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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
10 Waterview Blvd. 3rd floor
Parsippany, NJ 07054
Telephone (973) 331.4902

July 24, 2008

WARNING LETTER

CERTIFIED MAIL-
RETURN RECEIPT REQUESTED
Ronald Greenblatt, President & CEO
G & W Laboratories, Inc.
111 Coolidge Street
South Plainfield, New Jersey 07080

FILE NO.: 08-NWJ-07

Dear Mr. Greenblatt:

An inspection of G & W Laboratories, Inc. 111 Coolidge Street, South Plainfield, New Jersey was conducted by a Food and Drug Administration (FDA) investigator from December 3, 2007 through December 20, 2007. The inspection revealed significant deviations from the current good manufacturing practice (CGMP) for finished pharmaceuticals regulations, Title 21, Code of Federal Regulations (CFR), Parts 210 and 211, with regard to the production of pharmaceutical products by this facility. The deviations reported by the investigator caused your finished drugs to be adulterated within the meaning of 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 351(a)(2)(B)]. The deviations were presented to your firm on a FDA-483, List of Inspectional Observations, at the close of the inspection on December 20, 2007. In addition, your firm also manufactures unapproved new drugs and misbranded drugs in violation of the Act under sections 502(a) [21 U.S.C. § 352(a)], 502(c) [21 U.S.C. § 352(c)], 502(e) [21 U.S.C. § 352(e)], and 505(a) [21 U.S.C. § 355(a)].

CGMP Deviations

We acknowledge receipt of your letter dated January 15, 2008, as well as your updated responses dated January 31, 2008 and February 29, 2008. Examples of the deficiencies observed along with comments regarding your FDA Form 483 responses are as follows:

1. **Failure to reject drug products that did not meet established standards and other relevant quality control criteria [21 CFR § 211.165(f)].**

Specifically, the batch that your firm designated as a stand alone batch, Formulation R Hemorrhoidal Ointment, Lot 029807011, was released for distribution without a demonstration that this batch met relevant quality control criteria.

As Formulation R Hemorrhoidal Ointment, Lot 029807011 was not made in accordance with a validated manufacturing process, there is no assurance that it meets the required quality attributes. Therefore, the quality of this batch must be evaluated on its own merit. For a "stand alone" lot, relevant criteria, including appropriate statistical criteria, are needed to support a QC decision for rejection or release. The preamble to the current Good Manufacturing Practice Regulation, 21 CFR §211.165(f), states that "any other relevant quality control criteria" includes statistical criteria where appropriate. Your response failed to include appropriate justification to release this lot.

The Formulation R Hemorrhoidal Ointment product is purported to contain 100% of label claim. The product specification for Formulation R Hemorrhoidal Ointment is [redacted] of label claim, which allows for some normal variability around the target of 100%.

The sample data from Formulation R lot 029807011 for packaging order PK 90674 (the first packaging order filled) shows results clustered around the upper limit of the specification (i.e., the data is not centered around the 100% label claim but is near the upper specification limit). In addition, one of the sample results was [redacted] which exceeded the product specification. Our review of these data (e.g., time plot or histogram) indicates that a portion of that packaging order contains units that exceeded the specification.

Your January 15, 2008 response to the FDA483 stated, in part, that the batch was releaseable because: 1) the lot met finished product criteria; 2) the product does not have dosing information; and 3) the process validation test variation did not indicate a lack of adequate control in the manufacture of the batch. You concluded that the lot did not pose safety and efficacy issues and did not need to be rejected on the basis of GMPs. We disagree with your rationale for releasing this batch. The batch did not meet the finished product criteria and the appropriate statistical criteria were not established for this "stand alone" batch. Furthermore, the lack of specified dosing instructions for this ointment or the variability of patient use of the product is not a basis for an assessment of the batch quality and the decision to release or reject it. Significantly, our inspection found that mixing (to assure uniformity) was not properly controlled. Accordingly, we disagree with your conclusion that there was no reason for "rejection on GMP grounds." The batch should not have been released without further evaluation (e.g. testing and/or analysis). In addition to the 21 CFR § 211.165(f) citation other sections of the CGMP regulation (discussed below) were violated by your firm.

2. Failure to establish written procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess [21 CFR § 211.100(a)].

Specifically, your firm scaled up from a small to a large batch size for Formulation R Hemorrhoidal Ointment without a study to assess the impact of a change in process parameters on product quality. This lack of attention to process design appears to have been a factor in inadequate mixing of at least one batch of Formulation R product.

3. Failure to reject in-process material that did not meet the identity, strength, quality, and purity standards during production [21 CFR § 211.110(c)].

Specifically, the bulk Formulation R Hemorrhoidal Ointment, Lot 029807011, was sampled from the holding tank and tested prior to filling into the finished product containers. The sample result from the bottom of the holding tank was [redacted] of label claim, and exceeded your in-process acceptance criteria of [redacted] of label claim. Your firm did not reject the lot and there was no follow-up to address inadequate mixing at this significant process stage.

4. Failure to clean and maintain equipment and utensils used in the production of drug products in order to prevent contamination [21 CFR § 211.67(a)].

For example, deteriorating equipment was observed, including: tape flaking off filling equipment directly above an uncovered hopper containing product to be filled (Hydrocortisone Acetate Suppositories, Lot #050307039), a leaking gasket in the product transfer line during filling of Hydrocortisone Acetate Suppositories, Lot #050307039, and two leaks in the Purified Water system. While your response appears adequate, we are concerned about the condition of your manufacturing facility in that during the inspection our investigators observed multiple conditions of disrepair.

