



DEPARTMENT OF HEALTH & HUMAN SERVICES

T1790M

Public Health Service

JAN 21 1998

Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

WARNING LETTER  
FEDERAL EXPRESS

Mr. Alan Schwebel, President  
Mennen Medical, LTD.  
Kryat Weizman Science Park  
Rehovot, Israel 76100

Dear Mr. Schwebel:

During an inspection of your firm located in Rehovot, Israel, on September 10, 11, & 14, 1997, our investigator determined that your firm manufactures patient monitors. 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 within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for their manufacture, packing, storage, or installation are not in conformity with Good Manufacturing Practice (GMP) for Medical Devices Regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Failure to document the approval of a document with a signature and to promptly remove all obsolete documents from all points of use or otherwise prevented from unintended use, as required by 21 CFR 820.40(a). For example:
  - a. All of the device master records, approximately 400, available for the production and quality control departments, had only a typed name for the reviewing and approving personnel. There was no approval signature on these records.
  - b. The list of approved components are stored on the your terminal based, main server. There was no written list of approved components with an approval signature.
  - c. The approval page for the Horizon 9000WS Cathlab's software located in the document control department contained the signature of the originator of the document, but it lacked an approval signature. This approval page was different from the approval page for the same software located in the production department. The approval page located in the production department contained an approval signature, but it lacked the identity of the person responsible for initiating revision E through H.

- d. Copies of the assembly/production instructions for the "IP 960-318-000 REV.A," "Installation Procedure CBL-RGB Adapter Video Splitter (Multi Coax)," for the Horizon 9000WS CathLab located in the document department and the production department lacked an approval page. The approval page was stored in a personal computer located in the document department. A copy of the approval page was printed during the inspection. The printed copy contains the name of the person who approved this procedure, but no signature.
- e. Assembly /production procedures currently being used for the Horizon 9000WS Computerized Catheterization Laboratory have not been reviewed or approved.
- f. Outdated assembly instructions were being used for the Horizon XL/S.

Your response to (a. through d.) above appears to be adequate. You intend to train again your personnel in document control, to bring the device master records into full compliance with the GMP requirements, to maintain in the device master record file formally approved hard copies of all computerized documents, and to generate an index for each device master record.

Your response to (e.) above appears to be adequate. You state that the assembly/production procedures which have not been reviewed or approved will be submitted immediately through the change control process. Additionally, you will retrain your production/assembly personnel in change control procedures.

Your response to (f.) above appears to be adequate. You provided for our review a copy of a memorandum written by the Quality Assurance Manager to the Production Manager requesting that Work Order and Serial Number be handwritten onto the work instruction sheet. This procedure will be followed until all work instructions are updated.

- 2. Failure to implement procedures for acceptance of incoming product, as required by 21 CFR 820.80(b). For example, your written procedures require that approved incoming product be identified with the inspector's signature and the date. The contents of one of the numerous drawers in the Store Room which contains released components failed to have the inspector's signature or release date on the release label. Furthermore, the part stored in this drawer has a different part number than the two part numbers listed on the drawer. A check of the approved incoming product in the store room by your employees in a time span of about ten minutes revealed only two release labels which had been signed by the incoming product inspector. Two working days after these observations were made the "Incoming Inspection" area was checked again. Released components were observed that did not have a signature, date or a stamp.

Your response appears to be adequate with one exception. You did not address the storage of incoming approved product in drawers which have a different part number than the part number for the incoming approved product.

You state that the lack of a release label on the incoming components in the approved Stores Department was caused by two situations. One was the placing of the stickers used for the yearly inventory counts over the incoming product approval stickers. The other was the separation of incoming approved product from its original packaging material. You plan to resolve these situations by issuing a new written procedure.

Further, you state that all items that currently do not bear a release label in the Stores Department will be reprocessed through incoming inspection.

3. Failure of the device master record for each type of device to refer to the location of all of its required records, as required by 21 CFR 820.181. For example, Mr. Mazor of the firm stated that the firm has a list of all of the assemblies and sub-assemblies, for each device, but does not have a reference location for the elements of the device master records for those assemblies.

Your response appears to be adequate. Your response letter to the FDA 483 included a copy of your new Quality Master Record standard operating procedure (05-03-00) which covers the maintenance of the Device Master Record to include the location of the documents that comprise the Device Master Record for each product. The letter also stated that you will be creating a device master index for each device master record. Each index will provide a complete list and location of all documents that comprise the device master record.

