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DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

Dallas District
4040 North Central Expressway
Dallas, Texas 75204-3128

January 7, 2008

Ref: **2008-DAL-WL-05**

WARNING LETTER

VIA FEDERAL EXPRESS
RETURN RECEIPT REQUESTED

Mr. Phil Pylant, Owner
Village Compounding Pharmacy
975 Corbindale Rd., Suite 100
Houston, TX 77024

Dear Mr. Pylant:

We recently reviewed your firm's website, www.villagecompounding.com. As explained below, your website contains false and misleading claims for your firm's compounded hormone therapy drugs, causing those drugs to be misbranded in violation of Section 502(a) of the Federal Food, Drug, and Cosmetic Act (FDCA) [21 USC § 352(a)]. Additionally, your firm compounds a hormone therapy drug containing estriol, without an FDA-approved new drug application or an FDA-sanctioned investigational new drug application, in violation of Section 505 of the FDCA (21 USC § 355). Hormone therapy drugs containing estriol are also misbranded in violation of section 502(f)(1) of the FDCA [21 U.S.C. § 352(f)(1)] in that their labeling fails to bear adequate directions for use.

A. Misbranded Drugs Under Section 502(a) of the FDCA

Under section 502(a) of the FDCA, a drug is misbranded if its labeling is false or misleading in any particular. Section 201(n) of the FDCA [21 U.S.C. § 321(n)] provides that, in determining whether a drug's labeling or advertising "is misleading, there shall be taken into account . . . not only representations made or suggested . . . but also the extent to which the labeling or advertising . . . fails to reveal facts material in light of such representations . . . ."

Your website advises that you compound hormone therapy drugs that are available for purchase and distribution. These compounded hormone therapy drugs are misbranded within the meaning of section 502(a) of the FDCA for the following reasons:

1. Unsubstantiated Efficacy Claims

Your firm's website contains claims concerning your firm's compounded hormone therapy drugs, including:

- "BIO-IDENTICAL HRT HAS BEEN USED IN THE SUCCESS OF TREATING:
  Fibrocystic breasts
  Depression
  Poor concentration/Memory lapses
  Heart disease/Arteriosclerosis"
- "ESTROGENS:
  Decrease of blood pressure
  Memory and cognitive functions may be improved
  Sleep patterns, energy levels and moods may improve"

FDA regards these claims as false and misleading. FDA is not aware of substantial evidence (consisting of adequate and well controlled clinical investigations) that supports these claims.

2. Unsubstantiated Superiority Claims

Your firm's website contains a statement suggesting the superiority of your firm's compounded hormone therapy drugs:

- "The molecular structure of the replacement hormone must exactly match the molecular structure of the original hormone naturally produced and present in the human body in order to replicate the function of the original hormone. These structural differences that exist between bio-identical and synthetic or animal hormones may be responsible for the side effects women are experiencing when synthetic hormones are being taken for replacement therapy."

This statement represents and suggests that your firm's compounded hormone therapy drugs are superior to other hormone therapy products, including FDA-approved drugs. This claim—which is unsupported by substantial evidence (consisting of adequate and well controlled clinical investigations) —is false and misleading.

3. Unsubstantiated "Bio-identical" Claims

Your website claims that your firm's compounded hormone therapy drugs are "bio-identical." This claim implies that your compounded hormone therapy drugs are natural, or identical to the hormones made by the body. FDA is unaware of substantial evidence (consisting of adequate and well controlled clinical investigations) to support the claimed "bio-identical" nature of your hormone therapy drugs.

As explained above, the claims made for your hormone therapy drugs are false and misleading in that they are not supported by substantial evidence. These claims cause your hormone therapy drugs to be misbranded under section 502(a) of the FDCA.

