

Inspections, Compliance, Enforcement, and Criminal Investigations

Ohm Laboratories, Inc. 12/21/09



Department of Health and Human Services

Public Health Service
Food and Drug Administration
New York District
158-15 Liberty Avenue
Jamaica, NY 11433

December 21, 2009

VIA FEDERAL EXPRESS

WARNING LETTER
Ref: NYK 2010-07

Robert Patton, Vice President, General Manager
Ohm Laboratories, Inc.
34 West Fulton Street
Gloversville, NY 12078-2902

Dear Mr. Patton:

This letter describes FDA's concerns regarding a July 13 through August 12, 2009 inspection by FDA investigators of your pharmaceutical manufacturing facility, Ohm Laboratories, Inc., located at 34 West Fulton Street, Gloversville, NY. The inspection identified significant violations from the Current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals, Title 21, CFR Parts 210 and 211. These violations cause your drug product(s) 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)] in that the methods used in, or the facilities or controls used for, their manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with CGMP regulations.

In addition, you manufacture and distribute a prescription drug without an approved application. As described below, this drug is an unapproved new drug and by introducing it into interstate commerce, you are in violation of sections 301 (d) and 505(a) of the Act [21 U.S.C. §§ 331(d) and 355(a)].

Further, this inspection revealed your firm failed to report the quantity of a drug product distributed under an approved application in an annual report [21 CFR § 314.81 (b)(2)(ii)] and to submit an NDA-Field Alert Report within three working days of receipt of information concerning a failure of one or more distributed batches of a drug to meet the specifications established for it in the application [21 CFR § 314.81 (b)(1)(ii)].

We received your firm's September 11, 2009 response, and we note that it lacks sufficient corrective actions. In addition, we received your firm's October 12, November 11, and December 11, 2009 responses, indicating the status of and timeframes for the September 2009 proposed corrective actions.

Specific violations observed during the inspection include, but are not limited, to:

CGMP Violations

1. Your firm has not thoroughly investigated the failure of a batch or any of its components to meet its specifications, whether or not the batch has already been distributed, and failed to extend the investigation to other batches of the same drug product and other drug products that may have been associated with the specific failure or discrepancy [21 CFR § 211.192]. For example,

- a. Complaint investigation #2009-01830 concerning black particles in a single bottle of Metformin HCl Oral Solution, batch 1987071, concluded that the source of the particles may have originated from worn nozzle seals on the filling machines. The investigation did not include an assessment to determine whether the use of such defective equipment affected the quality of other batches of your product and other products that utilize the same filling machine.

Your response to observation 6a in the FDA 483, regarding the Metformin HCl Oral Solution complaint investigation, states that the investigation failed to identify a conclusive root cause and hypothesized that the particles came from the "food-grade nozzle seals" On the filling machine. We find inconsistencies between the description of the investigation in your response and our review of investigation #2009-01830, which attributed a root cause to the failures. In addition, we have determined your investigation to be inadequate.

Investigation #2009-01830 states that "over time the nozzle seals will become somewhat degraded and begin to 'flake' when removed from the nozzle shaft to change spacer settings, and the nozzle tip a-rings will wear from constant cycling of the filling nozzle during filling operation, at which time they are replaced with new seals." You have no knowledge of when the seals started to degrade or when it became a risk to the quality of your product. Your complaint investigation also states that microscopic evaluation of a **(b)(4)** seal yielded many similarities with the particles in the complaint sample and concluded that a worn nozzle seal on the filling equipment was the most probable source. You failed to extend the investigation to other batches of the same drug product and other drug products that may have been associated with the equipment failure.

Further, your response states that this was the only complaint you had ever received regarding visible particles in Metformin HCl Oral Solution since you started manufacturing this product in 2003. You assert that tracking and trending, to determine if additional or

similar complaints were received, may have been the appropriate disposition of this complaint. Although you did not limit this investigation to tracking and trending, we disagree with your premise that tracking and trending would have been sufficient. The CGMP regulations [21 CFR §211.198] require that you investigate complaints or provide a sufficient reason when an investigation is deemed unnecessary. Tracking and trending of a complaint is only part of a sufficient investigation and does not substitute for an investigation or provide adequate justification to circumvent the investigation requirement.

b. Your May 20 and July 7, 2008 investigations into fiber and cardboard particles found in three batches of Ranitidine HCl Solution were inadequate. The initial investigation was not thorough, nor did your investigation include an assessment to determine whether drug product in polyethylene terephthalate (PETE) bottles (confirmed to contain particles) should have been rejected. You released the batches of drug product based on questionable visual inspections of amber color bottles filled with product.

