DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

5046

Dallas District
3310 Live Oak Street
Dallas, Texas 75204-6191

December 5, 2000

Ref: 2001-DAL-WL-05

WARNING LETTER

CERTIFIED MAIL
RETURNED RECEIPT REQUESTED

Mr. William W. George
Chief Executive Officer and Chairman
Medtronic, Inc.
7000 Central Avenue, N.E.
Minneapolis, MN 55432

Dear Mr. George:

During an inspection of your firm, Medtronic Midas Rex, located at 4620 North Beach Street, Forth Worth, Texas, on July 31 to August 10, 2000, our investigator determined that your firm manufactures the Classic Midas Rex® Systems, Midas Rex® III Systems, Dissecting High-Speed Drill Systems, Power Surgical Instrument Systems, Safety Seals, and Attachments. These products are medical devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The inspection documented significant deviations from the Current Good Manufacturing Practice (CGMP) requirements for devices, therefore, your devices are adulterated pursuant to Section 501(h) of the Act. Additionally, your devices are misbranded pursuant to Section 502(t)(2) for failure to submit MDR reportable incidents and a report of correction.

We have received and reviewed your firm's written correspondence and attachments, dated August 30, September 29, and November 2, 2000, responding to our inspectional observations (FDA-483) issued at the completion of the inspection (copy attached) to Mr. Samuel Owusu-Akyaw, Vice President and General Manager, Medtronic Midas Rex. We acknowledge your commitment to correcting the deviations and outlining the anticipated corrective actions. However, in general, we find your responses incomplete. Your responses lack supporting documentation, and in some instances, do not address underlying issues that may have contributed to or resulted in the deficiencies.

Your 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 manufacturing, packing, storage, or installation are not in conformance with the Current Good Manufacturing Practice (CGMP) requirements of the Quality System Regulations, as specified in Title 21, Code of Federal Regulations (CFR), Part 820. Significant deviations include the:

1. Failure of the management with executive responsibility to ensure that an adequate and effective quality system has been established and maintained [21 CFR 820.20]. For example,

   a. Established procedures are not always followed (i.e., the Management Review, Quality System Audit, Training, Design Control, Risk Analysis, and Corrective Action Procedures) as cited in FDA-483, Items 2, 3, 5,7, 8 thru 12, and 16.

   b. Employee training was not controlled nor monitored to ensure that all employees received the necessary training to perform their duties.

   c. Adequate resources have not been provided for performing complaint handling activities, quality assurance functions, and assessment activities.

FDA-483, Item 1(a) and (b):
Your responses indicate that the Management Committee will review, maintain, correct, add, or delete standard operating procedures as necessary to establish relevance and would submit an action plan by November 2, 2000. However, you have not determined the possible root causes or why the above-referenced procedures were not always followed. Furthermore, your November 2, 2000, response indicates that your firm would not complete the action plan until March 31, 2001. Therefore, we consider your corrective action to be inadequate. It is critical to the quality of your medical devices that established procedures for production and process controls be in place as soon as possible, and personnel trained as necessary to gain compliance.

FDA-483, Item 1(c):
The investigator determined that Executive Management has not provided or allotted enough resources to perform and complete the complaint handling activities and quality assurance functions. Specifically, service/repair records, discrepant material reports, final acceptance test results, supplier performance and qualifications, and non-conforming materials were neither reviewed nor analyzed to identify developing trends because of the lack of personnel.

In the November 2, 2000, response, you indicate that since August 3, 2000, your firm has hired additional employees to address the shortcomings in the Regulatory and Quality Assurance Departments. However, you have not addressed whether new employees were given proper job training and have not provided examples of specific tasks assigned to the new employees to assure your CAPA system is adequately monitored.

2. Failure to maintain adequate documentation of management reviews [21 CFR 820.20(c)]. For example, your firm had not maintained a list of management attendees for all six management review meetings for the period of 5/1/00 to 7/31/00 (FDA-483, Item 3).

In the September 29, 2000, response, you indicate that Document #4010200, Management Review Procedure, will be revised to include the requirement for recording the Management Committee members present during management meetings and that this change will be issued by September 1, 2000.

However, our further review of previous procedures collected at the time of the inspection revealed that Section 3.0 of the 7/27/00 Management Review Procedure and Section 4.1.2 of the 9/24/99 Quality System Manual does require keeping records of management reviews, including those in attendance.

Please clarify the reason for not following the referenced procedures, and address the steps you have taken or will take to prevent the recurrence of this nonconformance.

