



APR 26 2002

WARNING LETTER

VIA FEDERAL EXPRESS

Dr. Bernard Cales
General Manager, Biomedical Ceramics & Specialty Products
St. Gobain Ceramiques Avancees Desmarquest
Rue de L'industrie, Z.I. No.1
27025 Evreux Cedex France

Dear Dr. Cales:

We are writing to you because between December 17 and 20, 2001, an investigator from the Food and Drug Administration (FDA) collected information that revealed serious regulatory problems involving your firm's Quality System. Under a United States (US) Federal Law, the Federal Food, Drug, and Cosmetic Act (the Act), this product is considered a medical device because it is used in the diagnosis of disease or medical condition, or in the treatment or prevention of a medical condition, or to affect the structure or function of the body.

The above-stated inspection revealed that the methods used in, or the facilities or controls used for, manufacturing, packaging, storage, or installation of this device are not in conformance with the Quality System Regulation, as specified in Title 21 Code of Federal Regulation (CFR) Part 820. In legal terms, the product is adulterated within the meaning of section 501(h) of the Act, as follows:

1. **Failure to adequately validate the tunnel furnace process with a high degree of assurance and approve according to established procedures, as required by 21 CFR 820.75(a).** For example, your [] furnace validation summary report and additional process validation information, dated March 11, 2002, do not document that the [] process parameters are consistently controlled and result in the desired product specifications. The process validation protocol, contained in your March 11, 2002, submission does not describe how the process parameters and product specifications are measured or tested.

Your process validation summary report was collected by our investigator during his inspection of your firm. On February 20, 2002, in a telephone conversation with Mr. Ed Levadnuk, we requested the complete process validation protocol and report for the [] furnace. This additional material, with a cover letter dated March 11, 2002, was received by us on March 18, 2002.

The material helps establish the reasoning behind the design of the furnace and some of the properties or features to be measured/tested to document that the furnace process produces the desired results. However, it is not process validation as required by 21 CFR 820.75. For example, the process validation report does not document that the [] furnace process itself results in a consistent, predictable outcome of product based upon specific operational process parameters for the furnace. In addition, the [] furnace process validation protocol included in your additional information is inadequate because it does not specify:

- all the data to be collected and the purpose of all the data to be collected;
- the test procedures to be used to measure the predetermined success criteria; or
- provide a statistical rationale for the number of device per run or the number of runs.

You need to properly validate the [] furnace process. Please supply a complete proposed validation protocol for the [] furnace. This protocol should specifically address if any aspect of this furnace is computer controlled and how the software will be validated. Enclosed are copies of the Process Validation Guidance issued by the Global Harmonization Task Force Study Group 3, the FDA's May 11, 1987, Federal Register Notice issuing guidance on General Principles of Process Validation and the FDA's "General Principles of Software Validation; Final Guidance for Industry and FDA Staff" dated January 11, 2002, to aid you in developing your protocol.

2. **Failure to establish and maintain adequate procedures for changes to a specification, method, process, or procedure that ensure that changes are:**
 - a. **verified or, where appropriate, validated according to 21 CFR 820.75, before implementation and that these activities are documented, and**
 - b. **approved in accordance with 21 CFR 820.40, as required by 21 CFR 820.70(b).**

For example, in 1998 your firm changed the manufacturing process for the zirconia femoral balls by adding a [] furnace to the manufacturing process. Contrary to your procedures, this process change was made for all femoral head designs without the necessary documentation, verification/validation, review and approval for all of the femoral head designs by your firm and/or the affected US orthopedic firm. In addition, your procedure "Management of Process Modification" does not adequately distinguish between changes that require validation and those that require verification only.

At the time of the inspection, your firm provided a non-certified English translation of your procedure for process change control entitled "Management of Process Modification." This translation contains apparent typographical errors resulting in nearly identical definitions for major and minor changes. Additionally, the procedure does not distinguish explicitly between changes that must be validated and those that simply require verification

Please provide a certified English translation of your revised "Management of Process Modification" procedure that fulfills all the requirements for making changes to specifications, processes or procedures. The procedure should address whether a process change must be validated or verified. In addition, explain how you intend to prevent the approval of future process changes without the required customer approval described in your procedure.

- 3. 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, your firm performed a design review for the [] femoral head and determined that the [] design did not meet your firm's design specification of not less than [] mm between stem cone trunion to the machined ball. Your firm revised the engineering drawing to reflect your firm's specification and returned it to [] for approval.

