Cosmecca Korea Co., Ltd. 2/2/18

10903 New Hampshire Avenue
Silver Spring, MD 20993

Via UPS **Warning Letter** 320-18-30
Return Receipt Requested

February 2, 2018

Mr. Im-Rae Cho
Chairman
Cosmecca Korea Co., Ltd.
17-12 Daegeum-ro 196 beon-gil, Daeso-myeon
Eumseong-gun, Chungcheongbuk-do, 27670
Korea

Dear Mr. Cho:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Cosmecca Korea Co., Ltd. at 17-12 Daegeum-ro 196 beon-gil, Daeso-myeon, Eumseong-gun, Chungcheongbuk-do, from September 18 to 22, 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 October 23, 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 over-the-counter (OTC) **(b)(4)** drug products without data to support their conformance to specifications (e.g., strength). During our investigator's review of batch records for five of your OTC products, you could not provide analytical data to support the release of these products. One of your lab personnel also stated that you did not test every lot of finished products prior to release.

2. Your firm failed to ensure that laboratory records included complete data derived from all tests necessary to assure compliance with established specifications and standards (21 CFR 211.194(a)).

Our investigator documented multiple examples of falsifying laboratory records. Your quality control laboratory employee stated that he fabricated laboratory data for untested finished drug products by manipulating electronic laboratory records. For example, he changed the file names for test results of previously tested drugs so that the file names appeared to reflect the results of other lots of product. Your firm used this falsified laboratory data to determine the strength of your OTC **(b)(4)** drug products. Your response stated that your quality assurance manager instructed laboratory analysts to manipulate, falsify, or fabricate data.

3. Your firm's quality control unit failed to review and approve all drug product production and control records to determine compliance with all established, approved written procedures before a batch is released or distributed (21 CFR 211.192).

Your OTC sunscreen drug product, **(b)(4)**, contains **(b)(4)** active ingredients: **(b)(4)**. Your batch records for lot **(b)(4)** of this product included concentration values for these active ingredients that did not match the data found in your instruments. You used the inaccurate data reported in your batch records to calculate potency results that were within specification, and you relied on these inaccurate results to release your product. However, when we used the instrument data instead of the results in your batch records to perform the same calculations, we found that the lot was out-of-specification (OOS) (superpotent) for **(b)(4)** active ingredients. Your quality unit did not identify this discrepancy prior to releasing this lot.

4. 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)).

Laboratory equipment used to generate analytical data for release purposes lacked restricted access. For example, analysts shared usernames and passwords, and all users had administrator rights that permitted them to delete or modify files in high-

performance liquid chromatography and *gas chromatography* equipment. You had no mechanism to facilitate traceability of the individuals who changed, adjusted, or modified data generated by computerized systems.

5. Your firm failed to establish laboratory controls that include scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity (21 CFR 211.160(b)).

Our investigator found that you failed to test incoming active pharmaceutical ingredients used to manufacture finished products for the United States using the U.S. Pharmacopeia (USP). Your specifications allow a higher level of impurities, such as **(b)(4)** and **(b)(4)**, than the limits established by USP.

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.

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 manufacture. We acknowledge that you are using a consultant to audit your operation and assist in meeting FDA requirements.

In response to this letter, provide the following.

A. A comprehensive investigation into the extent of the inaccuracies in data records and reporting. Your investigation should include:

- A detailed investigation protocol and methodology; a summary of all laboratories, manufacturing operations, and systems to be covered by the assessment; and a justification for any part of your operation that you propose to exclude.
- Interviews of current and former employees to identify the nature, scope, and root cause of data inaccuracies. We recommend that these interviews be conducted by a qualified third party.
- An assessment of the extent of data integrity deficiencies at your facility. Identify omissions, alterations, deletions, record destruction, non-contemporaneous record completion, and other deficiencies. Describe all parts of your facility's operations in which you discovered data integrity lapses.

- A comprehensive retrospective evaluation of the nature of the testing data integrity deficiencies. We recommend that a qualified third party with specific expertise in the area where potential breaches were identified should evaluate all 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 analysesof the risks to patients caused by the release of drugs affected by a lapse of data integrity, and 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. Your strategy should include:

- A detailed corrective action plan that describes how you intend to ensure the reliability and completeness of all the data you generate, including analytical data, manufacturing records, and all data submitted to FDA.
- A comprehensive description of the root causes of your data integrity lapses, including evidence that the scope and depth of the current action plan is commensurate with the findings of the investigation and risk assessment. Indicate whether individuals responsible for data integrity lapses remain able to influence CGMP-related data at your firm.
- Interim measures describing the actions you have taken or will take to protect patients and to ensure the quality of your drugs, such as notifying your customers, recalling product, conducting additional testing, adding lots to your stability programs to assure stability, drug application actions, and enhanced complaint monitoring.
- Long-term measures describing any remediation efforts and enhancements to procedures, processes, methods, controls, systems, management oversight, and human resources (e.g., training, staffing improvements) designed to ensure the integrity of your company's data.
- A status report for any of the above activities already underway or completed.

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 January 8, 2018.

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 17-12 Daegeum-ro 196 beon-gil, Daeso-myeon, Eumseong-gun, Chungcheongbuk-do, 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 or mail your reply to:

Ms. Rebecca Parrilla
Compliance 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 3010165567.

Sincerely,
/S/
Francis Godwin
Director
Office of Manufacturing Quality
Office of Compliance
Center for Drug Evaluation and Research