



DEPARTMENT OF HEALTH AND HUMAN SERVICE

Southwest Region

Food and Drug Administration
Denver District Office
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Denver, Colorado 80225-0087
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May 24, 2001

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Gerald G. Brew
President
Nicolet Biomedical, Inc.
5225 Verona Road
Madison, Wisconsin 53744

Ref. #: DEN-01-32

Dear Mr. Brew:

On March 19 through March 28, 2001 Investigator Lori A. Lahmann of our office conducted an inspection of Nicolet Vascular, Inc. in Golden, Colorado. Our investigator determined that your firm manufactures various products, including the Elite Series, PocketDop Series, CareDop, CT+, StethoDop, FreeDop, Imex Lab and 3000DX ultrasound units for vascular and obstetrical applications. 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 manufacturing, packing, storage, or installation are not in conformance with the Quality System/Good Manufacturing Practice (QS/GMP) for Medical Devices Regulation, as specified in Title 21, Code of Federal Regulations (21 CFR), Part 820. The deviations are as follows:

1. Inadequate failure investigations, as required by 21 CFR 820.198. Our inspection found that although your procedures require your QC department to initiate failure analysis actions and to notify the Director of QA and the Director of Engineering if such conditions are observed, there was no evidence that failure investigations are conducted on complaints. In at least two complaints reviewed, devices were returned to your firm three times for the same complaint. Each time the device was repaired and returned to the customer without evidence of any root cause analysis to determine the nature of the failures. Other complaints reviewed found a similar lack of failure analyses.

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6. Inadequate training as required by 21 CFR 820.25(b). There is no documented evidence that employees have received adequate training for the responsibilities assigned. For example, there is no evidence that Quality Control inspectors have been trained or tested to perform the final inspection procedure for the CareDop/Elite Probe, the Elite Versions, the PocketDop models or O.B. versions of your products. There are no criteria on which to evaluate the quality control inspector's (X X X X X X X X X X) (X X X) tested. Also, there is no evidence that the person evaluating complaints for MDR reportability has been trained in the criteria necessary to make a proper assessment.

We acknowledge receipt of your response dated April 4, 2001, signed by Mr. David W. Wagner. With regards to your response, we have the following comments:

1. In response to observation 1 regarding the lack of failure analysis of complaints, we are unable to evaluate your response as you have not included the new procedure. Our concerns with the procedures in place at the time of the inspection dealt with the fact that there was no evidence that your firm had reviewed, evaluated and investigated these complaints. It is your responsibility to ensure that your procedures address this requirement.
2. With regards to item 2(a), again we are unable to evaluate your response without reviewing your procedure. Regarding item 2(b), please be aware that your Corrective/Preventive Action Request does not address the use of (X X X X) to record preventive actions.
3. Your response is inadequate. We disagree with the manner in which your are sampling products. The use of ANSI/ASQC Z1.4 Sampling Procedures is not subject to interpretation. To use this sampling plan, you must first determine the inspection level and AQL you wish to use (i.e., normal, tightened or reduced). These are then taken in conjunction with the lot size to determine the sample. There is no evidence in your (X X X X X X) (X X X) procedure, that these elements have been incorporated into your plan. Depending upon the results of your sampling, the AQL may be adjusted (tightened or reduced) depending upon your findings. Again, your procedure does not address this. Your practice of changing the frequency of testing dependent upon the previous (X) lots/months' testing data and how close to the permitted maximum the previous (X) tested, is not an acceptable practice under the ANSI/ASQC Procedure.
4. Your response appears adequate.
5. Although your procedure now includes the statement that the audit plan must be signed and dated by the auditor prior to being used for the audit, your procedure still does not specifically name the areas, processes and procedures that are to be examined by the auditors. You must insure that all processes, areas and procedures are covered by your internal audits.
6. Your response is inadequate. Please see item #5 above under the objectionable deviations, (Inadequate design verification) for a discussion of our concerns.

PURGED

Page 4 - Nicolet Biomedical, Inc.
May 24, 2001

7. Your response appears adequate.

The above identified deviations are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure that your establishment is in compliance with all requirements of the Federal regulations. The specific violations noted in this letter and in the Form FDA-483 issued at the conclusion of the inspection may be symptomatic of serious underlying problems in your establishment's quality system. You are responsible for investigating and determining the causes of the violations identified by the FDA. You also must promptly initiate permanent corrective and preventive action on your Quality System.

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 Class III devices to which the QS/GMP deficiencies are reasonably related will be cleared until the violations are corrected. Also, no requests for Certificates to Foreign Governments will be approved until the violations related to the subject devices have been corrected.

In order to facilitate FDA in making the determination that such corrections have been made, thereby enabling FDA to withdraw its advisory to other federal agencies concerning the award of government contracts, to resume marketing clearance for Class III devices for which a 510(k) premarket notification or Premarket Approval application (PMA) have been submitted, and provide Certificates to Foreign Governments for products manufactured at your facility, we are requesting that you submit certification by an outside consultant to this office on the schedule below. Certification by an outside expert consultant should contain assurance that he/she has conducted an audit of your establishment's manufacturing and quality assurance systems relative to the requirements of the device QS/GMP regulation (21 CFR, Part 820). You should also submit a copy of the consultant's report with certification that you have reviewed the report and that your establishment has initiated or completed all corrections called for in the report.

The initial certifications of audit and corrections, and subsequent certifications of updated audits and corrections (if required) should be submitted to this office by the following dates:

- Initial certifications by consultant and establishment –by August 31, 2001.
- Subsequent certifications – bi-monthly thereafter until all corrections have been made.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by us without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please notify this office in writing within fifteen (15) working days of receipt of this letter of the specific steps you will be taking to comply with our request.

PURGED

Page 5 - Nicolet Biomedical, Inc.
May 24, 2001

Your response should be sent to Regina A. Barrell, Compliance Officer, Food and Drug Administration, Denver District, P. O. Box 25087, Denver, CO 80225-0087. If you have any further questions, please feel free to contact Ms. Barrell at (303) 236-3043.

Sincerely,



Thomas A. Allison
District Director

Cc:



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