3. Failure to review and update design plans to ensure they include the design and development activities and that they define responsibility for implementation [21 CFR 820.30(b)]. For example, the [redacted] design plan version did not:

   a. include the design activities performed between October 1999 and June 18, 2000 (FDA-483, Item 8);

   b. identify the area, group, or individual assigned the responsibility for completing the design activities for QC [redacted], fabrication of all components, and quality control inspection (FDA-483, Item 9).

4. Failure to establish and maintain procedures for approving the design input requirements [21 CFR 820.30(c)]. For example, the approval of the [redacted] design input requirements, including the date and signature of the individual approving the requirements, was not documented [FDA-483, Item 11].

Pages 1-2 of your November 2, 2000, response indicates that your firm has made the decision to [redacted] based on inconsistent design inputs, deficiencies in the design and development documentation, and failure to adhere to the Failure Mode and Analysis Procedure. Tab A of this response further states that to assure adherence to the requirements of design control, Document #4040100 Product Design Procedure will be revised to include reviews of the design history files for correctness and completeness at the time of design reviews throughout the life of the design project.

As written in Sections 5.0, 9.3, and 16.3 of the above revised Product Design Procedure, an audit of the design history file will be conducted after the completion of each design stage. We are requesting clarifications to the following questions:

Has your firm established a specific or generic audit procedure to audit the design control process or a particular design project for design control discrepancies?

How are audit discrepancies integrated into design reviews for detecting and resolving design problems?

If design control discrepancies are detected and resolved after each audit, does your established procedures require they be documented in design control records (i.e., the design history file) or in an audit report? FDA investigators will not request to review audit reports during inspections as per 21 CFR 820.180 General Requirements for Records. However, if audit results require changes or corrections to the device design (procedures, specifications, intended uses, etc.) after approval of initial design inputs or during commercial release, changes or corrections must be captured, documented, and are subject to FDA reviews as per 21 CFR 820.30(i) Design Changes.

5. Failure to establish and maintain procedures to ensure that formal documented reviews of the design results are planned and conducted at appropriate stages of design development and that those reviews are maintained in the design history file [21 CFR 820.30(e)]. For example, design reviews were not conducted to insure changes to the devices listed below are appropriate [FDA-483, Item 13]:

   a. Engineering Change Order (ECO) #990820, Release Date 9/03/99, to change the [redacted] vendor, [redacted] assembly machines, and [redacted] assembly procedures.

   b. ECO #990933, Release Date 10/04/99, to change the tolerance of the [redacted] by [redacted]

   c. ECO #991129, Originator Date 11/24/99, to change the [redacted] from [redacted] to [redacted] and the style of the [redacted].

The inspection findings revealed that your firm had not evaluated the impact of the above changes on the overall design and that a design review had not been conducted.

Tab G of your November 2, 2000, response indicates that a final design review was later conducted and signed 10/10/00. We note that this final design review, as submitted, does not comply with all of the design review elements as required by 21 CFR 820.30(e).

For example, this final design review does not address the identification of the design and the use of an outside specialist or independent reviewer was not specified.

We also note that six design review items were documented as incomplete or are still pending at the time of drafting your responses (i.e., re-evaluation of risk analysis, review of the sterilization methods, update of the inspection plans, approval of vendors by audits, and verification of supplier purchasing agreements). Have these outstanding review items been resolved? If these items are being resolved or have been resolved, you should attach documentation to the 10/10/00 final design review and provide the evidence of completion in the next written response to this office.

6. Failure to adequately validate the manufacturing process with a high degree of assurance [21 CFR 820.75]. For example,

   (a) your firm has not verified and/or validated the acceptance tests used for finished device testing of the MRIII motors [FDA-483, Item 15]; and

   (b) CAR 99-034 and ECR 000224 to change quality control procedures and motor heat specifications (in response to complaints of overheated motors) were incomplete at the time of inspection [FDA-483, Item 15].

The inspection findings show that your firm received at least 15 complaints of motors running hot in 1999 and 2000. Our review of complaints revealed that some physicians complained that the pneumatic motors were getting hot during surgical procedures.

On page 6 of your August 30, 2000, response, you indicated that the appropriateness for temperature performance of the Midas Rex III motor is based on the Standard [redacted], and that an acceptance temperature range was also established based on the same standard. We find your explanation incomplete and inadequate to address the issue of overheated motors. Please respond to the following questions:

Did your firm follow the Standard [redacted] during the design of the MRIII motors or did your firm start to adapt this standard after receiving these complaints as indicated in CAR 99-034 and ECR 000224?

Your response does not indicate a lower and upper limit for "an acceptance temperature range." How does this acceptance temperature range relate to the "[redacted]degree rise above the initial temperature measurement", as specified in the Procedure "Final Inspection of Midas III Motors, Document #4101400-03, Revision 6, dated 4/8/00"?

