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E.M.

Public Health Service

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
7200 Lake Ellenor Drive
Orlando, Florida 32809

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

WARNING LETTER

FLA-97-59

May 27, 1997

C. Richard Kinsolving, PhD, President
Immuno-Rx, Incorporated
7292 26th Court East
Sarasota, Florida 34243

Dear Dr. Kinsolving:

Inspection of your pharmaceutical development company from December 10, 1996 through February 3, 1997, and your contract research and production facility, located at the University of South Florida, 12901 Bruce B. Downs Boulevard, Tampa, Florida, from December 23, 1996 through January 10, 1997, by FDA Investigator Shari J. Hromyak, revealed serious violations of the Federal Food, Drug, and Cosmetic Act (the Act).

At your contract production facility, the investigator documented significant deviations from the Current Good Manufacturing Practice (CGMP) regulations [Title 21, Code of Federal Regulations, Parts 210 and 211 (21 CFR 210 and 211)] in conjunction with the production and release for distribution of IRex-2, a sterile injectable natural cytokine mixture, causing the product to be adulterated within the meaning of Section 501(a)(2)(B) of the Act.

Deviations from the CGMP regulations documented during the inspection include but are not limited to: failure to validate the IRex-2 production process; failure to establish an environmental monitoring program and perform testing in critical areas; the use of [REDACTED] .2 um filters not approved by the filter manufacturer for parenteral production; failure to establish procedures for calibration and maintenance of equipment; failure to establish batch production records; failure to document actual yields produced; failure to retain reserve samples; and failure to maintain distribution records.

Produced under the above conditions, there is no assurance that your IRex-2 has the strength, quality and purity it is represented to possess. A copy of the Inspectional Observations (FDA Form 483) issued to your chief scientific officer, John W. Hadden, MD, at the conclusion of the inspection is enclosed.

Inspection of your facility revealed that you obtained [REDACTED] vials of IRex-2, lot #17HA95, from Dr. Hadden's laboratory on January 16, 1995, and [REDACTED] vials of IRex-2, lot #2HA395, from Dr. Hadden's residence on March 14, 1995. On both occasions, these vials were packed in coolers with dry ice and were personally transported by you to [REDACTED] Mexico via a commercial airline.

The export of IRex-2 to Mexico is in violation of the requirements under 21 CFR 312.110(b) in that: 1) an Investigational New Drug application (IND) was not in effect for the drug under 21 CFR 312.40 at the time of export, or 2) authorization was not obtained from FDA prior to shipment of the drug for use in a clinical investigation. Additionally, you are in violation of Section 505(a) of the Act since you did not meet the aforementioned conditions for the exportation of IRex-2.

Since IRex-2 is an unapproved drug within the meaning of Section 505(a) of the Act and, at the time of shipment to Mexico, was not the subject of an investigational new drug exemption under Section 505(i), the drug is also misbranded in accordance with Section 502(f)(1) of the Act in that the label fails to bear adequate directions for use.

Please be advised that if you determine to continue to export IRex-2 to foreign countries for use in clinical investigations, you must comply with the requirements for export as outlined in Sections 801 and 802 of the Act (also known as the "FDA Export Reform and Enhancement Act of 1996") or the applicable regulations set forth in 21 CFR Part 312.

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facilities. As president, it is your responsibility to ensure that all drug products you produce and distribute are in compliance with the Act and the requirements of the CGMP regulations. You should take prompt action to correct these violations. Failure to correct these violations may result in administrative action, such as withdrawal of an approved IND, or regulatory action, including seizure and/or injunction without further notice.

We request that you notify this office in writing within fifteen (15) working days of receipt of this letter, of specific steps you have taken to correct these violations. If corrections cannot be completed within 15 working days, state the reason for the delay and the time frame within which corrections will be completed.

Your reply should be directed to Jimmy E. Walthall, Compliance Officer, U.S. Food and Drug Administration, 7200 Lake Ellenor Drive, Suite 120, Orlando, Florida 32809, telephone (407) 648-6823, extension 263.

Sincerely,



Douglas D. Tolen
Director, Florida District

Enclosure

cc: John W. Hadden, M.D.
12901 Bruce B. Downs Blvd.
Tampa, FL 33612