



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service d2041b

Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

SEP 17 1998

WARNING LETTER

Mr. Didier Parzy, President  
LOKKI Lasers Medicaux S.A.  
Le Cristal, Place Pierre Semard  
38200 Vienne FRANCE

Dear Mr. Parzy:

We have completed a review of your letter of July 3, 1998, responding to the FDA-483 observations identified during a U.S. Food and Drug Administration inspection conducted at your facility on June 8-12, 1998, by Ms. Michelle S. Dunaway. Our investigator determined that your firm manufactures dental lasers. 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 their manufacture, packing, storage, or installation are not in conformity with the Good Manufacturing Practice (GMP) requirements set forth in the Quality Systems Regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820 (copy enclosed). The reasons for this determination are discussed below.

21 CFR 820.30(f) Design verification.

Failure to establish procedures that are complete for verifying the device design.

The investigator noted that multiple changes were implemented prior to June 1, 1998, affecting the value of a capacitor, control of voltage, the number of diodes, and incorporating the addition of a buzzer. This was noted in Item #1 of the FDA-483. Verification activities for these changes were not documented either before or after June 1, 1998, the effective date of the design control requirements contained in 820.30(f).

Your response makes reference to a qualification test and the fact that the R&D Manager has been assigned the responsibility to update the "documentary file of the modified product." While your response may be adequate, it is difficult to make a determination due to the fact that the example provided, Notice de modification Buzzer E004, is in French.

21 CFR 820.30(i) Design changes.

Failure of the design changes procedure to identify changes requiring design validation or, where appropriate, design verification.

Item 1B on the FDA-483 concerns the fact that your procedure does not identify which changes require design verification vs. design validation. Our inspection report states that the investigator discussed both design verification and validation, after which Ms. Dunaway was advised that LOKKI would develop a procedure that would identify verification and validation requirements, and would provide additional comments in the firm's response. Unfortunately, much of your response is in French. We need all relevant information provided to this office in English.

It would appear that the changes incorporated into your procedure are the addition of a "Quality Insurance" member to the committee that reviews device modifications, the addition of a "qualification" test, and the R&D Manager being assigned the responsibility to update files for modified product. These revisions to the procedure do not appear to differentiate between design changes requiring validation vs. verification. Therefore, we consider your response to this observation inadequate.

You will note that the term, "qualification," is not a term that is utilized in our Quality System Regulation. It is not clear what you mean by the term, "qualification test" or for what purpose a qualification test is conducted. Is it conducted for purposes of validation or verification?

It is FDA's position that a design change must be validated to illustrate that the requirements for a specific intended use can be consistently fulfilled. However, a design change may be verified through testing, for example, when it is determined (and your procedure should specify how) that the change will not have a bearing upon the intended use but on whether the design output meets the design input requirements.

The phrase, "where appropriate," used in 820.30(i) of the requirement is discussed in the Scope portion of the regulation and can be found in 820.1(a)(3), page 52655. You may find it helpful to refer to this discussion.

21 CFR 820.30(g) Design validation and 21 CFR 820.75 Process validation.

Failure to:

- document that design validation had been performed to ensure that the device conformed to defined user needs and intended uses under actual or simulated use conditions; and,
- validate the sterilization process

For example, Observation #2 concerned the fact that your firm could not provide data to show the effectiveness of the sterilization technique specified for the fiber optic or the effects of multiple autoclaving cycles on the fiber optic.

It would appear from the test results provided with LOKKI's response that the sterilization technique (autoclaving) does not have an adverse effect on the function of the fiber optic, at least not for 10 cycles. Evaluating the affect the process has on the function of the device and its ability to meet user needs and fulfill the intended use is often referred to as product qualification when associated with process validation. This should be performed routinely as part of process validation.

Your response does not provide a protocol or summary validation data to show the effectiveness of the sterilization technique. Please provide this data, in English, to illustrate that the method for sterilizing the fiber optic is effective.

#### 21 CFR 820.22 Quality audit.

Failure to conduct quality audits to assure that the quality system is in compliance with established requirements.

