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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
555 Winderley Pl., Ste. 200
Maitland, Fl 32751

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

WARNING LETTER

FLA-08-27

September 2, 2008

Whitney Labs
c/o Colonial Management Group, LP
T. Mark Gallagher, President/CEO
14050 Town Loop Boulevard, Suite 204
Orlando, Florida 32837

Dear Mr. Gallagher:

On March 12, 13, 14, and 17, 2008, the United States Food and Drug Administration (FDA) conducted an inspection of Whitney Labs, your prescription drug products repackaging and relabeling facility located at 1095 North US Highway 1, Suites #1-4, Ormond Beach, Florida 32174-1921. The inspection revealed numerous significant deviations from the current good manufacturing practice (CGMP), Title 21 Code of Federal Regulations Parts 210 and 211 (21 CFR Parts 210 and 211), in the repackaging and relabeling of drug products, including, but not limited to, the Schedule II controlled substance Methadone HCl in solid and liquid oral dosage forms. These deviations cause your finished drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 351(a)(2)(B)]. Furthermore, the inspection revealed that your firm was responsible for manufacturing (b) (4) unit-doses of Methadone HCl 260mg/26mL in liquid oral dosage form that were mislabeled as 20mg/2mL Methadone HCl. These drug products are misbranded within the meaning of Section 502(b)(2) of the Act [21 U.S.C. 352(b)(2)] in that the labels for these packaged drug products did not bear an accurate statement of the quantity of the contents in terms of weight, measure, or numerical count.

We acknowledge receipt of your April 14, 2008 written response to the FDA 483, Inspectional Observations. We note that some corrections appear to have been implemented and that you have promised that others will soon be implemented. However, your response does not adequately address some of the deficiencies, as further discussed below. Specific areas of concern include, but are not limited to:

1. Failure to have a quality control unit *[21 CFR § 211.22]*. Specifically, you have neither designated in writing nor in practice a quality control unit with the following functions: the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging material, labeling, and drug products; the authority to review production records to assure that no errors have occurred or, if errors have occurred, that they have been fully investigated; and the responsibility for approving or rejecting all procedures or specifications impacting on the identity, strength, quality, and purity of drug products. We acknowledge your correspondence of April 14, 2008, in response to the FDA 483, which promises the establishment of a quality control unit and revised procedures describing its functions by July 1, 2008. However, your firm has not provided any documentation of these corrections. *(FDA 483 Observation 1)*

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)]*. For example, your firm's automated packaging line processes and their respective software systems have not been validated. Your response to the FDA 483 response is inadequate because it fails to include any detail on the specific steps your firm intends to take to verify the proper functioning of the referenced equipment. *(FDA 483 Observation 2)*

3. Failure to follow written production and process control procedures in the execution of the various production and process control functions and to document them at the time of performance *[21 CFR § 211.100(b)]*. For example, on February 11, 2008, your firm's production line employee(s) involved in the manufacture of liquid oral Methadone HCl failed to follow your firm's procedures and document their actions at the time of performance regarding label changeovers between production runs and verification of processing equipment, including settings prior to changing fill-sizes. As a result, (b) (4) unit-doses of 260mg/26mL liquid oral Methadone HCl were mislabeled as 20mg/2mL liquid oral Methadone HCl, (b) (4) (b) (4) unit-doses of which were subsequently distributed. Your FDA 483 response states that retraining of employees has already taken place, but does not describe any other measures you may have taken to ensure adherence to written procedures in the future. *(FDA 483 Observation 3)*

4. Failure to thoroughly investigate any unexplained discrepancies or failures of a batch or any of its components to meet any of its specifications *[21 CFR § 211.192]*. For example, the mislabeling of 300 unit-doses of 260 mg/26 mL liquid oral Methadone HCl and reports of leaking containers and missing labels received by your firm were not investigated to determine root causes and no corrective or preventive action was implemented. Your FDA 483 response is inadequate because it does not address the need to investigate unexplained discrepancies or failures of a drug product or component to meet specifications even when there is no complaint involved. *(FDA 483 Observation 5)*

5. Failure to establish written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, testing, approval, and rejection of components, containers, and closures *[21 CFR § 211.80(a)]*. For example, your firm has no procedures requiring testing of drug product components, containers or closures for solid and liquid oral dosage form Methadone HCl, 40cc unit-dose. The corrective action described in your FDA 483 response is inadequate because it does not state how your firm intends to address the specific inspectional observations concerning drug product components, containers and closures. *(FDA 483 Observation 4)*

6. Failure to establish and follow written procedures describing the handling of all written and oral complaints regarding drug products *[21 CFR § 211.198(a)]*. For example, your firm has not established written procedures describing the handling of complaints that include provisions for: 1) review by a quality control unit of any complaint indicating a possible failure of a drug product to meet its specifications, 2) a determination of the need for an investigation of any such possible failure or unexplained discrepancy, and 3) review to determine if the complaints represent serious and unexpected adverse drug experiences which are required to be reported to FDA. Your FDA 483 response states that revised procedures will be in place by June 1, 2008, that will address the specific inspectional observations. However, you have not provided any additional follow up documentation to demonstrate that corrective actions have been implemented. *(FDA 483 Observation 5)*