As to whether this acceptance temperature range is the same as or different from the [redacted] degree rise, has your firm validated, or when appropriate verified, the device design to ensure it meets user needs [21 CFR 820.30(g)]? How does this new acceptance temperature range address complaints of motors getting too hot and can physicians tolerate it during surgery?

Our investigator's review of service repair records indicated that motors were returned for repairs because they were running hot or overheating and that your firm was not reviewing these records to identify possible complaints (FDA-483, Item 23). What are the possible causes for motors running hot [21 CFR 820.100(a)(2)]?

In ECR/ECO 000224, your firm indicated to change the device specifications and QC procedures for Midas III Motors so that the maximum temperature a motor can reach during testing is [redacted] F. What are the specific changes [21 CFR 820.30(i) and 820.100(a)(5)]? This ECO was first initiated 12/14/99 and found to be incomplete at the time of the inspection; eight months has elapsed since the initiation of CAR 99-034. What is its status currently [21 CFR 820.100(a)(3) and (a)(4)]?

In the 2/17/00 memo (attached to CAR 99-034), your firm indicated that all Midas III motors in-process or in finished goods storage that do not meet the new upper temperature limit must be reworked in order to meet the new limit. Please describe the specific rework operations, the current status of reworking the units, and the effect the rework has made upon the devices [21 CFR 820.100(a)(4) and 820.90(b)(2)].

7. Failure to establish and maintain procedures for implementing corrective and preventive action [21 CFR 820.100]. For example, your firm:

(a) does not always follow the Corrective Action Procedure, Document # 4140100, Effective Date 8/5/99, by failing to routinely review service records for reliability information [FDA-483, Item 16];

(b) does not analyze service and repair records, discrepant material reports, nonconforming material reports, and finished device acceptance test data to identify existing and potential causes of nonconforming product and other quality problems [FDA-483, Item 18]; and

(c) is inconsistent in the assignment of failure and investigation conclusion codes used in the trending of complaint data [FDA-483 Item, 19(a)].

FDA-483, Item 16 and 18:
Your August 30, 2000, response indicated that the Corrective Action Procedure # 4140100 would be revised by November 30, 2000, and that associated training would be performed. However, you have not submitted the latest revision of this document and personnel training records for our review.

In addition, once the referenced procedure has been completely revised and proper personnel training provided, your firm should re-analyze and review all sources of past and current quality data to identify any existing and potential quality problems for corrective and preventive action. Please provide a status report in the next written response.

FDA-483, Item 19(a):
The investigator determined through record review that complaints of disintegrating/fuzzy motor safety seals were all received for the same root cause, yet your firm assigned different failure codes (i.e., code #9027, 9034, 9046, and no code).

Your November 2, 2000, response indicates that Document #4140200, Processing Customer Complaints, was revised to include the standardization and recording of all codes when completing the complaint form and report. However, this response and attached complaint handling procedure (Tab D) does not explain how failure codes are trended and reviewed to detect inconsistency in the assignment of failure and conclusion codes.

8. Failure to establish and maintain procedures for receiving, reviewing, and evaluating complaints [21 CFR 820.198]. For example, 74 of the 152 complaints reviewed had one or more of the following deficiencies [FDA-483, Item 20]:

   (a) Records of complaint investigations do not consistently include documentation of the corrective action taken;

   (b) Not all complaints are reviewed and evaluated to determine whether an investigation is necessary;

   (c) When necessary, complaints involving the possible failure of a device to meet any of its specifications are not investigated;

   (d) Records of complaint investigations do not include the nature and details of the complaint;

   (e) Records of complaints do not include the results of the investigation.

Your August 30, 2000, and November 2, 2000, responses indicate that the Complaint Handling Procedure #4140200 has been revised and associated personnel training performed. Your management of the firm agreed with the investigator's observation that the firm was behind in complaint handling and complaint investigation activities. We would like to emphasize that, in addition to revising the referenced complaint handling procedure, your corrective action should include a complete review of all past complaint records to determine if they have been adequately investigated for compliance with 21 CFR 820.198 – Complaint Files. Please provide a status report covering these activities in your next written response.

