



DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration
New Orleans District Office
6600 Plaza Drive, Suite 400
New Orleans, LA 70127 JEH

May 20, 2002

VIA FEDERAL EXPRESS – NEXT DAY

Mr. William S. Propst, Jr., President
Vintage Pharmaceuticals, LLC
150 Vintage Drive
Huntsville, AL 35811

Warning Letter No. 02-NSV-22

Dear Mr. Propst:

During an inspection of your facility on March 25-29, 2002, our investigators documented violations of the Current Good Manufacturing Practice Regulations (CGMPs), Title 21, Code of Federal Regulations, Part 211. These violations cause your drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act).

The inspection revealed inadequate process validation of drug manufacturing (as required by 21 C.F.R. §§ 211.100, 211.110(a), and 211.110(b)), failure to follow Standard Operating Procedures for change controls and process validation (as required by 21 C.F.R. §§ 211.100(b) and 211.22(d)), inadequate stability studies (as required by 21 C.F.R. § 211.166), and inadequate investigations of manufacturing and laboratory deviations (as required by 21 C.F.R. §§ 211.160(a), 211.165(a) & (f), and 211.192).

The above identification of violations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Current Good Manufacturing Practice Regulations.

Federal agencies are advised of the issuance of all warning letters about drugs so that they may take this information into account when considering the award of contracts. Additionally, pending NDA, ANDA, or Certificates to Foreign Governments requests will not be approved until the above violations are corrected.

We acknowledge your response of April 19, 2002 to our investigators' observations noted on the Form FDA 483 and have the following comments:

Observation No. 1a – We acknowledge your re-evaluation of the seven (7) products listed in attachment 2 of your response which indicates that each product has been successfully validated. However, we have concerns about your procedures and conclusions, and about why you did not commit to re-evaluate all products. You performed new evaluations for these seven products without addressing acknowledged deficiencies, and before the additional studies promised in your response were completed. Thus, the manufacturing process for those products cannot be

considered adequately validated, as required by 21 C.F.R. §§ 211.100(a), 211.110(a), and 211.110(b).

Observation No. 1b – Your response states that product re-evaluations include evaluations of friability, bulk density, tapped density and particle size data. Although such data are included in the reports, we did not find any acceptance criteria or evaluation of the data, as promised, and as required by your procedures. The Current Good Manufacturing Practice Regulations require compliance with written procedures. See 21 C.F.R. §§ 211.100(b) and 211.22(d).

Observation No. 2 – Your response did not include any validation report for CDP/Clidinium in attachment 2. Without it, FDA does not have adequate assurance that the process for manufacturing CDP/Clidinium is validated, as required by 21 C.F.R. §§ 211.100(a), 211.110(a), and 211.110(b).

Observation No. 4 – We have concerns if Lot No. 001G1 of Phenobarbital ¼ grain tablets has been released for distribution. During the inspection it appeared this lot failed USP Content Uniformity and Assay. Your response does not indicate the original results are invalid. The response does not address the cause of the original failure, provide any information about the investigation or re-testing done, or identify any corrective actions to prevent a recurrence. Under 21 C.F.R. § 211.165(f), drug products failing to meet established standards or specifications or any other relevant quality control criteria shall be rejected.

Observation No. 5 - We have concerns that you re-opened previously completed investigations, and reached different conclusions than previously reported. In some cases, your response contained little justification or information about how the new conclusions were reached, as required by 21 C.F.R. §§ 211.160(a) and 211.192. This was the case for Guaifenesin/PSE and Phenobarbital products. We also have concerns that out of specification (OOS) investigations of Q Bid LA lots, manufactured in the time frame between the 2 sets of validation lots, are not discussed in either validation report, thus providing insufficient assurance that the manufacturing process for Q Bid LA is validated, as required by 21 C.F.R. §§ 211.100(a), 211.110(a), and 211.110(b).

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

You should notify this office in writing within fifteen (15) working days of receipt of this letter of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations.

If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the time within which the corrections will be completed. Your reply should be directed to the attention of Joseph E. Hayes, Compliance Officer, Food and Drug Administration, 297 Plus Park Boulevard, Nashville, TN 37217.

Sincerely,

A handwritten signature in black ink, appearing to read "Carl E. Draper". The signature is fluid and cursive, with a long, sweeping line extending from the end of the name.

Carl E. Draper
Director, New Orleans District

CED:JEH:man

Enclosure: 21 CFR Part 211