



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Central Region

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Telephone (973) 526-6004

Food and Drug Administration
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

May 20, 1999

WARNING LETTER

CERTIFIED MAIL

RETURN RECEIPT REQUESTED

Chris Fuhrmann, CEO
Glenwood LLC
One New England Avenue
Piscataway, New Jersey 08855

FILE NO.: 99-NWJ-23

Dear Mr. Fuhrmann:

This letter is regarding an inspection of your facility located at One New England Avenue, New Jersey by the U.S. Food and Drug Administration from March 17 through May 4, 1999. During the inspection our investigator documented serious deviations from the current Good Manufacturing Practices (cGMP) Regulations (Title 21, Code of Federal Regulations, Part 210 and 211) in conjunction with your firm's manufacture of prescription drugs.

These deviations were presented to your firm's attention on a FDA-483, List of Inspectional Observations, at the close of the inspection on May 4, 1999. The cGMP deficiencies cause your products to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act.

The significant observations are as follows:

1. Your firm failed to evaluate the gross discoloration of the product Glenwood, Bichloracetic Acid, which is included in your Treatment Kits, Replenishment, and Restocking Units. The firm has received numerous Consumer Complaints regarding the discoloration of the Biochloracetic Acid liquid. The product is labeled as a clear colorless liquid. An examination of the firm's retained samples and current product inventory revealed that lots #49382, #49642, #49650, #48843, #48309, #48310, and #49649, were discolored with sealed bottles containing yellow to dark-brown liquid. The above referenced lots are all within expiration. There has been no investigation into the root cause or adverse effects of the discoloration.

Additionally, the titration analytical method being used is not validated and is non-stability indicating. Neither the supplier nor Glenwood has performed analysis of the Biochloracetic Acid and its impurities.

2. Your firm has no assurance that the manufacturing process for the product Iodoquinol tablets, USP, will consistently produce a product that meets all quality attributes throughout the labeled shelf life. The Retrospective Validation Study completed by your firm failed to evaluate the [REDACTED] retrospective batches for critical steps and controls, including drying times, temperature, equipment, or batch size. Retrospective batches were evaluated for only Assay, Content Uniformity, and Tablet specifications, with portions of the data missing for 11 of the retrospective batches.
3. The Process Validation for the product Yocon 5.4 mg. tablets is inadequate in that it fails to demonstrate that the blending process could produce a blend that meets all acceptance criteria. Sample sets were taken in [REDACTED] and analyzed selectively based on results from the first set tested. The blend sample results showed acceptance criteria were met for only two of the blender sample sets, both from lot V49726 (2nd and 3rd sets) and only one set of drum sample sets, lot V49730.
4. The analytical data used to support the process validation for Yocon 5.4 mg was obtained using a non-validated method. For example, the Tablet Content Uniformity data for lot V49726 was collected from two different analytical methods. Neither of the methods was validated at the time they were used to analyze lot V49726. The data obtained by both methods was reported as acceptable in the Analytical Report.

In addition, the firm permitted the Yucon 5.4 mg Process Validation Studies to begin prior to validating an analytical method for the product. There is no documentation in the Analytical Report for lot V49726, or in the Process Validation Report that two different analytical methods had been used to obtain the data.

5. The Process Validation Report for the product Potaba capsules is inadequate in that it fails to demonstrate the ability to manufacture product with consistent, uniform results from batch to batch, and will meet predetermined specifications. For Example:
 - a. Lot #49746 noted capsule weight inconsistencies. An incident report stated that during Quality Assurance (QA) In-Process testing the average capsule weight was below minimum range of [REDACTED]. QA approved the partial release of the batch.

- b. Lot #49684 noted capsule weight inconsistencies. Deviation Report #97-004 was included for OOS weight results. The report stated that due to poor compaction, the material was transferred and encapsulated using a different encapsulator [REDACTED], which is an unvalidated process. No investigation was performed on the unusual characteristics of the material that led to the poor compaction.
6. The Process Validation Report for Potaba tablets fails to provide assurance that the product can be made of consistent quality, using the established manufacturing process. For example, Lot #V49791 produced low assay results from mixer samples [REDACTED] which was attributed to a "possible short injection". The investigation which determined the failure to a short injection was never documented. The samples were retested and again the results did not meet specification ([REDACTED]). The Potaba tablet assay specification is [REDACTED]. The laboratory accepted the results without QA approval.
7. Failure to validate the manufacturing processes for the products, Barium Sulfate Tablets, Epifoam Concentrate, Boro Pak 2.7 g (Burow's Solution), and PALS (chlorophyllin copper complex).
8. Your firm has no assurance that the Validation Reports accurately evaluate and summarize raw data. Unacceptable and untraceable data was used for the Method Validation Report of the product Carbiset 300 mg. tablets. The firm utilized failing results from the dissolution method for Carbinoxamine Maleate, active pharmaceutical ingredient (API) as part of the validation data. The raw data does not demonstrate that the method met the validation acceptance criteria. For Example:
- a. % Recovery Studies for Carbinoxamine Maleate failed to meet the acceptance criteria of a Relative Standard Deviation (RSD) of less than [REDACTED]. This unacceptable data was used to compile the Method Validation Report.
- b. The linearity data and graphs for the two unacceptable % Recovery studies were used interchangeably in the validation report.
- c. An incorrect passing value for the Average % Recovered and RSD was reported in the laboratory notebook #123. The incorrect results were reviewed and signed by a second analyst.

