



August 27, 1998

WARNING LETTER
CHI-34-98

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

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Glen E. Tullman, President
Allscripts, Inc.
2401 Commercial Drive
Libertyville, IL 60048-4464

Dear Mr. Tullman:

During an inspection of your facility from June 24 to July 9, 1998, Investigators Nicholas Lyons and Ruth Smith documented deviations from the Current Good Manufacturing Practice Regulations (Title 21, Code of Federal Regulations, Parts 210 & 211). These deviations cause your drug products to be adulterated within the meaning of Section 501 (a)(2)(B) of the Federal Food, Drug, and Cosmetic Act. The deviations reported included:

Failure to conduct process validation studies for the repackaging of liquid, suspension or syrup drug products.

Failure to have the approval by the Quality Control branch of the written procedures currently used by your firm covering the repackaging of liquids, suspensions and syrup products.

Failure to have an ongoing testing program to verify product stability after the shelf life has been determined to be appropriate. Some stability studies that have been conducted have not included microbiological or preservative effectiveness testing.

Failure to conduct stability studies, which support the six-month expiration date, assigned to repackaged unit-of-use containers for Hydrocodone/Homatropine MBR Syrup and Ferrous Sulfate Elixir.

Failure to handle and store components and drug product containers in a manner to prevent contamination. For example, the investigators reported that your firm receives penicillin and cephalosporin drug products in a common shipping and receiving area also used to receive non-penicillin and non-cephalosporin drug products. The investigators reported that during the inspection they observed the receipt by your firm of containers of

cephalosporin containing drug products in the common dock area. They observed an employee working in the receiving area handling damaged containers of cephalosporin drug products and that the spillage from the containers was accumulating on the employee's hands. The same employee handled containers of non-cephalosporin and non-penicillin drug products also. The investigators also reported that your firm does not have written procedures that address the receipt and handling of penicillin and cephalosporin drug products.

Failure to maintain a record covering the maintenance, cleaning, sanitizing, and inspection of equipment used in the repackaging of drug products.

Failure to validate equipment cleaning procedures.

Failure of employees to follow written procedures covering the cleaning and maintenance of equipment. For example, the investigators reported observing an employee cleaning equipment used for repackaging of Biaxin 500 mg. with compressed air rather than with alcohol directed by the written SOP.

Failure of batch production and control records to include complete information relating to the production and control of each batch. For example, the batch records for two products, Procardia XL 30 mg. and Tessalon 100 mg., did not include a copy of complete labeling and a statement of actual yield and percentage of theoretical yield at appropriate phases of processing.

Failure to follow written procedures in the investigation and reporting of product complaints.

Failure to investigate stray peaks found on HPLC chromatograms of Albuterol Sulfate stability assays. The firm could not identify the stray peak. There is no assurance the impurity is not introduced by the repeaking process.

This letter, as well as the Form FDA 483, is not intended to be an all-inclusive list of deficiencies at your facility. Rather, they represent unacceptable practices documented during our most recent inspection of your facility. It is your responsibility to insure that all requirements of the Act, and regulations promulgated thereunder, are being met.

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

We acknowledge receipt of Mr. Dave Mullen's written response, dated July 16, 1998, to the Form FDA 483 that was issued and discussed with Mr. Mullen by Investigators Lyons and Smith. His response to the Form FDA 483 indicated that several promised corrective actions would be completed by specified dates. Mr. Mullen indicated that, in some cases, the corrective action to be taken involved the preparation of new or the revision of current written procedures.

The response indicated that Allscripts is evaluating whether the firm will continue to repackage liquid products, have a private contractor do the repackaging or just discontinue providing liquids to your customers. The response stated that Allscripts will make that decision by August 31, 1998, and would advise us of your plans in this area. One of the options Mr. Mullen indicated Allscripts is evaluating is option 1 in which you indicate Allscripts will continue to repackage liquids, in which case Allscripts will address all the Form FDA items (items 6-14, 17, 19 and 34). Based on these comments, it is our understanding that Allscripts continues to repackage liquid drug products under the conditions and controls reported by Investigators Lyons and Smith. We cannot condone or agree to the continued distribution of these types of drug products.

We consider the response to the Form FDA 483, in most instances, to be adequate in terms of actions you plan to take and the time frames you cited. However, we have additional comments/questions:

The response to item #9 of the Form FDA 483 indicated that Teva Pharmaceutical, the manufacturer of Albuterol Sulfate, provided an explanation of the chromatogram peaks for the 3-month, 9 month and 12 month samples. The letter, dated July 14, 1998, from Teva indicated that Albuterol Sulfate, lot number 2203, was used in the stability study. The stability study was performed by Missouri Analytical Laboratories, Inc. The records covering this stability study indicated that the Albuterol Sulfate lot number involved in the study, lot number 3085078, was assigned by Missouri Analytical Laboratories, Inc. sample number 8807. Is lot #2203 (Teva's #) and lot #8807 (Missouri Analytical's #) the same lot of Albuterol Sulfate? In the letter, Teva indicates that this peak appears to be atypically large as compared to other samples analyzed. Is the comparison Teva made to the 3-month room temperature study (Allscripts' test) or in comparison to Teva Pharmaceutical's own stability profile? In addition, Allscripts assigns a twenty-four month shelf life for this product. Investigators Lyons and Smith only observed room temperature stability data covering a twelve-month shelf life. Does Allscripts have data which supports the twenty-four month assigned expiration date?

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Your response to item #35 of the Form FDA 483 indicates that Allscripts current process “involves the use of stringent controls in returning a partial bottle back to bulk stock to be utilized in the next repackaging of the product.” As you know, there are some drug products that are sensitive to moisture, light or oxygen and therefore may be affected by that exposure. These factors may affect a product’s shelf life. We question whether “stringent controls” can be utilized in this area unless you have information which enables you to evaluate the effect conditions such as light, humidity, temperature exposure, and the frequency and length of time the containers can be re-opened.

The corrections you indicated in your response to the Form FDA 483 will be evaluated during future inspections of your firm.

In your response, you indicated that you would like to obtain a copy of the Cleaning Validation Guideline published by the Center for Drug Evaluation and Research (CDER). All guidelines pertaining to the pharmaceutical industry that have been written by CDER can be purchased from the National Technical Information Service (N.T.I.S.) located in Springfield, Virginia 22161. The telephone number is (703) 605 6000. The publication number for the Cleaning Validation Guideline document is PB 96-127246. You can also find additional information in this area via the FDA Website (<http://www.fda.gov/>) on the CDER home page.

Please notify this office in writing within 15 working days of receipt of this letter regarding the specific steps, in addition to those contained in your response letter of July 16, 1998, you have taken to correct the violations. Please submit your response to the Warning Letter to the attention of George F. Bailey, Compliance Officer.

I received a letter from Clifford E. Berman, Senior Vice President, Regulatory & Legislative Affairs, in which he listed the dates Allscripts is available to meet with the FDA. You should also contact Mr. Bailey to schedule the meeting.

Sincerely,

Raymond V. Mlecko
District Director