DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Minneapolis District Office
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December 22, 2005

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Refer to MIN 06 – 17

James M. Cornelius
Chairman and Chief Executive Officer
Guidant Corporation
111 Monument Circle
Indianapolis, Indiana 46204-5129

Dear Mr. Cornelius:

During an inspection of your establishment located in St. Paul, Minnesota, on August 22 - September 1, 2005, our investigators determined that your firm manufactures implantable cardioverter defibrillators (ICDs) and pacemakers. 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 under section 501(h) of the Act [21 U.S.C. 351(h)] in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformance with the Current Good Manufacturing Practice (CGMP) requirements for medical devices which are set forth in the Quality System regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820. Significant deviations include, but are not limited to, the following:

1. Failure to adequately ensure that when the results of a process cannot be fully verified by subsequent inspection and test, the process shall be validated with a high degree of assurance and approved according to established procedure, as required by 21 CFR 820.75(a). For example:

    a. The Automated Optical Inspection (AOI) laser measurement test method was not adequately validated as part of the solder printing process for the hybrid assembly processes or independently as a test method for process screening and acceptance.

b. The AOI laser measurement test method was not adequately validated as part of the mount/pick/place process for the Tachy hybrid assembly process or independently as a test method for process screening and acceptance. Operational Qualification activities did not include testing with reference hybrids at the worst case conditions and the Performance Qualification part of the process validation was not conducted.

c. Manual visual inspection methods were not validated as part of the Brady or Tachy hybrid assembly processes or independently as test methods for process screening and acceptance.

2. Failure to establish and maintain adequate procedures for when changes or process deviations occur, to ensure the review and evaluation of the process and to ensure that revalidation is performed where appropriate, and to document all these activities, as required by 21 CFR 820.75(c). For example, the solder printing process for Brady hybrid assembly was originally validated using test boards and the AOI laser measurement test method. In April 2005 the AOI equipment was removed from service without adequate assessment of the change and without validation of the solder printing process with manual visual inspection.

3. Failure to establish and maintain adequate procedures to identify the action(s) needed to correct and prevent recurrence of nonconforming product and other quality problems, as required by 21 CFR 820.100(a)(3). For example:

a. Adequate and timely actions were not identified for the correction and prevention of the Insignia Real Time Clock issue with relationship to the risk the nonconformance posed to the patient. Further, users had not been informed of the potential for the Insignia pacemakers to fail in a no output failure mode due to a failure in the real time clock described in TR 05013 Rev B, INSIGNIA Real Time Clock Issues, dated 06/22/05. As of September 1, 2005, there were a total of 14 confirmed failures.

b. Adequate and timely actions were not identified for the correction and prevention of the Insignia Rate Fault Reset Loop issue with relationship to the risk the nonconformance posed to the patient. Further, users had not been informed of the potential for the Insignia pacemakers to fail in a no output failure mode due to a loose particle/foreign material problem described in TR 03030 Rev E, INSIGNIA Rate Fault Reset Loop, dated 07/21/05. As of September 1, 2005, there were a total of 35 confirmed failures due to foreign material in the crystal component.

4. Failure to analyze sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems, as required by 21 CFR 820.100(a)(1). For example:

    a. Failure data collected from the AOI equipment following the solder printing and mount processes are not routinely collected and analyzed. The AOI identifies nonconformance as to the component and pin locations.

    b. The AOI used on the Tachy hybrid assembly line at pre-solder reflow is not routinely analyzed to identify existing and potential causes of nonconforming product and other quality problems. The AOI equipment captures and maintains nonconforming product images. The images are not routinely analyzed for quality nonconformances from defects occurring from the component mounting equipment.

5. Failure to establish and maintain adequate procedures for changes in a specification, method, process, or procedure where such changes shall be verified or validated before implementation and these activities shall be documented and approved in accordance to section 820.40, as required by 21 CFR 820.70(b). For example, the removal of the AOI from the Brady hybrid assembly line in April 2005 did not have a documented process change order or completed work order with implementation date, approval signature, and approval date.

6. Failure to establish and maintain adequate procedures for process controls necessary to ensure conformance to specifications, as required by 21 CFR 820.70(a). For example, several process control charts that describe specific criteria for stopping production for process adjustments were located on the hybrid assembly line. These production limits were set without documented evidence that ensured products were meeting specifications. Further, the use of these control charts were not documented in established manufacturing instructions.

7. Failure to document rework and reevaluation activities in the Device History Record (DHR), as required by 21 CFR 820.90(b)(2). For example, solder touch-ups that occur after solder printing were not considered to be a rework operation and were not captured in the DHRs.

8. Failure to adequately maintain Device History Records (DHR) that include acceptance records which demonstrate the device is manufactured in accordance with the Device Master Record (DMR), as required by 21 CFR 820.184(d). For example, several DHRs for the solder printing did not document the completion of acceptance inspection activities, the type of inspection (manual or AOI), and the results of the acceptance inspection.

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 Form FDA-483 issued at the close 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. 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 approval applications for Class III devices to which the Quality System regulation deficiencies are reasonably related will be approved until the violations have been corrected. Also, no requests for Certificates to Foreign Governments will be granted until the violations related to the subject devices have been corrected.

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

FDA acknowledges Guidant's September 22, 2005, communication to physicians regarding failures within the INSIGNIA and NEXUS family of pacemakers, which addresses the concern noted above in point number 3.

We have also received and reviewed your letters dated September 15, October 5, October 18, November 17, and December 15, 2005, which describe actions taken by your firm to address the FDA-483 Inspectional Observations and the deviations cited in this Warning Letter. You have failed to address all of the significant violations listed in the Form FDA-483, and will receive additional correspondence detailing the inadequacy of your response.

Please notify this office in writing within 15 working days of receipt of this letter and provide an update on the status of your corrective actions. Your response should be sent to Timothy G. Philips, Compliance Officer, at the address on this letterhead.

Sincerely,

W. Charles Becoat

W. Charles Becoat
Director
Minneapolis District

TGP/HTW/ccl