9. No assurance that the firm's Quality Control Laboratory performed method validation work in accordance with an approved validation protocol. For example, the Method Validation Protocol for the product Iodoquinol was approved on 10/23/98. The Method Validation Report, including the method, was approved on 10/26/98. The chromatograms that are included with the report, show method validation work being performed in May 1998, five months before the approval of the validation protocol.
10. Your firm began process validation studies for the product Carbiset prior to completing validation of the analytical methods. The first product validation batch, VMBR-49812, was started on 1/23/98, while the Carbiset Analytical Method Validation Report was not approved until 6/3/98. There is no assurance that acceptance criteria and product specifications were established before the actual analytical work and process validation results. In addition, all three validation lots contained tablets with weights in excess of tablet weight specifications.
11. Glenwood LLC does not routinely perform investigations into batch manufacturing and/or analytic testing deviations and failures. Examples:
 - a. During production of the product Potaba Envules 2g, Lot #49810, bulk flow problems caused weight variations. The filled envules were transferred back to the original bulk drum containers. This material was then used to manufacture Potaba Capsule, Lot #49828. No investigation was conducted into the abnormal characteristics of the bulk material, or the undocumented transfer of material. Lot #49828 was released.
 - b. The raw material used for Yucon 5.4 mg. tablets Validation lot #V49734, was contaminated. The validation documentation noted that the raw material, Sodium Starch Glycolate, used for the lot was bug infested. The firm's incident report referenced raw material lot # 98382, Dibasic Calcium Phosphate. The report referenced raw material lot #98382, Dibasic Calcium Glycolate, stated "dark specks[sic]" were observed in some finished tablets. No investigation was conducted to determine what the dark spots were. The compressed tablets were inspected and released.
 - c. The batch size for Potaba Envules 2 g, lot #49696, was reduced from [REDACTED] active to [REDACTED]. The batch failed to meet assay specifications and content uniformity requirements. No investigation was conducted into the reason for the decreased batch size, failing content uniformity and OOS results.

12. The firm does not always test stability samples placed in the stability program, at the required time intervals. Examples:

Bichloroacetic Acid

LOT #	CONDITION	SCHEDULED TIME INTERVAL	TESTED
49649, 10 ml	[REDACTED]	3 months	6 months
49649, 75 ml	[REDACTED]	2 months	6 months
49649, 75 ml	[REDACTED]	3 months	6 months
49642, 75 ml	[REDACTED]	3 months	7 months
49642, 75 ml	[REDACTED]	6 months	7 months

Yodoxin Tablets

49835, 650 mg.	CRT	3 months	4.5 months
49835, 650 mg.	CRT	6 months	7 months

13. Failure to conduct Performance Qualification on the laboratory instruments that are used to analyze raw materials and finished products, including two (2) [REDACTED] three (3) [REDACTED] and one (1) GC.

14. Failure to validate the software programs, Shimadzu and [REDACTED] that are used to run the laboratory HPLC equipment, during analysis of raw materials and finished products. The [REDACTED] software does not secure data from alterations, losses, or erasures. The software allows for overwriting of original data. There are no written procedures for the use of passwords, levels of access, or data back-up.

The above identification of violations is 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 Practices Regulations. We request that you take prompt action to correct any noted violations not already corrected and undertake a comprehensive evaluation of your cGMP compliance. You should respond within 15 working days with any information regarding the steps you are taking to correct the identified deficiencies and assure a comprehensive approach to compliance with cGMP's. Failure to promptly correct these violations may result in regulatory action without further notice. This includes seizure and/or injunction.

Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so that they may take this information into account when considering the award of contracts. In addition, pending new drug applications (NDA's), abbreviated new drug applications (ANDA's) or export approval requests may not be approved until the aforementioned violations are corrected.

Any additional information you wish to submit should be sent to the Food and Drug Administration, New Jersey District Office, 10 Waterview Blvd, 3rd Floor, Parsippany, New Jersey 07054, Attention: Andrew Ciaccia, Compliance Officer.

Very truly yours,

A handwritten signature in cursive script, appearing to read "Douglas Ellsworth for".

DOUGLAS ELLSWORTH
District Director
New Jersey District Office

AC: slm