DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

WARNING LETTER

Certified Mail
Return Receipt Requested

Reference No: 07-HFD-45-0102

JAN 19 2007

Mr. Ali N. Syed,
President
Avlon Industries
1999 N. 15th Avenue
Melrose Park, IL 60160

Dear Mr. Syed:

Between March 8 and 15, 2006, investigator Mr. Russell Riley, of the Food and Drug Administration (FDA), conducted an inspection of your firm to audit your activities related to the testing of an investigational drug product in humans. Specifically, he inspected a study you sponsored for [ ].

This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to monitor conduct of research, to ensure that the rights, safety, and welfare of the human subjects have been protected. Mr. Riley presented and discussed Form FDA 483, Inspectional Observations, with you at the conclusion of the inspection.

Based on our evaluation of inspectional reports and related documents, the Center for Drug Evaluation and Research (CDER) concludes that you violated FDA regulations governing the protection of human subjects participating in clinical investigations. Specifically, you failed to obtain approval from an Institutional Review Board (IRB) or assure proper informed consent for the [ ]study, as required by 21 CFR Parts 56 and 50. CDER also concludes that you violated FDA regulations governing the use of investigational new drugs by initiating a clinical investigation without submitting an investigational new drug (IND) application, as required by 21 CFR Part 312 and that you failed to meet the obligations of a sponsor under applicable regulations as noted below.

1. FAILURE TO CONDUCT THE STUDY UNDER AN IND [21 CFR 312.20]

FDA regulations require that a sponsor submit an IND to FDA if the sponsor intends to conduct a clinical investigation with an investigational new drug [21 CFR 312.20(a)] and have an IND in effect before the investigational new drug is administered to study subjects [21 CFR 312.40(a)(1)]. A sponsor is a person who takes responsibility for and

initiates a clinical investigation [21 CFR 312.3(b)]. A clinical investigation is defined as "any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects" [21 CFR 312.3(b)]. The definition of a drug includes, among other things, "articles other than food intended to affect the structure or any function of the body of man or other animals" [Section 201(g)(1)(C) of the Act]. Our investigation indicates that you initiated and were responsible for the conduct of a clinical investigation designed to determine whether[ ], an investigational drug, is effective in[ ] in humans.

At the close of the inspection, you claimed that you intend to submit an abbreviated new drug application (ANDA) for your product. Although[ ]is the active ingredient in several marketed topical solutions, there is no approved application for a cream dosage form. Thus, to submit an ANDA based on 505(j) of the Federal Food, Drug and Cosmetic Act, you must file a Suitability Petition to request a change in dosage form from the listed drug[ ]solution 2%) to the proposed drug product[ ] cream 2%). Because you did not file a Suitability Petition that sought permission to file an ANDA for your proposed product, an IND was required to test your investigational new drug[ ]in human subjects [21 CFR 312.20(a)].

2. FAILURE TO ASSURE IRB REVIEW [21 CFR 56.103(a)]

You failed to assure IRB review of your clinical investigation for[ ] FDA's inspection of your facility and records found that[ ] (topical [ ] cream 2%) was administered and dispensed to human subjects without IRB approval of a study protocol. As noted above, you initiated and were responsible for the conduct of a clinical investigation designed to determine whether[ ] (topical[ ]cream 2%), an investigational drug, and therefore subject to the requirement to assure IRB review. Your[ ]does not qualify for the IRB review exemptions described in 21 CFR 56.104

3. FAILURE TO PROTECT SUBJECT'S LEGAL RIGHTS [21 CFR 50.20]

You failed to protect the subjects' legal rights in that the document provided to human subjects in the[ ]study, entitled "RELEASE for Hair, Scalp & Skin testing at Avlon Industries, Inc., Bedford Park, IL," contained exculpatory language through which the subject is made to waive or appear to waive legal rights, or releases or appears to release the investigator, the sponsor, the institution, and its agents from liability for negligence, in violation of 21 CFR 50.20.

For example, the document you provided to the study subjects contained the following statements:

a. "I, and the parent or legal guardian thereof if a minor, do hereby release and hold harmless Avlon Industries, Inc., and its subsidiaries and affiliates and all their respective employees, officers, directors, representative, independent contractors and agents (collectively referred to as "Affiliates") from any and all liability or damage

due in whole or part from my participation in this test, and further agree that I shall bring no claims, demands, actions and causes of action against Avlon or its Affiliates for any injuries, death or damages which may not exist or which may hereafter occur which are a result of my participation in this test."

b. "I have read completely and fully understand this release and freely and voluntarily consent to its terms without duress and with full knowledge of what I am doing and the rights that I am relinquishing forever."

4. FAILURE TO OBTAIN PROPER INFORMED CONSENT [21 CFR 50.25]

The informed consent document is required to contain eight basic elements [21 CFR 50.25(a). Our investigation found that the informed consent document used in your [ ] study, entitled "RELEASE for Hair, Scalp & Skin testing at Avlon Industries, Inc., Bedford Park, IL," did not contain the following required elements.

a. The consent form failed to disclose any reasonably foreseeable risks or discomforts to the subject and appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

b. The consent form failed to disclose the extent, if any, to which confidentiality of records identifying the subject will be maintained and the possibility of Food and Drug Administration inspection.

c. The consent form failed to describe available medical treatments and further information in case of an injury.

d. The consent form failed to describe the purposes of the research, the procedures to be followed, and the expected duration of the subject's participation.

e. The consent form failed to include a statement that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

5. VIOLATIONS RELATED TO SPONSOR'S RESPONSIBILITIES [21 CFR 312.50 and 21 CFR 312.23]

As a sponsor conducting a clinical investigation, you failed to maintain an effective IND as required by 21 CFR 312.50. You failed to submit supporting data and a study protocol with the required elements specified in 21 CFR 312.23, including:

a. Chemistry, manufacturing, and control information for the drug substance and the product, as required by 21 CFR 312.33(b)(7)

You failed to provide technical information related to the investigational drug, including source and purity of the drug substance.

b. A protocol for each planned study, as required by 21 CFR 312.33(a)(6).

You failed to submit a protocol describing the clinical procedures and other measures that would be taken to monitor the effects minoxidil cream on human subjects and procedures for identifying, collecting and reporting adverse events.

This letter is not intended to be an all-inclusive list of deficiencies with your clinical study of an investigational drug. It is your responsibility to ensure adherence to each requirement of the law and relevant FDA regulations. You must address these deficiencies and establish procedures to ensure that any on-going or future studies will be in compliance with FDA regulations. Failure to promptly correct these deviations may result in regulatory action without further notice. These actions include, but are not limited to, seizure or injunction.

Within 15 working days of your receipt of this letter, you must notify this office in writing of the actions you have taken or will be taking to prevent similar violations in the future. Failure to adequately and promptly explain the violations noted above may result in regulatory action without further notice.

Your reply should be sent to:

C.T. Viswanathan, Ph.D.
Associate Director, Bioequivalence
Chief, GLP & Bioequivalence Investigations Branch
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
7520 Standish Place, Room 116
Rockville, MD 20855
(301) 594-0020

Sincerely,

Joseph P. Salewski for

Gary Della'Zanna, D.O., M.Sc
Director
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research