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Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

WARNING LETTER

AUG 17 1999

Dr. Gennaro D'Andrea
Division Director
Biocoatings, srl
Via A. Volta, 3
43040 Rubbiano Di Solignano (Parma)
ITALY

Dear Dr. D'Andrea:

During an inspection of your facility, Flametal, S.p.A., located in Fornovo Tara (Parma) ITALY, on April 13-15, 1999, our investigator determined that your firm provides contract non-sterile titanium and hydroxyapatitic powder coating of endosseous and orthopedic implants. The endosseous implants are devices as defined by Section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act).

The current inspection disclosed that your firm had corrected all of the previously cited observations, however, new significant deficiencies have been observed at your facility. These new deficiencies deviate from the Good Manufacturing Practices as set forth in the Quality System Regulation as indicated by the delineation's below.

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 follows:

1. Failure to validate your process with a high degree of assurance and approval according to established procedures, as required by 21 CFR 820.75(a). For example, although your firm has conducted process validation studies for coating orthopedic implants they failed to conduct the same studies for the endosseous implants. This study would assess the impact of the coating process if the firm deviated from the specified process parameters.
2. Failure to establish and maintain procedures for changes to a specification, method, process, or procedure; to verify or where appropriate validate such changes according to Sec. 820.75 before implementation; and approve changes in accordance with Sec. 820.40, as required by 21 CFR 820.70(b).

For example, no formal engineering change control system has been established to control projects such as modifying production processes or equipment, i.e., an isolated room for cleaning pieces before and after coating was introduced without an engineering change order. Also, the work process FCL 6968 or the associated test report form was changed, and now the atomizer settings [REDACTED] and [REDACTED] °C specified in the work process instruction disagree with the [REDACTED] bar and [REDACTED] °C of the test report form.

3. Failure to establish and maintain process control procedures that describe any process controls necessary to ensure conformance to specifications. These procedures must include documented instructions, standard operating procedures (SOP's), and methods that define and control the manner of production, as required by 21 CFR 820.70(a)(1). For example, there is no preventative maintenance procedures established for DI water systems supplying water for ultrasonic cleaning and HA powder production, and no limit has been established for the conductivity parameter being used.
4. Failure to maintain device master records (DMR's) that included device specifications including appropriate composition, formulation, component specifications, quality assurance procedures and specifications including acceptance criteria to be used, as required by 21 CFR 820.181(a) & (c). For example, the raw material acceptance records for titanium powder granulometric distribution does not agree with acceptance specification. Presently, the acceptance test results show the percentage (%) of granule sizes between [REDACTED] microns to be approximately [REDACTED] lower than the [REDACTED] required by the raw material specification. Additionally, the specification require < [REDACTED] (Na), but the laboratory tests do not check specifically for Na content.
5. Failure to establish and maintain procedures to ensure that equipment is routinely calibrated, inspected, checked, and maintained, as required by 21 CFR 820.72. For example, the springs required for adhesion testing per ASTM F1501 have not been included in the calibration schedule.
6. Failure to maintain complaint files. The failure to establish and maintain procedures for receiving, reviewing, and evaluating complaints by a formally designated unit, as required by 21 CFR 820.198(a). For example, the review of the past two years of nonconformance reports (~40 reports) revealed that two customer complaints were not documented with "Nonconformance Report form". Additionally, the failure to document all activities required under this section, and their results, as required by 21 CFR 820.100(b). For example, a corrective action consisting of increased monitoring of incoming [REDACTED] tape was not 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 requirement of the Act and regulations.

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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.

Therefore, federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information in to account when considering the award of contracts.

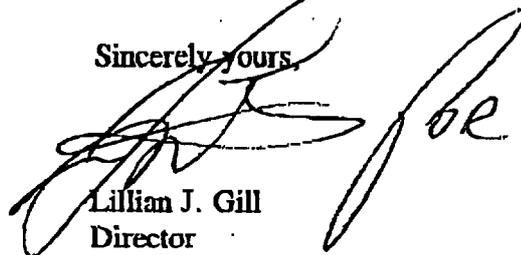
Given the serious nature of these violations of the Act, devices coated by your firm, located in Fornovo Tara (Parma), ITALY and manufactured by Micromeccanica, in Milan, Italy, may be detained upon entry into U.S. until these violations are corrected.

In order to remove this firm's (Micromeccanica) device 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 has been verified this firm products may resume entry into this country.

Please notify this office in writing within 15 days of receipt of this letter, 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 system problems necessary to assure that similar violations will not recur. Any and all 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.

Your response should be sent to the attention of Mr. Ronald L. Swann, Dental, ENT, and Ophthalmic Devices Branch, at the above Gaither Road address.

Sincerely yours,



Lillian J. Gill
Director
Office of Compliance
Center for Devices and
Radiological Health