Pharmagen Laboratories, Inc 10/24/14

Department of Health and Human Services

Public Health Service
Food and Drug Administration
New England District
One Montvale Ave.
4th Floor
Stoneham, MA 02180

WARNING LETTER
CMS # 435786

UNITED PARCEL SERVICE
OVERNIGHT DELIVERY

October 24, 2014

Mr. Mackie Barch,
Chief Executive Officer
Pharmagen, Inc.
9337 Fraser Ave.
Silver Spring, MD 20901

Dear Mr. Barch:

From August 5 to August 23, 2013, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility located at 30 Buxton Farms Road, Suite 110, Stamford, CT 06905. The investigators observed serious deficiencies in your practices for producing sterile drug products. For example, investigators observed that your firm's operators did not use proper aseptic technique to don sterile gowning prior to aseptic operations, and they were observed putting on sterile gowns without gloves and not wearing sleeve covers. In addition, FDA observed operators leaning with forearms on the horizontal work bench surfaces on which aseptic operations are performed. Furthermore, FDA investigators found that your firm failed to demonstrate through appropriate studies that your hoods were able to provide adequate protection of the ISO 5 area in which sterile products were processed. Therefore, your products were produced in an environment that poses a significant contamination risk. A Form FDA-483 was issued to your firm on August 23 and 26, 2013.

Although we acknowledge your email dated July 24, 2014, that indicated Pharmagen, including this facility in Stamford, CT, has closed and is no longer in business, based on this inspection, it appears that you were producing drugs that violate the Federal Food, Drug, and Cosmetic Act (FDCA).

FDA acknowledges that Pharmagen registered its facility with FDA as a 503B outsourcing facility on January 21, 2014.

A. Compounded Drugs Under the FDCA

At the time FDA inspected your facility, there were conflicting judicial decisions regarding the applicability of section 503A of the FDCA [21 U.S.C. § 353a], which exempts compounded drugs from several key statutory requirements if certain conditions are met.**[1]** Nevertheless, receipt of valid prescriptions for individually-identified patients prior to distribution of compounded drugs was relevant for both section 503A of the FDCA and the agency's Compliance Policy Guide 460.200 (CPG) (2002), which was then in effect.**[2]** During the FDA inspection, the investigators observed that your firm did not receive valid prescriptions for individually-identified patients for a portion of the drug products you produce. Based on this factor alone, those drugs were not entitled to the statutory exemptions for compounded drugs described in section 503A of the FDCA and did not qualify for the agency's exercise of enforcement discretion set forth in the CPG.**[3]**

Since FDA inspected your facility, Congress enacted and the President signed into law the Compounding Quality Act (CQA),**[4]** which amended FDCA section 503A by eliminating the advertising restrictions that had been the basis for conflicting judicial decisions. The CQA otherwise left section 503A intact, and so clarified that the remainder of section 503A, including the requirement of valid prescriptions for individually-identified patients, is applicable in every federal judicial circuit.

The CQA also established a new section 503B in the FDCA [21 U.S.C. § 353b]. Under section 503B(b) of the FDCA, a compounder may elect to become an outsourcing facility by registering with the FDA.**[5]** 21 U.S.C. § 355] and the requirement to label products with adequate directions for use under section 502(f)(1) of the FDCA [21 U.S.C. § 352(f)(1)] if the requirements in section 503B of the FDCA are met. In addition, prescriptions for individually-identified patients are not required for products produced under section 503B of the FDCA. As noted previously, Pharmagen registered its Stamford, Connecticut facility with FDA as a section 503B outsourcing facility on January 21, 2014. Drug products compounded in a registered outsourcing facility can qualify for exemptions from the FDA approval requirements in section 505 of the FDCA [

To qualify for the exemptions under section 503B of the FDCA, the drug products must be compounded in a 503B outsourcing facility that meets all of the conditions set forth in section 503B of the FDCA, which include, but are not limited to, reporting serious adverse events, labeling compounded products with certain information, and compounding drug products by or under the direct supervision of a licensed pharmacist. In addition, outsourcing facilities must comply with other provisions of the FDCA, including the current good manufacturing practice (CGMP) regulations under section 501(a)(2)(B) of the FDCA [21 U.S.C. § 351(a)(2)(B)] and the prohibition on making, packing or holding drugs in insanitary conditions found in section 501(a)(2)(A) of the FDCA [21 U.S.C. § 351(a)(2)(A)].

Generally, CGMP requirements for finished drug products are established in Title 21 of the Code of Federal Regulations (CFR) parts 210 and 211. As discussed further below, Pharmagen did not comply with certain CGMP requirements.

B. Violations of the FDCA

The drug products that you manufactured and distributed without valid prescriptions for individually-identified patients before registering as an outsourcing facility were not the subject of approved applications, and they are therefore unapproved new drugs in violation of section 505(a) of the FDCA. In addition, because these products were intended for conditions that are not amenable to self-diagnosis and treatment by individuals who are not

medical practitioners, adequate directions could not be written for them so that a layman could use these products safely for their intended uses. Consequently, their labeling fails to bear adequate directions for their intended uses, causing them to be misbranded under section 502(f)(1) of the FDCA.

In addition, your sterile drug products were prepared, packed, or held under insanitary conditions whereby they may have been contaminated with filth or rendered injurious to health. As such, all sterile drug products you manufacture are adulterated within the meaning of section 501(a)(2)(A) of the FDCA. Furthermore, because you manufactured and distributed a portion of your drugs without valid prescriptions for individually-identified patients, the manufacture of those drugs was also subject to FDA's CGMP regulations for Finished Pharmaceuticals, Title 21 CFR parts 210 and 211. FDA investigators observed significant CGMP violations at your facility, causing such drug product(s) to be adulterated within the meaning of section 501(a)(2)(B) of the FDCA.

