



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Atlanta District Office

60 8th Street, N.E.
Atlanta, Georgia 30309

August 2, 1999

VIA FEDERAL EXPRESS
RETURN RECEIPT REQUESTED

Kevin D. Lynch
Owner
Ag-Mark, Inc.
d/b/a Animal Health Sales, Inc.
US Route 113 & Clndnl A
Selbyville, Delaware 19975

WARNING LETTER
(99-ATL-24)

Dear Mr. Lynch:

An inspection of your facility, Ag-Mark, Inc., located in Teachey, North Carolina, was conducted on April 12-15, 1999. Investigator Amy H. Ruble found that you manufacture veterinary drug products and repack human drug products under the "PINEE" label. The three veterinary products are "PINE-I'DINE LIVESTOCK PREPARATION", "CANINE PREPARATION", and "LIVESTOCK PREPARATION". The human product is labeled as "AN UNMIXED OIL OF THE LONG LEAF PINE".

As labeled, promoted, and formulated these products are intended for use as topical healing and antiseptic agents establishing the products as drugs as defined Section 201(g) of the Federal Food, Drug, and Cosmetic Act (the Act). The Act defines a drug as any article intended for use in the diagnosis, mitigation, cure, treatment, or prevention of disease in man or animals. Unless an animal drug is generally recognized as safe and effective by scientific experts, for its labeled intended use, it is regarded as a "new animal drug" under the law (Section 201 (w)(1)). A new animal drug may not be legally marketed unless it is the subject of an approved New Animal Drug Application (NADA). NADAs may be approved by the FDA only on the basis of adequate scientific data that the applicant submits as evidence of the safety and effectiveness of the product under the labeled conditions for use.

The status of these products was brought to the attention of your firm in a letter to Thomas M. Morris, General Manager, dated January 31, 1997. This letter was issued from the FDA Center for Veterinary Medicine, Division of Compliance, in response to your firm's request to review and comment on labeling for these products. This letter (copy enclosed) not only addressed the new drug issue but also discussed safety and labeling concerns. You were

requested to submit target safety information supporting the use of high concentrations of pine oil on damaged or wounded skin of large and small animals as indicated by your labeling. Any historical or scientific data to support the use claims of antiseptic and healing agents, was requested also. You were requested to submit this information if you wished to pursue marketing of these products. It is not clear why your company ignored this letter since it was noted to be on file during the course of the current inspection. These Pinee® products are considered to be adulterated new animal drugs within the meaning of Section 501(a)(5) of the Act which are unsafe within the meaning of Section 512.

Your "PINEE AN UNMIXED OIL OF THE LONG LEAF PINE" product, promoted for human use, is currently under review by the Center for Drug Evaluation and Research to determine if it also is a "new drug" in accordance with Section 201(p) of the Act. The review will include a determination if pine oil is generally recognized as safe and effective under the conditions recommended or suggested in the product labeling. We will immediately notify you of the results of this review.

Your firm has not registered with FDA as a repacker of the human drug product as required. This product is misbranded in accordance with Section 502(o) of the Act in that it is repacked in an establishment not duly registered under Section 510 of the Act and the drug has not been listed as required by Section 510(j).

The inspection also revealed numerous significant deviations from the Current Good Manufacturing Practice Regulations (GMPs) as set forth in Title 21, Code of Federal Regulations (21 CFR), Part 211. These deviations cause the veterinary drugs you manufacture, and the human drug you repack, to be adulterated within the meaning of Section 501(a)(2)(B) of the Act.

You have failed to establish appropriate approved master production and control records for the drug products you manufacture. These products include the human product and two of the three veterinary products. There were no established specifications for any of the finished products or the processes used for their manufacture or repacking. You could not provide any documented evidence which established a high degree of assurance that the current manufacturing procedures and processes were effective and could consistently produce products meeting their predetermined specifications and quality attributes. None of your manufacturing or repacking processes has been validated to assure that each batch would meet its purported identity and strength.

You have failed to maintain appropriate batch production records to include complete information relating to each significant step of the production and control of each batch. The Batch Sheets maintained failed to document the manufacturing steps conducted. There was no Batch Sheet for the production of the PINE-I'DINE lot. There was no documentation available that the batch sheets had been reviewed and approved by a responsible individual prior to product release. Although there is a signature on these documents, our investigator was told that it did not indicate review or approval of the batch sheet. The individual had been instructed merely to sign the sheets.

