



DEPARTMENT OF HEALTH & HUMAN SERVICES

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New York District

Food & Drug Administration
850 Third Avenue
Brooklyn, NY 11232

WARNING LETTER

**CERTIFIED MAIL
RETURN RECEIPT REQUESTED**

July 23, 1999

David Seltzer, President
Hi-Tech Pharmacal Co., Inc.
369 Bayview Avenue
Amityville, New York 11701

re: NYK-1999-55

Dear Mr. Seltzer:

During inspections of your facility at 369 Bayview Avenue, Amityville, New York conducted January 5 to March 19, 1999 and May 25, 1999 to June 15, 1999 our investigators observed significant deviations from the Current Good Manufacturing Practice Regulations for the manufacturing, processing, packing, or holding of drugs (Title 21, Code of Federal Regulations, Parts 210 and 211). In addition, we acknowledge your letters of March 31, 1999 and June 24, 1999 responding to the investigators' observations (FDA 483) for the inspections conducted January 5 to March 19, 1999 and May 25 to June 15, 1999. The following violations were observed:

1. Failure to maintain a complete record of all data secured in the course of each drug test. With regard to the reprocessing of chromatograms (items #1, 10a, and 10b of the FDA 483 issued March 19, 1999), we agree with your response of March 31, 1999 that your new SOP QC-058 corrects and explains the violation observed. We point out the neomycin testing was questioned in the FDA 483 issued July 21, 1998 item number 1. We found that data obtained from assays conducted in May 1997 were replaced by data from assays conducted months later and not all of your records adequately recorded the correct assay dates. Again in the FDA 483 issued March 19, 1999 items 14, 26, and 29, it was observed that the test dates listed in stability summary reports do not represent the actual dates of the analyses performed.

Your responses state that the deficiencies will be corrected, however, your commitments are unclear. In addition, these items are of particular concern because they could represent a pattern. We believe that all test dates in stability summary tables, submitted to FDA or kept as your own records, should be accurate, for current as well as past analyses, for approved applications representing marketed drugs as well as pending applications. It is not clear in your March 31, 1999 item 14 response (re: Timolol Maleate Ophthalmic Solution ANDA 75-163) when past submissions containing inaccurate test dates will be corrected by submissions to the application. It is not clear in your March 31, 1999 response to item 26 and 29 (re: Neomycin Sulfate Oral Solution and Polymyxin/Neomycin/Hydrocortisone Otic Solution, AADAs 65-010 and 65-014) if the revised sheets enclosed with the FDA483 response have also been submitted to the applications.

2. Failure to have specifications of a drug product that were scientifically and appropriately established. The stability degradant limit compared to the initial degradant limit for Prednisolone Sodium Phosphate oral solution (addressed in the FDA 483 issued March 19, 1999 item 21) was indicated in your March 31, 1999 response to have been changed. It is not appropriate to change the specification by advising the district in your response and then fail to update the application. If the dates of the assays are misreported (as discussed above items 14, 26, and 29 of the FDA 483 issued March 19, 1999 and item number 1 of the FDA 483 issued July 21, 1998) there does not appear to be a capability to scientifically and appropriately establish a stability specification.

3. Failure to have test procedures that were established using scientifically sound and appropriate procedures. The methods producing the chromatograms in question for the first part of item number 1 above should be scientifically developed and validated such that reprocessing is not generally necessary. The criteria that justify reprocessing (for example, an inadequate baseline or a peak with an inadequate area) should likewise be appropriately established for each method and in writing. The test procedures once established should be secure from unauthorized change. Your response of March 31, 1999 regarding protection of the chromatograph system settings with a password (FDA 483 issued March 19, 1999 item 10b) indicates that your system has the facility to protect access with a password. The response, however, fails to commit you to use the protection or to indicate which of your personnel will have access and how the protection will be used.

4. Failure to have manufacturing procedures that were established using scientifically sound and appropriate methods. Our investigator in the FDA 483 issued June 15, 1999 found that Calcionate Syrup lots were marketed with an inadequate sorbitol proportion such that precipitation occurred. Your response of June 24, 1999 reports that the validation has been conducted and the reformulated product is now being marketed. However we wish to point out the procedures and formulations, and their validations, are required to be established and completed prior to marketing.

5. Failure to follow established procedures. The procedures for the control and issuance of labeling materials (FDA 483 issued March 19, 1999 item #4) were not being followed, and new procedures were devised during the inspection and revised for your March 31, 1999 response.

6. Failure to conduct and complete cleaning validations. The investigator observed you had not conducted testing for detergent residues, reported in the FDA 483 issued July 21, 1998 (item number 3). The observation was repeated in the FDA 483 issued March 19, 1999 (item number 6). Moreover, the investigators observed that testing for the validation of the cleaning procedures was inadequate in that only 4 products were validated and swab samples for chemical validation were done for only one product.

We comment on the following items for information and ask for your response. With regard to the March 19, 1999 FDA 483 observation item 2a through 2d, your response does not address our investigators' observation that only two bottles of the stability samples of Hydroxyzine HCl lot 801-796 appeared to have been removed from the storage cartons. This observation compared to the stability study test results showing that the testing for three separate stability stations, months apart, had been completed for the lot needs to be explained.

We also bring to your attention the problems involving crossouts, transcription and other errors, and/or missing records, as pointed out in the March 19, 1999 FDA 483 items, 15, 16, 20, 22, 27, 18, and 19. Although your March 31, 1999 response adequately answers the individual instances involved, our concern is the discrepancies could represent a pattern. Our files show these kinds of discrepancies, as well as the discrepancies discussed in the above item number 1, are found by our investigators in past inspections. Please provide a more global response to these discrepancies, such as by providing employees basic training in areas such as record keeping and ethics.

The remaining responses appear to have adequately answered our concerns, again because they adequately address the individual instances involved. In general, however, we cannot conclude as to the adequacy of your responses without your further response, verification of corrections by further inspection, and without coordination with FDA reviewers of affected applications. We will specifically refer concerns involving actual test dates and the establishment of stability degradant specifications to the reviewers of your applications, as the scientific significance of the discrepancies and concerns can only be judged on a case by case basis by the reviewers.

The above-identified deviations are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure that your facility is in compliance with all requirements of the federal regulations. You should take prompt action to correct these and all violations at your firm. Failure to achieve prompt corrective action may result in further regulatory action without further notice. These actions include seizure and/or injunction.

Please notify this office in writing, within 15 days, of the specific steps you have taken to correct the noted violations and to prevent a recurrence of similar violations. 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.

Your response should be sent to the Food and Drug Administration, 850 Third Avenue, Brooklyn NY 11232, Attention: William Friedrich, Compliance Officer. Mr. Friedrich can be telephoned at 718/340-7000 ext. 5532.

Sincerely,



Brenda J. Holman
District Director