Inspections, Compliance, Enforcement, and Criminal Investigations

Avella of Deer Valley, Inc. 1/17/14

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Los Angeles District
Pacific Region
19701 Fairchild
Irvine, CA 92612-2506
Telephone: 949-608-2900
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WARNING LETTER

VIA UNITED PARCEL SERVICE
SIGNATURE REQUIRED

January 17, 2014

WL# 10-1

Dr. John D. Musil, CEO/Founder
Avella of Deer Valley, Inc.
1606 W. Whispering Wind Dr., 2nd floor
Phoenix, AZ 85085

Dear Dr. Musil:

From February 19, 2013, to February 25, 2013, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, Avella of Deer Valley, Inc., 23620 N. 20th Drive, Suite 12, Phoenix, AZ 85085-0621. During the inspection, the investigators noted that you were not receiving valid prescriptions for individually-identified patients for a significant number 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. For example, during the inspection we observed your technicians performing aseptic operations while wearing non-sterile gowns and with skin exposed. These observations and others were noted on a Form FDA 483, issued on February 25, 2013. We acknowledge receipt of your firm's response to the FDA Form 483 dated March 7, 2013.

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 the 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] Because your firm was in the Ninth Circuit, at the time of our inspection, FDA applied the enforcement policy articulated in Compliance Policy Guide 460.200 ["Pharmacy Compounding"], issued by FDA on May 29, 2002, [see Notice of Availability, 67 Fed. Reg. 39, 409 (June 7, 2002)] to your compounding of human drugs. The CPG identified a non-exhaustive list of factors for the FDA to consider in deciding whether to initiate an enforcement action with respect to the compounding of human drugs. 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 Pharmacy Compounding CPG.[2]

Since the FDA inspected your facility, Congress enacted and the President signed into law the Compounding Quality Act (CQA)[3], 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.[4]

During the FDA inspection, 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. 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.[5]

B. Violations of the FDCA

Because the drug products that you manufacture and distribute without valid prescriptions for individually-identified patients are not the subject of approved applications, they are unapproved new drugs and misbranded drugs in violation of sections 505(a) and 502(f)(1) [21 U.S.C. §§ 355(a) and 352(f)(1)] of the FDCA, respectively. 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 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 drugs without valid prescriptions for individually-identified patients, the manufacture of those drugs is 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)].

Unapproved New Drug Products

You do not have any FDA-approved applications on file for the drug products for which you have not obtained valid prescriptions for individually-identified patients.[6] Under sections 301(d) and 505(a) of the FDCA [21 U.S.C. §§ 331(d) and 355(a)] a new drug may not be introduced into or delivered for introduction into interstate commerce unless an application approved by FDA under section 505 of the FDCA [21 U.S.C. § 355] is in effect for the drug. Your marketing of these products, or other applicable products, without an approved application violates these provisions of the FDCA.

Misbranded Drug Products

Additionally, 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 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). The introduction or delivery for introduction into interstate commerce of these products therefore violates sections 301(a) of the FDCA [21 U.S.C. § 331(a)]. It is also 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 those conditions include that technicians were performing aseptic operations while wearing non sterile gowns and with exposed skin in the face and neck area.

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 or follow appropriate written procedures that are designed to preven 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 ensure that manufacturing personnel wear clothing appropriate to protect drug product from contamination (21 CFR 211.28(a)).

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

C. Corrective Actions

In your response to the Form FDA 483 dated March 7, 2013, you referenced your purported compliance with United States Pharmacopeia (USP)-National Formulary (NF) General Chapter <797>, “Pharmaceutical Compounding - Sterile Preparations.” As noted above, your firm has manufactured and distributed 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 th minimum requirements of 21 CFR part 211, and there is no assurance that the drug product(s) produced by your firm without valid prescriptions for individually-identified patients conform to these basic quality standards that ensure safety, identity, strength, quality, and purity.

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 consultan with relevant sterile drug manufacturing expertise could be useful in conducting this comprehensive evaluation.

D. 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 ensure 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. Other federal agencies may take this Warning Letter into account when considering the award o contracts.

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 the corrective actions cannot be completed within fifteen working days, state the reason for the delay and the time frame within which the corrections will be implemented.

Your written reply should be addressed to:

Blake Bevill, Director
Compliance Branch
U.S. Food and Drug Administration
19701 Fairchild
Irvine, CA 92612

If you have questions regarding any issues in this letter, please contact Ms. Jessica Mu, Compliance Officer, at 949-608-4477.

Sincerely,
/S/
Steven E. Porter, Acting Director
Los Angeles District

cc:

Harland (Hal) Wand, Executive Director
Arizona State Board of Pharmacy
1616 West Adams
STE 120
Phoenix, AZ 85007

[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] *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.").
[3] H.R. 3204 / Public Law 113-54, Drug Quality and Security Act (Nov. 27, 2013; 127 Stat. 587; 54 pages).
[4]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
[5] 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.
[6] The specific products made by your firm are drugs within the meaning of section 201(g) of the Act, [21 U.S.C. § 321(g)] because they are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of diseases. Further, they are "new drugs" within the meaning of section 201(p) of the FDCA [21 U.S.C. § 321(p)] because they are not generally recognized as safe and effective for their labeled uses.

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