You have failed to implement sufficient controls to assure that incoming raw materials meet appropriate written specification of identity, strength, quality, and purity. No examination, testing, or formal approval is performed on incoming drug component, container, closure, labeling or packaging materials as required. No identity testing is performed on each drug component as required. Certificates of analysis were not available for most incoming lots of your predominant active ingredient, pine oil. Two of the three certificates available for pine oil had been faxed in after you were notified of our inspection. None of these could be correlated with the two lots of pine oil currently on hand. Review of these certificates revealed that the product is not consistently tested to established standards. No certificates could be provided for the [REDACTED] or [REDACTED] components. Significant concern remains over the use of these industrial chemicals in your products. No verification is conducted to determine the reliability of the suppliers' certificates of analysis.

You have failed to implement appropriate laboratory determination of satisfactory conformance to final specifications for your drug products, including the identity and strength of the active ingredients, prior to release. No finished product testing has been conducted for any of the drug products manufactured or repacked. No evidence was available that there was any formal review or approval of finished drug product prior to release for distribution.

You could provide no assurance that your drug products meet applicable standards of identity, strength, quality, and purity throughout their commercial shelf life or the expected period of use. No stability testing program has been implemented and no stability test data was available. Expiration dating is currently not enforced for human over the counter drug products if their labeling does not bear dosage limitations. Although you do not place expiration dates on your human drug product, you should have at least three years of stability data for this drug. No retain samples are maintained from each batch of drug products manufactured as required. Samples from the last two years of production were reported to have been discarded in preparation for this inspection.

You have failed to provide an appropriate facility for the manufacture, processing, packing, and holding of your drug products. You have failed to implement appropriate controls to keep environmental contaminants such as dust from entering the manufacturing area. The manufacturing room is exposed to the outdoors. Birds were noted to be flying in the storage area adjacent to the manufacturing room. No efforts were noted to control the temperature of your storage area although several of your raw materials require cool storage. Drug product container closures were observed stored in opened cartons exposed to dusty environmental conditions. Our investigator was also told that manufacturing and filling equipment was never cleaned.

You have failed to ensure that each person engaged in the manufacture, processing, packing, or holding of your drug products, and each person responsible for supervising these activities, has the education, training, and experience to enable that person to perform their assigned functions in such a manner as to provide assurance that your drug products have the quality and purity that they purport to or are represented to possess. This training must not only be in the particular operation that the employee performs but also include current good

manufacturing practice as it relates to the employee's functions. It is readily apparent that no one at your firm has received appropriate training commensurate with their responsibilities as evidenced by the lack of familiarity with the most basic GMP requirements.

At the conclusion of the inspection, our investigator issued her Inspectional Observations (FDA 483) to, and discussed the findings with, Donald W. Blake, General Manager. A copy of the FDA 483 is enclosed for your review. Neither the above discussion of deficiencies, nor the FDA 483, should be construed as an all-inclusive list of violations that may be in existence at your facility. The violations noted in this letter and in the FDA 483 are symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. It is your responsibility to ensure adherence to each requirement of the Act.

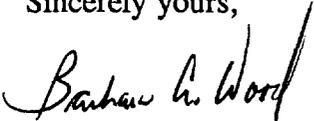
You should take immediate action to correct these violations. Failure to promptly correct these deviations may result in legal sanctions provided by the law such as product seizure and/or injunction, without further notice to you. Federal agencies are advised of the issuance of warning letters involving drugs so that they may take this information into account when considering the award of contracts.

You are requested to notify this office within fifteen (15) working days of receipt of this letter of all steps you have taken, or intend to take, to correct the noted violations, including an explanation of each step being 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 corrections will be completed.

We do acknowledge that Mr. Blake stated that he was going to cease production until corrective actions could be completed and you could be advised of the problems. However, he also advised of his intention to continue distributing the remaining inventory of these products. Your management expressed no surprise over the inspectional findings and in fact stated that they were aware of all deficiencies. We would question your commitment to bringing this firm into compliance. You had failed to follow your own procedures in the Pinee Operations Manual which calls for maintenance of production records, review of production records, maintenance of certificates for all incoming shipments of pine oil, review of incoming packaging and labeling materials, and maintenance of reserve samples. In addition to this you failed to respond to previous warnings and concerns expressed to your facility through correspondence from the Center for Veterinary Medicine.

Your response should also address any proposed actions regarding any drug product lots currently in distribution. Your response should be addressed to Philip S. Campbell, Compliance Officer, at the address noted in the letterhead.

Sincerely yours,


for Ballard H. Graham, Director
Atlanta District

Enclosures

cc: Donald Blake
General Manager
Ag-Mark Inc.
P.O. Box 127
Teachey, NC 28464