



U.S. FOOD AND DRUG ADMINISTRATION

NEW YORK DISTRICT
850 THIRD AVENUE, BROOKLYN, NEW YORK 11232

405

Telephone: [718] 340-7000 [Ext 5301]

WARNING LETTER

CERTIFIED MAIL **RETURN RECEIPT REQUESTED**

Ralf Lange
President and CEO
Luitpold Pharmaceuticals, Inc.
One Luitpold Drive
Shirley, NY 11967

September 5, 1997

Ref: 73-NYK-97

Dear Mr. Lange:

During an inspection of your drug manufacturing facility conducted on August 5 through 15, 1997, our investigators documented deviations from Current Good Manufacturing Practice for Finished Pharmaceuticals Regulations (Title 21, Code of Federal Regulations, Parts 210 and 211). These deviations cause drug products manufactured by your firm to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act).

The deviations include your firm's failure to validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process materials and finished drug products. For example:

- There was no documentation of performing validation of the manufacturing processes for the following marketed drug products: Aminocaproic Acid Injection USP, Bretylium Tosylate Injection, Dopamine HCl Injection USP, Hydroxyzine HCl Injection USP, Mannitol Injection USP, Methyldopate HCl Injection USP, and Potassium Chloride for Injection Concentrate USP.
- Your firm is using a retrospective approach to validating some of its older marketed drug products. However, there was no written standard operating procedure established and followed for performing such retrospective validation.
- The retrospective validation reports for Potassium Chloride Injection USP, Dexamethasone Sodium Phosphate Injection USP, and Furosemide Injection USP do not state whether the batches included in the retrospective analysis were manufactured with the same formulations, same manufacturing processes, and same in-process specifications. Further, the reports for Potassium Chloride Injection USP and Dexamethasone Sodium Phosphate Injection USP do not state whether any manufacturing deviations occurred or if any batches were rejected. It was explained to the investigator that your firm uses a limited random sampling approach to reviewing batch records for retrospective validation. This approach does not address any

deviations that may have occurred in other batches (not included in the random record review sample) that were included in the retrospective time frame.

- The retrospective validation report for Furosemide Injection USP contained information on manufacturing deviations and rejects for batches that were included in the retrospective analysis. However, the report failed to mention whether these manufacturing deviations and rejects were taken into consideration during the retrospective analysis.

- According to the retrospective validation report, critical process parameters were assessed during evaluation of all the annual product review data for finished product manufactured since 1991. The annual product review document that was in the validation report does not contain any information that could lead to the evaluation of critical parameters.

Neither the above identification of violations nor the inspectional observations (Form FDA 483) presented to Richard P. Lawrence, Acting Director of Quality Control/Quality Assurance at the conclusion of the inspection is intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with each requirement of the Act and its implementing regulations. Federal agencies are advised of the issuance of all warning letters about drug products so that they may take this information into account when considering the award of contracts. Additionally, pending Antibiotic Form 6, NDA, ANDA, or export approval requests may not be approved until the above violations are corrected.

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

You should notify this office in writing, within 15 working days after receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step taken to prevent the 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 reply should be sent to the attention of Bruce A. Goldwitz, Compliance Officer, Food and Drug Administration, 850 Third Avenue, Brooklyn, NY 11232.

Sincerely,



Brenda J. Holman
District Director

Attachment: Form FDA 483 dated August 15, 1997