Degasa S.A. De C.V. 4/18/18

U.S. FOOD & DRUG ADMINISTRATION

10903 New Hampshire Avenue
Silver Spring, MD 20993

Via UPS
Return Receipt Requested

Warning Letter 320-18-46

April 18, 2018

Mr. Guillermo Rodriguez Fernandez
Managing Director
Degasa S.A. De C.V.
Prolongación Canal de Miramontes No. 3775
Col. Ex Hacienda San Juan C.P. 14300
Delegación Tlalpan
Ciudad de México
México

Dear Mr. Fernandez:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Degasa S.A. De C.V. at Calle 13 Este No. 580, Civac, Juitepec, Morelos, from September 4 to 8, 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).

In addition, your drug products Dynarex Povidone Iodine Prep Solution, Dynarex Povidone Iodine Surgical Scrub Solution, Dukal Povidone Iodine USP 10% Prep Solution, Dukal Antiseptic Sudsing Skin Cleanser Scrub Solution, and Medi Choice Scrub Solution Antiseptic Bactericidal Sudsing Skin Cleanser are misbranded under section

502(c) of the FD&C Act, 21 U.S.C. 352(c). Furthermore, your drug products Dynarex Povidone Iodine Prep Solution, Dynarex Povidone Iodine Surgical Scrub Solution, Cardinal Health Scrub Solution Povidone Iodine 7.5% (32 fl. oz.), and Cardinal Health Scrub Solution Povidone Iodine 10% (32 fl. oz.) are misbranded under section 502(x) of the FD&C Act, 21 U.S.C. 352(x).

We reviewed your September 28, 2017, response in detail and acknowledge receipt of your subsequent correspondence.

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

1. Your firm does not have, for each batch of drug product, appropriate laboratory testing, as necessary, of each batch of drug product required to be free of objectionable microorganisms (21 CFR 211.165(b)).

Your firm failed to implement adequate microbial testing for your drug products. For example, your povidone-iodine antiseptic products are intended for significant indications such as "**(b)(4)**," "preparation of skin prior to surgery," "prevent infection in minor cuts, scrapes, and burns," "**(b)(4)**," and "helps to reduce bacteria that can potentially cause skin infection." You lacked testing of these products for microbial attributes, including absence of objectionable microbial contamination, or sterility, where appropriate.

It is essential that your drug products are produced in a manner that is suitable for their intended uses and that each batch is tested for conformance to appropriate microbial quality specifications.

In your response to this letter, address the following:

- An action plan for promptly testing retain samples of all batches in the U.S. market that are still within expiry to determine their microbial quality. These tests should be performed and results provided to the FDA within 30 days of receipt of this letter. Include complete analytical records for each of these tests, and full information on the name and location of the testing laboratory performing the analyses. If any test results reveal that you released drug products that did not meet appropriate microbial specifications, specify the corrective actions you have taken or will take, including notifying customers or recalling products.
- For each of your drug products, provide microbiological test methods and finished product release specifications for microbiological quality. Include tests for either microbial limits (i.e., total counts and objectionable microbes) or sterility, depending on the intended use of the product.
- Provide validation studies for each microbiological testing method (e.g., microbial limits, sterility, antimicrobial effectiveness) used for your drug products.
- Provide an independent, comprehensive assessment of the manufacturing operations used to manufacture each of your topical drug products, with special emphasis on material inputs, enhanced bioburden controls, and contamination prevention.

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)).

Your firm was unable to provide complete raw data related to the qualification of your "**(b)(4)**" water system. You lacked basic information (including missing sanitization data) to assess water system performance. According to your employee, half the data you generated over a year was lost.

Your laboratory also lacked data such as weight of samples, test methods, records of calculations performed, standards used for release of final products, and water monitoring data.

Our inspection also indicated that your water system is not suitable for its intended use. Specifically, our findings indicate that your water system was not appropriately designed, controlled, and maintained to consistently produce high-purity water.

Water is a major ingredient in your drug products. It is essential that you employ a water system that is robustly designed, and that you effectively control, maintain, and monitor the system to ensure it consistently produces water suitable for pharmaceutical use that conforms to the USP monograph for purified water and appropriate microbial standards.

We acknowledge your commitment to update your procedure for laboratory records. However, you did not address how you will assure that procedures are appropriate, properly implemented, and followed. You also did not adequately address the impact of your insufficient data on decisions made by your firm regarding manufacturing and product quality.

