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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Los Angeles District
Pacific Region
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Irvine, CA 92612-2506

Telephone: 949-608-2900
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WARNING LETTER

VIA FEDERAL EXPRESS

December 16, 2008 W/L 07-09

Mr. Ari S. Schafer
Civic Center Pharmacy
7331 E. Osborn Road, Suite 208
Scottsdale, AZ 85251-6420

Dear Mr. Schafer:

On July 15-16, 2008, the United States Food and Drug Administration (FDA) conducted an inspection of your firm located at 7331 E. Osborn Road, Suite 208, Scottsdale, AZ. This inspection revealed that your firm compounds a hormone therapy drug containing estriol without an FDA-approved new drug application or an FDA-sanctioned investigational new drug application.

The Federal Food, Drug, and Cosmetic Act (FDCA) establishes Agency jurisdiction over "new drugs," including compounded drugs. Compounded drugs fit within the FDCA's definition of "new drug": "[a]ny drug (except a new animal drug . . .) [that] is not generally recognized . . . as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof." 21 U.S.C. § 321(p)(1). See Weinberger v. Hynson, Westcott & Dunning, 412 U.S. 609, 619, 629-30 (1973) (explaining the definition of "new drug"). There is substantial judicial authority supporting FDA's position that compounded drugs are not exempt from the new drug definition. See Medical Ctr. Pharm. v. Mukasey, 536 F.3d 383 (5th Cir. 2008) ("compounded drugs are not exempt from the FDCA's 'new drug' definition, § 321(p), nor are they uniformly exempt from the FDCA's 'new drug' requirements, §§ 351(a)(2)(B), 352(f)(1), 355"); Prof'ls & Patients for Customized Care v. Shalala, 56 F.3d 592, 593 n.3 (5th Cir. 1995) ("Although the [FDCA] does not expressly exempt 'pharmacies' or 'compounded drugs' from the new drug ... provisions, the FDA as a matter of policy has not historically brought enforcement actions against pharmacies engaged in traditional compounding."); In the Matter of Establishment Inspection of: Wedgewood Vill. Pharmacy, 270 F. Supp. 2d 525, 543-44 (D. N.J. 2003) ("The FDCA contains provisions with explicit exemptions [from] the new drug . . . provisions. Neither pharmacies nor compounded drugs are expressly exempted."), aff'd, Wedgewood Vill. Pharmacy v. United States, 421 F.3d 263, 269 (3d Cir. 2005). The drugs that pharmacists compound are not FDA-approved and lack an FDA finding of safety and efficacy. Because compounded drugs are "new drugs" under the FDCA that are unapproved, the statute generally prohibits their introduction into interstate commerce.

However, FDA has long recognized the important public health function served by traditional pharmacy compounding. FDA regards traditional compounding as the extemporaneous combining, mixing, or altering of ingredients by a pharmacist in response to a physician's prescription to create a medication tailored to the specialized needs of an individual patient. See Thompson v. W. States Med. Ctr., 535 U.S. 357, 360-61 (2002). Traditional compounding typically is used to prepare medications that are not available commercially, such as a drug for a patient who is allergic to an ingredient in a mass-produced drug, or diluted dosages for children. As a matter of Agency discretion, FDA has historically not taken enforcement action against traditional compounding in recognition of the benefit that it affords patients when FDA-approved, commercially available drugs are inadequate or unavailable

In 1997, Congress enacted, as part of the Food and Drug Administration Modernization Act of 1997 (FDAMA), a provision that related to pharmacy compounding, codified in section 503A of the FDCA (21 U.S.C. § 353a). In 2001, the Ninth Circuit Court of Appeals declared this section invalid because it included unconstitutional restrictions on commercial speech and those restrictions could not be severed from the rest of section 503A. W. States Med. Ctr. v. Shalala, 238 F.3d 1090 (9th Cir. 2001). The Supreme Court affirmed the Ninth Circuit ruling that the advertising restrictions violated the First Amendment, but it did not consider whether these restrictions could be severed from the rest of section 503A. Thompson v. W. States Med. Ctr., 535 U.S. 357 (2002). In 2008, the Fifth Circuit Court of Appeals held that the restrictions on commercial speech could be severed from the rest of section 503A and that the remainder of 503A is valid and in force. Medical Ctr. Pharm. v. Mukasey, 536 F.3d at 405. Thus, the decisions of the Fifth and Ninth Circuits directly conflict on whether the non-advertising provisions of section 503A are valid and in effect.

