Phase 4 Pharmaceutical LLC 4/18/18

U.S. FOOD & DRUG ADMINISTRATION

Office of Pharmaceutical Quality Operations,
Division 2
4040 N. Central Expressway, Suite 300
Dallas, Texas 75204

April 18, 2018

CMS Case # 533923

WARNING LETTER

VIA UPS OVERNIGHT

Stephen M. Lapidus, Owner
Phase 4 Pharmaceutical, LLC
21055 N.E. 37th Ave., Suite 2202
Aventura, Florida 33014

Mr. Lapidus:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Phase 4 Pharmaceutical, LLC (FEI: 3008862488) at 21055 N.E. 37th Ave., Suite 2202, Aventura, Florida 33014, from April 26 to May 2, 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 May 22, 2017, response in detail.

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

1. Your firm failed to establish a quality control unit with the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging materials, labeling, and drug products (21 CFR 211.22(a)).

Your firm repackages over-the-counter (OTC) transdermal patch drug products in zippered plastic bags. You lacked a quality control unit for your drug repackaging operation and you lacked written procedures for repackaging operations and quality control unit responsibilities.

In your response, you provided a quality control procedure that references food regulations that are not applicable to drug product manufacturing. You also state you have the “intention to migrate all of our skin patches to non-drug forms, such as homeopathic topical applications.”

Note that Section 201(g)(1) of the FD&C Act (21 U.S.C. 321(g)(1)) defines the term "drug" to mean articles recognized in the official United States Pharmacopeia (USP), official Homeopathic Pharmacopeia of the United States (HPUS), or official National Formulary (NF), or any supplement to them. Simply switching your products to “homeopathic topical applications” will not necessarily render your products “non-drug forms.” Moreover, homeopathic drugs generally must meet the standards for strength, quality, and purity set forth in the Homeopathic Pharmacopeia, and homeopathic drug products must be manufactured in conformance with current good manufacturing practice. See sections 501(b) and 501(a)(2)(B) of the FD&C Act and 21 CFR parts 210 and 211.

In your response to this letter, provide your procedure detailing the responsibilities of the quality control unit, and outline your repackaging operations with their corresponding procedures as required by drug CGMP regulations.

See FDA’s guidance document, Quality Systems Approach to Pharmaceutical CGMP Regulations, for help implementing quality systems and risk management approaches that meet the requirements of drug CGMP regulations (21 CFR parts 210 and 211), at
https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070337.pdf (https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070337.pdf)

2. Your firm failed to establish and follow written procedures designed to assure that correct labels, labeling, and packaging materials are used for the products, including procedures to prevent mix-ups and crosscontamination by physical or spatial separation from operations on other drug products (21 CFR 211.130(a))

Your firm lacks controls and/or records necessary to prevent product mix-ups during repackaging and labeling operations. Your firm receives bulk deliveries of different kinds of transdermal patches from a contract manufacturer, and you then repackage your drug products into zippered plastic bags along with the product labels. These different drug products are similar in appearance and have no identifying labels on them, which may result in product and labeling mix-ups at your firm.

In response to this letter, provide a detailed action plan describing the changes and improvements made in your packaging and labeling operations to control the possibility of product/labeling mix-ups.

3. Your firm failed to establish a system by which the distribution of each lot of drug product can be readily determined to facilitate its recall if necessary (21 CFR 211.150(b)).

Your firm lacked any procedures describing your drug distribution system. You do not document the lot numbers of products distributed, and therefore cannot trace products adequately throughout the marketplace should a recall be necessary.

In your response, you provided a procedure outlining your shipping activities. However, your response is inadequate because you did not address your firm's lot number documentation practices to ensure product traceability after distribution.

4. Your firm failed to ensure that its drug product bore an expiration date that was supported by appropriate stability testing (21 CFR 211.137(a)).

You repackage OTC skin patches into zippered plastic bags that are not labeled with expiration dates. In addition, you have no stability data to support the use of zippered plastic bags as an appropriate container-closure system for your drug products.

In your response, provide the summary of your stability studies indicating appropriate expiration dates for your drug products in their container-closure system.

FDA Sampling and Testing of your Products

FDA testing of your drug products – Power Patch, Female Libido Formula Patch, DHEA Skin Patch for Men, and Skin Patch for Women – found multiple samples to be subpotent with no active ingredient content. In addition, FDA testing found nondeclared ingredients (DHEA and pregnenolone), in samples of your Power Patch.

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.

Correct the violations cited in this letter promptly. Failure to promptly correct these violations may result in legal action without further notice including, without limitation, seizure and injunction. Unresolved violations in this warning letter may also prevent other Federal agencies from awarding contracts.

Until these violations are corrected, we may withhold approval of pending drug applications listing your facility. We may re-inspect to verify that you have completed your corrective actions. We may also refuse your requests for export certificates.

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 written response to Mr. Mark W. Rivero, Compliance Officer, at **ORAPHARM2_RESPONSES@fda.hhs.gov (mailto:ORAPHARM2_RESPONSES@fda.hhs.gov)**. Please identify your response with FEI 3008862488 and CMS Case # 533923.

If you have questions regarding any issues in this letter, please contact Mr. Rivero, Compliance Officer, at (504) 846-6103.

Sincerely,
/S/

Monica R. Maxwell
Program Division Director
Office of Pharmaceutical Quality Operations,
Division II

CC:
Renee Alsobrook, Chief
Department of Business and Professional Regulation
Division of Drugs, Devices and Cosmetics
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