Item 4 on the FDA-483 concerns the fact that LOKKI had not conducted any internal audits; in fact, the procedure had only been established in May 1998.

Your response stated that a complete audit would be conducted during the first and second week of this month, and you provided a preliminary internal audit. Your response is not acceptable in view of the fact that the preliminary internal audit provided with your response is in French. We cannot determine what is, or is not, to be covered during your internal audits or how often they are to be conducted. Consequently, we cannot determine the adequacy of your procedure. Please advise whether your complete internal audit has been completed, and provide an English translation of your internal audit procedure.

#### 21 CFR 820.30(i) Design changes.

Failure to establish and maintain procedures for the identification, documentation, validation, or where appropriate, verification, review and approval of design changes before their implementation.

Items 4A and B on the 483 concern the fact that modifications were implemented prior to going through a formal approval procedure – the effective dates of the modifications precede the approval dates.

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Your response advises that your procedure would be changed to require formal approval. It further states that once a change is qualified, the Note of Modification (NM) is issued by R&D, who also updates the documentary file, and the NM will include the date of implementation and/or the appliance number when the modification will be applied.

Please clarify whether implementation date means the date of approval and whether date of application is the starting date for the change to be incorporated into the device.

21 CFR 820.90 Nonconforming product.

Failure to establish and maintain procedures to address the identification, documentation, evaluation, and disposition of nonconforming product.

Item 5 on the 483 concerned the replacement of a fiber optic on 3/7/98 for a unit sold on 2/16/98. Information was not obtained in order to determine whether this represented a nonconformity.

Your response indicated that LOKKI's "After Sale Service Sheet" has been revised to include a box to check when the service required is considered a nonconformity. This is not an adequate response.

The fact that you have changed your service sheet does not mean that your procedure is adequate to meet the requirements of 820.90. How is a nonconformity determined in order to check the box on the After Sale Service Sheet? What is to happen once a nonconformity is identified, as indicated by the checked box on the service sheet? The procedure should outline the steps to be followed in order to identify a nonconformity as well as what to do once one has been identified. Please provide an English translation of your procedure for identifying, documenting, evaluating and disposing of nonconforming product.

21 CFR 820.100(a)(6) Corrective and preventive action.

Failure to ensure that information related to quality problems or nonconforming product is disseminated to those directly responsible.

Item 6 on the 483 indicates that the firm's corrective action procedure does not provide for notifying the supplier responsible for nonconforming product found during production or after distribution.

It will be necessary for us to have a copy of your procedure for treatment of nonconformities in English in order to evaluate whether it adequately addresses observation #6 on the FDA-483.

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21 CFR 820.40 Document controls.

Failure to establish and maintain procedures to control all documents.

Item 7 on the 483 concerns the fact that documents that should be updated as a result of design changes are not identified in the firm's procedures. The example given is a schematic diagram in the Device Master Record that had not been updated to reflect the change from one capacitor to two.

Your response is considered inadequate because your revised procedure does not specify what files should be changed, e.g., design history file; device master record, etc.

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 actions.

We acknowledge that you have submitted a response dated July 3, 1998, however, your response does not adequately address each of the problems identified on the FDA-483.

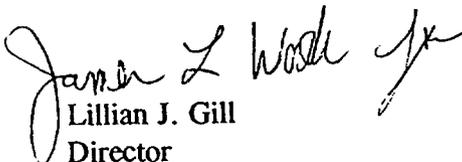
Federal agencies are advised of the issuance of all warning letters about devices so that they may take the information into account when considering the award of contracts.

Please notify this office, in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted deficiencies. Please include any and all documentation in English 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. Please send your response to me at the letterhead address.

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If you have any questions, please contact Sharon Kalokerinos at the above address or at (301) 594-4613 ext. 139 or FAX (301) 594-4638.

Sincerely yours,

A handwritten signature in cursive script, appearing to read "Lillian J. Gill".

Lillian J. Gill

Director

Office of Compliance

Center for Devices and Radiological Health

Enclosure: As Stated