



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service  
Food and Drug Administration

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

April 5, 2000

Ref: 2000-DAL-WL-7

WARNING LETTER

CERTIFIED MAIL  
RETURN RECEIPT REQUESTED

Mr. Emile Battat, CEO & President  
Quest Medical, Inc.  
One Allentown Parkway  
Allen, Texas 75002-4211

Dear Mr. Battat:

During an inspection of your firm located in Allen, Texas, on August 16-27, and September 3-7, 1999, our investigator determined your firm manufactures Myocardial Protection System (MPS) Cardioplegia Delivery Sets and Vacuum Relief Valves (VRV-II). These products are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The referenced inspection revealed 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 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 Federal Regulations (CFR), Part 820.

We have reviewed Quest's response letter and attachments, dated September 30, 1999. Our evaluation of the response leaves this office and CDRH with continued concerns for the lack of appropriate controls used in the production of medical devices by Quest Medical, Inc. We continue to see significant deviations where Quest has failed to conduct and document a thorough investigation of failed devices prior to effecting changes in device design as a result of device complaints, or as a result of Quest's efforts to improve efficiency in production.

The following deviations were documented during the inspection; note that some of these deviations are repeat observations from the previous inspection concluded on September 9, 1998.

Failure to establish and maintain procedures for the identification, documentation, validation or verification, review, and approval of design changes, as required by 21 CFR 820.30(i). For example, document reviews were not performed to ensure that the results of the changes listed below are appropriate:

1. The check valve was replaced with a [REDACTED] in the MPS Cardioplegia Delivery Set, per ECO #100075, dated 5/18/98;
2. The [REDACTED] of the [REDACTED] in the heat exchanger of the MPS Cardioplegia Delivery Set was [REDACTED], per ECO #100278, dated 11/20/98;
3. The changes made to the MPS Cardioplegia Delivery Sets, including a [REDACTED] process for the heat exchanger, the acceptance requirements for the amount and location of adhesive, and the criteria for [REDACTED] rejections on the heat exchangers, per ECO #100334, dated 12/22/98, and
4. There were changes to the Checkmate Anesthesia Sets to replace [REDACTED] sterilization with [REDACTED] sterilization, per ECO #100439, dated 4/5/99.

Failure to establish and maintain procedures to ensure that formal documented reviews of the design results are planned and conducted at appropriate stages and those reviews are maintained in the Design History File, as required by 21 CFR 820.30(e). For example, you did not perform and document design reviews to ensure the results of the changes listed below are appropriate:

1. The check valve was replaced with a [REDACTED] in the MPS Cardioplegia Delivery Set, per ECO #100075, dated 5/18/98.
2. The [REDACTED] of the [REDACTED] in the heat exchanger of the MPS Cardioplegia Delivery Set was [REDACTED] per ECO #100278, dated 11/20/98.
3. The changes made to the MPS Cardioplegia Delivery Sets, including a [REDACTED] process for the heat exchanger, the acceptance requirements for the amount and location of adhesive, and the criteria for [REDACTED] rejections on the heat exchangers, per ECO #100334, dated 12/22/98.

4. There were changes to the Checkmate Anesthesia Sets to replace [REDACTED] sterilization with [REDACTED] sterilization, per ECO #100439, dated 4/5/99.

Failure to establish and maintain procedures for verifying the device design to confirm that the design output meets the design input requirements, and that these documents are maintained in the Design History File, as required by 21 CFR 820.30(f). For example, design changes were implemented without performing and documenting testing to determine whether the design outputs met the functional and operation requirements in the following instances:

1. A design change from a check valve to a [REDACTED] for the Myocardial Protection System (MPS) Cardioplegia Delivery Set, per ECO #100075, dated 5/18/98;
2. An [REDACTED] in the [REDACTED] of the [REDACTED] in the heat exchanger of the MPS Cardioplegia Delivery Set, per ECO #100278, dated 11/29/98; and
3. The change of the heat exchanger design to a [REDACTED] for the MPS Cardioplegia Delivery Set, per ECO #100428, dated 3/15/99.