In your response to this letter, provide the following:

- A comprehensive independent evaluation of the water system design, including a thorough corrective action and preventive action plan (CAPA) to install and validate a suitable water system.
- An effective program for ongoing control, maintenance, and routine monitoring that ensures the remediated system consistently produces water that meets USP Purified Water monograph specifications and appropriate microbial limits. Regarding the latter, your topical products necessitate significantly tighter total count action limits than those currently used by your firm.
- Investigation of the missing water system data, including root causes, and your CAPA plan. Include a risk assessment of the impact on product quality of using water from this system in the manufacture of your drug products.
- A retrospective review of both in-process and finished product test results to determine where product quality may have been compromised due to your practice of not maintaining complete analytical data.
- A comprehensive assessment of the documentation systems used throughout your manufacturing and laboratory operations to determine where else you lack complete records. Include a detailed CAPA plan with systemic remediations to assure your facility maintains complete records. The CAPA should include, but not be limited to, revised procedures, training, and systemic actions implemented to assure integrity of all CGMP records.

Quality Unit Authority

Significant findings in this letter indicate that your quality unit is not able to fully exercise its authority and/or responsibilities. Your firm must provide the quality unit with the appropriate authority, sufficient resources, and staff to carry out its responsibilities and consistently ensure drug quality.

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. The third-party review of your operation should comprehensively assess and assist with remediating your operations, including but not limited to: water system, process design and bioburden control, the laboratory system, equipment, facilities, microbiology specifications, qualification/validation program, and the quality unit.

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.

Misbranding Charges

"Dukal Povidone Iodine USP 10% Prep Solution, Dukal Antiseptic Sudsing Skin Cleanser Scrub Solution, Medi Choice Scrub Solution Antiseptic Bactericidal Sudsing Skin Cleanser, Dynarex Povidone Iodine Prep Solution, Dynarex Povidone Iodine Surgical Scrub Solution, Cardinal Health Povidone Iodine Scrub Solution Povidone Iodine 7.5% (32 fl. oz.) and Cardinal Health Povidone Iodine Scrub Solution Povidone Iodine 10% (32 fl. oz.)"

Examples of claims observed on your product labels for Dukal Povidone Iodine USP 10% Prep Solution, Dukal Antiseptic Sudsing Skin Cleanser Scrub Solution, Medi Choice Scrub Solution Antiseptic Bactericidal Sudsing Skin Cleanser, Dynarex Povidone Iodine Prep Solution, Dynarex Povidone Iodine Surgical Scrub Solution, Cardinal Health Povidone Iodine Scrub Solution Povidone Iodine 7.5% (32 fl. oz.) and Cardinal Health Povidone Iodine Scrub Solution Povidone Iodine 10% (32 fl. oz.) that establish the intended uses of the products include, but may not be limited to, the following:

Dukal Povidone Iodine USP 10% Prep Solution Prep Solution and Dukal Antiseptic Sudsing Skin Cleanser Scrub Solution

Dukal Povidone Iodine USP 10% Prep Solution:

"…for preparation of the skin prior to surgery"
"First aid antiseptic to help prevent infection in minor cuts, scrapes and burns"

Dukal Antiseptic Sudsing Skin Cleanser Scrub Solution:

"…for preparation of the skin prior to surgery"
"…for handwashing to reduce bacteria on the skin"

Medi Choice Scrub Solution Antiseptic Bactericidal Sudsing Skin Cleanser (Medi Choice Skin Cleanser)

"Scrub Solution"
"For preparation of the skin prior to surgery"
"…for handwashing to reduce bacteria on the skin"

Dynarex Povidone Iodine Prep Solution and Dynarex Povidone Iodine Surgical Scrub Solution

"A primary professional/hospital antiseptic and medicated cleanser"
"Effective in destroying certain bacteria…to provide antiseptic and wound cleansing"

Cardinal Health Povidone Iodine Scrub Solution Povidone Iodine 7.5% (Cardinal Health Scrub Solution Povidone Iodine 7.5%) and Cardinal Health Povidone Iodine Scrub Solution Povidone Iodine 10% (Cardinal Health Scrub Solution Povidone Iodine 10%)

"Antiseptic / First Aid Antiseptic"
"For preparation of the skin prior to surgery"

Based on the above claims, Dukal Povidone Iodine USP 10% Prep Solution, Dukal Antiseptic Sudsing Skin Cleanser Scrub Solution, Medi Choice Scrub Solution Antiseptic Bactericidal Sudsing Skin Cleanser, Dynarex Povidone Iodine Prep Solution, Dynarex Povidone Iodine Surgical Scrub Solution, Cardinal Health Povidone Iodine Scrub Solution Povidone Iodine 7.5% (32 fl. oz.) and Cardinal Health Povidone Iodine Scrub Solution Povidone Iodine 10% (32 fl. oz.) are "drugs" as defined by section 201(g)(1)(B) of the FD&C Act, 21 U.S.C. 321(g)(1)(B), because they are intended for the diagnosis, cure, mitigation, treatment, or prevention of disease, and/or under

section 201(g)(1)(C) of the FD&C Act, 21 U.S.C. 321(g)(1)(C), because they are intended to affect the structure or any function of the body. Specifically, these products are intended as patient preoperative skin preparations and/or surgical scrubs.