5. Failure to conduct and document a thorough investigation of any unexplained discrepancy or failure of a batch or any of its components to meet its specifications, or to extend the investigation to other batches which may have been associated with the particular failure or discrepancy [21 CFR § 211.192].

For example, unexplained discrepancies and/or incomplete investigations were conducted or documented in the following:

- Investigation Control #0535-0515: Formulation R Suppositories, Lot #053507006, was rejected due to the presence of black particles. Your investigation indicated that the [redacted] pump was replaced during the production of the lot. The December 2006 batch record does not document any equipment replacement or problems with the equipment. The black particles were not analyzed. You did not extend the investigation to extend to other batches.

We note your January 15, 2008 response stated, "No further analysis was performed on the black particles, since the source was evident from the investigation." We disagree that further sample analysis was not necessary, as testing the sample would have provided conclusive results of the black particles found in the batch. In addition, the investigation also noted the shift mechanic who incorrectly assembled the sine pump was a new employee; however, there was no indication that an assessment was conducted to determine whether other batches may have been impacted and investigated.

- Investigation Control #4-6610-01122007: Positive results were identified for E.coli from Purified Water samples taken from Ports 9-12. Your investigation concluded the sample was contaminated during microbiological testing. This investigation was incomplete in that it did not adequately address the failure of personnel to determine if any follow up was necessary and the need for training in this area.

Your January 15, 2008 response acknowledged the analyst that performed the testing for the water samples that resulted in contamination was "partially trained," and that his training was completed after the incident. Your response does not indicate how you will ensure that untrained or incompletely trained employees will not perform tasks in the laboratory, manufacturing, or production areas, as appropriate. In addition, your response did not include the location in the water system where the sample was taken and the sampling error occurred.

6. Failure to follow written procedures that describe the in-process controls and tests to be conducted on appropriate samples of in-process materials of each batch [21 CFR § 110(a)].

Specifically, your firm failed to test Formulation R Hemorrhoidal Ointment, process validation Lots #029807012, #029807013 and #029807015 for content uniformity of the preservatives (Methylparaben and Butylparaben).

Your January 15, 2008 response stated your firm would complete additional analyses for preservative testing. However, your response lacked timeframes for completion.

Misbranded and Unapproved New Prescription Drugs

Based on the information your firm submitted to FDA's Drug Registration and Listing System and the labeling collected during the inspection of your facility, you manufacture the following prescription drugs:

- Chloral Hydrate Rectal Suppository (Chloral hydrate: 500 mg x 25 suppositories; 500 mg x 100 suppositories)
- Anucort-HC (Hydrocortisone acetate: 25 mg x 12 suppositories; 25 mg x 24 suppositories; 25 mg x 100 suppositories)

The above products are drugs within the meaning of Section 201(g) of the Act, [21 U.S.C. § 321(g)] because they are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of diseases. Further, they are "new drugs" within the meaning of Section 201(p) of the Act [21 U.S.C. § 321(p)] because they are not generally recognized as safe and effective for their labeled uses. Under Sections 301(d) and 505(a) of the Act [21 U.S.C. §§ 331(d) and 355(a)] a new drug may not be introduced into or delivered for introduction into interstate commerce unless an FDA-approved application is in effect for the drug. Based on our information, you do not have any FDA-approved applications on file for these drug products.

Additionally, the above products are misbranded because, as prescription drugs, adequate directions cannot be written for them so that a layman can use these products safely for their intended uses. Consequently, their labeling fails to bear adequate directions for use as required under Sections 502(f)(1) of the Act [21 U.S.C. § 352(f)(1)] and because they lack required approved applications, they are not exempt from this requirement under 21 CFR § 201.115.

The introduction or delivery for introduction into interstate commerce of these products without approved new drug applications violates Sections 301(a) and (d) of the Act [21 U.S.C. §§ 331(a) and (d)]; therefore, you should discontinue manufacturing and distributing all of your unapproved new drugs at all facilities immediately, with the exception of Anucort-HC products. If you decide to discontinue marketing Anucort-HC products, please notify the Agency to assist us in avoiding any undue burdens on consumers or disruption in the market. If you elect to continue marketing Anucort-HC products, FDA approvals for products are necessary to bring them into compliance with the Act. The Unapproved Drugs Coordinator in the Office of New Drugs may be able to assist you in obtaining information regarding the application process and can be reached at 301-796-0700. Also, please note that if you are no longer marketing these products, you must update the Drug Listing files in accordance with 21 CFR § 207.30 (a)(2).

The issues and violations cited in this letter are not intended to be an all-inclusive statement of violations that exist at your facility. You are responsible for investigating and determining the causes of the violations identified above and for preventing their recurrence or the occurrence of other violations. It is your responsibility to assure that your firm complies with all requirements of federal law and FDA regulations.

You should take prompt action to correct the violations cited in this letter. Failure to promptly correct these violations may result in legal action without further notice, including, without limitation, seizure and injunction. Other federal agencies may take this Warning Letter into account when considering the award of contracts. Additionally, FDA may withhold approval of requests for export certificates, or approval of pending new drug applications listing your facility as a manufacturer until the above violations are corrected. A reinspection may be necessary.

Within fifteen working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct violations. Include an explanation of each step being taken to prevent the recurrence of violations, as well as copies of related documentation. If you cannot complete corrective action within fifteen working days, state the reason for the delay and

the time within which you will complete the correction. If you no longer manufacture or market any drugs, your response should so indicate, including the reasons and the date on which you ceased production.

Your reply 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.

Sincerely,

Diana Amador-Toro

Diana Amador-Toro
Acting District Director
New Jersey District Office

AC:slm