Failure to maintain procedures for the review and disposition of nonconforming product as required by 21 CFR 820.90(b). For example, incoming lots of components were initially rejected and later released by the MRB (Material Review Board) without adequate documentation justifying the need for use of the nonconforming product and the need for an investigation (FDA-483 Item 2a-d). This is a repeat observation from the previous inspection concluded on September 9, 1998 (FDA-483 Item 5).

The current use of initially rejected components include the following:

- Quest's Receiving Inspection/Disposition Report (QAID #74718), dated 12/15/98, documented vendor lot #10490-2 and 10490-03 were initially rejected due to hair and black particle material inside the MPS cassette.
- Receiving Inspection/Disposition Report (QAID #78229), dated 5/27/99, documented the vendor lot #10899-01 was initially rejected due to MPS cassette units containing [REDACTED] and failing the [REDACTED] test.

Quest stated on the reports that excess material was not an issue and the cassette pump could be used as-is. Quest failed to include or reference detailed

rationale and/or failure investigation documentation supporting its position and substantiating the acceptance of out-of-specification components.

In the September 30, 1999 response, you indicated that in order to resolve some difficulties encountered in the manufacturing of the MPS cassette pumps by the supplier, Quest [REDACTED] manufacture the MPS pump [REDACTED]. The effectiveness of this corrective action will be verified during the next scheduled inspection.

**Failure to investigate the cause of nonconformities relating to product, processes, and the quality systems as required by 21 CFR 820.100(a)(2).** For example, root causes for the sticking of [REDACTED] valves and low vacuum pressure in the VRVII have not been determined (FDA-483 Item 3).

**Failure to identify the action(s) needed to correct and prevent recurrence of nonconforming product as required by 21 CFR 820.100(a)(3).** For example, Quest has not implemented corrective action to address the complaints of sticking valves and low pressure (FDA-483 Item 3).

The problems with occluded and sticking [REDACTED] valves were observed during the 9/98 and 9/99 inspection of Quest, respectively. Quest was first made aware of the problem with slits sticking in 10/97, and Quest continued to receive 27 similar complaints of no flow, low vacuum, or slow flow from September 1998 to August 15, 1999.

Your investigation records indicated that sticking valves and occluded valves were two separate problems even though they both caused a reduction in [REDACTED]. Quest first initiated CAR 707 on 10/23/97 and completed it on 3/10/98 to instruct the valve supplier, [REDACTED] to discontinue the [REDACTED] process to prevent the recurrence of sticking valves.

After CAR 707, Quest initiated CAR 820, another corrective action, on 11/17/98 to address the same sticking valve problem. CAR 820 was lost and resulted in the third CAR (99075). However, these actions did not correct the problem because Quest continued to receive similar complaints in 1998 and 1999. Quest, therefore, has failed to verify or validate the corrective actions [21 CFR 820.100(a)(4)].

During the 9/98 inspection, you indicated that as corrective action to the October 1997 recall of occluded VRV-II valves, Quest implemented [REDACTED]% visual and functional testing to verify that the valves are open. Your response to the 1998 inspectional findings stated that the valve testing process was properly validated. We are quite concerned with your testing, valve calibration, and process validation because they fail to detect a reduction in [REDACTED] during production regardless of whether it is a problem with sticking valves or occluded

valves [21 CFR 820.80 – Acceptance Activities; 21 CFR 820.75 – Process Validation].

Quest should conduct the necessary investigation to determine if [REDACTED] particles have or have not been cleared from the valves as a result of the supplier discontinuing the [REDACTED] process. A summary of that investigation should be provided to this office and should adequately address the following concerns as well:

- Quest's failure to confirm the root causes of valve blockage [21 CFR 820.100(a)(2) – Investigating the cause of nonconformities].
- Quest's failure to provide a preventive action plan to control the sources of [REDACTED] contamination at Quest or at the supplier [21 CFR 820.100(a)(3)].
- Quest's failure to provide purchasing control requirements for defining acceptance criteria for [REDACTED] defects and excess materials for [REDACTED] parts received from the supplier [21 CFR 820.50 – Purchasing Controls].

