



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration  
g2054d

December 14, 2001

Dallas District  
4040 North Central Expressway  
Dallas, Texas 75204-3145

Ref: 2002-DAL-WL-06

**WARNING LETTER**

**CERTIFIED MAIL**  
**RETURN RECEIPT REQUESTED**

Mr. Donald Smothers, President  
Natural Technology, Inc.  
350 Apache Trail  
Terrell, Texas 75160

Dear Mr. Smothers:

During an inspection of your drug, dietary supplement, and cosmetic manufacturing facility located in Terrell, Texas, conducted on September 25-28, 2001, our investigators documented deviations from the Current Good Manufacturing Practice Regulations for Finished Pharmaceuticals (Title 21, Code of Federal Regulations, Parts 210 & 211). These deviations cause your drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act. Examples include:

- Failure to establish control procedures which monitor the output and validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product [21 CFR 211.110(a)]. For example, there is no manufacturing process validation in place for drug products and the associated equipment utilized in drug manufacturing.
- Failure to establish and maintain written records of investigations into unexplained discrepancies, the failure of a batch or any of its components to meet its specifications and failure to include conclusions and follow-up of such investigations [21 CFR 211.192]. For example, on May 19, 2000 microbial testing on RoEzIt batch number 00503, lab number N5040, revealed positive results on both Standard Methods Agar and [REDACTED] Agar plates. The Aerobic Plate count for this sample was too numerous to count (TNTC). On May 22, 2000, microbial testing of the same RoEzIt batch

number 00503, lab number N5043, had an Aerobic Plate count TNTC. A second random sample taken the same date May 22, 2000, with lab number N5044 and batch number 00503 had an Aerobic Plate count TNTC. A total of [REDACTED] microbial tests were conducted for this product, yet there was no documented investigation into these discrepancies nor was there any conclusion or follow-up.

- Failure to establish testing and release criteria that determines satisfactory conformance to the identity and strength of each active ingredient prior to release of drug products [21 CFR 211.165(a)]. For example, potency testing is only performed for sunscreen products and fails to include all other drug products manufactured by your firm.
- Failure to validate the performance and reliability of test methods used in the determination of conformance of drug products to established standards [21 CFR 211.165(e)]. For example, the procedure for determining the viscosity of drug products has not been validated.
- Failure to establish and maintain a stability testing program that appraises the stability of drug products [21 CFR 211.166]. For example, documentation of stability testing or an established protocol could not be provided.
- Failure to establish and follow written procedures that evaluate at least annually, provisions for reviewing product complaints, product recalls, returned and/or salvaged drug products as well as procedures describing how investigations into these events are to be conducted [21 CFR 211.180(e)(2)]. For example, written procedures or documentation of reviews pertaining to such events could not be provided.
- Failure to establish and follow distribution procedures [21 CFR 211.150]. For example, written distribution procedures could not be provided.
- Failure to maintain records of calibration checks and inspections of automatic, mechanical, or electronic equipment [21 CFR 211.68(a)]. For example, incubator and refrigerator thermometers associated with equipment that stores microbiological media have not been calibrated.
- Failure to establish written procedures designed to prevent the growth of objectionable microorganisms in drug products not requiring sterility [21 CFR 211.113(a)]. For example, these procedures could not be provided.
- Failure to examine and test components, containers, and closures to determine conformance to established standards and acceptance for use [21 CFR 211.84(d)]. For example, [REDACTED] testing to determine the identity of components is not an acceptable procedure. Validation of vendor's testing to

assure reliability of test results that pertain to containers and closures has not been performed.

- Failure to establish and follow control procedures for drug components, containers and closures that are designed to prevent contamination in finished drug products [21 CFR 211.80]. For example, written procedures lacked sufficient detail describing the receipt, identification, storage, sampling, handling, testing, approval, and rejection of components, drug product containers, and closures. The reverse osmosis water system used as a component in human drug products contained an approximate 2-1/2 foot dead leg and a leaking valve.
- Failure to identify and control quarantined products and components until they have been tested or examined as appropriate [21 CFR 211.82(b)]. For example, drug product containers and closures are not stored under quarantine prior to their release.
- Failure to establish time limits for completion of various production phases as appropriate [21 CFR 211.111]. For example, mixing procedures for OTC drugs specify indefinite timeframes to achieve completion such as “agitate until solution complete”.
- Failure to include complete information in batch production records [21 CFR 211.188]. For example, a statement of yield, samples or copies of product labeling, and examinations of labeling for correctness are not included in batch production records.

The above deviations are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence with each requirement of the Good Manufacturing Practice Regulations. Federal agencies are advised of the issuance of all warning letters involving drugs, so that they may take this information into account when considering the award of contracts. Additionally, NDA, ANDA, or export approval requests may not be approved until the above deviations are corrected.

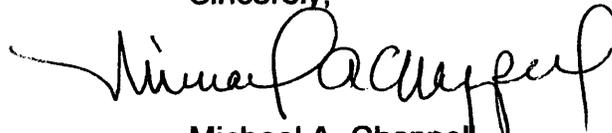
We are aware of your firm's agreement to correct various deficiencies documented during the inspection, however targeted dates, responsible departments and/or persons, and specific corrections to be accomplished were not detailed.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. Possible actions include seizure and/or injunction.

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Please notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted deviations and to prevent their recurrence. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. Your reply should be sent to the Food and Drug Administration, Dallas District Office, Attention: Brenda C. Baumert, Compliance Officer, at the above letterhead address.

Sincerely,

A handwritten signature in black ink, appearing to read "Michael A. Chappell". The signature is fluid and cursive, with a long horizontal stroke at the beginning and a large loop at the end.

Michael A. Chappell  
Dallas District Director

MAC: bcb