Your response to observation 6b in the FDA 483, regarding the Ranitidine HCl Solution investigations, states that subsequent investigation of this matter indicated that "the particulates may not have been related to the specific lot of bottles in question, but rather to the handling of the bottles prior to charging them into the filling line. The removal of the plastic wrap from the bottles may cause electrostatic buildup that can attract any loose particles present in the secondary container (cardboard boxes)." Your response and process deviation report PRO13/08 also state that you conducted "AQL final product inspections" to release batches of product that used the same batch of "PETE" bottles confirmed to contain particles.

Based on your assessment, the presence of particles in your bottles may have occurred previously due to your similar handling of the bottles plastic wrap, yet you did not extend the investigation to other batches of drug product that were treated in the same manner. In addition, you released batches of drug product despite inadequate AQL inspections conducted on amber color bottles filled with product and on equipment (i.e., bottle washer) that was not qualified for its intended use (i.e., removal of particles from PETE bottles). Please provide information to demonstrate that visual AQL inspections on amber color bottles of Ranitidine HCl Solution are effective. It is your responsibility to ensure that the release of drug products is based on validated methods of inspection and that the equipment is qualified for its intended use.

c. Your July 5, 2007 investigation into an Out-of-Specification (OOS) assay result (by HPLC) for anhydrous morphine content of Opium Tincture USP (Deodorized), batch 1781499, disregarded the initial 88.6% OOS result (specification **(b)(4)**%). Instead, you replaced the 88.6% OOS result with a 95.9% result (obtained by reinjection) and investigated the 95.9% result as an Out-of-Trend (OOT) result. You invalidated the OOS result without justification, conjectured that "there could be possible unidentified analytical error," and released the batch.

Your response to observation 6c in the FDA 483, regarding the Opium Tincture OOS investigation, acknowledges that the analyst involved in this investigation did not document the investigation as required by the OOS procedure (SOP 2802). However, this incident is not simply a documentation error but a failure to acknowledge the initial OOS result and to thoroughly investigate what may have caused the OOS result. It is your responsibility to ensure that you thoroughly investigate the cause of the OOS results before continuing your investigation with the retesting and re-sampling of additional samples (e.g. bulk, retain, stability). Please include corrective actions to prevent recurrence of similar deviations. For

example, review and revise your OOS procedure, if necessary, or conduct 100% audit of your OOS investigations to ensure the OOS procedure is followed.

In addition, it is your responsibility to ensure that you have established adequate procedures for investigating unexplained discrepancies (e.g., OOT results). We acknowledge your commitment to create an OOT procedure and to revise the OOS procedure by October 30, 2009. Please include corrective actions to prevent recurrence of similar deviations (i.e., lack of procedures). For example, we recommend that you schedule periodic evaluations of your procedures by conducting gap analysis between your firm's procedures and corporate policies and procedures to ensure they are in alignment and to identify missing procedural CGMP requirements.

2. Your firm has failed to comply with its written stability program [21 CFR § 211.166(a)], failed to establish an adequate written stability program designed to assess the stability characteristics of drug products in order to determine appropriate storage conditions and expiration dates [21 CFR § 211.166(a)], and failed to maintain a record of the number of batches of each drug product that are tested to determine an appropriate expiration date [21 CFR § 211.166 (b)]. For example,

a. You failed to follow SOP 2805, **(b) (4)** when your QCU failed to analyze stability samples maintained under long term stability conditions within **(b) (4)** working days from the date withdrawn. Your QCD tested stability samples between 77 to 153 days after removal from the stability chambers. The following are examples of batches of drug products that were not tested within **(b) (4)** days from the date the samples were withdrawn from their stability chambers.

Product	Batch	Pack	Test Time Point (mo.)	Difference (days)
	1326373			
Metformin HCl Solution	1327834	40 oz HDPE	(b) (4)	153
	1328455			
	1728799			
Sertraline HCl Concentrate	1728800	2 oz Glass	(b) (4)	114
	1729098			
(b) (4)	1680581	160 oz Glass	(b) (4)	81
(b) (4)	(b) (4)	(b) (4)	(b) (4)	77