Drug products such as Dukal Povidone Iodine USP 10% Prep Solution, Dukal Antiseptic Sudsing Skin Cleanser Scrub Solution, Medi Choice Scrub Solution Antiseptic Bactericidal Sudsing Skin Cleanser, Dynarex Povidone Iodine Prep Solution, Dynarex Povidone Iodine Surgical Scrub Solution, Cardinal Health Povidone Iodine Scrub Solution Povidone Iodine 7.5% (32 fl. oz.) and Cardinal Health Povidone Iodine Scrub Solution Povidone Iodine 10% (32 fl. oz.) intended as Topical Antimicrobials are being evaluated as part of the OTC Drug Review. The labeling for such drugs, like all OTC drugs, must comply with all the requirements of section 502 of the FD&C Act and all pertinent regulations found in Title 21 of the Code of Federal Regulations (21 CFR). However, your products are misbranded for the reasons provided below.

Dukal Povidone Iodine USP 10% Prep Solution and Dukal Antiseptic Sudsing Skin Cleanser Scrub Solution are misbranded under section 502(c) of the FD&C Act, 21 U.S.C. 352(c). Specifically, their labels contain labeling information in English, Spanish and French. Dual language labeling with English and another language is permissible when labeled in accordance to 21 CFR 201.15 and not otherwise false or misleading. Please note, 21 CFR 201.15 states that “all words, statements, and other information required by or under authority of the act to appear on the label or labeling shall appear thereon in the English language” . . . and “if the label contains any representation in a foreign language, all words, statements, and other information required by or under authority of the act to appear on the label shall appear thereon in the foreign language.” These statements describe what conditions must be met if you wish to have your OTC drug label contain both English and a foreign language. If you wish to distribute dual-language (English/Spanish or English/French) versions of OTC drug labels and labeling, you are responsible for ensuring that such labels and labeling are complete and accurate. The labels for Dukal Povidone Iodine USP 10% Prep Solution and Dukal Antiseptic Sudsing Skin Cleanser Scrub Solution are not labeled in accordance to 21 CFR 201.15 because their labels do not include a “Drug Facts” panel in Spanish and French.

Dukal Antiseptic Sudsing Skin Cleanser Scrub Solution and Medi Choice Skin Cleanser are misbranded within the meaning of section 502(c) of the FD&C Act, 21 U.S.C. 352(c), because the label fails to bear a complete statement of identity as required under 21 CFR 201.61. In the case of a drug that has an established name, the statement of identity must contain the established name and the general pharmacological action(s) or principal intended action(s) of the drug in the principal display panel. The labels for these products fails to include the established name of the drug, povidone iodine, as part of the statement of identity.

Dynarex Povidone Iodine Prep Solution and Dynarex Povidone Iodine Surgical Scrub Solution are not labeled in accordance with the “Drug Facts” labeling requirements described in 21 CFR 201.66. Therefore, these products are misbranded under section 502(c) of the FD&C Act, 21 U.S.C. 352(c), because the information that is required to appear on the labeling is not prominently placed thereon with such conspicuousness and in such terms, as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use. Specifically, their labels lack the “Drug Facts” title and formatting as specified under 21 CFR 201.66.

Furthermore, Dynarex Povidone Iodine Prep Solution, Dynarex Povidone Iodine Surgical Scrub Solution, Cardinal Health Scrub Solution Povidone Iodine 7.5% and Cardinal Health Scrub Solution Povidone Iodine 10% are misbranded under Section 502(x) of the FD&C Act, 21 U.S.C. 352(x), because the products’ labels fail to disclose a domestic address or domestic telephone number through which the responsible person may receive a report of a serious adverse event with such drug. Please note that Section 201(k) of the FD&C Act defines the term "label" as "...a display of written, printed, or graphic matter upon the immediate container of any article; and a requirement made by or under the authority of the FD&C Act that any word, statement, or other information appear on the label shall not be complied with unless such…also appears on the outside container….”

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.

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 refusing admission of articles manufactured at Degasa S.A. De C.V. at Calle 13 Este No. 580, Civac, Juitepec, Morelos, 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:

Ms. Chhaya Shetty
Interdisciplinary Scientist, 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 3004555163.

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

cc: Ms. Veronica Ley Fuentes
Corporate Manager of Quality Assurance and Regulatory Affairs
Degasa S.A. De C.V.

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