7. Failure to adequately train employees engaged in the manufacture, processing or holding of a drug product in CGMP or in the particular operations performed by the employees *[21 CFR § 211.25(a)]*. For example, employees engaged in the production of 260mg/26mL liquid oral Methadone HCl, lot #5464L, which was mislabeled as 20mg/2mL, did not follow your firm's written procedures pertaining to product changeover on the Auto Labe labeling system or those requiring documentation of filler settings. In addition, according to employee training records as maintained in the human resource files for employees engaged in the production of 260mg/26mL liquid oral Methadone HCl, lot #5464L, those employees received no GMP training, conducted on a continuing basis and with sufficient frequency, to ensure familiarity with applicable CGMP requirements. Whitney Labs also failed to comply with Section 1.4.1 of its training procedure to implement and document new hire training activities for employees engaged in the production of drug products. Your FDA 483 response states that retraining of employees on existing procedures took place on May 15, 2008. In addition, the response states that training will be on a continuing basis; however, details are not provided regarding the frequency of the retraining. *(FDA 483 Observation 8)*

8. Failure to establish a written testing program designed to assess the stability characteristics of your firm's repackaged solid and liquid oral dosage form Methadone HCl to determine appropriate storage conditions and expiration dates *[21 CFR § 211.166(a)]*. For example, your firm's procedure whereby an expiration date of one year past the date of repackaging is assigned to unit dose containers is not sufficient to

provide assurance that the drug products will meet all applicable standards of identity, strength quality and purity at time of use since it does not include an assessment of the expiration date of the bulk drug product or address the effect of multiple openings of the bulk drug product container prior to repackaging. Pursuant to 21 CFR § 211.137, expiration dates must be supported by appropriate stability testing described in a written program, which your firm has not established. The corrective action described in your FDA 483 response is unsatisfactory because it does not address how your firm intends to assign expiration dates to repackaged unit-dose drug products while the stability studies are being conducted. *(FDA 483 Observation 6)*

9. Failure to retain reserve samples from representative lots or batches of drug products and to conduct visual examinations of such samples for evidence of deterioration on an annual basis [*21 CFR § 211.170(b)*]. Specifically, your firm does not retain reserve samples. The corrective action described in FDA 483 response appears to be satisfactory. However, your firm has provided no documentation of this correction. *(FDA 483 Observation 7)*

10. Failure to establish written procedures for conducting annual reviews to evaluate the quality standards of each drug product to determine the need for changes in drug manufacturing or control procedures *[21 CFR § 211.180(e)]*. Specifically, no annual product reviews are conducted and your firm does not maintain written procedures for conducting such reviews. Your FDA 483 response does not address conducting annual product reviews. *(FDA 483 Observation 7)*

In addition, we have determined that the aforementioned (b)(4) [redacted] unit-doses of 260mg/26mL Methadone HCl in liquid oral dosage form that your firm mislabeled as 20mg/2mL Methadone HCl, Lot #5364L, are misbranded within the meaning of Section 502(b)(2) of the Act [21 U.S.C. 352(b)(2)] in that the labels for these packaged drug products do not bear an accurate statement of the quantity of the contents in terms of weight, measure, or numerical count.

This letter is not intended to be an all-inclusive list of the violations at your facility. It is your responsibility to ensure compliance with applicable laws and regulations administered by FDA.

As we noted above, we have received your firm's written response to the FDA 483 and we appreciate the statement by your Operations Manager, Ms. Hunter, that your firm is "prepared to take all necessary steps to ensure compliance in all areas." We acknowledge that your firm's Corrective Action Plan, which provides an outline of your firm's proposed corrective actions for each of the objectionable observations listed on the FDA 483, includes an expected date of completion for all corrective actions of September 1, 2008. We also acknowledge that, during the inspection, Ms. Hunter reported to our investigator that, as of February 15, 2008, your firm had identified the locations of all (b) (4) [redacted] unit-doses of the misbranded Methadone HCl, (b) (4) [redacted] unit-doses of which were distributed by your firm to narcotic detoxification treatment clinics located in New Hampshire, North Carolina, Alabama, and Florida. However, we are concerned that, as of

the time of the inspection, only one (1) of the six (6) treatment centers receiving affected drug products had returned the misbranded Methadone HCl for destruction.

Your firm's April 14, 2008, response is not adequate, in that your proposed corrective actions to the CGMP violations do not, for the reasons listed above, alleviate our concerns regarding the identity, strength, quality and purity of drug products repackaged and relabeled by your firm.

Moreover, FDA has evaluated the degree of the health hazard associated with use of these misbranded unit-doses of Methadone HCl by the general adult population and has determined that overdose with methadone is highly likely to cause fatal respiratory depression and cardiac arrhythmia. Due to the life-threatening health risk of methadone overdose to patients for whom your firm's misbranded Methadone HCl, Lot #5364L, was intended, your firm's response is also inadequate in that no documentation regarding the final disposition of the entire lot of affected drug product was provided, without which we cannot evaluate and determine the effectiveness of your corrective actions.

Please notify this office in writing within fifteen (15) working days from the date you receive this letter of the specific steps you have taken to correct the noted violations. Include documentation of the corrective actions you have taken, such as: any new or revised procedures or policies, including validation protocols; training records; and copies of records documenting the final disposition of all unit-doses of Methadone HCl, Lot #5364L. Regarding your planned corrections that will occur over time, please include any appropriate revisions to the timetable for implementation of corrective actions (i.e., the Corrective Action Plan) that was previously submitted with your response dated April 14, 2008. If corrective actions cannot be completed within 15 working days, state the reason(s) for the delay and the time within which the corrections will be completed.

You should take prompt action to correct the violations addressed in this letter. Failure to promptly correct these violations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure and injunction. Also, 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.

Please send your response to the U.S. Food and Drug Administration, Attention: Matthew B. Thomaston, Compliance Officer, 555 Winderley Place, Suite 200, Maitland, FL 32751. If you have questions regarding any issue in this letter, please contact Mr. Thomaston at (407) 475-4728.

Sincerely,

for Emma R. Singleton
Director, Florida District