During the course of the inspection you indicated to the investigator that your firm does not perform design control activities. However, during the inspection you have also described activities that fall under the design control regulations and provided non certified English translation of your design transfer procedures. Discussion between the investigator and employees of your firm, indicates that your firm is involved in activities such as design transfer, design review, design changes prior to production, design verification (i.e., burst testing, proof testing, fatigue testing, etc.), design changes stemming from process change and document change control (21 CFR 820.40).

You must clarify with your customers which party is responsible for all the design control activities as required in 820.30(a)-(j) in the GMP regulation. Once you have clarified your firm's role, provide certified English translations of procedures that satisfy the requirements of the portions of the design control regulation your firm is responsible for performing. At a minimum, these procedures will need to address the requirements outlined in Design Changes 820.30(i), Design Review 820.30(e), Design Transfer 820.30(h) and Document Change 820.40.

- 4. Failure to establish and maintain corrective and preventive action (CAPA) procedures for analyzing oral complaints to identify existing and potential causes or nonconforming product or other quality problem, as required by 21 CFR 820.100(a)(1).** For example, complaint handling procedures were not established, defined, documented, or implemented to ensure that all oral complaints of device failures are documented upon receipt. Specifically, oral complaints of device failures received by the firm were not entered into the CAPA system in a timely manner as evidenced by, in at least one instance, when the firm was verbally informed of a device failure on October 9, 2000. The device failure was not entered into the CAPA system until March 15, 2001, when written notification from the customer reporting the failure was received.

On January 4, 2002, your firm responded to the observations on the form FDA-483. Your firm has implemented new procedures where all complaints are evaluated for possible MDRs and has created a new complaint form to capture all complaints, non-conformities and device failures for the CAPA system. The response appears to address this citation adequately.

- 5. Failure to establish and maintain procedures for receiving, reviewing and evaluating all complaints by a formally designated unit, as required by 21 CFR 820.198.** For example, complaint handling procedures were not established or implemented to ensure that all complaints are evaluated to determine whether the complaint should be filed as a medical device report (MDR).

On January 4, 2002, the firm responded to the observations on the form FDA-483. You provided a procedure entitled “Procedure for Medical Device Reporting.” This procedure identified Dr. Bernard Cales as the person in charge of MDRs in France and Mr. Edward Levadnuk as the firm’s US representative for MDRs. This procedure is a high level SOP that addresses the specific items identified in the FDA-483 observation regarding MDRs but it does not address the overall lack of procedures for assessing all complaints.

It is not clear from your response that your firm is properly capturing and documenting complaint information. The translated procedures leave doubt that all the aspects of 21 CFR 820.198 are fulfilled by your firm’s quality system. Please provide us with a copy of your procedures that satisfy all the requirements of 21 CFR 820.198 Complaint Files.

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 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 action.

We acknowledge that you have submitted to this office a response, dated January 4, 2002, concerning our investigator’s observations noted on the form FDA 483. We have reviewed your response and concluded that it does not address fully all of the observations noted on the form FDA-483. An evaluation of specific responses is described above after the relevant deviations listed above.

Given the serious nature of these violations of the Act, your implantable femoral head devices may be detained without physical examination upon entry into the United States until these violations are corrected.

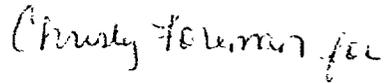
United States Federal Agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Also, no requests for Certificates for Products for Export will be approved until the violations related to the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

It is necessary for you to take action on this matter now. Please let this office know, in writing, within fifteen (15) working days from the date that you received this letter, the steps you are taking to correct the problem. We also ask that you explain how you plan to prevent this from happening again. If you need more time, let us know why and when you expect to complete your correction. If the documentation is not in English, please provide a translation to facilitate our review. Please address your response to:

Ms. Erin Keith
FDA/CDRH/OC
Division of Enforcement III (HFZ-343)
2094 Gaither Road
Rockville, MD 20850
USA

If you have any questions regarding this matter please feel free to contact Ms. Keith at the address above or at (301) 594-4659, extension 117, or fax (301) 594-4672. You may obtain general information about all of FDA's requirements for manufacturers of medical devices by contacting our Division of Small Manufacturers, International and Consumer Assistance at (301) 443-6597, or through the Internet at <http://www.fda.gov>.

Sincerely yours,



Larry D. Spears
Acting Director
Office of Compliance
Center for Devices and Radiological Health

Enclosures: As stated

cc: Mr. Ed Levadnuk
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Raleigh, NC 27615