**Failure to investigate and follow-up on complaints in a timely manner as required by 21 CFR 820.198 (a)(1).** For example, a complaint of blood leaks on [REDACTED] % of the temperature probes of the MPS Standby Delivery Set and a complaint of [REDACTED] leaks were not further investigated for approximately 6 months after initial receipt of the complaints (FDA-483 Item 5b and Item 7a).

**Failure of the complaint handling procedures to determine the cause of the nonconforming product as required by 21 CFR 820.100(a)(2) and 820.198(c).** For example, testing of the finished goods sample (customer returned stock) was not done to confirm the root causes of the failures until the issue was raised in the current FDA inspection (FDA-483 Item 5b). Complaints of [REDACTED] leaks were open with no documented failure investigation (FDA-483 Item 7a).

FDA-483 Item 5b:

On March 17, 1999 Quest received a hospital complaint (Complaint #9907604) that [REDACTED] % of the temperature probes of the MPS Standby Delivery Set leaked blood no matter how tight the connector was tightened on the temperature probe, and that the temperature probe had to be cut out to avoid the problem. The MPS Standby Delivery Set is a manual back-up unit in case the MPS system fails.

The hospital also provided Quest with the lot number and percentage of the quantity affected. This complaint record documented that Quest had not been able to confirm the report since a sample was not available.

In an internal e-mail, dated 3/19/99, Quest indicated that the supplier was notified of the event and Quest had some units in stock and would test them. However, in-stock units were not tested and the complaint was closed two days later on 3/19/99 following Quest's initial receipt of the complaint on 3/17/99.

Since 3/19/99 Quest has not followed up with the supplier for additional information on the complaint. This issue was raised during the FDA inspection, and in response to the observation Quest sent a September 18, 1999 letter to the supplier requesting an additional response (Appendix 5B of your written response). This letter demonstrated to us that Quest has not conducted any follow-up for six months, since the receipt of the complaint on 3/19/99 [21 CFR 820.198(a)(1)].

Furthermore, in the September 18, 1999 letter, you indicated to the supplier that you included a representative sample of the defect that was pulled from customer returned stock. Quest's testing of the sample showed a leak at the connection between the temperature probe and the [REDACTED] fitting at a pressure of [REDACTED]. We have questions regarding your firm's manner of sampling and testing, and if that sampling and testing is representative of the lot. Only [REDACTED] was tested from stock and information has not been provided on the lot number and lot size. Quest's letter did not indicate if other units from different lots were tested to determine the extent of the leak problem.

FDA-483 Item 7a:

The file for Complaint #9908901, Item 1 of 1 received on 3/30/99 was reviewed on 8/25/99 and was found by the investigator to be open with no documentation of a failure investigation. Additionally, no data was available regarding a root cause of the failure. There were attached records to the complaint, however, including the Lot Inquiry Record showing [REDACTED] units of Lot 9290.03K were scrapped during production. The reason for scrapping these units is not addressed in the complaint file. Nor is scrapping addressed in the Device History Record (DHR) for the lot.

Additionally, the DHR for this lot documents a significant number of the heat exchanger components (supplier lots [REDACTED], [REDACTED] and [REDACTED] failing for [REDACTED] and [REDACTED] tests.

Finally, additional handwritten notes, dated 2/16/99, reference the need to check batch trends as a result of leaks identified the week before. All of these findings indicated a need for a complete and thorough investigation of a failed device.

Your written response declared Complaint #9908901 was closed 10/1/99 and included a memo of investigation, dated 9/30/99, which was initiated 9/21/99 and concluded 9/29/99, six months following the receipt of the complaint.

Failure to report to FDA reportable device malfunctions as required by Medical Device Reporting (MDR) Regulations (21 CFR 803). The investigator also determined that Quest's MPS Cardioplegia Delivery Sets are 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 (MDR) Regulation, CFR 21 Part 803.

