DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

m3882n

Food and Drug Administration
Rockville MD 20857

VIA FEDERAL EXPRESS

JUN 22 2000

WARNING LETTER

Mr. Jean-Claude Mas
Chief Executive Officer
Poly Implants Protheses, Sa
337 Avenue De Bruxelles
La Seyne, Sur Mer
France

Dear Mr. Mas:

During an inspection of your firm located in La Seyne, Sur Mer, France on May 11 through May 17, 2000, our investigator determined that your firm manufactures saline pre-filled mammary implants. These are devices as defined by section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above-stated inspection revealed that these devices are adulterated within the meaning of section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Good Manufacturing Practice (GMP) for Medical Devices Regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as listed below.

1. Failure to establish and maintain procedures for verifying the device design and to confirm that the design output meets the design input requirements, as required by 21 CFR 820.30(f). For example, there are no established and maintained written procedures for verifying the device design confirms that the design outputs meet the design input requirements.

2. Failure to establish and maintain procedures for validating the device design to include validation and to perform design validation under defined operating conditions on initial production units, lots, or batches, or their equivalents; and failure to ensure that devices conform to defined user needs and intended uses and to include testing of production units under actual or simulated use conditions including software validation and risk analysis where appropriate, as required by 21 CFR 820.30(g). For example, there are no established and maintained written procedures for validating the device design to ensure the devices conform to defined user needs and intended uses and to include testing of production units under actual or simulated use conditions.

3. Failure to establish and maintain procedures to control all documents that are required providing for the designation of an individual(s) to review for adequacy and approve prior to issuance all documents established to meet the requirements, as required by 21 CFR 820.40(a). For example, the written procedures for change control are inadequate, in that they do not identify those persons who have the authority and responsibility to approve changes and specifications and assign initiation dates.

4. Failure to establish and maintain procedures for implementing corrective and preventive action including requirements for analyzing processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned product, and other sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems, and to employ appropriate statistical methodology where necessary to detect recurring quality problems, as required by 21 CFR 820.100(a)(1). For example, procedures for analyzing data on defective prostheses from Medical Device Reporting (MDR), complaint files, returned devices, and the production area are non-existent or inadequate. There were no procedures for the statistical analysis of complaints or returns. In addition, the document entitled, "PROCEDURE FOR THE STATISTICAL MANAGEMENT OF THE NONCONFORMITIES COMING FROM THE PRODUCTION", reference SQ 1/20 PCD 001, Index B, on page 13 of 13, Application date: 03/08/1999, states that a total defect rate of up to [redacted] is acceptable.

5. Failure to establish and maintain procedures for implementing corrective and preventive action including verifying or validating the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device, as required by 21 CFR 820.100(a)(4). For example, there are no written procedures for verifying or validating corrective and preventive action to ensure the action is effective. You stated that your procedure for verifying correction was to wait one year after the correction had been introduced onto the market and review the number of complaints. If the number was reduced, the correction must have worked.

6. Failure to establish and maintain procedures for implementing corrective and preventive action including implementing and recording changes in methods and procedures needed to correct and prevent identified quality problems, as required by 21 CFR 820.100(a)(5). For example, there is no written procedure for implementing and recording changes in methods and procedures needed to correct and prevent identified quality problems. The procedures provided were inadequate to aid in complying with the regulation.

7. Failure to document all activities required under Section 21 CFR 820.100 and their results, as required by 21 CFR 820.100(b). For example, there is no written record of the investigations into the trends associated with deflation of the saline filled implants or leaks from filling needles.

8. Failure to establish procedures for quality audits and to conduct such audits 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, audits of the quality system were not conducted on an annual basis. This is required by your procedure entitled, "PROCEDURE FOR ORGANIZING AND CONDUCTING INTERNAL AUDITS", Reference SQI/17 PCD 001, Index B, page 6 of 9, application date: 14/10/2000.