FDA has determined that it will apply the non-advertising provisions of section 503A to entities covered by this provision that are located within the jurisdiction of the Fifth Circuit (i.e., Texas, Louisiana, and Mississippi) as well as to the plaintiffs that brought the Medical Center case. Elsewhere, FDA will continue to apply the enforcement policy articulated in Compliance Policy Guide section 460.200 ["Pharmacy Compounding"], issued by FDA on May 29, 2002 (see Notice of Availability, 67 Fed. Reg. 39, 409 (June 7, 2002)). The CPG identifies a non-exhaustive list of factors that the Agency considers in deciding whether to initiate an enforcement action with respect to compounding. These factors include, among other things, compounding drugs in anticipation of receiving prescriptions (except in very limited amounts), using active pharmaceutical ingredients that are not components of FDA-approved drugs, compounding for third parties who resell to individual patients, and compounding drugs that are essentially copies of commercially available drugs.

As mentioned above, one of the factors identified in the CPG on human drug compounding is whether a firm compounds finished drugs from bulk active ingredients that are not components of FDA approved drugs without an FDA sanctioned investigational new drug application (IND) in accordance with 21 U.S.C. § 355(i) and 21 CFR 312.
The recent FDA inspection revealed that your firm compounds drugs using the bulk substance estriol, which is not an active ingredient contained in any FDA-approved drug and has not been demonstrated under FDA standards to be safe and effective for any use. FDA does not sanction

the use of estriol in pharmacy compounding and will not exercise enforcement discretion with respect to drug products that contain estriol.

The estriol product compounded by your firm is a drug within the meaning of section 201(g) of the FDCA [21 U.S.C. § 321(g)]. It is also new drug under section 201(p) of the FDCA [21 U.S.C. § 321(p)] because it is not generally recognized by qualified experts as safe and effective for its labeled uses. This product may not be introduced or delivered for introduction into interstate commerce under section 505 of the FDCA [21 U.S.C. § 355] because no approval of an application filed pursuant to section 505 of the FDCA [21 U.S.C. § 355] is in effect for it. Its introduction or delivery for introduction into interstate commerce violates section 301(d) of the FDCA [21 U.S.C. § 331(d)]. In addition, this drug is misbranded under section 502(f)(1) of the FDCA [21 U.S.C. § 352(f)(1)] because its labeling fails to bear adequate directions for their use, and it is not exempt from this requirement under 21 CFR § 201.115, and does not otherwise comply with section 505(i) of the FDCA [21 U.S.C. § 355(i)].

Section 301(a) of the FDCA [21 U.S.C. § 331(a)] prohibits the introduction or delivery for introduction into interstate commerce of any misbranded drug, and section 301(k) of the FDCA [21 U.S.C. § 331(k)] prohibits any act with respect to a drug if the act is done while the drug is held for sale after shipment in interstate commerce and results in the drug being misbranded.

FDA permits the production of drugs with active ingredients that - like estriol - are not components of FDA-approved drugs pursuant to an Investigational New Drug Application (IND). INDs are important to patient safety. Information regarding obtaining an IND for estriol can be found at http://www.fda.gov/cder/pharmcomp/estriol.htm. It should be noted that the IND is obtained by the prescribing physician and not the pharmacy.

The violations cited in this letter are not intended to be an all-inclusive statement of violations that exist at your facility, and they may not be limited to the above-cited drug products. You are responsible for investigating and determining the causes of the violations identified above and for preventing their recurrence and 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. Other federal agencies may take this Warning Letter into account when considering the award of contracts.

In addition to the violations noted above, we note that, in reviewing a listing of compounded products sold by your pharmacy, there may be drugs produced and marketed by your firm that are copies of FDA-approved commercially available drugs. These include, but are not limited to 200mg Testosterone Cypionate, 40 mg Estradiol Valerate, and 5 mg Estradiol Cypionate. As mentioned above, one of the factors identified in the CPG on human drug compounding is whether a firm compounds drugs that are essentially copies of commercially available drugs. Pharmacies should not compound drugs that are essentially copies of FDA-approved drugs without a documented, patient-specific medical need, determined by a licensed healthcare provider, for their variation from the FDA-approved, commercially-available drugs.

Within fifteen working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct the cited violations. Include an explanation of each step being taken to prevent the recurrence of violations, as well as copies of related documentation. If you cannot complete corrective action within fifteen working days, state the reason for the delay and the time within which you will complete the correction.

Your response should be sent to:

John J. Stamp, Compliance Officer
Los Angeles District Domestic Compliance Branch
U.S. Food & Drug Administration
19701 Fairchild
Irvine, CA 92612

If you have any questions, please contact Mr. Stamp at (949) 608-4464.

Sincerely,

Alonza E. Cruse
Director
Los Angeles District
U.S. Food and Drug Administration

cc: Hal Wand
Executive Director
Arizona Board of Pharmacy