WARNING LETTER

Adamson Analytical Laboratories, Inc.

MARCS-CMS 614644 — AUGUST 17, 2021

Delivery Method:

Via Email

Product:

Drugs

Recipient:

Mr. Peter B. VanCouvering

General Manager/CEO

Adamson Analytical Laboratories, Inc.

220 Crouse Dr.
Corona, CA 92879-8093
United States

Issuing Office:

Division of Pharmaceutical Quality Operations IV

United States

WARNING LETTER

August 17, 2021

Dear Mr. VanCouvering:

The U.S. Food and Drug Administration (FDA) inspected your contract testing laboratory, Adamson Analytical Laboratories, Inc., FEI: 3000204955, at 220 Crouse Dr., Corona, California, from March 8 to 23, 2021. Our inspection determined that you are a contract testing laboratory for prescription and over-the-counter finished drug products and active pharmaceutical ingredients (API).

This warning letter summarizes significant violations of Current Good Manufacturing Practice (CGMP) regulations for finished pharmaceuticals. See Title 21 Code of Federal Regulations (CFR), parts 210 and 211 (21 CFR parts 210 and 211).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drugs are adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

We reviewed your April 13, 2021, response to our Form FDA 483 in detail and acknowledge receipt of your subsequent correspondence. Your response is inadequate because it did not provide sufficient detail or evidence of corrective actions to bring your operations into compliance with CGMP.

During our inspection, our investigators observed specific violations including, but not limited to, the following.

1. Your firm failed to exercise appropriate controls over computer or related systems to assure that only authorized personnel institute changes in master production and control records, or other records (21 CFR 211.68(b)).

Your firm lacked sufficient controls over your gas chromatography (GC) data acquisition systems used to test drug product before release of analytical data. Specifically, your GC (GC **(b)(4)** and GC **(b)(4)**) data acquisition systems did not have sufficient controls to prevent deletion or alteration of raw data files. During the inspection, our investigators observed that laboratory personnel performing drug analyses had administrative privileges to the **(b)(4)** operating software for the GC equipment. These privileges included, but were not limited to, the ability to delete data sequences, change and/or delete methods, as well as enable and disable audit trails.

In addition, from at least April 2018, until February 2021, the high performance liquid chromatography (HPLC) and GC instruments were found to be operating in the absence of an activated audit trail to record information about each analytical test, such as:

- Type of injection
- Date and time
- Identity of analyst
- Reason for action taken (e.g., modifying a record)

You have also failed to validate electronic worksheets used by laboratory personnel for microbial challenge efficacy testing. Microbial worksheets reviewed were found to use unvalidated cell formulas resulting in erroneous data generation such as negative log reductions and percent reductions including **(b)(4)** percent and **(b)(4)** percent for *Staphylococcus aureus* and *Pseudomonas aeruginosa* species, respectively. These unvalidated calculations call into question the validity of the data generated from these spreadsheets.

We acknowledge that your firm changed ownership and had implemented a new organizational structure, as well as assigned new responsible individuals in April 2018. However, this is a repeat violation observed at your facility in a previous warning letter (WL # 38-16, dated August 2, 2016), in which FDA cited a similar CGMP violation. The previous management proposed specific remediation for the violation in their August 22, 2016, response to the warning letter. However, repeated failures and delays in the implementation of appropriate controls demonstrate that executive management oversight and control over laboratory operations remain inadequate. We also note that you use the same processes to test both human drug products and API.

In your response, you committed to changing analyst privileges to prevent **(b)(4)** Administrator rights for employees who perform analyses. However, the supporting documentation provided in additional correspondence demonstrates that you did not implement the appropriate controls to which you had committed. Specifically, the users continue to have improper administrative privileges.

Your customers rely on the integrity of the laboratory data that you generate to make decisions regarding drug quality. It is important to maintain strict control over CGMP electronic data to ensure that all laboratory data is retained and that all additions, deletions, or modifications of information in your electronic records are authorized and appropriately documented.

In addition, you committed to performing **(b)(4)** reviews of only a subset of audit trails for future laboratory analyses. Your response is inadequate because 21 CFR 211.22 requires data review prior to batch release including audit trail data. In response to this letter provide:

• A list of all laboratory instruments and software identifying which have activated audit trails.

• Documentation verifying configuration changes for GC-**(b)(4)** and GC-**(b)(4)** employee-specific data privileges which you state have been corrected for all analysts and applicable operating software for electronic laboratory equipment.

• A list of all software configurations (both equipment software and laboratory information system (LIMS)), details of all user privileges up to and including administrator rights, and oversight roles for each of your laboratory systems. Regarding user privileges, specify user roles and associated user privileges for all staff levels who have access to the laboratory computer systems and their organizational affiliation and title. Describe in detail how you will ensure that administrative privileges are fully segregated and completely independent of QU laboratory personnel.

