



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Atlanta District Office

60 8th Street, N.E.
Atlanta, Georgia 30309

MAYSEN

HF 135

August 2, 1999

VIA FEDERAL EXPRESS
RETURN RECEIPT REQUESTED

Danny J. Cress
President/General Manager
E.M.T.-Rx
9400 Ransdell Road
Suite 10
Raleigh, North Carolina 27603

WARNING LETTER
(99-ATL-23)

Dear Mr. Cress:

An inspection of your firm was conducted on May 24-26, 1999, by Investigator E. Harold Blackwood. Our investigator found that you are manufacturing prefilled syringes for intravenous catheter flushes. These syringes contain 0.9% sodium chloride solution or heparin mixed in a saline solution. These products are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

Our investigator documented several significant deviations from the Quality System Regulation as set forth in Title 21 Code of Federal Regulations (21 CFR), Part 820. These deviations cause the devices you manufacture and distribute to be adulterated within the meaning of Section 501(h) of the Act.

You have failed to properly validate the manufacturing processes currently utilized for the syringe products. You could not provide documented evidence which established a high degree of assurance that the manufacturing processes were effective and could consistently produce a product meeting its predetermined specifications and quality attributes. No written procedures had been established for conducting a validation of the aseptic fill process. The validation documents available included no explanation of what the acceptance criteria would consist of. The available validation was limited to testing [REDACTED] samples as representative of lots, which can range up to [REDACTED] syringes.

You have failed to establish and maintain procedures for finished device acceptance to ensure that each device meets acceptance criteria. Lot #990202A, Heparin Sodium in 0.9% Sodium Chloride, was released with labeling declaring 100 heparin sodium units per milliliter. The

batch records for this lot indicate that the heparin concentration was only ten heparin sodium units per milliliter. There was no documentation available that pyrogen testing was performed on lots #990108A and #990108B, Heparin Sodium in 0.9% Sodium Chloride, prior to their release. There is no requirement for a pH check of the sample prior to running the pyrogen test, as suggested by the pyrogen test kit manufacturer. In fact, you did not initiate pyrogen testing on your products until October 1998. This was approximately six months after you began distributing your products.

There was no documentation available for lot #990222A to indicate the concentration of Heparin Sodium utilized in the product. There is no testing performed on any of the heparin concentrations prepared by mixing heparin with saline solution. No documentation was available to indicate the accuracy or reliability of the heparin mixing conducted at your facility.

The procedure in place for the Control of Nonconforming Material or Process was inadequate to deal with failing finished product testing. A finished product pyrogen test in November 1998 for lot #981109B was noted to give a positive result. The procedure was rewritten to allow for retesting of the lot. This lot was retested and released for distribution. No investigation was performed into the initial positive result nor were any documented attempts made to invalidate the initial positive result. The current Inspection and Test Procedure does not describe how to handle unacceptable test results or how to appropriately respond to an out of specification result.

You could provide no documentation to substantiate the twelve-month expiration date currently placed on your devices. The expiration date was extended from six months to twelve months in January 1999 without appropriate justification. No test results were available to support the expiration dates currently placed on your products.

You have failed to establish and maintain device master records for your device products. All procedures in use during our inspection were in draft form. None of these procedures had any indication that they had been reviewed and approved for use by a responsible individual at the firm. A few procedures had the name of an individual who had prepared the procedure although most lacked any names or dates of review and preparation. These procedures included all aspects of compliance with the QSR to include your quality policy, design control, process control, inspection and testing, quality audits, and quality records. No written procedures were available that addressed the handling and evaluation of complaints, to include reporting requirements under Section 21 CFR Part 804.

You have also failed to establish procedures for identifying training needs and to ensure that all personnel are trained to adequately perform their assigned responsibilities. The draft Quality Policy made reference to establishing training procedures but no such procedures were provided to our investigator. No documentation was available as to what training any of your employees had received, as required.

Since January 1991, an Intercenter Agreement (ICA) (copy enclosed), published in the Federal Register (F.R. #58760, November 21, 1991) has been in existence between FDA's Center for Devices and Radiological Health (CDRH) and the Center for Drug Evaluation and Research (CDER). This agreement provides industry with a guide to the regulatory requirements regarding certain generic categories of drug and device products. The regulatory requirements pertaining to products subject to the ICA are typically determined by the indications for use found on the product labeling. In particular, according to this agreement, products intended to be used to flush intravenous catheters are regulated as devices. Under section VII.C. of the agreement: Liquids, gases, or solids intended for use as devices, (e.g., implants or components, parts or accessories to devices) are to be regulated as devices.

As a device manufacturer, you are required to register your firm with the FDA's Center for Devices and Radiological Health, and provide a listing of the devices you manufacture to the Agency. The regulations for these requirements are found in 21 CFR Part 807. A copy of these regulations is enclosed for your convenience. If you fail to register your firm and list your devices, the devices may be misbranded within the meaning of section 502(o) of the Act. The Division of Small Manufacturers Assistance (DSMA) of CDRH is available to provide manufacturers with information, forms, 510(k) packages, and many other resources needed by device manufacturers. You may call or fax DSMA at (301) 443-6597 and (301) 443-8818, respectively, to request information.

In addition, a device manufacturer is required to submit a premarket notification under section 510(k) of the Act and to notify the FDA at least 90 days prior to the introduction of a device into commercial distribution in the United States. An order issued by the FDA allowing a manufacturer to begin distributing devices must be received by the manufacturer before commencing distribution. Information necessary to comply with the premarket notification [510(k)] requirement may be found in 21 CFR Part 807, Subpart E - Premarket Notification Procedures (copy enclosed). Please be advised that promotion and distribution of these devices without the submission of a 510(k) and the receipt of the order may result in the device being misbranded under section 502(o) of the Act and adulterated under section 501 of the Act.

Devices intended for use only as intravenous catheter flushes must have adequate labeling for this intended use. For example, the indications for use for devices, which contain such ingredients as sodium chloride and heparin sodium, must be specific. Devices labeled solely as "flushes" without identifying the specific intention for use, i.e., for flushing intravenous catheters, are not labeled adequately and are misbranded. An example of adequate device labeling for products intended to be used to flush catheters would include the statement, "...heparin sodium lock flush syringe for IV flush only..." These devices are subject also to the labeling requirements necessary for prescription devices which are found in 21 CFR Part 801 (enclosed).

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. At the close of the inspection, the Inspection Observations (FDA 483) was issued to and discussed with you. The specific violations noted in this letter and in the FDA 483 are symptomatic of serious underlying problems in your firm's 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.

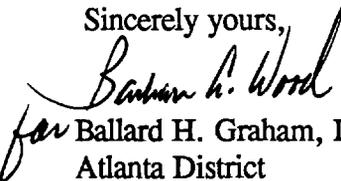
Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Also, no request for Certificates for Products for Export will be approved until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory actions being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please notify this office in writing within fifteen (15) 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 15 working days, state the reason for the delay and the time within which the corrections will be completed.

We are in receipt of your June 7, 1999, response to the FDA 483. Although extensive corrective actions were promised, the response lacked any specificity as to how the problems were going to be addressed. Many of the corrections were to be addressed within the month, so it is difficult to assess the adequacy of those actions until completed. These corrections would need to be verified during our next inspection however. We are also in receipt of your June 29 response, which stated that your company was suspending production so you could evaluate this product line. Your response should be sent to Philip S. Campbell, Compliance Officer, at the address noted in the letterhead. We also request that you notify this office if a decision is made in the future to resume production of this product line.

Sincerely yours,


for Ballard H. Graham, Director
Atlanta District

Enclosures