Medical Device Manufacturers are required to report within 30 days whenever the manufacturer receives or otherwise becomes aware of information that reasonably suggests a device marketed by the manufacturer has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur [CFR 21 Part 803.50(a)(2)].

Quest failed to report reportable events to FDA within 30 days of receiving information on malfunctions of the MPS Cardioplegia Delivery Sets, for example:

- Complaint #9911801, Item 1 of 1, dated 4/28/99, reported by a user that a Cardioplegia Delivery Set with/Arrest, Additive, showed the presence of blood on the front of the housing of the heat exchanger following a case. A review of this complaint during the current inspection determined the complaint was still open, even though Quest's evaluation notes indicated the complaint had been confirmed. Quest had not submitted an MDR report for the complaint, and there was no documentation in the MDR file (21 CFR 803.18) indicating Quest had made a decision the event was not reportable (21 CFR 803.17).

Post inspection information provided to the district in the September 30, 1999, response indicated inconsistency about when the event had occurred. This complaint was confirmed by Quest and it meets the criteria for "reasonably suggests" because leaks can occur from heat exchangers and cause or contribute to a death or serious injury. The leak problem is documented by Quest's device history record and in various MDR reports submitted for this same, and similar problems. The device or a similar device would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

- Complaint #9911603, Item 1 of 1, dated 4/27/99, reported a loss of system pressure during a case. The user reported blood leaking from the MPS. Quest classified the complaint with an alleged defect of no [REDACTED] or weak [REDACTED] on the main cassette. The defect identified in this complaint is the same type of defect that was identified in the May, 1999 recall of the MPS Cardioplegia Delivery Sets.

This defect meets the requirement for reporting a malfunction [21 CFR 803.50(a)(2)]. The MPS malfunctioned, e.g., blood leaked due to weak [REDACTED]. The malfunction is likely to cause or contribute to a death or serious injury if the event were to recur. The serious injury threshold was established when the leak resulted in medical or surgical intervention to prevent blood loss. This action met the MDR criteria for "medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure", i.e., blood loss.

- Complaint #9911101 - the initial event (Complaint #9911101, Item 1 of 3) on 4/21/99, reported that upon attempting to deliver a third dose of cardioplegia, the seam on the main pump cassette gave way and would not deliver. This event was reported 5/5/99. However, two other related events (involving two different MPS Cardioplegia Delivery Sets occurred during the same case with the same patient) were not reported to FDA until 8/23/99, during the FDA inspection.

The second event (Complaint #9911101, Item 2 of 3, dated 4/21/99) reported a tear on an out-of package disposable for the MPS Cardioplegia Delivery Set. The third event (Complaint #9911101, Item 3 of 3, dated 4/21/99) reported an occluded Arrest Agent Pouch during the same case. All three events involved malfunctions that appear to have led to the termination of surgery without completing the planned procedures. Quest did not report the second and third event within the 30-day time frame as required.

In addition, the MPS system is a Class III device and is considered to be life-sustaining/life-supporting. The preamble to the MDR regulation stipulates that malfunctions with "a device that is considered to be life-sustaining/life-supporting and thus essential to maintaining human life" are reportable.

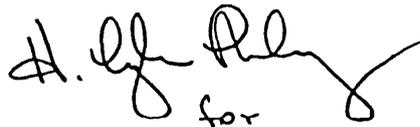
This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is Quest's responsibility to ensure adherence to each requirement of the Act and the regulations. The specific violations noted in this letter and in the FDA-483 (copy attached) issued at the closeout of the 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 violations. Failure to promptly correct these violations 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 15 working days of receipt of this letter, of the specific steps you have taken to identify and correct any underlying systems problems necessary to assure that similar violations will not recur. 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 James R. Lahar, Compliance Officer, at the above letterhead address.

Sincerely,

A handwritten signature in black ink, appearing to read "M. A. Chappell", with a large flourish at the end. Below the signature, the word "for" is written in a smaller, cursive script.

Michael A. Chappell  
Dallas District Director

MAC:jrl

Enc. Form FDA-483

cc: Doug Bryan, Plant QA/RA Manager