



JAN 14 1998

Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

REGISTERED MAIL - RETURN RECEIPT REQUESTED  
WARNING LETTER

Mr. Roberto Reghetti, President  
Innosan S.r.l.  
Via S. Donato 156  
Bologna, Italy

Dear Mr. Reghetti:

During an inspection of your firm located in S. Pietro in Casale (BO), Italy, on [redacted] our investigator determined that your firm manufactures oxygen concentrators. 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 Quality System for Medical Devices Regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Failure to establish and maintain procedures to ensure that equipment is routinely calibrated, inspected, checked, and maintained and to document calibration activities, as required by 21 CFR 820.72(a). For example, there was no procedure to ensure that the following measuring and testing equipment in the manufacturing area was calibrated: the [redacted]  
[redacted]  
[redacted] There was no calibration record for any of these devices.

Your written response dated [redacted] revealed that all measuring and testing equipment listed on the FDA 483 was calibrated since the inspection. The procedure was in Italian so the procedure could not be evaluated for adequacy. This response is inadequate because the procedure could not be evaluated. You must re-submit the procedure in English.

2. Failure to establish and maintain procedures to adequately control environmental conditions where these environmental

conditions could reasonably be expected to have an adverse effect on product quality, as required by 21 CFR 820.70(c).

For example, there was no written procedure referencing [redacted] controls during production of the [redacted]. An employee was observed handling [redacted] without any protection or grounding to eliminate [redacted].

Your written response dated [redacted] indicated that an effort was made to write and submit an [redacted] procedure; however, the document was submitted in Italian and could not be evaluated. This response is inadequate because the procedure could not be evaluated. You must re-submit the procedure in English.

3. Failure to document approval of all documents established to meet the requirements of part 820, including the date and signature of the individual(s) approving the document, as required by 21 CFR 820.40(a). For example, the device master record was not signed or dated to indicate approval, and the master and working copies of Software for EPROM used in the [redacted] were not signed and dated as approved.

Your written response dated [redacted], indicated that your device master record is now dated and signed appropriately. This response is adequate.

In your written response dated [redacted] you indicated that the programmer signed and dated the document. For your information, typically, the person performing the approval is not the same person who has completed the task. To ensure objectivity of the task completed and to assure that specifications can be met, the approval of a procedure should be signed by an impartial employee.

4. Failure to establish and maintain procedures to control all documents that are required by this part and provide for the review and approval of changes, as required by 21 CFR 820.40. For example, there is no formal engineering change order (ECO) procedure.

At the close out of the inspection, your ECO procedure was provided to and verified by Investigator Gessesse. This response is adequate.

5. Failure to conduct quality audits that the quality system is in compliance with the established quality system requirements and to determine the effectiveness of the quality system, as required by 21 CFR 820.22. For example, the internal quality audit due ~~2000~~ was not performed.

Your written response dated [redacted], indicated that your audit was performed [redacted] and that the next is scheduled for [redacted]. This response is adequate.

These devices are also misbranded within the meaning of Section 502(t)(2) in that you failed to comply with requirements of the Medical Device Reporting regulation described in 21 CFR 803, Subpart B as follows:

6. Failure to have a written MDR procedure, as required by 21 CFR 803.17. For example, you did not have a written MDR procedure.

Your written response dated [redacted] indicated that an effort was made to write an MDR procedure; however, the document is in Italian. For your information, MDR procedures must be translated into English as required by 21 CFR 803.13(a). This response is inadequate because all documents must be submitted in English so they can be evaluated for completeness.

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 on 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.

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. Additionally, no premarket submissions for devices to which the GMP deficiencies are reasonably related will be cleared until the violations have been corrected.

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Innosan S.r.l.

Please notify this office, in writing, within 15 working days of receipt of this letter of the specific steps you have taken to correct 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 the documentation is not in English, please provide a translation to facilitate our review. Please address your responses to:

Edgardo Santiago  
Food and Drug Administration  
Center for Devices and Radiological Health  
Division of Enforcement III  
Orthopedic, Physical Medicine  
& Anesthesiology Branch, HFZ-343  
2098 Gaither Road  
Rockville, MD 20850

If you have any questions, please contact Brenda Hayden at (301) 594-4659.

Sincerely yours,



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