Your response to observation 11a in the FDA 483, regarding the failure to analyze drug products within **(b) (4)** days from the date of removal from the stability chambers, states

that the products covered by the observation "span a period from 2003 to 2007." Your response also states that "Normal staff fluctuations... occasionally impact sample analysis timeframes" and that you "have successfully managed these factors to limit delays." We have concerns regarding your commitment to ensure that your stability program is in compliance with CGMP regulations and your adherence to it, once it is adequately established. We disagree with your comment that you have been successfully managing factors to limit delays in your stability program. You acknowledge that you have had a systematic failure in your stability program from 2003 to 2007, yet you now propose working on initiatives to ensure compliance with your stability SOP 2805. Please explain why this observation has remained unresolved since 2003. In addition, we note that the failure to have an adequate number of qualified personnel is not justification to neglect your commitments to the stability program. Please submit your corrective action to prevent recurrence of similar deviations.

b. Your Standard Operating Procedure SOP 2805, **(b) (4)** is not adequate. The procedure does not establish time limits for the initiation of the stability studies and clearly describe the stability protocol contents to (1) specify when to test "On Demand" samples that are stored at refrigerated condition (i.e., **(b) (4)** °C); and (2) describe the intended purpose of the test for "On Demand" samples stored at refrigerated condition. For example, **(b) (4)** batch **(b) (4)** was manufactured in May 2006, and the stability study was not initiated until June 2007. In addition, the stability protocols provide inadequate instructions regarding the purpose of testing. For example, **(b) (4)** stability protocol, STB-016/06, states that samples stored at refrigerated condition "shall be analysed only on demand, when required."

Your response to observation 3a in the FDA 483, regarding the failure to maintain stability records, states that the samples to be stored under refrigerated condition are protocol driven; termed "On Demand" samples from exhibit batches; and intended for research and troubleshooting purposes. We note that the terms "On Demand" and "exhibit batches" are not described in your stability SOP 2805. SOP 2805 describes the procedure for your product stability program and does not reference samples intended for research by your research department (i.e., PD/TS).

In addition, your response states that "On Demand" samples are not collected or used for stability purposes and are not subject to the stability program sample control practices. Despite this statement, you use the stability protocols governed by the stability procedure SOP 2805 to include "On Demand" samples as part of the stability program. Further, your response to observation 3d regarding inconsistencies in the number of units placed on stability states that the stability protocols "specifically indicate that these samples are to be analyzed '...only on demand when required.'" Please note that the terms "when required" and "On Demand" are ambiguous, and neither is defined in your stability protocols. Your stability program is inconsistent and inadequate. Please submit your corrective actions to your stability program.

Be advised that it is not adequate to place a product on stability, for example, one year from the time it is manufactured. This could result in non-conforming product remaining on the market for an unjustifiable period of time because you failed to begin stability testing (starting at Day 0) at an appropriate interval to provide timely information to protect the public.

We acknowledge your commitment to immediately terminate the practice of collecting "On

Demand" samples. However, we advise you to review and correct all stability related procedures and protocols to ensure that your stability program is adequately designed and followed. In addition, we recommend that you revise your quality assurance program to prevent similar deviations and to ensure that your procedures are adequate and in compliance with your corporate policy, procedures, and CGMP regulations.

c. You have not established a laboratory control system to trace the movement of stability samples (including units of product without tamper evident seal) stored in your refrigerators. Specifically, you are not maintaining a record that includes product description, batch number, dates, the person(s) responsible for the movement of samples in and out of the refrigerator, and the quantity of product to ensure that stability studies are reliable. Examples of samples required by stability protocols and stored inside the refrigerators **(b) (4)** and **(b) (4)** include: **(b) (4)** lots **(b) (4)** and **(b) (4)** and Ranitidine HCL Solution, lot 5750601.

Your response to observations 4a and 4b in the FDA 483 states that the samples stored in the refrigerators are not stability samples but "On Demand" samples that are collected and stored as required by your stability protocols (SOP 2805). Be advised that these stability protocols are part of your stability program, and SOP 2856, which requires stability documentation for the tracking of stability samples, also applies to your "On Demand" samples (i.e., instructions to place stability samples intended for testing in the stability chambers that include refrigerated conditions). Hence, your assertion that "On Demand" samples are not stability samples is contradicted by your stability procedures.

In addition, your response states that "It has never been Ranbaxy's policy to analyze 'On Demand' samples for stability purposes and there is no evidence that 'On Demand' samples have been used in this manner." You have not demonstrated that "On Demand" samples have never been used for stability purposes because you have not established a control system to ensure the accountability and traceability of samples stored in your refrigerators. Please submit your corrective actions to your stability program.

d. SOP 2856 **(b) (4)**, requiring stability documentation for the tracking of stability samples is not adequate. SOP 2856 states that quality personnel submit collected stability samples to the stability coordinator. Under this procedure, the stability coordinator initiates the stability protocol, and upon approval of the protocol, the samples are labeled and placed in the stability chambers. However, this sequence of events in the procedure is inadequate and inconsistent with your current practice. The collection of the samples from the packaging line by quality personnel cannot precede the stability protocol's approval because you do not know the number of samples to be collected without the study protocol.

