



M3905n

**WARNING LETTER**  
**VIA EXPRESS**Food and Drug Administration  
Center for Devices and  
Radiological Health  
2098 Gaither Road  
Rockville, MD 20850

JUN 19 2000

Mr. Patrick Choay  
President  
Laboratoires Prodimed  
ZI-4, Avenue de l'Europe  
60530 NEUILLY-EN-THELLE, FRANCE

Dear Mr. Choay:

During an inspection of your firm located at Neuilly-en-Thelle, France, on March 27-30, 2000, Jane Donnelly, Auditor, SGS Yarsley and FDA investigator Teresa Jimenez, San Juan, Puerto Rico determined that your firm manufactures Pipelle de Cornier and assisted pregnancy devices. These products 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 Quality System Regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Failure to establish and maintain procedures for validating the device design that include ensuring that devices conform to defined user needs and intended uses and testing of production units under actual or simulated use conditions, as required by 21 CFR 820.30(g). For example:
  - a. Design validation did not ensure that devices conform to defined user/patient needs and intended uses. Specifically, there is no documentation showing that the design fulfils the user requirements or intended use for program [REDACTED] (assisted reproduction device).
  - b. The design was not validated using production units or their equivalents. Specifically, the prototype for project [REDACTED] was made by a Technician not production personnel. Subsequent production was not verified as being equivalent to the prototype.
2. 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, the original design project [REDACTED] specified that the device would be sterilized by [REDACTED]; but during the design stage it was changed to [REDACTED]. Procedures do not ensure that design outputs that are essential for the proper functioning of the device are completely identified or verified. Specifically, how irradiation affects the mechanical properties of the device and the impact of irradiation on the shelf life of the device.

3. Failure to establish and maintain procedures to ensure that the design requirements relating to a device are appropriate, address the intended use of the device, including the needs of the user and patient, and have a mechanism for addressing incomplete, ambiguous or conflicting requirements, as required by 21 CFR 820.30(c). For example, procedures to ensure that a device's design input requirements are appropriate and address its intended use, including physical characteristics; user/patient needs; addressing incomplete, ambiguous, or conflicting design input requirements are not defined. Specifically, procedure CRD001C dated July 99 do not define the design input stage or refer to controlled documents used during these stages such as D\_CON02.
4. Failure to validate the process with a high degree of assurance where as the results of the process cannot be fully verified by subsequent inspection or testing and approved according to established procedures, as required by 21 CFR 820.75(a). For example, a process, whose results cannot be fully verified by subsequent inspection and test, has not been fully validated and approved according to established procedures. Specifically, there has been no substantiation of [REDACTED] as a sterilizing dose to deliver a [REDACTED] for [REDACTED] assisted reproduction devices, as required by EN 552 or ISO 11137.
5. Failure to adequately document activities for a revalidation process, as required by 21 CFR 820.75(c). For example, documentation for the sterilization revalidation of the gynaecological sampling device (1999) is not complete. Specifically, there is no revalidation protocol, no documentation showing the location of biological indicators or functional pouch testing as required in the report.
6. Failure to develop, conduct, control and monitor production processes to ensure that a device conforms to its specifications, as required by 21 CFR 820.70(a). For example, there was no procedure defining the bioburden alerts and action limits and the actions to take if the specification is exceeded, bioburden trending and characterization.
7. Failure to establish and maintain procedures for implementing corrective and preventive action that include the requirements for analyzing all sources of quality data to identify existing and potential causes of nonconforming product or quality problems, as required by 21 CFR 820.100(a)(1). For example, not all sources of quality data are analyzed to identify existing and potential causes of nonconforming product and other quality problems. Specifically, nonconforming reports and weekly analysis of scraps have not been analyzed for trends or to identify root causes.
8. 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, finished product acceptance procedures is not documented. Specifically, for gynaecological sampling device there is no procedure defining
  - a. the responsibilities for who releases the batches
  - b. the criteria for release

- c. how is the distributor informed of the release.
9. Failure to establish and maintain procedures to adequately control the environmental conditions, as required by 21 CFR 820.70(c). For example, appropriate procedures have not been implemented for controlling environmental conditions. Specifically,
    - a. Air pressure differentials have been below tolerance on several occasions.
    - b. The class of clean room has been recorded as being nonconforming (class 100,000 not class 10,000) at the last validation for clean room fabrication, clean room 1 and clean room 4. There was no authorization to continue, or any specification change or deviation, by an authorized person.
  10. Failure to establish and maintain procedures to control documents including ensuring that obsolete documents are removed and ensuring the usage of the current version is adequate to fulfill its intended purpose, as required by 21 CFR 820.40(a). For example, responsibilities for employees who manage work affecting quality have not been defined. Specifically, the quality manual gives responsibilities for the quality assurance manager and plant manager which are inaccurate and out of date. Personnel changes have occurred including responsibility changes which have not yet been documented.
  11. Failure to maintain procedures that cover all the requirements of the Medical Device Reporting regulation, as required by 21 CFR 803.17. For example, the procedures for the Medical Device Reporting does not cover all the requirements of the MDR regulations.

We acknowledge that you have submitted a response dated "March 13, 2000" (incorrect date - dated prior to the issuance of the FDA-483), concerning the investigator's observations noted on the form FDA-483. Your response has been reviewed and has been found to be inadequate in that the corrections noted and documentation to support your response were not submitted for review.

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 conclusion of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance system. You are responsible for investigating and determining the causes of the violation identified by the Food and Drug Administration. If the causes are determined to be systems problems, you must promptly initiate permanent corrective action.

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. Given the serious nature of these violations of the Act, all devices manufactured by Laboratoires Prodimed, Neuilly-en-Thelle, France may be detained upon entry into the United States (U.S.) until these violations are corrected.

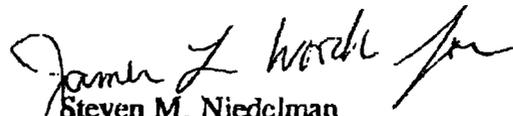
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In order to remove the devices from this detention, it will be necessary for you to provide a written response to the charges in this Warning Letter for our review. After we notify you that the response is adequate, it will be your responsibility to schedule an inspection of your facility. As soon as the inspection has taken place, and the implementation of your corrections have been verified, your devices may resume entry into this country.

Please notify this office in writing within 15 days of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. Please include any and all documentation to show that adequate correction has been achieved. In the case of future corrections, an estimated date of completion, and documentation showing plans for correction, should be included with your response to this letter. If documentation is not in English, please provide an English translation to facilitate our review. Please address your response and any questions to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Enforcement II, OB/GYN, Gastroenterology, and Urology Branch, HFZ-332, 2098 Gaither Road, Rockville, Maryland 20850, to the attention of Mr. Paul Tilton.

If you have any questions, please contact Lynette Salisbury or Sharon Murrain-Ellerbe at the above address or at (301) 594-4616 or FAX (301) 594-4638.

Sincerely yours,

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