• Your action plan, with timelines, describing your interim controls and when audit trails will be enabled for all applicable laboratory instruments and electronic data systems, as well as when procedures will be implemented for the review of audit trails before release of analytical results subject to CGMP.

• Your investigation into the failure to enable the audit trail functionality in your laboratory instruments and electronic data systems and the impact this recurring failure could have on generated data.

2. Your firm failed to establish and follow required laboratory control mechanisms (21 CFR 211.160(a)).

You failed to adequately control critical changes to electronic laboratory monitoring operations using documentation, assessment, and approval of the QU. Specifically, critical changes to laboratory operations without QU oversight included, but are not limited to, the following:

• Implementation of electronic worksheets for tracking and monitoring standards and reagents

• Changes to microbial testing worksheets pre-populated with analyst identification

• Activation of instrument software audit trails on February 16, 2021, without any governing procedures or change control.

In your response, you committed to updating your change control form (PAR A-0037) as well as your written procedure governing change control over laboratory operations. We could not determine the adequacy of your response because you did not provide copies of PAR A-0037 and the updated Standard Operating Procedure for our review. In addition, you've failed to commit to a systematic retrospective review of changes implemented to your operations as well as the applicable impact to drug analyses subject to CGMP.

In response to this letter provide:

A comprehensive, independent assessment of your change management system. This assessment should include, but not be limited to, your procedures to ensure changes are justified, reviewed, and approved by your quality assurance unit. Your change management program should also include provisions for determining change effectiveness.

Data Integrity Remediation

Your quality system does not adequately ensure the accuracy and integrity of data to support the safety, effectiveness, and quality of the drugs you test. See FDA's guidance document *Data Integrity and Compliance With Drug CGMP* for guidance on establishing and following CGMP compliant data integrity practices at https://www.fda.gov/media/119267/download (/media/119267/download).

We strongly recommend that you retain a qualified consultant to assist in your remediation. In response to this letter, provide the following:

A. A comprehensive investigation into the extent of any inaccuracies in data records and reporting including results of the data review for drugs distributed to the United States. Include a detailed description of the scope and root causes of your data integrity lapses.

B. A current risk assessment of the potential effects of the observed failures on the quality of your drugs. Your assessment should include analyses of the risks to patients caused by the release of drugs affected by a lapse of data integrity and analyses of the risks posed by ongoing operations.

C. A management strategy for your firm that includes the details of your global corrective action and preventive action plan. The detailed corrective action plan should describe how you intend to ensure the reliability and completeness of all data generated by your firm including microbiological and analytical data, laboratory records, and all data submitted to FDA.

Responsibilities of a Contract Testing Lab

FDA considers contractors as extensions of the manufacturer's own facility. Your failure to comply with CGMP may affect the quality, safety, and efficacy of the drugs you test for your clients. It is essential that you understand your responsibility to operate in full compliance with CGMP, and that you inform all your customers of any out-of-specification results or significant problems encountered during the testing of these drugs. For additional information refer to FDA Guidance for Industry Contract Manufacturing Arrangements for Drugs: Quality Agreements (https://www.fda.gov/media/86193/download (/media/86193/download)).

CGMP Consultant Recommended

Because you failed to correct repeat violations, we strongly recommend engaging a consultant qualified as set forth in 21 CFR 211.34 to assist your firm in meeting CGMP requirements. Your use of a consultant does not relieve your firm's obligation to comply with CGMP. Your firm's executive management remains responsible for resolving all deficiencies and systemic flaws to ensure ongoing CGMP compliance.

Conclusion

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

Correct any violations promptly. Failure to promptly and adequately address this matter may result in regulatory or legal action without further notice including, without limitation, seizure, and injunction. Unresolved violations may also prevent other Federal agencies from awarding contracts.

Failure to address violations may also cause FDA to withhold issuance of Export Certificates. FDA may withhold approval of new applications or supplements listing your firm as a contract testing laboratory until any violations are completely addressed and we confirm your compliance with CGMP. We may re-inspect to verify that you have completed corrective actions to address any violations.

This letter notifies you of our findings and provides you an opportunity to address the above deficiencies. After you receive this letter, respond to this office in writing within 15 working days. Specify what you have done since our inspection to correct your violations and to prevent their recurrence. In response to this letter, you may provide additional information for

our consideration as we continue to assess your activities and practices. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion.

Send your electronic reply to ORAPHARM4_Responses@FDA.HHS.GOV or mail your reply to:

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV
U.S. Food & Drug Administration
19701 Fairchild Road
Irvine, California 92612-2506

Please identify your response with unique identifier **614644**.

If you have any further questions, please contact Nayan Patel, Compliance Officer, by email at Nayan.Patel1@fda.hhs.gov or by phone at (303) 236-3010.

Sincerely,
/S/

Steven E. Porter, Jr.
Program Division Director
Division of Pharmaceutical Quality Operations IV

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