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August 22, 2001

Chicago District
300 S. Riverside Plaza, Suite 550 South
Chicago, Illinois 60606
Telephone: 312-353-5863

WARNING LETTER
CHI-45-01

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Harry Jansen Kraemer, Jr.
President & CEO
Baxter Healthcare Corp.
One Baxter Parkway
Deerfield, IL 60015

Dear Mr. Kraemer:

During the inspection of your firm's I.V. Systems/Medical Products Business Unit (located at Route 120 & Wilson Road, Round Lake, IL) from September 12 to November 15, 2000, Investigator Chad Schmeier determined your firm manufactures infusion pumps. Infusion pumps are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The 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 regulation for medical devices, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Failure to establish and maintain procedures to include requirements that ensure that information related to quality problems are disseminated to those directly responsible for assuring the quality of infusion pumps. For example:
 - 1.1. EIS -Large Volume Pump Quality Reviews conducted for quarter 4/1999, quarter 1/2000, and quarter 2/2000 did not include review of corrective and preventive actions as per procedure #PHG177. Also, procedures did not discuss review of engineering studies/investigations or production data related to pump design. The related information was not presented during the quality reviews.
 - 1.2. Engineering management did not respond to an internal memorandum that discusses the cause of premature main battery failures. The information was not contained in the corrective and preventive action system.
2. Failure to complete the investigation of nonconformities. Failure to justify the halt or delay of an investigation of nonconformities. For example:
 - 2.1. The report for study # [REDACTED] explained that further studies would be conducted to investigate influences that may have contributed to slightly larger increases in delivery error for trials 7 and 12. No further investigation was conducted. No explanation for the discontinuation was documented.

Additionally, your firm's infusion pumps are misbranded within the meaning of Section 502(t)(2) in that your firm has not provided an adequate explanation for not submitting MDR Malfunction Reports as required by 21 CFR Part 803.50(a)(2).

Specifically, your firm's rationale for not submitting malfunction reports includes the "adverse reporting Guidance for Medical Device Manufacturer or its Authorized Representative." The Global Harmonization Task Force, Study Group (SG) II drafted this document. The SG II document does not reflect current MDR policy and cannot be used to make MDR reporting decisions. Therefore, the firm has not provided or documented an adequate reason for its failure to submit the referenced MDR Malfunction Reports.

In addition, your firm's current MDR policy regarding failure codes and MDR reporting does not appear to be compliant with 21 CFR Part 803.50(a)(2) – malfunction reporting. During the inspection, the firm's policy was reported as, "Baxter's current policy is not to submit MDRs for complaints related to failure codes unless the information suggested that an injury occurred or medical intervention was required." This policy conflicts with the malfunction reporting requirements in 21 CFR 803.50(a)(2) because a reportable malfunction by definition involves an event that is likely to cause or contribute to a death or serious injury. An actual injury or medical intervention would be reportable as a serious injury.

Also, there is a lack of information about patient medical treatment in your firm's investigations. For example, your firm has no way of determining if the device is likely to cause or contribute to an injury or death if there is no information about the medication being infused. The risk to the patient is affected by the nature of the drug being infused. For example, is the patient receiving saline, a narcotic, a cancer drug, a cardiac drug, etc.?

The Corrections and Removals regulation requires manufacturers, importers, and distributors to report promptly to FDA corrections or removals of devices undertaken to reduce risk to health within 10 working days. Your firm's Colleague® single channel infusion pumps are misbranded within the meaning of Section 502(t)(2) of the Act in that your firm failed to submit information to FDA required by 21 CFR Part 806, Medical Device Corrections and Removals, promulgated under Section 519(f) of the Act. For example, your firm failed to submit a Report of Correction and Removal to FDA for adding a second additional battery to the Colleague® single channel infusion pump to correct numerous reported battery failures. The Correction and Removal began in September 1999, and is currently ongoing. If you have not done so already, you are required to submit a report of all corrections and removals to the FDA, within 30 working days of the receipt of this letter, of which your firm has conducted since May 18, 1998. Please send your report to our office and address it to Ms. Kathleen E. Haas, Recall & Customer Complaint Coordinator.

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 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 Quality System/GMP deficiencies are reasonably related will be cleared or approved until the violations have been 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, and thereby enabling FDA to withdraw its advisory to other federal agencies concerning the award of government contracts, and to resume marketing clearance for Class III devices for which a 510(k) premarket notification or Premarket Approval application (PMA) has been submitted, and Certificates to Foreign Governments for products manufactured at your I.V. System Division facilities, we are requesting that you submit to this office on the schedule below, certification by an outside expert consultant 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, and certification by your establishment's Chief Executive Officer (if other than yourself) that he or she has reviewed the consultant's report and that your establishment has initiated or completed all corrections called for in the report. The attached guidance may be helpful in selecting an appropriate consultant.

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: December 31, 2001

**Subsequent certifications: December 31, 2002
 December 31, 2003**

We acknowledge the receipt of your firm's responses to our Investigators' FDA-483, dated November 28, 2000, and January 9, February 15, April 1, and June 27, 2001. We do not consider your responses to be adequate because of the following:

11/28/00 Response to FDA-483 # 1:

Your firm did not discuss how management would assure Baxter's quality systems not covered during the inspection are in compliance with the Quality System Regulation.

