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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
New Orleans District
404 BNA Drive
Building 200 – Suite 500
Nashville, TN 37217

Telephone: (615) 366-7801
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January 28, 2008

WARNING LETTER NO. 2008-NOL-07

FEDERAL EXPRESS
OVERNIGHT DELIVERY

Michael Reitermann, President
Siemens Medical Solutions USA, Inc.
Molecular Imaging Division
2501 North Barrington Drive
Hoffman Estates, Illinois 60192

Dear Mr. Reitermann:

During an inspection of your firm, located at 810 Innovation Drive, Knoxville, Tennessee on July 16, 2007 through August 7, 2007, investigator(s) from the United States Food and Drug Administration (FDA) determined your firm manufactures molecular imaging diagnostic equipment device(s). Under Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), [21 United States Code (21 USC) 321(h)], these products are devices because they are intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or are intended to affect the structure or function of the body.

This inspection revealed these devices are adulterated within the meaning of Section 501(h) of the Act [21 USC 351(h)], in the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with the Current Good Manufacturing Practice (CGMP) requirements of the Quality System (QS) regulation found at Title 21, *Code of Federal Regulations*, Part 820 (21 CFR 820). We received a response letter from Vice-President of Regulatory Affairs and Quality Assurance, Ron Nolte and you, dated August 20, 2007, concerning our investigator's observations noted on Form FDA 483, List of Inspectional Observations, issued to Mr. Nolte. We have reviewed your response and concluded it is inadequate in relation to each of the noted violations, which include, but are not limited to, the following:

1. Your firm failed to establish and maintain adequate procedures to control design validation, including software validation and risk analysis, where appropriate, as required by 21 CFR 820.30(g). For example:

a. Because you failed to follow your procedure, the acceptance criteria were not complete prior to the performance of validation activities. Specifically, [redacted] for ECAT scanners introduced an error in the scan start time used in the decay correction algorithm. This error was most pronounced in the TTTT/EEEE mode which was not tested during the validation of the software update.

b. Risk analysis is incomplete. The risk analysis for the hazard of linking PET/CT scans to the incorrect patient was performed after a June 2006 incident. The risk analysis has not been re-assessed/updated for increased probability given the three subsequent incidents. Your firm's Standard Operating Procedure directs risk analysis be reviewed and updated upon receipt of safety-related complaints. However, no risk analysis was performed for complaints related to incorrect normalization values in [redacted] PET/CT scanners. Complaint 07-0215, received on or about February 28, 2007 concerning incorrect normalization values, states the complaint review board directed a risk analysis be performed. Two subsequent complaints were received but no risk analyses were performed.

You did not provide the newly-created acceptance criteria for future revisions to the software nor documentation to substantiate your claim of reevaluation of the hazard analysis for ECAT systems. You did not provide copies of the procedure [redacted]. Also, the response indicates the two risk analyses were performed, and complaint and risk analysis procedures were revised, but copies were not provided. Please provide these documents for our review.

2. Your firm failed to establish and maintain adequate procedures for implementing corrective and preventive action (CAPA) to ensure the analyzing of sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems and employ appropriate statistical methodology, where necessary, to detect recurring quality problems, as required by 21 CFR 820.100(a)(1). For example, your firm's CAPA procedures inadequately identify quality data to be analyzed or the statistical methods to be used to analyze quality data.

   You did not submit copies of the revised CAPA and new trending procedures for review. You also did not provide evidence of implementation of these procedures. Your response should address preventive actions to ensure identified sources and statistics chosen are capturing the necessary information to proactively address quality problems and/or issues.

3. Your firm failed to establish and maintain adequate procedures are conducted which assure the investigation of the cause of nonconformities relating to product, processes, and the quality system, as required by 21 CFR 820.100(a)(2). For example, a formal process does not exist to document investigation into returned parts.

   You did not provide copies of the revised CAPA and complaint procedures nor the eCAPA process for returned parts for our review. Please provide evidence of implementation of the corrective measures taken.

4. Your firm failed to establish and maintain adequate procedures to identify 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. At least four complaints were received concerning PET/CT scans linked to the wrong patient. Complaint PC0000295 was entered into your firm's complaint system on September 27, 2005; complaint PC0000636 was entered on June 12, 2006; complaint 07-0098 was reported to your firm on January 30, 2007; and, complaint 07-0663 was reported to your firm on June 11, 2007. The software bug has been corrected in devices distributed since July 2006, but neither a software fix nor user notification has been distributed to customers who have devices received prior to July 2006.

   b. Your firm's current CAPA procedures inadequately address preventive activities to be considered.

   c. The corrective and preventive actions for ECAT PET scanner malfunctions caused by software deficiencies and the required Medical Device Reporting submissions did not include documented preventive actions considerations.

