HFD-205

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

AUG - 5 1998

WARNING LETTER

Mr. Kenneth L. Evenstad
President
Upsher Smith Laboratories, Inc.
14905 23rd Avenue
Minneapolis, Minnesota 55447

Re: 98-HFD-312-04

Dear Mr. Evenstad:

This letter is in reference to your firm's marketing of "**AMLACTIN™** 12% Cream" and "**AMLACTIN™** 12% Lotion" for topical application. **AMLACTIN™** 12% Cream and **AMLACTIN™** 12% Lotion are drugs as described in section 201(g) of the Federal Food, Drug, and Cosmetic Act (Act) and new drugs as described in section 201(p) of the Act. Accordingly, neither product may be introduced or delivered for introduction into interstate commerce under section 505(a) of the Act because they are not the subject of approved applications under section 505(b) of the Act.

The Agency has reviewed the product labeling along with promotional offerings, advertising, and correspondence that accompanies these products. This material and the circumstances surrounding the distribution of these articles (see Title 21 of the Code of Federal Regulations (CFR) section 201.128), demonstrate that these products are intended for use in the "cure, mitigation, treatment, or prevention of disease," or are intended "to affect the structure or any function of the body," as described in section 201(g) of the Act.

This material and these circumstances include:

- Labeling for **AMLACTIN™** 12% Cream and Lotion that states that each of these products "has beneficial effects on dry, scaly skin and itching associated with this condition." The labeling also includes a caution statement that states in relevant part: "Avoid contact with eyes, lips and mucous membranes. Irritation may occur on the face of fair skinned individuals. A mild stinging, burning or peeling may occur on sensitive or irritated skin areas. If irritation or sensitivity occurs, discontinue use and consult a physician for appropriate therapy."

- A promotional sheet directed to family practitioners and dermatologists states that **AMLACTIN™** 12% Cream is an effective, non-prescription alternative to a prescription drug formulation when, in fact, **AMLACTIN™** 12% Cream contains the same basic formulation as the approved prescription drug products. The promotional sheet states: "Give your patients the freedom of no prescription restriction . . . Freedom of Choice . . . New cream formulation available in 140g tube gives your patients the freedom to choose between a cosmetic cream or lotion formulation with **no prescription restriction**." An advertisement placed in the April 1998 **Skin & Allergy News**, "The Leading Independent Newspaper for the Dermatologist," makes a similar claim: "NO PRESCRIPTION RESTRICTION . . . New **AMLACTIN™** 12% Cream . . . Freedom of Choice . . ."

- "Dear doctor" letters with patient samples of **AMLACTIN™** 12% Lotion encourage physicians to recommend this product to their patients in place of the prescription drug product with the same formulation. The letters state in part: "As you know, **AMLACTIN™** 12% Lotion contains ammonium lactate equivalent to 12% lactic acid . . . is available behind the counter in pharmacies everywhere. So recommend economical **AMLACTIN™** 12% Lotion by name for your patients."

- Both **AMLACTIN™** 12% Cream and **AMLACTIN™** 12% Lotion contain 12% *ammonium lactate, a formulation which is known to act as a keratolytic agent on the skin* and that is the subject of an approved new drug application.

- The publication by your firm of **AMLACTIN™** 12% Lotion in the 1998 Physicians Desk Reference, suggests that the product is a drug, along with the use of the over-the-counter (OTC) drug designation, a number that follows the format of the National Drug Code (NDC number) [1], and an address for additional "medical information."

Based on the above, **AMLACTIN™** 12% Cream and **AMLACTIN™** 12% Lotion are positioned as prescription drug substitutes, and use a formulation that is commonly associated with treatment of the conditions described above. Because the preceding claims and circumstances suggest individually and collectively that your products are intended to cure, mitigate, treat, or prevent a disease, or are intended to affect the structure or any function of the body, your products are drugs as described in section 201(g) of the Act.

Further, the Food and Drug Administration is unaware of any scientific evidence that these drugs are generally recognized as safe and effective for their intended uses. These products, although offered for sale OTC, do not comply with the general regulations covering OTC drugs found in 21 CFR, Part 330, nor do they comply with specific final or tentative final OTC drug product monographs. These products are considered "new drugs" under section 201(p) of the Act and may not be legally marketed in the United States since they are not the subject of an approved application as described in section 505(b) of the Act.

These drugs are misbranded as described in section 502(f)(1) in that their labeling fails to bear adequate directions for the uses for which they are being offered since the products are unapproved "new drugs" (section 201(p) of the Act).

The above list of violations is not intended to be an all inclusive list of deficiencies at your firm. It is your responsibility to ensure that the drug products you distribute meet all the requirements of the Act and its implementing regulations. Federal agencies are advised on the issuance of all Warning Letters about drugs and devices so that they may take this information into account when considering the award of contracts.

We request that you take prompt action to correct these violations. Failure to promptly correct these violations may result in regulatory action without further notice. Such actions may include seizure and/or injunction.

Please notify this office in writing within fifteen (15) working days of receipt of this letter of the specific actions you will take to correct these violations. Your response should also include an explanation of each step being taken to prevent recurrence of similar violations. If corrections cannot be completed within fifteen (15) working days, please state the reason for the delay and the time within which corrections will be completed.

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[1] Our information also indicates that the Medicaid Program for the state of Louisiana has declared **AMLACTIN™** 12% Cream as a drug for reimbursement purposes.

Your reply should be addressed to William G. Nychis, Compliance Officer, U.S. Food & Drug Administration, OTC Compliance Team (HFD-312), at the address noted above.

Sincerely,

/S/

Bradford W. Williams
Director
Division of Labeling and
Nonprescription Drug Compliance
Center for Drug Evaluation and Research