

HFD-36



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Central Region d1867b

Food and Drug Administration
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone (973) 526-6006

June 9, 1998

WARNING LETTER

Mr. Burgise F. Palkhiwala
President
AccuMed Inc.
2572 Brunswick Pike
Lawrenceville, NJ 08648

FILE NO: 98-NWJ-25

Dear Mr. Palkhiwala:

An inspection of your drug manufacturing facility located in Lawrenceville, NJ, was conducted by the Food and Drug Administration on April 23, 24, 27, 28 and May 4, 7, 1998. This inspection found significant deviations from Current Good Manufacturing Practice regulations for Finished Pharmaceuticals, (Title 21, Code of Federal Regulations, Part 211). These deviations cause finished pharmaceuticals to be adulterated within the meaning of Section 501 (a) (2) (B) of the Federal Food, Drug and Cosmetic Act (the Act).

- 1). There was no process validation protocol or process validation data for the following products: Accumide, Gas Relief Infant Drops, Accuseptic Menthol Spray, Accumed Medicated Pads, Accufrin Nasal Spray, Accufrin Nasal Spray Pump, Accuspray Saline Mist, Accucal Ultra Assorted Calcium Antacid, Accucal Calcium Antacid Peppermint, Accucal Assorted, Gas Relief, Accuson Tablets 90s, Accucon Tablets 250s, and Accusen Plus.
- 2). The process validation conducted for Accuotic Ear Drops was not adequate in that there was no validation protocol with predetermined specifications, there was inadequate sampling and testing of in-process and finished product, and your firm was unable to supply the data for the validation report.
- 3). There are no established hold times for bulk liquid products between manufacturing and filling.
- 4). There was no qualification of manufacturing and packaging equipment including blenders (excluding the Double Cone Blender), mixers, tablet presses, liquid filling lines (excluding Filling Line #3), tablet filling lines, and packaging lines.
- 5). The qualification protocols for Filling Line #3 and the Double Cone Blender were not adequate due to a lack of complete in-process and finished product sampling. The finished reports also lacked any supporting data.

- 6). Failure of production batch records to provide consistent, complete, and controlled manufacturing of finished products. For example:
- a. There were inconsistent overages of Carbamide Peroxide, USP used in the formula of Accuotic Ear Drops. Batches AM801013 and AM710006 were given a [REDACTED] overage while batches AM802011, AM802015, and AM802014 were given a [REDACTED] overage.
 - b. Lot numbers # AM802015, AM802014, and AM802011 do not include documentation that the proper mixing time of [REDACTED] was followed.
 - c. There was a repeated use of white-out to correct errors made on batch production records, test data, and results.
- 7). Failure to have a cleaning validation protocol and cleaning validation data for the following products: Accumide, Gas Relief Infant Drops, Accuseptic Menthol Spray, Accumed Medicated Pads, Accufrin Nasal Spray, Accufrin Nasal Spray Pump, Accuspray Saline Mist, Accucal Ultra Assorted Calcium Antacid, Accucal Calcium Antacid Peppermint, Accucal Assorted, Gas Relief, Accuson Tablets 90s, Accucon Tablets 250s, and Accusen Plus. Your cleaning validation should provide assurance that your equipment is appropriately cleaned between batches of similar and different products.
- 8). The stability program does not provide consistent, controlled conditions for storage of samples and generation of reliable test results at each stability station. For example:
- a. The stability chambers [REDACTED] have not been qualified to show consistent, uniform temperature and humidity conditions throughout the chamber over an extended period of time.
 - b. Humidity levels are not monitored in the Room Temperature chamber and temperatures during the weeks beginning December 24, 1998, February 4, 11, and 18, 1998, were not consistently maintained at the USP 23 specification of 25 degrees +/- 2 degrees. These temperatures were also not within your Standard Operating Procedure (SOP) level of [REDACTED].
 - c. Your SOP titled "Stability Program and Expiration Dating" lists a specification of [REDACTED]. Unless you can show that your current methods are equal or better to the current USP 23, you need to follow the current USP 23 specifications for temperature and humidity during long-term stability testing. The current USP 23 specifications are 25 +/-2 degrees and 60 +/- 5% RH.

- d. Temperature charts were not maintained for the weeks of August 19, 1997 and October 29, 1997.
- 9). Your Waters HPLC hardware and software system used for assay testing of products in the laboratory has not been qualified or validated. There are also no written procedures for the security of data files, password control, access levels, and functions, or preventative maintenance.
 - 10). Failure to conduct an investigation into why 18 bottles of Gas Relief Infant Drops Lot #8001 were rejected without any explanation on your batch record.
 - 11). A contract laboratory performed a check analysis on Accusen Plus tablets, Lot #8006. They obtained a reading of 85.2 to 88.3%. Your result from this same batch was 100.3%. Your firm did not conduct an adequate investigation to determine why these two results were different. You closed this matter by accepting a subsequent telephone report of 93% by the contract laboratory.
 - 12). The warehouse system does not provide adequate identification of materials regarding their status (i.e. Approved, Rejected, On Hold) and their identification. For example:
 - a. Select Brand Antacid Peppermint Tablets, 75's, Lot #7026, manufactured on March 1997, was placed "On Hold", but was not physically labeled as such, nor did the computerized inventory system indicate this status.
 - b. Accucal Calcium Antacid Peppermint Tablets, 150's, Lot #7075 was marked "Rejected" as stored in the warehouse, but this status was not indicated in the computerized inventory system used to delegate material to filling and packaging departments.
 - c. Two bulk 55 gallon drums located in the warehouse contained an unidentified material and were labeled as "To be Returned." The drums were not labeled with contents or manufacturer information.
 - 13). Failure to maintain required records and logbooks. For example:
 - a. There were no equipment and use logs documenting the batches manufactured in specific equipment, the cleaning of the equipment, or the maintenance of the equipment.
 - b. Your laboratory did not maintain a record of samples that they received and tested listing the batch number, date received, and status of the sample.

The above is not intended to be an all-inclusive list of violations. As a manufacturer of finished pharmaceuticals, you are responsible for assuring that your overall operation and the products you manufacture and distribute are in compliance with the law.

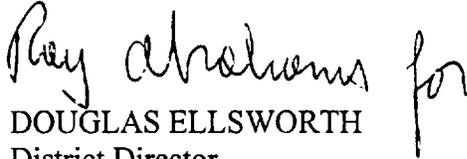
Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so that they may take this information into account when considering the award of contracts.

You should take prompt action to correct these violations and to establish procedures to prevent their recurrence. Failure to promptly correct these violations may result in regulatory action without further notice, such as seizure and/or injunction.

We acknowledge receipt of your response dated June 3, 1998. This response is currently under review. We will provide comments to you when this review is complete.

Any questions that you have concerning this Warning Letter should be directed to Diane Boucher, Compliance Officer, Food and Drug Administration, New Jersey District Office, 10 Waterview Blvd., Parsippany, NJ 07054. Diane Boucher's phone number is (973) 526-6006.

Very truly yours,

Handwritten signature of Doug Ellsworth in cursive, followed by the word "for" in a smaller, less legible cursive script.

DOUGLAS ELLSWORTH
District Director
New Jersey District

CERTIFIED MAIL-
RETURN RECEIPT REQUESTED

DEB:np