



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 24 1996

WARNING LETTER

Mr. Joseph S. Gallagher
Manager and Director
Biosil Limited
127 Deerdynes View
Cumbernauld, Scotland, U.K.

Dear Mr. Gallagher:

During an inspection of your manufacturing facility located at Cumbernauld, Scotland, U.K. on October 15-18, 1996, our investigator confirmed that you manufacture saline-filled breast implants. These products are devices as defined by Section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act). The current inspection was scheduled as a pre-clearance inspection to support your premarket approval document K962184. The current inspection revealed that your firm has Good Manufacturing Practice deficiencies regarding manufacturing validation, environmental control, record keeping, finished device testing and inadequate calibration procedures. The devices manufactured by your firm are or may become adulterated in accordance with Section 501(h) of the Act because the methods used in, and the facilities and controls used for the manufacture, packaging, storage, and installation of devices are not in conformity with the Medical Device Good Manufacturing Practice Regulations as prescribed by Title 21, Code of Federal Regulations Part 820, as follows:

1. Failure to establish and implement specification control measures to assure that the design basis for the device and packaging is correctly translated into approved specifications, as required by 21 CFR 820.100(a)(1). For example:
 - a) The retrospective validation study performed covering the patching of the RTV shells is based on an analysis of production records for the period of April 2 - June 28, 1996. These production records do not include documentation of the operational settings for the vulcanization process. The validation conclusions were approved based on the assumption that the operating parameters were within the acceptable range.
 - b) There have been no validation studies covering the packaging materials, or process.
 - c) The protocols for shell dipping and texturing do not specify the number of products to be manufactured and/or sampled.
2. Failure to control environmental conditions, such as lighting, ventilation, temperature, filtration, or microbiological contamination, to prevent contamination of the device and to provide proper conditions for each of the operations performed, as required by 21 CFR

820.46. For example, corrective actions and/or investigations that are undertaken when microbial limits are exceeded are not documented. The monthly microbiological monitoring of the cleanroom performed between June and September 1996 included TNTC colonies at multiple sites, but there is no documentation of the corrective actions or investigations that may have been performed, although the procedure Microbiological Control [REDACTED] states that investigations and documented corrective actions shall be undertaken when limits are exceeded.

3. Failure of the Device Master Record to include device specifications including appropriate drawings, composition, formulation, and component specifications, as required by 21 CFR 820.181(a). For example, your firm performs bioburden testing on its products for every sterilization lot. However, no limits have been set and there is no documentation of any corrective action or investigation performed when TNTC colonies were obtained on sample [REDACTED] taken from lot [REDACTED].

4. Failure to have written procedures for acceptance of components and inspecting, sampling, and testing components for conformance to specifications as required by 21 CFR 820.80(a). Your firm lacks sampling, test, and acceptance criteria for components received from Biosil Ltd. in Ashby, U.K. For instance, the standard dome valve assembly is sampled and measured to specification upon receipt but this is not specified in the inspection instructions.

5. Failure of the Device History Record to include critical information such as dates of manufacture, quantity manufactured, and quantity released for distribution, as required by 21 CFR 820.184. For example, the Sterilization Manifest and Batch Release Records which are part of the Device History Record for the saline-filled breast implants contain blank signature fields and blank data fields, and over-writes which lack explanation.

6. Failure to adequately check and, where necessary, test each production run, lot, or batch for conformance with device specifications prior to release for distribution, as required by 21 CFR 820.160. For example, corrective action plans for non-conformance reports do not always address the root cause of the problem. Non-conformance reports [REDACTED], [REDACTED], and [REDACTED] highlight problems with fibers, bubbles and FM in product.

7. Failure to have adequate calibration procedures which include specific directions, limits for accuracy and precision, and provision for remedial action when accuracy and precision limits are not met, as required by 21 CFR 820.61(a). For example, records for instrument calibration showed that the equipment was calibrated to a setpoint rather than a range. Incubators Nos. 1 and 2 were both calibrated at one point ([REDACTED] and [REDACTED] degrees C, respectively).

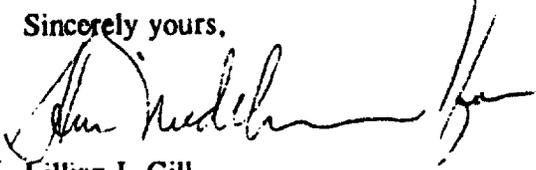
This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the closeout of the inspection may be symptomatic 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 Food and Drug Administration. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions. In addition, 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.

Validation of your manufacturing processes is extremely important in producing a product that consistently meets specifications. Past microbiological monitoring of your cleanrooms showed several TNTC results. Bioburden testing showed one TNTC result. If bioburden on the product is excessive, the sterilization process may not be adequate to sterilize the product.

Initial review of your October 28, 1996 response to the FDA-483 issued to you by Ms. Lynch appears to adequately address the observations. However, part of your corrective action will not be completed until the end of January 1997. It will be necessary for us to inspect your firm to verify the implementation of your corrections. Until these corrections are verified, your premarket submission (K962184) will be on hold status. It is your responsibility to reschedule another inspection of your facility. You may contact the Food and Drug Administration, Division of Emergency and Investigational Operations Branch, 5600 Fishers Lane, Room 1371, (HFC-133), Rockville, MD 20857 to reschedule.

Should you require any assistance in understanding the contents of this letter, please contact Ms. Madalyn Sheldon at (301) 594-4618, or at the letterhead address.

Sincerely yours,



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

cc: [REDACTED]