Because your facility is now registered as section 503B outsourcing facility, this letter focuses on the insanitary conditions and violations of CGMP requirements that continue to apply even though you registered your facility as outsourcing facility. Although you notified us that Pharmagen, including this facility in Stamford, CT, has closed and is no longer in business, you have not de-registered as an outsourcing facility.

Insanitary Conditions Observed During FDA's Inspections

Based on the August 2013 inspection, FDA investigators noted that your sterile drug products were prepared, packed, or held under insanitary conditions whereby they may have been contaminated with filth, or rendered injurious to health, causing your drug products to be adulterated within the meaning of section 501(a)(2)(A) [21 U.S.C. §351(a)(2)(A)] of the FDCA. For example, our investigators observed that your firm's operators did not use proper aseptic technique to don sterile gowning prior to aseptic operations, and they were observed putting on sterile gowns without gloves and not wearing sleeve covers. In addition, FDA investigators observed operators leaning with forearms on the horizontal work bench surfaces on which aseptic operations are performed. Furthermore, our investigators found that your firm failed to demonstrate through appropriate studies that your hoods were able to provide adequate protection of the ISO 5 area in which sterile products were processed. Therefore, your products are produced in an environment that poses a significant contamination risk. As noted above, outsourcing facilities, like any other compounder, may not prepare, pack, or hold drugs under insanitary conditions (section 501(a)(2)(A) of the FDCA).

CGMP Violations Observed During FDA's Inspection

FDA investigators also noted CGMP violations at your facility, causing the drug products for which you did not obtain valid prescriptions for individually identified patients to be adulterated within the meaning of section 501(a)(2)(B) [21 U.S.C. §351(a)(2)(B)] of the FDCA. Such violations observed at your facility include, for example:

1. Your firm failed to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes (21 CFR 211.113(b)).

2. Your firm failed to establish an adequate system for monitoring environmental conditions in aseptic processing areas (21 CFR 211.42(c)(10)(iv)).

3. Your firm failed to ensure that manufacturing personnel wear clothing appropriate to protect drug product from contamination (21 CFR 211.28(a)).

4. Your firm does not have, for each batch of drug product purporting to be sterile and/or pyrogen-free, appropriate laboratory determination of satisfactory conformance to final specifications for the drug product (21 CFR 211.167(a)).

As noted above, outsourcing facilities must comply with current good manufacturing practice (CGMP) requirements under section 501(a)(2)(B) of the FDCA. On July 1, 2014, FDA issued a draft guidance, *Good Manufacturing Practices — InterimGuidance for Human Drug Compounding Outsourcing Facilities under Section 503B of the FD&C Act.* Until final regulations are promulgated, FDA intends to describe its expectations regarding outsourcing facilities and the CGMP requirements in 21 CFR Parts 210 and 211 through guidance. If you continue to operate as an outsourcing facility, you should consult this draft guidance regarding particular provisions in 21 CFR Parts 210 and 211 cited above, pending the development of final guidance or new regulations.

Corrective Actions

We acknowledge your email dated July 24, 2014, that indicated Pharmagen, including this facility in Stamford, CT, has closed and is no longer in business. FDA strongly recommends that if you decide to resume production of drugs, your management first undertake a comprehensive assessment of your operations, including facility design, procedures, personnel, processes, materials, and systems. In particular, this review should assess your aseptic processing operations and design.

Conclusion

The violations cited in this letter are not intended to be an all-inclusive statement of violations at your facility. You are responsible for investigating and determining the causes of the violations identified above and for preventing their recurrence or the occurrence of other violations. It is your responsibility to assure that your firm complies with all requirements of federal law and FDA regulations.

If you decide to resume operations, you should take prompt action to correct the violations cited in this letter. Failure to promptly correct these violations may result in legal action without further notice, including, without limitation, seizure and injunction.

If you intend to resume production of drugs in the future, please include an explanation of each step being taken to prevent the recurrence of violations, as well as copies of related documentation. If you do not believe that the products discussed above are in violation of the FDCA, include your reasoning and any supporting information for our consideration.

In addition to taking appropriate corrective actions, you should notify this office prior to resuming production of any sterile drugs in the future.

Your response should be addressed to Karen N. Archdeacon, Compliance Officer New England District: One Montvale Ave, Stoneham, MA 02180. If you have questions regarding any issues in this letter, please contact our office at 781-587-7491.

Sincerely,
/S/
Mutahar Shamsi
District Director
New England District

Cc:
Scott K. Morton

Executive Vice President
Pharmagen Laboratories, Inc.
30 Buxton Farms Road, Suite 110
Stamford, CT 06905

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[1] *Compare Western States Med. Ctr. v. Shalala*, 238 F.3d 1090 (9th Cir. 2001) *with Medical Ctr. Pharm. v. Mukasey*, 536 F.3d 383 (5th Cir. 2008).

[2] The CPG set forth a non-exhaustive list of factors that FDA considered in determining whether to take enforcement action when the scope and nature of a pharmacy's activities raised concerns. This CPG has been withdrawn in light of new legislation. See below.

[3] *See* 21 U.S.C. § 353a(a) (granting compounded drugs statutory exemptions if, among other things, "the drug product is compounded for an identified individual patient based on the . . . receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient . . . ."); CPG at 2 ("FDA recognizes that pharmacists traditionally have extemporaneously compounded and manipulated reasonable quantities of human drugs upon receipt of a valid prescription for an individually-identified patient from a licensed practitioner. This traditional activity is not the subject of this guidance.").

[4] Drug Quality and Security Act, Public Law 113-54, 127 Stat. 587 (Nov. 27, 2013).

[5] *See* Draft Guidance for Industry, "Registration for Human Drug Compounding Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act," (December, 2013).