Inspections, Compliance, Enforcement, and Criminal Investigations

Nora Apothecary Pharmacy 2/14/14

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Detroit District
300 River Place
Suite 5900
Detroit, MI 48207
Telephone: 313-393-8100
FAX: 313-393-8139

WARNING LETTER

2014-DET-05

February 14, 2014

VIA UPS

Charles A. Lindstrom
Owner
Nora Apothecary and Alternatives Therapies, Inc.
1101 E. 86th Street
Indianapolis, IN 46240-3729

Dear Mr. Lindstrom:

From March 19, 2013, to March 21, 2013, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, Nora Apothecary and Alternative Therapies, Inc., located at 1101 E. 86th Street, Indianapolis, Indiana 46240. From May 14, 2013, to May 15, 2013, investigators returned to your facility for a follow-up review of your sterile compounding records. During the inspection and follow-up review, the investigators noted that you were not receiving valid prescriptions for individually-identified patients for a portion of the drug products you were producing. In addition, the investigators observed serious deficiencies in your practices for producing sterile drug products, which put patients at risk. All sterile products produced on or before Friday, April 19, 2013, and still within expiry were recalled as a result of these observations. These observations and others were noted on the FDA Form 483 issued on March 21, 2013.

During a teleconference with your firm on April 19, 2013, we expressed our concerns with multiple observations made during the inspection of your firm. For example, we observed that your ISO-5 aseptic processing area is not located within an ISO-7 or better clean room, but instead is located within an unclassified area. Furthermore, the gowning room, which should be ISO-8 or better, is also unclassified. Appropriately designed, qualified, controlled, and maintained cleanrooms are essential to assure that microbial and particulate levels in the air are consistently minimized, and the cleanroom environment does not compromise ISO-5 aseptic operations. In addition, manual manipulations within the ISO-5 area were not slow and deliberate, risking the disruption of the unidirectional air protecting the vials from microbial contamination. These practices place your firm's aseptically-produced injectable products at considerable risk of microbial contamination.

Based on this inspection, it appears that you are producing drugs that violate the Federal Food, Drug, and Cosmetic Act (FDCA).

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 on Pharmacy Compounding (CPG) (2002), which was then in effect (CPG) (2002).[2] During the FDA inspection, investigators observed that your firm does 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. Accordingly, the drugs you compound without valid prescriptions for individually identified patients are not entitled to the exemptions in section 503A.[5]

In addition, we remind you that there are a number of other conditions that must be satisfied to qualify for the exemptions in section 503A of the FDCA.[6]

B. Violations of the FDCA

The drug products that you manufacture and distribute without valid prescriptions for individually-identified patients are misbranded drugs in violation of section 502(f)(1) [21 U.S.C. § 352(f)(1)] of the FDCA. In addition, your sterile drug products are prepared, packed, or held under insanitary conditions whereby they may have been contaminated with filth, or whereby they may have been rendered injurious to health. As such, all sterile drug products you manufacture are adulterated within the meaning of section 501(a)(2)(A) [21 U.S.C. § 351(a)(2)(A)] of the FDCA. Furthermore, because you manufacture and distribute a portion of your drugs without valid prescriptions for individually-identified patients, the manufacture of those drugs are also subject to FDA's Current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals, Title 21, Code of Federal Regulations (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 [21 U.S.C. § 351(a)(2)(B)].

Misbranded Drug Products

Because the drug products for which you have not obtained valid prescriptions for individually-identified patients are intended for conditions that are not amenable to self-diagnosis and treatment by individuals who are not medical practitioners, adequate directions cannot be written for them so that a layman can use these drug 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 [21 U.S.C. § 352(f)(1)], and they are not exempt from the requirements of section 502(f)(1) of the FDCA (*see*, *e.g.*, 21 C.F.R. § 201.115). It is a prohibited act under section 301(k) of the FDCA [21 U.S.C. § 331(k)] to do any act with respect to a drug, if such act is done while the drug is held for sale after shipment in interstate commerce of the components used to make the drug and results in the drug being misbranded.