3. Your firm has not established laboratory control mechanisms and documented the execution of laboratory control functions at the time of performance [21 CFR § 211.160(a)]. For example,

a. Your QCU did not document the dates at the time samples were allegedly withdrawn from the stability chambers for analysis. The attendance record shows that your stability coordinator was absent from your firm during those dates in which the coordinator recorded the withdrawal of samples from the stability chambers (see examples below).

Product	Lot#	Protocol#	Interval	Date	Day	Attendance recor
(b) (4)	(b) (4)	STB-016/06	(b) (4)	mo7/7/2007	Saturday	Stability coordina was absent from the firm
(b) (4)	(b) (4)	STB-016/06	(b) (4)	mo10/7/2007	Sunday	Stability coordina was absent from the firm
(b) (4)	(b) (4)	STB-003/07	(b) (4)	mo9/1/2007	Saturday	Stability coordina was absent from the firm
(b) (4)	(b) (4)	STB-006/07	(b) (4)	mo7/29/2007	Sunday	Stability coordina was absent from the firm
(b) (4)	(b) (4)	STB-006/07	(b) (4)	mo9/29/2007	Saturday	Stability coordina was absent from the firm
(b) (4)	(b) (4)	STB-006/07	(b) (4)	mo3/29/2007	Saturday	Stability coordina was absent from the firm
(b) (4)	(b) (4)	STB-005/08	(b) (4)	mo5/30/2007	Saturday	Stability coordina was absent from the firm
(b) (4)	(b) (4)	STB-008/07	(b) (4)	mo9/22/2007	Saturday	Stability coordina was absent from the firm
(b) (4)	(b) (4)	STB-008/07	(b) (4)	mo2/22/2007	Sunday	Stability coordina was absent from the firm
Metoclopramide Solution	3020801	STB-004/08	(b) (4)	mo1/4/2009	Sunday	Stability coordina was absent from the firm
Opium Tincture USP (Deodorized)	1684894	STB-012/06	(b) (4)	mo9/22/2007	Saturday	Stability coordina was absent from the firm
Opium Tincture USP (Deodorized)	1684894	STB-012/06	(b) (4)	mo3/22/2008	Saturday	Stability coordina was absent from the firm
Ranitidine HCL Solution	5750601	STB-003/06	(b) (4)	mo3/22/2008	Saturday	Stability coordina was absent from the firm
Nortriptyline HCl Solution	1505270	STB-002/05	(b) (4)	mo1/7/2006	Saturday	Stability coordina was absent from the firm
Nortriptyline HCl Solution	1505270	STB-002/05	(b) (4)	mo4/7/2007	Saturday	Stability coordina was absent from the firm

Your response to observation 5a in the FDA 483, regarding the failure to document the withdrawal of stability samples at the time of performance, acknowledges that your stability coordinator mistakenly recorded the date of sample collection to coincide with the date specified in the stability protocol. Your response also states that the responsibilities of this former employee have been transferred to another qualified employee. Although

responsibilities were transferred to another employee, we still have concerns regarding your corrective actions. This type of deficiency in your CGMP quality system is indicative of the failure by your QCU to provide effective training and adequate oversight to assure that no errors occur. We recommend that you develop an internal audit program that will assist you in identifying and correcting similar deviations. We also recommend that you revise your training program to include an evaluation of training effectiveness. Please submit your corrective actions to prevent recurrence of similar deviations.

b. Your QCU has not established a control system to prevent mixups, to assure the traceability of samples in the laboratory, and to assure the proper storage of samples before testing. Your QCU uses a walk-in cage, known as the Test Sample Room, to store units of expired and unexpired finished drug products. This collection represents exhibit and process validation batches, samples already tested, and stability samples. Your firm does not maintain an inventory of the cage contents, does not track the status of the products, and uses the cage as backup storage for stability samples. Examples of products stored in the cage include: **(b) (4)** batches **(b) (4)** batch **(b) (4)**; Sertraline HCl Concentrate, batch 3020801; Nortriptyline HCl Solution, 1684894; and Ranitidine HCl Solution, batch 5750601.

c. Your QCU has not established a record control system that assures the reliability of the laboratory raw data. Your QCU documented raw data (e.g. date of analysis, batch numbers, calculations) in spiral pocket notebooks that lack controls to prevent the deletion and traceability of analytical raw data.