The Midas Rex® (MR) Motors and Safety Seals are also misbranded within the meaning of Section 502(t)(2) of the Act in that information was not submitted to FDA as required by the Medical Device Reporting Regulation, 21 CFR 803.50. The investigator determined that your firm had failed to submit at least 20 complaints received between January 1999 and July 2000 as MDR reports as required. For example:

> Complaint #0199-0008 received 1/19/99: The safety seal broke and came out during a spinal fusion procedure. The doctor was concerned about the contamination issue.
>
> Complaint #0399-00066 received 3/11/99: During a case, the safety seal came out of the motor during use. The patient's wound site was irrigated and cleaned.
>
> Complaint #1099-00125 received 10/14/99: The safety seal blew out and released oil mist during a recent surgery.
>
> Complaint #1299-00163 received 12/20/99: A Midas Rex III Motor leaked oil into the sterile field during surgery.
>
> Complaint #1299-00162 received 12/30/99: A Midas Rex III Motor leaked excessive oil during surgery. The safety seal was black and had oil throughout the seal. The motor housing was coated with oil. The doctor changed gloves twice during the procedure.
>
> Complaint #0100-0002 received 1/04/2000: Oil leakage during surgery.
>
> Complaint #0400-0126 received 4/05/2000: During a craniotomy procedure, there was a black substance that leaked into the patient. The wound was flushed with antibiotics. The safety seal appeared to have dislodged.
>
> Complaint #0500-0151 received 5/24/2000: Oil leaked from the motor into the sterile field. The Technical Support contact advised the complainant to treat the surgical site as if the oil were not sterile.

Your responses indicate that the 20 MDR reports were submitted on September 11, 2000, and were included in Tab B of the September 29, 2000, response. During the inspection your firm indicated to our investigator that MDR reports would be submitted for the 20 complaints the investigator reviewed. We would like to remind you that the 20 complaints identified were only a sample and that your firm should conduct a comprehensive review of all complaints for a decision on MDR reportable events and submit reports as required by 21 CFR 803.50. Because of the serious deficiencies found in your firm's complaint handling and MDR reporting systems, a status report should be submitted on the MDR issue in your next written response to this office.

The MR Motors and Safety Seals are further misbranded within the meaning of Section 502(t)(2) of the Act in that a report of correction or removal was not submitted to FDA as required by Section 519(f)(1) of the Act. The Correction and Removal Regulation (21 CFR 806), promulgated under Section 519(f)(1), requires manufacturers, importers, and distributors to promptly report to FDA any correction or removal of a device to reduce a risk to health within 10 working days.

The inspection revealed that the safety seals were expanding in the autoclave during the sterilization process before each use. When the MR motors were running, the safety seals would shred. Records reviewed indicated that your firm had received at least 23 complaints of defective seals. Your firm's internal failure investigation (CA #00-013) determined that the returned safety seals displayed "fuzzy" and disintegration characteristics, and that the supplier had changed the [redacted] material without notifying your firm of the change. Your firm's corrective action was to change the supplier, scrap all safety seals in stock from Lot # 5031 to Lot #5348, and to send replacement seals (from acceptable lots) to only those customers who had complained.

The safety seals are accessories to the Classic and Midas III Motors and serve as redundant seals to prevent oil leakage from the motors. Safety seals from the defective lots resulted in an increased chance of oil leaks and seal material disintegration, thereby increasing the chance of sterile field contamination. Your firm's action to send replacement seals to customers meets the definition of a "correction" as defined in 21 CFR 806.2(d) and 21 CFR 806.10(a)(1), which requires manufacturers to submit a written report to FDA of any correction or removal of a device if the correction or removal was initiated to reduce a risk to health.

We are also concerned that your firm's action was not adequate to notify customers, other than those who had submitted complaints, of the problem with the defective safety seals. Please respond in writing to these concerns and provide the justification for not addressing all users.

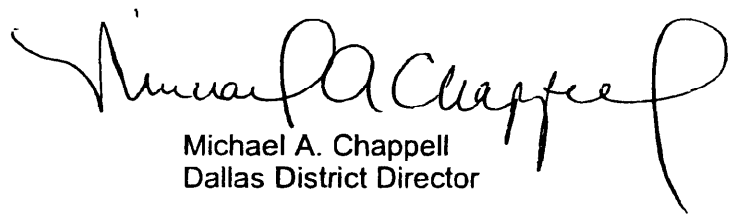
This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA-483 issued at the closeout of the inspection may be symptomatic 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.

Until these violations are corrected, and FDA has documentation to establish that such corrections have been made, federal agencies will be advised of the issuance of this Warning Letter so that they may take this information into account when considering the award of contracts.

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 penalties.

Please provide this office in writing within 15 working days of receipt of this letter a report of the specific steps you have taken or will take to identify and correct any underlying systems problems necessary to assure that similar violations will not recur. Include your responses to the specific clarifications and documentation requested in this letter. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time frame within which the corrections will be completed. Your reply should be directed to Mr. Thao Ta, Compliance Officer, at the above letterhead address.

Sincerely,



Michael A. Chappell
Dallas District Director

Enclosures:

cc: Mr. Samuel Owusu-Akyaw
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