



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

g1757d

19900 MacArthur Blvd., Ste 300
Irvine, California 92612-2445
Telephone (949) 798-7600

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

September 19, 2001

W/L 76-01

Tony DeVos
President
Cardinal Laboratories
710 Ayon Avenue
Azusa, CA 91702

Dear Mr. DeVos

Your firm manufactures a variety of veterinary and human products, including products which are classified as veterinary and human drugs. During an inspection of your manufacturing facility located in Azusa, California, conducted between April 19 and June 11, 2001, our investigators found significant deviations from the Current Good Manufacturing Practice (cGMP) regulations for finished pharmaceuticals (Title 21, Code of Federal Regulations, Part 211). Such deviations cause human and veterinary drugs manufactured at this facility to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (henceforth the "Act").

Section 501 (a)(2)(B) of the Act states that a drug shall be deemed adulterated if the methods used in, or the facilities or controls used for its manufacture, processing, packing, or holding do not conform to or are not administered in conformity with cGMP, to assure that such drug meets the quality and purity characteristics which it purports or is represented to possess.

Our inspection found the following deficiencies:

A. Your firm is not testing each shipment of drug ingredients. For example, you are not performing identity testing of each lot of component [21 CFR 211.84(d)(1)]; and you are not establishing and verifying the reliability of certificates of analyses for purity, strength and quality of each component in lieu of testing each component. [21 CFR 211.84(d)(2)]

B. Your firm is not testing each batch of finished drug product for conformance with final specifications prior to release. For example, your firm did not complete finished product testing for the veterinary drug product Medisel shampoo, lot #0K06D and for the human drug product [REDACTED] UV Protective Lotion SPF-30, lot #1B28D. [21 CFR 211.165(a)]

C. Requirements for stability testing of drug products are not being met. For example, you do not have, as part of the storage condition, any documentation that stability samples are maintained at the designated temperature [21 CFR 211.166(a)(2)]; and you do not have appropriate stability data to support the 4 year expiration date for the veterinary drug product Hydrocortisone Shampoo. [21 CFR 211.166(b)]

D. Your firm follows the unwritten practice of incorporating remnants of finished lots as components of in-process lots with no assessment as to the impact on the identity, quality, strength and purity. For example, a remnant of the veterinary drug product Hydrocortisone lotion 0.5%, lot #0F06D was added as a component to lot #0I20A of the same product. This represents a deviation without justification from the written production and process controls. [21 CFR 211.100]

E. Written procedures for production and process control are deficient in that your firm lacks validation of your DI water system. [21 CFR 211.100]

F. Each lot of components is not withheld from use until the lot has been sampled, tested, or examined, as appropriate, and released for use by the quality control unit in that your firm does not conduct routine testing of the water produced from your backup system which you use regularly in the production of drug products. [21 CFR 211.84]

G. Your firm's equipment cleaning and maintenance procedures do not assure the absence of contamination in human and veterinary drug products. Your firm lacks documentation and corrective actions in response to TNTC (too numerous to count) microbial test results obtained from at least 10 samples collected from filling equipment

during calendar 2001. In addition, you have no documentation that assures that your drug products are free of drug, detergent or other residues. [21 CFR 211.67(a)]

H. Laboratory controls, including the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality and purity are required. Your firm has not performed blend uniformity studies for the veterinary drug products hydrocortisone lotion, hydrocortisone shampoo, hydrocortisone cream, medicated shampoo, Medisel shampoo, and wormicide, as well as the human drug products antibacterial soap and sunscreen SPF 30 to assure compliance. Additionally, your firm has not performed preservative effectiveness testing for the veterinary drug products hydrocortisone lotion, hydrocortisone cream hydrocortisone shampoo or wormicide. [21 CFR 211.160]

I. Your firm has failed to maintain complete batch production and control records. For example, your batch records are not complete in that batch records do not always reflect a different employee verifying the performance of a production step (hydrocortisone lotion, lot #0I20A); white-out and pencil are used in/on batch records; temperature is not being recorded for production steps with temperature requirements (hydrocortisone lotion, lot #0F06D); and viscosity test results are not included as part of the batch record. [21 CFR 211.188]

J. Your firm is not destroying obsolete and outdated labels as required. For example, our investigator reported "dead product" labels along with labels for products which had been subject to changes in formulation or label claims were maintained in the area used for storage of current product labels. [21 CFR 211.122(e)]

The above is not intended to be an all-inclusive list of violations. As a manufacturer of human and veterinary drugs, you are responsible for assuring that your overall operations and the products you manufacture and distribute are in compliance with the law. Several of the violations noted during this inspection are similar to those previously brought to your attention. You should take prompt action to correct these violations and to establish procedures to prevent their recurrence. Failure to promptly correct these violation may result in regulatory action without further notice, such as seizure and/or injunction. Other Federal Agencies are informed about the Warning Letters issued so they may consider this information when awarding government contracts for drug products.

You should notify this office in writing within fifteen (15) working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an

Letter to Mr. DeVos

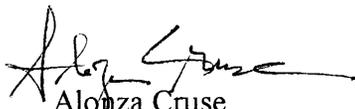
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explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the time within which the corrections will be completed. Also include copies of any available documentation demonstrating that corrections have been made. If you have any questions or need clarification regarding this letter prior to your written response, you may contact Barbara Rincon, Compliance Officer at telephone number (949) 798-7739.

Your reply should be directed to:

Thomas L. Sawyer
Director, Compliance Branch
U.S. Food & Drug Administration
19900 MacArthur Blvd., Ste. 300
Irvine, CA 92612

Sincerely,


Aloyza Cruse
District Director