Your response fails to address the violation. You must establish adequate controls to assure the reliability of laboratory records. Please include your corrective actions to address this violation.

4. Your firm has not established scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality, and purity [21 C.F.R § 211.160(b)]. For example, your sampling plan intended for stability studies (i.e., batch record sampling instructions and stability protocol) is not adequate. The number of samples collected for stability purposes during the manufacturing process, as documented in your batch manufacturing records, differs significantly from the number of samples required by your stability protocols to be placed on stability (e.g., Ranitidine HCl Solution, batch 5750601; **(b) (4)** batches **(b) (4)** and **(b) (4)** Metformin HCl, batches AA192 through 194; and **(b) (4)** batch **(b) (4)**).

Your response to observation 3a in the FDA 483, regarding the failure to maintain records of the number of drug product batches tested for stability purposes, acknowledges that there is a difference in the number of stability samples between the batch record and the stability protocol. You also state that this difference is managed during "execution of the exhibit batch" by either collecting additional samples or destroying the surplus. Please include your corrective actions to ensure that the number of stability samples collected during manufacturing is consistent with your stability program. In addition, you need to ensure that all collected samples are adequately documented and accounted for.

5. Your firm has not exercised appropriate controls over computer or related systems to assure that changes in control records or other records are instituted only by authorized

personnel [21 CFR § 211.68(b)]. For example, one user account is established for two analysts to access the laboratory instrument's software on the computer system attached to HPLC systems **(b) (4)** and **(b) (4)**. The user account provides full system administrative rights, including editing of the methods and projects. In addition, data security protocols are not established that describe the user's roles and responsibilities in terms of privileges to access, change, modify, create, and delete projects and data.

Your response to observation 17 in the FDA 483, regarding the failure to establish a procedure that defines the user account responsibilities and privileges and ensures the use of a unique user name and password for each analyst, is not adequate. It states "A user account with 'Analyst' privileges was used during the demonstration.... However, it is not equivalent to the permissions of an 'Administrator' account, which has full access to all levels of the software." As observed by our investigators, your analysts did not know their roles and responsibilities in terms of privileges to the subject software during what your response now characterizes as a demonstration. Your response also states that unique usernames and passwords have been issued with "Analyst" access privileges. Please submit supporting information to demonstrate that your corrective actions address the violation.

6. Your firm has not established written procedures to monitor the output and to 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, the manufacturing process of Opium Tincture USP (Deodorized) does not include in process controls to monitor and confirm that the filtration step is effective. We note that your complaint investigation #2008-01394 for particulate matter in two bottles of Opium Tincture USP (Deodorized), batch 1781499, concluded that "the subject particles present in the complaint sample are inert organic sediment," and you have not provided supporting documentation to confirm the conclusion.

7. Your firm has not established an adequate number of qualified personnel to perform and supervise the manufacture, processing, packing, or holding of each drug product [21 CFR § 211.25(c)]. Specifically, your firm does not have an adequate number of personnel to ensure that your firm's manufacturing operations are adequately conducted and completed. For example,

a. Your OCU personnel stated that no data back-up of the **(b) (4)** HPLC Systems has been performed since May 26, 2009 due to insufficient time to perform such activity.

b. Based on your stability coordinator's explanation, it is difficult for the coordinator to routinely find the two employees that are required to open the "vault" to access samples because of a lack of personnel.

8. Your firm has not used equipment that is routinely calibrated, inspected, or checked according to a written program designed to assure performance [21 CFR § 211.68(a)] example, stability chambers **(b) (4)** and **(b) (4)** (installed August 2000); **(b) (4)** (installed February 2004); **(b) (4)** (installed March 2003); and **(b) (4)** (installed February 2003) have not been calibrated since installation. In addition, vault #2 used for storage of Opium Tincture stability samples (e.g., batches 2016450, 1997891, 1959526) has never been calibrated.

Your response to observations 14d and 14e in the FDA 483 regarding the failure to calibrate stability chambers is not adequate. The response does not address the reasons why the QCU failed to ensure equipment is calibrated, nor does it include corrective actions to prevent recurrence. In addition SOP 2854 **(b) (4)** submitted with your response is not adequate because it does not describe how to perform the calibration.

