Cellex-C International Inc. 8/2/17

10903 New Hampshire Avenue
Silver Spring, MD 20993

Via UPS
Return Receipt Requested

Warning Letter 320-17-44

August 2, 2017

Mr. John Chilver
President
Cellex-C International Inc.
9 New St.
Toronto, Ontario M5R 1P7
Canada

Dear Mr. Chilver:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Cellex-C International Inc. at 9 New Street, Toronto, from January 16 to 19, 2017.

This warning letter summarizes significant violations of current good manufacturing practice (CGMP) regulations for finished pharmaceuticals. See 21 CFR, parts 210 and 211.

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drug products 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 February 7, 2017, response in detail.

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

1. Your firm failed to have, for each batch of drug product, appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient, prior to release (21 CFR 211.165(a)).

You released your **(b)(4)** drug products without testing any of them for conformance to specifications, including identity and strength.

Your response indicated that you will have a contract laboratory test all finished drugs for active ingredients. Your response is inadequate because it lacks sufficient detail about the selection, qualification, and oversight procedures you will use to engage your contract testing laboratory. You also have not provided your action plan and timelines for conducting tests to determine the identity and strength of active ingredients in all drug products within expiry that you previously released without performing such testing.

2. Your firm failed to test samples of each component for conformity with all appropriate written specifications for identity, purity, strength, and quality (21 CFR 211.84(d)(1), (2)).

You failed to test incoming active pharmaceutical ingredients and other components you use in manufacturing **(b)(4)** drug products to determine their identity, purity, strength, or other appropriate specifications.

Your response claimed that because it is not feasible for you to perform component identification testing, you would instead rely on your supplier's certificate of analysis (COA) for the identity of each incoming component. Your response is inadequate for two reasons. First, you must conduct at least one specific identity test to analyze all incoming components. You may not rely on your supplier's COA to verify the identity of your components. Your response was also inadequate because you did not indicate how you would address your failure to test all incoming components for specifications other than identity.

3. Your firm failed to establish written responsibilities and procedures applicable to the quality control unit (21 CFR 211.22(d)).

Your firm lacked critical procedures to ensure that your quality unit has the appropriate authority to carry out its responsibilites. You lacked, for example, procedures to handle complaints and review production records.

According to your response, you will establish a quality procedure with "clear job descriptions." Your response is inadequate because you failed to provide this proposed written procedure, and because you have not demonstrated how establishing "clear job descriptions" will ensure that your firm has appropriate written responsibilities and procedures applicable to the quality control unit.

4. Your firm failed to establish adequate written procedures for production and process control designed to assure that the drug products you manufacture have the identity, strength, quality, and purity they purport or are represented to possess (21 CFR 211.100(a)).

You have not validated the manufacturing processes for your drug products. You lack assurance that your manufacturing processes result in batch uniformity, integrity, and consistent drug quality.

In your response, you committed to validating the manufacturing processes for your drug products. Your response is inadequate because you did not provide an action plan and timelines for validating your drug manufacturing processes.

5. Your firm failed to prepare batch production and control records with complete information relating to the production and control of each batch of drug product produced (21 CFR 211.188).

Your batch production records were incomplete. They lacked information regarding critical steps in your filling and packaging operations.

According to your response, you have revised your manufacturing formulation worksheet. Your response is inadequate. The worksheets you provided still omitted information about your manufacturing processes, such as identification of all critical equipment used during manufacturing, descriptions of the final drug product containers and closures, and details about in-process and finished product sampling.

CGMP consultant recommended

Based upon the nature of the violations we identified at your firm, 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 fully resolving all deficiencies and ensuring ongoing CGMP compliance.

Conclusion

Violations cited in this letter are not intended as an all-inclusive list. You are responsible for investigating these violations, for determining the causes, for preventing their recurrence, and for preventing other violations.

FDA placed your firm on Import Alert 66-40 on June 2, 2017.

Until you correct all violations completely and we confirm your compliance with CGMP, FDA may withhold approval of any new applications or supplements listing your firm as a drug manufacturer.

Failure to correct these violations may also result in FDA continuing to refuse admission of articles manufactured at Cellex-C International Inc., 9 New Street, Toronto, into the United States under section 801(a)(3) of the FD&C Act, 21 U.S.C. 381(a)(3). Under the same authority, articles may be subject to refusal of admission, in that the methods and controls used in their manufacture do not appear to conform to CGMP within the meaning of section 501(a)(2)(B) of the FD&C Act, 21 U.S.C. 351(a)(2)(B).

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. 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 **CDER-OC-OMQ-Communications@fda.hhs.gov (mailto:CDER-OC-OMQ-Communications@fda.hhs.gov)** or mail your reply to:

Daniel W. Brisker
Consumer Safety Officer
U.S. Food and Drug Administration
White Oak Building 51, Room 4359
10903 New Hampshire Avenue
Silver Spring, MD 20993
USA

Please identify your response with FEI 3003525539.

Sincerely,
/S/
Thomas J. Cosgrove
Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research