11/28/00 Response to FDA-483 # 2:

Procedure PHG173 does not discuss the format for presenting information during management review meetings to ensure uniformity from meeting to meeting. Also, the procedure does not discuss the requirements for elevating information obtained during CAPA's and engineering studies/investigations to the management review. PHG177 does not discuss how information will be summarized or presented during the quality meeting.

11/28/00 Response to FDA-483 # 3.1:

EIS Large Volume Pump Quality Review reports did not discuss the significance of the CAPA's, the relationship to the complaints, or what information related to the CAPA was reviewed. Pages 3 and 4 of the quality review reports did not include a summary of any corrective/preventive actions. Also, PHG177 does not discuss how information will be summarized or presented during the quality meeting.

11/28/00 Response to FDA-483 # 3.2:

Your firm provided no documentation in the response to support the statement that some points in the memo were deemed without merit and did not pertain to actual conditions seen in the Colleague[®] pump.

11/28/00 Response to FDA-483 # 4.1:

Your firm did not address the perceived instability in the study group due to the stress on the pump. Your firm provided no information during the inspection suggesting that users expose the battery to 55°C for less than one hour. Your firm explained that the results of study [redacted] (Colleague[®] III study) apply to the Colleague[®] I design due to the same circuit used in the Colleague[®] III. We remain concerned with this response because the Colleague[®] III pump has two main batteries, whereas the Colleague I had one main battery. Your firm proposed no additional investigation to study the effects of temperature on battery performance.

11/28/00 Response to FDA-483 # 5.1:

Your firm's responses did not make clear how decisions not to investigate and how the rationale for those decisions would be documented. The CAPA system does not appear to have procedures to track issues brought to the CAPA group for which no investigation was deemed necessary.

11/28/00 Response to FDA-483 # 7.1 and 7.3:

We remain concerned that nonconforming results of [redacted] were considered acceptable due to a non-verification study that was for informational purpose only. Your firm did not identify the actions that address design output not meeting input requirements for this design.

11/28/00 Response to FDA-483 # 7.2:

The current PRD, as reviewed during the inspection, did not discuss the inaccuracy of the battery charge level indicator or battery charge/discharge indicator. Your firm has not identified any actions that address design output not meeting input requirements for this design.

11/28/00 Response to FDA-483 # 8:

The underlining cause of the failure code was not evaluated to determine if the device malfunctioned. Also, complaint # 99101213 did not include information regarding whether or not medical intervention was necessary. Your firm did not provide any corrective action for this observation.

11/28/00 Response to FDA-483 # 11.1:

Study [redacted] was conducted on a dual battery pump, not a single battery pump as in EIS-96-078. The proposed study included with the response does not discuss the equivalency between simulated cycling and actual pump cycling. The study does not discuss the recharge time period or how a rate of 100ml/hr was chosen as a typical operating condition. Additionally, the study does not discuss how rates above 100ml/hr (up to 1200ml/hr) will affect battery performance.

11/28/00 Response to FDA-483 # 11.2:

Your firm's responses did not discuss correction of the operator's manuals currently in the field that list the storage temperature range as -29° to 57° C.

11/28/00 Response to FDA-483 # 11.5:

During the inspection, Investigator Schmeier did not observe tubing dimensions discussed in EIS-96-096. Additionally, no study observed during the inspection evaluated tubing dimensions in order to verify accuracy specifications.

11/28/00 Response to FDA-483 # 12.2:

Study () was conducted to predict the affect of tubing dimensions on pump accuracy under specific laboratory conditions. The study did not discuss operation ranges as evaluated in EIS-92-073 and () the studies that were reviewed did not discuss evaluating pump accuracy at worst case operating conditions and tubing dimensions.

6/27/01 Response:

We reviewed the Study Report Number 12371, entitled Colleague® Yuasa Battery Cycling Evaluation, issued June 15, 2001, that your firm submitted in the response dated June 27, 2001. We noticed that the raw data shows that at () and () cycles, the time from the low battery alert to the depleted battery alarm is less than the specification of () minutes for several pumps. The report does not address this apparent failure to meet specifications and contains no failure investigation.

We request that you 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 notify this office, in writing, within 30 working days of receipt of this letter of the specific steps you have taken to correct the 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. If corrective action cannot be completed within 30 working days, state the reason for the delay and the time within which the corrections will be completed.

In a meeting with your firm's representatives on December 14, 2000, Ms. Margaret Foss, Vice President Quality Management, explained that in June 2001 your firm intended to finish replacing the single-battery design of Colleague® infusion pumps with a dual-battery design. We need to know if your firm finished implementing this correction/removal to all Colleague® infusion pumps in the field. Please send this office a detailed status report regarding your firm's efforts regarding this correction/removal.

Your response should be sent to Michael Lang, Compliance Officer. If you have any questions regarding this letter, please contact Mr. Lang at (312) 353-5863 x171.

Sincerely,

RS\

Raymond V. Mlecko
District Director

Attachments

cc: Ms. Margaret Foss
Vice President Quality Management
Baxter Healthcare Corporation
I.V. Systems Division
Route 120 & Wilson Road
Round Lake, IL 60073-0490

Mr. Herbert Musolf
Vice President Reliability and Quality Engineering
Baxter Healthcare Corporation
I.V. Systems Division
Route 120 & Wilson Road
Round Lake, IL 60073-0490