4. Failure to establish and maintain procedures to adequately control all documents, as required by 820.40. For example:
  - a. There is no documentation that the changes made to the Device Master Record, specifically the production/assembly instructions for the Horizon XL Cardiac Monitor and the Horizon 9000WS Cath Lab Cardiac Monitor, have been updated in the production and quality control area copies of the device master record.
  - b. Procedures were not followed for Engineering Change Instructions, WI05-05-00, which include procedures for the distribution of Engineering Change Notice (ECN) and the generation of a monthly list of all ECN that took effect the preceding month. Correction Request #7664 located in the Document Control Area is different from the one located in the Production Department. Typed signatures and dates appear on the Correction Request located in the Document Control area, while handwritten signatures and dates appear on the one located in the Production Department. The concentrated list of Engineering Change Notices are distributed once every three months instead of once per month.

Your response to (a.) above appears to be adequate. You state that procedures for controlling documentation are currently being reviewed and revised to ensure that all changes in the device master record are communicated to appropriate individuals in a timely manner, and that obsolete versions of the documentation are handled in accordance with their work instructions (W105-07-00 and 05-02-00). You also state that employees will be retrained to follow your revised procedures and work instructions for handling new and obsolete documentation and that the retraining activities will be documented in personnel files.

Your response to (b.) above appears to be adequate. You state that employees will be retrained to follow their Engineering Change Instructions WI05-05-00 which require that Engineering Change Notices be distributed promptly to appropriate personnel and that a monthly list of approved Engineering Change Notices be generated. Further, you state that the Quality Assurance Department will monitor implementation of this work instruction to ensure compliance.

5. Failure to develop, conduct, control, and monitor production processes to ensure that a device conforms to its specifications, as required by 21 CFR 820.70. For example, there are no written procedures for the transfer of the approved version 1.7.2 Master copy of the Horizon Cathlab System 9000WS, from research and development to production.

Your response appears to be adequate. You have provided for our review a copy of an approved and implemented procedure (WI04-08-01) for the transfer of the approved version of the Master copy for the Horizon Cathlab System 9000WS to the production department.

6. Failure to validate with a high degree of assurance and approved according to established procedures, where the results of a process cannot be fully verified by subsequent inspection and test, as required by 21 CFR 820.75(a). For example, the procedure for the transfer of the approved current version, 1.7.2 of the Master copy of the Horizon Cathlab System 9000WS, to the production department for loading onto the finished device has not been validated.

Your response appears to be adequate with one exception. You did not provide for our review a copy of the validation results. You state that a procedure (WI04-08-02) for validating the transfer from the approved Master copy to the production department for loading onto the finished device has been approved and implemented. You only provided for our review a copy of the validation procedure.

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 regulation. The specific violation 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.

We acknowledge that you have submitted a response dated September 28, 1997, concerning our investigator's observations noted on the Form FDA 483. The adequacy of your responses are discussed above in our review. There are certain documents/corrective actions identified above which we will need to receive for our review prior to our conducting a follow-up inspection. We list these documents/corrective actions again below for your reference:

1. Please address the action that will be taken to prevent the storage of incoming approved product in drawers which have a different part number than the part number for the incoming approved product.
2. You did not provide for our review a copy of the validation results. You state that a procedure (WI04-08-02) for validating the transfer from the approved Master copy to the production department for loading onto the finished device has been approved and implemented. You only provided for our review a copy of the validation procedure.

After we have reviewed the above requested documents/corrective actions and have found them to be adequate, we will be in contact with you to schedule a follow-up re-inspection. Until the adequacy of the corrections by inspection can be confirmed, clearance of premarket submission, I 7, and any other premarket submissions for similar devices will be withheld. To arrange for a mutually convenient time for the inspection, please contact Kent A. Berthold at:

Food and Drug Administration  
Center for Devices and Radiological Health  
Division of Enforcement III  
Cardiovascular and Neurological Devices Branch, HFZ-341  
2098 Gaither Road  
Rockville, Maryland 20850

He may also be reached at (301) 594-4648 or by FAX at (301) 594-4672.

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.

You should take prompt action to correct these and any other manufacturing or quality systems deviations identified by your internal audits. Failure to promptly correct these deviations may be identified in a follow-up inspection, and may result in the detention of your device(s) without physical examination upon entry into the United States.

Page 6 - Mr. Alan Schwebel, President  
Mennen Medical, LTD., Rehovot, Israel

Please notify this office, in writing, within 15 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. Please include any and all documentation to show that adequate correction has been achieved. In the case of future corrections, an estimated date of completion, and documentation showing plans for correction, should be included with your response to this letter. If the documentation is not in English, please provide a translation to facilitate our review. Please address your response to:

Donald W. Serra  
Chief, Cardiovascular and Neurological Devices Branch, HFZ-341  
Food and Drug Administration  
Center for Devices and Radiological Health  
Office of Compliance  
Division of Enforcement III  
2098 Gaither Road  
Rockville, Maryland 20850  
USA

If you have any questions, please contact Kent A. Berthold at the above address, by telephone at (301) 594-4648, or by FAX at (301) 594-4672.

Sincerely yours,



Lillian J. Gill  
Director  
Office of Compliance  
Center for Devices and  
Radiological Health