9. Failure to establish and maintain procedures for changes to a specification, method, process, or procedure, and to verify or where appropriate validate the changes according to Section 820.75, before implementation and these activities shall be documented and approved in accordance with Section 820.40, as required by 21 CFR 820.70(b). For example:

   a. There are no records of the meetings where the change to approve the new glue, [redacted] for the filling needle holes was reportedly approved.

   b. The Corrective Action Request (CAR) #AQ 99/04, which was identified as the change control document for the approval of the new glue [redacted] for the filling of needle holes, was signed as approved January 10, 2000. The effective date for the change was July 1, 1999. The first production using the new glue was July 2, 1999, lot #99175.

10. Failure to report any complaint that represents an event which must be reported to FDA under part 803 or 804 of this chapter and to promptly review, evaluate, and investigate by a designated individual(s) such complaint, as required by 21 CFR 820.198(d). For example, saline implant complaints received from countries other than the U.S. that qualify as MDRs were not reported to FDA. There were approximately 100 complaints reported to France since January 6, 1997, and at least 20 received from other countries.

11. Failure to establish procedures for identifying training needs and ensure that all personnel are trained to adequately perform their assigned responsibilities, as required by 21 CFR 820.25(b). For example, no personnel have received any formal training in the Quality System Regulation, as outlined in the training procedures calling

for department leaders to evaluate the training needs for their employees. There is no training identified in the training schedules for 1999 or 2000.

Your device is also misbranded under Section 502(t)(2) of the Act in that your firm failed or refused to furnish any material or information required by or under section 519 respecting the device. For example, saline pre-filled implant complaints received from countries other than the U.S. that qualify as reportable to the FDA were not reported. There were approximately 100 complaints reported to France since January 6, 1997, that qualify as reportable, and at least 20 received from other countries. The 100 reportable complaints received from other countries were not reported to FDA.

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 requirement of the Act and regulations. The specific violations noted in this letter and in the 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 Food and Drug Administration. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

In order to facilitate FDA in making the determination that such corrections have been made and thereby enabling FDA to withdraw its advisory to other federal agencies concerning the issuance of government contracts, we are requesting that you submit to this office on the schedule below, certification by an outside expert consultant that s/he has conducted an audit of your establishment's manufacturing and quality assurance systems relative to the GMP requirements of the Quality System Regulation (21 CFR, Part 820). You should also submit a copy of the consultant's report, and certification by your firm's Chief Executive Officer (CEO) (If other than yourself) that your firm has initiated or completed all corrections called for in the report. The attached guidance may be helpful in selecting an appropriate consultant.

The certification of audits should be submitted to this office by the following date:

- Initial certification by an outside consultant no later than December 15, 2000

We have received a copy of your Telefaxed response dated May 26, 2000 to Ms. Marje Hoban. The response includes a plan to answer the FDA 483 observations issued to you at the close of the

inspection. Your response states that a written answer to each observation will be prepared and forwarded to this office. However, given the serious nature of these violations of the Act, all devices manufactured by Poly Implants Protheses, Sa, 337 Avenue De Bruxelles, La Seyne, Sur Mer, France, may be detained without physical examination upon entry into the United States (U.S.) until these violations are corrected.

In order to remove the devices from detention, it will be necessary for you to provide a written response to the charges in this Warning Letter for our review, and have an outside consultant certify your compliance with the Quality System Regulation no later than December 15, 2000. After we notify you that your response is adequate, it will be necessary to schedule an inspection of your facility. Our Division of Emergency and Investigational Operations will contact your facility about scheduling the inspection. As soon as the inspection has taken place, and the implementation of your corrections has been verified, your products may resume entry into this country.

If documentation is not in English, please provide an English translation to facilitate our review.

Your response should be sent to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Enforcement I, General Surgery Devices Branch, 2098 Gaither Road, Rockville, Maryland 20850, to the attention of Carol Shirk.

Sincerely yours,

Steven Niedelman
Acting Director
Office of Compliance
Center for Devices and
Radiological Health

Enclosure: Selecting a Consultant?

Cc:

President
Poly Implants Protheses America
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Miami, Florida 33157