Apotheca Supply, Inc 4/7/16

April 7, 2016

WARNING LETTER NO. 2016-NOL-02

UNITED PARCEL SERVICE
Delivery Signature Requested

Chris Lemley, President & CEO
Apotheca Supply, Inc. dba Apothecares
3220 Highway 31 South
Building B
Decatur, Alabama 35603-1731

Dear Mr. Lemley:

The U.S. Food and Drug Administration (FDA) inspected your pharmaceutical manufacturing (repackaging and relabeling) facility, Apotheca Supply, Inc. dba Apothecares, at 3220 Highway 31 South, Building B, Decatur, Alabama, from February 10-12, 2015.

We identified significant deviations from current good manufacturing practice (CGMP) for the manufacture of active pharmaceutical ingredients (API).

These deviations cause your drugs to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 United State Code (USC) 351(a)(2)(B), because 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.

We reviewed your February 23, 2015, response in detail; and, note it lacks sufficient corrective actions. We also acknowledge receipt of your subsequent correspondence.

Our investigator observed specific deviations during the inspection, including, but not limited to, the following:

1. Your quality unit failed to review and approve all quality related documents; and, the main responsibilities of your quality unit were not described in writing.

During our inspection, we found your quality unit did not approve your written standard operating procedures (SOPs) for numerous critical processes, such as quality unit responsibilities, expiration date extension, material quarantine, product distribution, equipment cleaning, product return, complaint handling, product recalls,

supplier qualification, raw material testing, and annual product reviews. We also found your quality unit did not review and approve quality-related documents, batch records, certificates of analysis, and the extension of API expiration dates. Specific examples include:

a. Your quality unit did not routinely release or reject all API. We found that your firm's office manager releases your drugs from quarantine to distribution, even though this person is neither identified as a member of your quality unit nor has documented CGMP training.

b. Your quality unit did not routinely complete annual product quality reviews for your repacking operations as required in your SOP *Procedural Review*. This deficiency is similar to deficiencies we found during our June 2009 and January 2010 inspections.

c. Your quality unit did not approve your master production record instructions for the API cyclobenzaprine HCL, estradiol, levofloxacin hemihydrate, and sildenafil citrate.

d. Your quality unit did not review and approve certificates of analysis (CoA) for repackaged API. You generated CoAs by **(b)(4)**. We identified CoA generated by your firm containing inaccurately **(b)(4)** assay specifications and results.

e. You generated inaccurate CoA that extended the expiration date of APIs. Specifically, you extended the expiration dates of coenzyme Q10 USP, carprofen USP, bupivacaine HCL USP, ursodiol EP, and itraconazole EP. You authorized the extension of these expiration dates with signature approvals from employees not identified as members of the quality unit and with no documented CGMP training.

In your response, dated March 23, 2015, you submitted SOP *Responsibilities of the Quality Assurance Unit*, which states your quality assurance unit is responsible for the review and approval of all quality-related documents. Your response is inadequate because you did not provide a risk assessment evaluating the potential effect of your deviations on the quality of API you previously repackaged and released.

In response to this letter, conduct a risk assessment and provide us with a summary of the risks your deviations posed to the quality of your API. Include in your risk assessment all API within expiry that were repackaged and distributed within the United States. Evaluate the product batch records and CoAs not approved by your quality unit and address them in your risk assessment. Ensure each CoA you generated contains accurate information. Also, provide adequate justification for your risk assessment.

Provide your plan for ensuring continuous compliance with your annual product quality review procedure. It is your responsibility to adhere to procedures established at your facility and commitments made in your correspondence to the FDA.

Additionally, provide an organizational chart that specifies the personnel authorized to release API and provide evidence that quality unit personnel are adequately trained in current good manufacturing practice.

