U.S. Department of Health & Human Services

U.S. Food and Drug Administration

Inspections, Compliance, Enforcement, and Criminal Investigations

AMPAC Fine Chemicals, LLC 6/25/10

Department of Health and Human Services

Public Health Service
Food and Drug Administration
San Francisco District
Pacific Region
1431 Harbor Bay Parkway
Alameda, CA 94502-7070
Telephone: 510-337-6700
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Warning Letter

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

June 25, 2010

Mr. Aslam Malik, Ph.D., President
AMPAC Fine Chemicals, LLC
Highway 50 and Hazel Avenue
Rancho Cordova, CA 95670

Dear Dr. Malik:

During our February 9-19, 2010 inspection of your active pharmaceutical ingredient (API) manufacturing facility, AMPAC Fine Chemicals, LLC, located at Highway 50 and Hazel Avenue, Rancho Cordova, CA, investigator(s) from the Food and Drug Administration (FDA) identified significant deviations from Current Good Manufacturing Practice (CGMP) for the manufacture of APIs. These deviations cause your APIs 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.

We have reviewed your firm's response dated March 12, 2010, and note that it lacks sufficient corrective actions.

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

1. Failure to properly maintain buildings used in the manufacture of API production in a manner that prevents contamination.

For example, dirt, blistering paint, rust, and oil droplets were found to be in close proximity to manufacturing equipment in several building locations.

In addition, on January 9,2009, operators observed paint chips in the material while manufacturing Temozolomide API, which was later rejected. Your variance report, **(b)(4)** indicates that paint chips could have fallen into the reactor during solid charging (e.g., during preparation of the crude or during the purification of the material). Your variance report, **(b)(4)** listed **(b)(4)** locations that could have been the source of the contamination. In addition, in the report you stated that the implemented corrective actions following the investigation were not effective and you provided no information concerning subsequent corrective actions implemented to reduce the risk of contamination.

In your response, you state that your cleaning procedures will eliminate the dirt, corrosion, blistering paint, and oil droplets before initiating manufacturing operations. You also state that you currently have adequate "controls and methods of detection" to prevent contamination and/or inadvertent release of product containing foreign matter. However, your response is inadequate because you do not describe such controls and methods of detection.

2. Failure to ensure documentation of cleaning of major equipment after each batch is processed; and failure to clean non-dedicated equipment between the production of different APIs to prevent cross-contamination.

For example, your cleaning log for a processing room (building **(b)(4)**) indicates that cleaning was performed on December 22, 2009. This room was used to manufacture the chlorambucil API from January 4 to 18,2010. On January 22, 2010, the room was released by your Quality Engineer and Production Manager for the manufacture of another material, temozolomide API, without performing any cleaning. According to your **(b)(4)**," the Quality Engineer and Production Manager are required to perform and document a room readiness audit (using the **(b)(4)** Form) verifying that the subject area is clean and suitable for use (including an audit of the cleaning logs) prior to the start of a manufacturing process. Although the cleaning log for the processing room lacked documentation of cleaning, the **(b)(4)** Form contains affirmations that the cleaning log was "complete and up-to-date."

In your response, you state that this occurrence was an "isolated incident, and not indicative of the effectiveness of [your] overall facility audit process." Your response is inadequate because
you do not describe how you will ensure that cleaning was performed or will be performed prior to starting manufacturing operations between different batches of APIs.

3. Failure to identify and quarantine returned APIs.

For example, you stored a drum of returned temozolomide API (batch 07-185-385) in the warehouse storage area with other drums of temozolomide API that were labeled as accepted and ready for release. The returned drum was not properly identified (e.g., tag or attached status

label).

In your response, you state that you have developed new procedures regarding rejected batches. Your response is inadequate because you have not addressed how you will manage returned APIs. It is your responsibility to ensure that returned APIs are properly identified and quarantined separately from material approved for distribution.

The deviations detailed in this letter are not intended to be an all-inclusive statement 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. It is your responsibility to assure compliance with all requirements of federal law and FDA regulations.

You should take prompt action to correct the deviations detailed in this letter. Failure to promptly correct these deviations 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 deviations are corrected. FDA may re-inspect to verify corrective actions have been completed.

Within fifteen (15) working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct deviations. Include an explanation of each step
taken to prevent the recurrence of deviations and copies of supporting documentation. If you cannot complete corrective action within fifteen (15) working days, state the reason for the delay and the date by which you will have completed the correction.

Your reply should be sent to the following address: Mr. Carl Lee, Compliance Officer, Food and Drug Administration, San Francisco District, Pacific Region, 1431 Harbor Bay Parkway, Alameda, CA 94502. If you have any questions about the content of this letter please contact Mr. Lee at (510) 337-6737 or by fax at (510) 337-6703.

Sincerely,
/S/

Gerald Berg

Acting District Director

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