Adulteration Charges

Additionally, FDA investigators noted that your sterile drug products were prepared, packed, or held under insanitary conditions, whereby they may have become contaminated with filth or rendered injurious to health, causing your drug products to be adulterated under section 501(a)(2)(A) of the FDCA [21 U.S.C. § 351(a)(2)(A)]. Examples of these conditions include the placement of the ISO-5 aseptic processing area in a room that is not controlled for airborne particles and microbes. Additional insanitary conditions include staff hand movements within the ISO-5 area not being slow and deliberate, risking the disruption of the unidirectional air protecting the vials from microbial contamination.

FDA investigators also noted CGMP violations at your facility, causing the drug products for which you have not obtained valid prescriptions for individually-identified patients to be adulterated under section 501(a)(2)(B) of the FDCA [21 U.S.C. § 351(a)(2)(B)]. The violations 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 and follow an adequate written testing program designed to assess the stability characteristics of drug products and to use results of such stability testing to determine appropriate storage conditions and expiration dates (21 CFR 211.166(a)).

3. 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)).

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

5. Your firm fails to segregate operations relating to processing of penicillin in facilities from those used for other drug products for human use (21 CFR 211.42 (d)).

It is a prohibited act under section 301(k) of the FDCA [21 U.S.C. § 331(k)] to do any act with respect to a drug, if such act is done while the drug is held for sale after shipment in interstate commerce of the components used to make the drug and results in the drug being adulterated.

C. **Corrective Action**

In your response to the Form FDA 483, you referenced your purported compliance with United States Pharmacopeia (USP)-National Formulary (NF) General Chapter <797> Pharmaceutical Compounding--Sterile Preparations. However, as noted above, your firm has manufactured and distributed some drugs without valid prescriptions for individually-identified patients, and the manufacture of such drugs is subject to FDA's drug CGMP regulations, 21 CFR Parts 210 and 211. Your firm's planned corrections do not meet the minimum requirements of 21 CFR part 211, and there is no assurance that these drug product(s) produced by your firm conform to the basic quality standards that ensure safety, identity, strength, quality, and purity.

In your response to the Form FDA 483, you also indicated that you would suspend "high risk compounding" and described several corrective actions. To address this issue, and also to ensure compliance with section 501(a)(2)(A) [21 U.S.C. § 351(a)(2)(A)], FDA strongly recommends that your management immediately undertake a comprehensive assessment of your manufacturing operations, including facility design, procedures, personnel, processes, materials, and systems. In particular, this review should assess your aseptic processing operations. A third party consultant with relevant sterile drug manufacturing expertise could be useful in conducting this comprehensive evaluation. We are aware that you are not currently producing sterile drug products. We expect that you will notify this office before resuming production of sterile injectable drug products.

In addition, you should correct the violations of FDCA section 502(f)(1) [21 U.S.C. § 352(f)(1)] noted above.

D. Conclusion

Please note that 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.

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.

Within fifteen (15) working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct violations. 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. If you cannot complete corrective action within 15 working days, state the reason for the delay and the time within which you will complete the correction. Your notification should be addressed to:

Tina M. Pawlowski, Ph.D., Compliance Officer
FDA Detroit District Office
U.S. Food and Drug Administration
300 River Place, Suite 5900
Detroit, MI 48207

If you have questions regarding any issues in this letter, please contact Compliance Officer Pawlowski at 313-393-8217 or by email at tina.pawlowski@fda.hhs.gov.

Sincerely,
/S/
Glenn T. Bass
District Director
Detroit District Office

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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]The CQA contains a number of other provisions, including new exemptions and requirements for compounders seeking to operate as outsourcing facilities. A discussion of the CQA and the agency's plans to implement the new law may be found at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/default.htm.
[6] For example, section 503A also addresses anticipatory compounding, which includes compounding (not distribution) before receipt of a valid prescription order for an individual patient. We are not addressing anticipatory compounding here.