



DEPARTMENT OF HEALTH & HUMAN SERVICES

g/1707d

Food and Drug Administration

466 Fernandez Juncos Avenue
Puerta De Tierra
San Juan, Puerto Rico 00901-3223

February 20, 2001

WARNING LETTER
SJN-01-07

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Saleh Yassin
President
Creative Medical Corporation
Box 29166
65th Infantry Station
Rio Piedras, P.R. 00739

Dear Mr. Yassin:

From November 28, 2000 to December 21, 2000, our office conducted an inspection of your OTC drug and dietary supplement manufacturing facility, Creative Medical Corporation, Road 172 Km. 9.4, Bayamocito Ward, Cidra, Puerto Rico. Our evaluation of the information obtained during the inspection determined that the OTC drugs manufactured at the facility are adulterated within the meaning of Section 501 (a)(2)(b) of the Federal Food, Drug and Cosmetic Act (the Act) because they were not manufactured in accordance with Good Manufacturing Practice Regulations (GMP) as defined by Title 21, Code of Federal regulations, Part 211 (21 CFR 211).

We acknowledge receipt of your letter dated January 4, 2001, responding to the FDA 483 issued at the close of the inspection. We have reviewed the contents of your responses have determined that the corrective actions proposed for observations # 1,3,6,7,8 & 9 when appropriately implemented, should correct these deviations. With regard to the remaining observations, the response did not adequately address all of our concerns as outlined.

1. Your firm relies on contract laboratories to conduct laboratory testing for all products. No audit of the contract laboratories, as required by 21 CFR 211.22(a), was performed by your quality control unit to assure that the laboratories were operating in conformance with 21 CFR 211.160. After out-of-specification (OOS) results were reported by one laboratory, for one product investigation determined that the laboratory results were inaccurate and the contract laboratory refused to conduct an in-depth investigation to determine the cause of the problem.

The questionnaire for laboratory audits you supplied with your response letter is not appropriate because it does not address issues, which are specific for laboratory operations.

2. Failure to have adequate procedures for evaluating the quality & purity of drug product components as required by 21 CFR 211.84 (d)(2). For example:

Purified water used for equipment cleaning and as a component of drug products was determined to fail USP specifications after it was used to manufacture drug products. No evaluation of the vendor was made prior to use of the water.

3. Investigations into failures of drug products or components to meet established specifications are not always adequate to comply with 21 CFR 211.192 requirements. For example:

The report of investigation into the failure of process water to meet Total Organic Carbons (TOC) specifications did not include all relevant information such as the date of occurrence, the products affected, test results and corrective actions.

4. Failure to follow all instructions in SOP 005-001, Investigation of Failures, as required by 21 CFR 211.100(b) in that:

a) According to Section 6.4, a log book of all failure investigations must be kept in sequential order by product, reflecting report number, product name, lot number, and investigation start and completion dates. No record or tracking of failure investigations was done.

b) The investigation report discussed in # 3 above was generated 11 months after the problem was discussed instead of within 30 days as required in the SOP.

5. Failure to have adequate validations of cleaning procedures as required by 21 CFR 211.61 (b). For example:
 - a) The cleaning validation protocol for Maslac required two additional lots for completion when the production operation was transferred. Your firm performed only a verification test of the cleaning process at the new facility but failed to have review and approved from the Quality Assurance Manager prior to implementing the procedure.
 - b) There is no written justification for the limit of detergent residue established in the cleaning validation protocol for Fullson 128. Your response that the sensitivity of the analytical method determined the acceptable level is not sufficient. Other factors must be considered in the determination.

Neither this letter nor the list of inspectional observations is meant to be an all-inclusive list of deviations at your facility. It is your responsibility to ensure that your facility is in compliance with the provisions of the Federal Food, Drug, and Cosmetic Act and all applicable regulations and standards. Federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information into account when considering that award of contracts.

Please notify the San Juan District office in writing, within 15 working days of receipt of this letter, of your responses to the violations identified in this letter. Corrective actions addressed in your letter may be referenced in your response to this letter as appropriate. Failure to promptly correct these deviations may result in regulatory action without further notice. These include seizure and/or Injunction.

Mr. Saleh Yassin
February 15, 2001
Page 4

Your reply should be sent to the Food and Drug Administration, San Juan District Office,
466 Fernandez Juncos Avenue, San Juan, Puerto Rico 00901-3223, Attention: Mary L.
Mason, Compliance Officer.

Sincerely,


Mildred Barber
District Director

CC: Maria Santiago
Operations Manager
Creative Medical Corporation
Road 172, Km 9.4
Bayamoncito Ward
Cidra, P.R. 00739