedures for finished device acceptance to ensure that each production run, lot, or batch of finished devices meets acceptance criteria, as required by 21 CFR 820.80(d). For example, electrodes with bubbles in the gel have been accepted for release; this contradicts the specifications given in the Device Master Record.

You state in your response dated April 7, 2003, that the air bubble specification for the gel has been changed to limit the air bubble diameter in the gel to half the size of the coating thickness.

This response is not adequate. You should summarize the design change control procedures used to implement this change, along with a summary of the proper verification or validation of this change. Also, explain the manner in which the procedures for acceptance activities will be implemented to ensure that the proper procedures are being followed.

5. 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 and the requirements of Part 820, as required by 21 CFR 820.184. For example, the parameters for storage and mixing (time stirring speed, temperature) of the ingredients for the electrode gel are not recorded in the DHR.

In your response of April 7, 2003, you state that a form sheet has been incorporated for the production process of the Disposable Therapy Electrode Department. The ingredient parameters are to be recorded and documented on this sheet during the gel production.

This response may be adequate. In order to confirm the adequacy of the response, submit an English translation of the “Form Sheet for Gel Mixture” dated March 31, 2003. Confirm that this information is also documented in the Device History Record.

6. Failure to examine the labeling for accuracy, including, where applicable, the correct expiration date, before releasing labeling for use, as required by 21 CFR 820.120(b). For example, a batch of disposable non-sterile therapeutic electrodes in the finished goods warehouse was labeled with a shelf-life of 2 ½ years rather than the specified 1 ½ year shelf-life.

In your response dated April 7, 2003, you state that instructions for the Disposable Electrode Production have been modified. The modifications include monitoring of the packaging, the Production Department’s records, and the electrodes by the Quality Management Department. The Quality Management Department will use a form sheet to document their monitoring procedures. It appears as though the Form Sheet “Charge Testing” dated March 31, 2003, will be used for this documentation.

This response is not adequate. Confirm that the “Charge Testing” form sheet (dated March 31, 2003) is the form sheet that will be used for the Quality Management Department’s monitoring procedures. Please submit an English translation of this form sheet.

Please submit an English translation of the labeling procedures including the procedures for monitoring the labeling and documentation in the Device History Record. If these procedures are already included in the “Operating Instructions for the Disposable Electrode Production System,” Version 4 dated March 31, 2003, please make reference to the applicable sections within this procedure.

7. Failure to establish and maintain procedures to control all documents that are required by Part 820, including the review and approval of document changes, as required by 21 CFR 820.40(b). There are examples of 2 incident reports and 2 test reports that were corrected without identification of the person who made the correction or the date of the correction.

You state in your response dated April 7, 2003, that SOP 721, “Documentation and Records” has been modified to state that handwritten records and documentation are to be dated and accompanied by the signature of the responsible person.

This response may be adequate. In order to determine the adequacy of this response, submit English translations of SOP 721, “Documentation and Records.”

8. Failure to conduct quality audits in accordance with established quality audit procedures to assure that the quality system is in compliance with the established quality system requirements and to determine the effectiveness of the quality system, as required by 21 CFR 820.22. For example, the 2002 quality audit plan did not include an audit of the company management responsibility program according to the firm's written procedures that require that every department be audited.

You state in your response dated April 7, 2003, that the contents of the Quality Management Handbook which were not completely covered will be corrected in the changes to Chapter 7 of the Quality Management Handbook. You also state that management must read the Audit Report with documentation on the audit plan and that incomplete portions will be corrected.

This response may be adequate. In order to determine the adequacy of the response, please submit an English translation of Chapter 7 of the Quality Management Handbook.

At the time of the inspection, the following observations were noted; however, these observations have been corrected and were verified by the investigator at the time of the inspection:

9. Failure to establish procedures for quality audits that include the conduct of quality audits by individuals who do not have direct responsibility for the matters being audited, as required by 21 CFR 820.22. For example, the internal audit procedures (SOP 751) do not require that the audits be conducted by individuals who do not have direct responsibility for the matters being audited.
10. Failure to document the dates and results of quality system reviews, as required by 21 CFR 820.20(c). For example, the management review procedures do not state that the results and date of the management review be documented.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each applicable requirement of the Act and regulations. The specific violations noted in this letter and in the list of Inspectional Observations (Form FDA 483) issued at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

If you fail to take prompt action to correct these deviations, FDA may take regulatory action without further notice to you. Under Section 801(a) of the Act, for example, FDA could detain your products without physical examination upon entry into the United States, on the ground that they appear to be adulterated under section 501(h). In addition, United States federal agencies

Page 7 – Mr. Bernd Zimmer

are advised of the issuance of all Warning Letters about medical devices so that they may take this information into account when considering the award of contracts. Also, no requests for Certificates For Products For Export will be approved until the violations related to the subject devices have been corrected.

Please notify this office in writing within 15 working days 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 all documentation of the corrective action you have taken. If you plan to make any corrections in the future, include those plans (including timeframes) with your response to this letter as well. If the documentation is not in English, please provide a translation to facilitate our review.

Your response should be submitted to:

Food and Drug Administration
Center for Devices and Radiological Health,
Office of Compliance, Division of Enforcement B
Orthopedic, Physical Medicine and Anesthesiology Devices Branch
2098 Gaither Road
Rockville, Maryland 20850 USA

Please send your response to the attention of Ms. Christy Foreman.

We acknowledge that you have submitted a response, dated April 7, 2003, concerning our investigator's observations noted on the form FDA 483. We have reviewed your response and have concluded that it is inadequate for the reasons cited above.

If you need help in understanding the contents of this letter, please contact Ms. Christy Foreman at the above address or at (301) 594 - 4659 or FAX (301) 594 - 4672.

Sincerely yours,



Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health