2. Your firm failed to have stability data to support the extension of expiration dates.

You extended API manufacturers' expiration dates by as much as two years and listed the new expiration dates in your CoAs for APIs repackaged at your facility. You tested APIs to verify that the results complied with the manufacturers' specifications. However, you did not perform stability testing to ensure that APIs met all specifications for the expiration dates you listed on your CoAs. You have no scientific justification for extending the expiration dates. For example, our investigator found unsupported extension of expiration dates for the following APIs:

API	Lot #	Manufacturer's expiration date	Apotheca's expiration date
Coenzyme Q10 USP	**(b)(4)**	**(b)(4)**	September 2016
Carprofen USP	**(b)(4)**	**(b)(4)**	September 2016
Bupivacaine HCL USP	**(b)(4)**	**(b)(4)**	March 2016 (retest date)
Ursodiol EP powder	**(b)(4)**	**(b)(4)**	August 2016
Itraconazole EP	**(b)(4)**	**(b)(4)**	September 2016

This deviation is similar to one found during our January 2010 inspection of your facility. In your response, you state you have stopped the practice of extending the manufacturer's API expiration dates. In response to this letter, provide a description of your process for ensuring this practice will not recur; and, provide your plan to ensure your CoAs are accurate and complete.

3. Your firm failed to ensure the cleanliness of your facility and equipment.

Your firm weighs and repackages bulk powder APIs including hormones, tricyclics, muscle relaxants, NSAIDS (non-steroidal anti-inflammatory drugs), antifungals and quinolones in non-dedicated suites using non-dedicated equipment. During the inspection, the investigator found expired cleaning products that your cleaning procedure or operators identified as cleaning agents for the suite and equipment. These include **(b)(4)** detergent **(b)(4)** (expiration 10/13), **(b)(4)** (expiration 10/12), and **(b)(4)** Sterile **(b)(4)**(expiration 05/2010). In addition, your operators used cleaning agents that are not documented in your cleaning procedure. Specifically, **(b)(4)** are used to clean surfaces of the non-dedicated suites. Neither of these cleaning agents are listed in your cleaning procedure.

Moreover, you have not performed cleaning validation studies to determine the effectiveness of your current cleaning agents to remove residual powders following repackaging operations in order to prevent cross contamination.

This CGMP deficiency is similar to one we found during our January 2010 inspection. In your response, you state you are developing a cleaning validation program to evaluate the effectiveness of your cleaning process. In response to this letter, provide your cleaning validation protocol, the timeline for its execution, and your justification of its effectiveness for the various drugs you repackage and

cleaning procedures you use. Provide your process for ensuring that no unapproved cleaning agents will be used in your facility.

To ensure your APIs meet the quality and purity characteristics they purport, or are represented to possess, please reference the FDA-issued ICH guidance entitled *Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients* available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073497.pdf.

The deviations cited in this letter are not intended to be an all-inclusive list of deviations that exist at your facility. You are responsible for investigating and determining the causes of the deviations identified above and for preventing their recurrence and the occurrence of other deviations.

If, as a result of receiving this letter or for other reasons, you are considering a decision that could reduce the number of APIs produced by your facility, FDA requests you contact CDER's Drug Shortages Staff immediately at drugshortages@fda.hhs.gov so we can work with you on the most effective way to bring your operations into compliance with the law. Contacting the Drug Shortages Staff also allows you to meet any obligations you may have to report discontinuances in the manufacture of your drug under 21 USC 356C(a)(1); and, allows FDA to consider, as soon as possible, what actions, if any, may be needed to avoid shortages and protect the health of patients who depend on your products. In appropriate cases, you may be able to take corrective action without interrupting supply, or to shorten any interruption, thereby avoiding or limiting drug shortages.

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 15 working days of receipt of this letter, please notify this office in writing of the specific steps you have taken to correct and prevent the recurrence of deviations, and provide copies of supporting documentation. If you cannot complete corrective actions within 15 working days, state the reason for the delay and the date by which you will have completed the corrections. Additionally, if you no longer distribute the APIs at issue, provide the date(s) and reason(s) you ceased production. Please identify your response with FEI No. 3006406317.

Please address all correspondence to Rebecca A. Asente, Compliance Officer, at the address above. If you have questions regarding the contents of this letter, please contact Ms. Asente at (504) 846-6104.

Sincerely,
/S/
Ruth P. Dixon

District Director
New Orleans District