Post Marketing Violations

1. Failure to report the quantity distributed of a drug product under an approved application in an annual report to FDA [21 CFR § 314.81(b)(2)(ii)]. Specifically, your February 10, 2009 Annual Report for ANDA 78-448, Ranitidine HCl Solution USP, 15 mg/mL, covering the review period of December 13, 2007 - December 12, 2008 failed to include the distribution data under the subject application of all lots manufactured at your site and distributed from your site. The Annual Product report declared that "no product has been manufactured or distributed during the reporting period." Production records show at least **(b) (4)** lots were manufactured and distributed during this period: batches **(b) (4)** and **(b) (4)**. Furthermore, batch # **(b) (4)** was rejected because the operators failed to add the required amount of active pharmaceutical ingredient during processing.

2. Failure to submit an NDA-Field Alert Report within three working days of receipt of information concerning a failure of one or more distributed batches of a drug to meet the specifications established for it in the application [21 CFR § 314.81(b)(1)(ii)]. Specifically:

a) Your firm received a complaint on March 23, 2009 related to particles in Metformin Oral Solution, batch #1987071 which was confirmed on April 1, 2009. The test for clarity requires that the sample should be **(b) (4)**. Your May 22, 2009 investigation concluded that the particles may be attributed to a worn nozzle seal on the filling machine. This event was not reported.

b) You became aware of an OOS result for an antioxidant at the **(b) (4)** month stability point on March 17, 2009 for ANDA 78-053, Sertraline Hydrochloride Oral Concentrate, 20 mg/mL, batches 1728799, 1728800, and 1729098. The NDA-Field Alert Report was not filed until March 26, 2009.

Unapproved Drug and Misbranding Violations

In regard to your unapproved drugs, on June 8, 2006, FDA issued a guidance entitled "Marketed Unapproved Drugs-Compliance Policy Guide (CPG)," which explains FDA's policies aimed at ensuring that all drugs marketed in the U.S., prescription and over-the-counter, have been shown to be safe and effective. This guidance can be found on FDA's webpage at

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070290.pdf>. Other related information can be found on <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/SelectedEnforcementActionsonUnapprovedDrugs/ucm118990.htm>.

The guidance clearly articulates FDA's expectation that illegally marketed products, those products marketed without required FDA approval, be removed from the market. The guidance also outlines FDA's enforcement policies aimed at efficiently and rationally bringing all drugs requiring approved applications into the approval process. As described in the CPG, all drugs marketed without required applications are subject to enforcement action at any time, without additional notice.

During the July 13 - August 12, 2009 inspection, we found that your firm is manufacturing and distributing the prescription drug Opium Tincture USP (Deodorized - 10 mg/mL). Based on our information, there are no FDA-approved applications on file for this drug product. You should contact FDA's unapproved drugs coordinator, Dr. Sally Loewke, at 301-796-0710 for assistance in communicating with the FDA on the application process for your unapproved drug.

The violations cited in this letter are not intended to be an all-inclusive list of your firm's unapproved drugs or statement of violations that exist at your facility. You are responsible for investigating and determining the complete status of all of the drugs manufactured by your firm and the causes of the violations identified above and for preventing their recurrence and the occurrence of other violations. It is your responsibility to assure compliance 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 drug applications listing your facility, until the above violations are corrected. FDA may re-inspect to verify corrective actions have been completed.

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 taken to prevent the recurrence of violations and copies of supporting documentation. If you cannot complete corrective action within fifteen working days, state the reason for the delay and the date by which you will complete the corrective actions. Additionally, your response should state if you no longer manufacture or distribute the drug product(s) manufactured at this facility, and provide date(s) and reason(s) you ceased production.

Finally, we note that the CGMP violations listed in this letter include similar violations to those cited in the June 2006 and September 2008 Warning Letters issued to other Ranbaxy Laboratories facilities (i.e., the corporation). It is apparent that Ranbaxy's attempts to make global corrections after past regulatory actions by the FDA have been inadequate. We remind you that Ranbaxy is responsible for ensuring that all Ranbaxy drug manufacturing operations comply with applicable US requirements, including the CGMP regulations. FDA expects Ranbaxy immediately to undertake a comprehensive assessment of its global manufacturing operations to ensure that all sites manufacturing drug for the US market conform to US requirements.

Your reply should be sent to the attention of Dean Rugnetta, Compliance Officer, at the following address:

Compliance Branch
Food and Drug Administration
300 Pearl St., Suite 100
Buffalo, NY 14202

Sincerely,

/S/

Laurence D. Daurio
Acting District Director
New York District