   Regarding item a, you did not provide a copy of the reassessment of the risk analysis which was performed. Since your firm has two different risk mitigations for the same problem, you should provide documentation showing both choices (software fix and user notification) address the problem and are compliant with your current risk management procedures. You did not provide the finalized copies of the user notification letter, risk management procedure and complaint handling procedure. You also should provide the training documentation which assures affected personnel have been trained on the revised procedures and/or practices.

   Regarding item b, you did not provide a copy of the revised CAPA procedure [redacted] for our review.

   Regarding item c, you did not provide the newly-created acceptance criteria for future revisions to the software, and provide documentation to substantiate your claim of reevaluation of the hazard analysis for ECAT systems.

5. Failure to establish and maintain adequate complaint procedures for receiving, reviewing, and evaluating complaints, as required by 21 CFR 820.198(a). For example:

   a. Complaints are not handled in a uniform and timely manner as specified by your procedures. Specifically, there are instances where the assignee of a complaint did not notify the complaint coordinator and indicated an expected date of investigation completion after the 60 day due date which is specified by the complaint handling procedures.

   b. There was no documentation to indicate complainants were notified and informed of complaint resolutions after the complaint was closed, as required by current complaint handling procedures.

c. The complaint handling procedures do not address how multiple complaints regarding the same defect will be handled. Multiple complaints were observed during the inspection concerning "Main User Interface Crashes".

d. A complaint form indicates Siemens was notified on June 15, 2006, of asymmetry in a whole body scan. This incident was not entered into the complaint handling system until March 21, 2007, after receipt of subsequent complaints of asymmetry in brain scans.

You did not provide the revised complaint handling procedure, the newly-created trending procedure, the revised procedure [redacted] and the training records of the affected personnel.

6. Your firm failed to establish and maintain adequate procedures to control documents and ensure all obsolete documents are promptly removed from use or otherwise prevented from unintended use, as required by 21 CFR 820.40(a). For example, approximately nine observations were made of complaint data being recorded on obsolete versions of complaint forms. Specifically, Complaint 07-0341 was observed to document a "Date of Event" as March 17, 2007, and [redacted] as March 17, 2007; however, the revision date of the form was [redacted] introduced in 2004. A list of complaint form revisions was provided to the investigators by firm management, which indicated five revisions during 2005 and 2006.

   You did not provide the training documentation, the revised complaint handling procedure and the documentation pertaining to the newly-implemented electronic device and your electronic complaint system.

You should take prompt action to correct the violations addressed in this letter. Failure to promptly correct these violations may result in regulatory action without further notice, including seizure, injunction, and/or civil money penalties. Federal agencies are advised of the issuance of all warning letters about devices so they may take this information into account when considering the award of contracts. Additionally, premarket approval applications for Class III devices to which the QS regulation deviations are reasonably related will not be approved until the violations have been corrected. Requests for Certificates to Foreign Governments will not be granted until the violations related to the subject devices have been corrected.

Please notify this office in writing within fifteen (15) working days from the date you receive this letter of the specific steps you have taken to correct the noted violations, including an explanation of how you plan to prevent these violations, or similar violations, from reoccurring. Include documentation of the corrective action you have taken. If your planned corrections will occur over time, please include a timetable for implementation of those corrections. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your response should be sent to Kari L. Batey, Compliance Officer, U.S. Food and Drug Administration at the above address. If you have any questions about the content of this letter, please contact Ms. Batey at (615) 366-7808.

This letter is not intended to be an all-inclusive list of violations at your facility. It is your responsibility to ensure compliance with applicable laws and regulations administered by FDA.

The specific violations noted in this letter and in the List of Observations, Form FDA 483, issued at the closeout of the inspection, may be symptomatic of serious problems in your firm's manufacturing and quality assurance systems. You should investigate and determine the causes of the violations, and take prompt actions to correct the violations and bring your products into compliance.

Sincerely,

H. Tyler Thornburg
District Director
New Orleans District

Enclosures: FDA 483 dated August 7 and 8, 2007

cc: Kenneth F. Baker, Vice President of Operation
Siemens Medical Solutions USA, Inc.
810 Innovation Drive
Knoxville, TN 37932-2571