B. Unapproved New Drug Under Section 505 of the FDCA: Estriol

Because your products are intended to treat, mitigate, and prevent disease (a conclusion supported by the claims described above), the estriol products compounded by your firm are drugs within the meaning of section 201(g) of the FDCA [21 U.S.C. § 321(g)]. Further, as these products are not generally recognized by qualified experts as safe and effective for their labeled uses, they are new drugs, as defined by section 201(p) of the FDCA [21 U.S.C.§ 321(p)]. No FDA-approved applications pursuant to section 505 of the FDCA [21 U.S.C. § 355] are effective with respect to these drugs. Accordingly, their introduction or delivery for introduction into interstate commerce violates section 505(a) of the Act [21 U.S.C. § 355(a)].

The FDCA establishes agency jurisdiction over "new drugs," including compounded drugs. Compounded drugs are "new drugs" within the meaning of 21 U.S.C. § 321(p), because they are not "generally recognized, among experts . . . as safe and effective" for their labeled uses. *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 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 Village Pharmacy,* 270 F. Supp. 2d 525, 543-44 (D.N.J. 2003), *aff'd, Wedgewood Village Pharmacy v. United States,* 421 F.3d 263, 269 (3d Cir. 2005) ("The FDCA contains provisions with explicit exemptions from the new drug . . . provisions. Neither pharmacies nor compounded drugs are expressly exempted."). Because they are "new drugs" under the FDCA, compounded drugs may not be introduced into interstate commerce without FDA approval.[1]

The drugs that pharmacists compound are not FDA-approved and thus lack an FDA finding of safety and efficacy. 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. Western States Medical Center,* 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

[1] In August 2006, the U.S. District Court for the Western District of Texas issued a ruling in *Medical Center Pharmacy v. Gonzales* interpreting, among other things, the application of the "new drug" provisions of the FDCA to compounded drugs. *See Medical Center Pharmacy v. Gonzales,* MO-04-CV-130, (W.D. Tex, Aug. 30, 2006). The government has appealed this decision to the U.S. Court of Appeals for the Fifth Circuit.

patient who is allergic to an ingredient in a mass-produced drug, or diluted dosages for children.

FDA's current enforcement policy with respect to the compounding of human drugs is 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)).[2] The CPG identifies factors that the Agency considers in deciding whether to initiate enforcement action with respect to compounding.[3] These factors include whether a firm is "[c]ompounding 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."

Your firm is compounding drugs containing estriol, which is not a component of an FDA-approved drug, without an FDA-sanctioned IND. These are unapproved new drugs and their compounding violates section 505(a) of the FDCA. Based on FDA's consideration of the circumstances here, FDA is prepared to take enforcement action to halt your compounding of drugs containing estriol.

C. Misbranded Drugs Under Section 502(f)(1) of the FDCA: Estriol

The estriol drugs compounded by your firm are also misbranded under section 502(f)(1) of the FDCA [21 U.S.C. § 352(f)(1)] in that their labeling fails to bear adequate directions for their use. Further, these drugs are not exempt from this requirement under 21 CFR § 201.115 because they are new drugs within the meaning of section 201(p) of the FDCA and they lack approved applications filed pursuant to section 505 of the FDCA.

D. **Conclusion**

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.

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[2] Although Section 503A of the FDCA [21 U.S.C. § 353a] addresses pharmacy compounding, this provision was invalidated by the Ninth Circuit's ruling in *Western States Medical Center v. Shalala*, 238 F.3d 1090 (9th Cir. 2001), that Section 503A included unconstitutional restrictions on commercial speech and those restrictions could not be severed from the rest of 503A. In *Thompson v. Western States Medical Center*, 535 U.S. 357 (2002), the Supreme Court affirmed the Ninth Circuit ruling that the restrictions in question violated the First Amendment, but it did not consider whether these restrictions could be severed from the rest of section 503A. FDA shares the Ninth Circuit's view that section 503A is now void.

[3] As stated in the CPG, "[t]he . . . list of factors is not intended to be exhaustive." *See* CPG section 460.200 ["Pharmacy Compounding"].

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.

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.

Please direct your response to the U.S. Food and Drug Administration, Dallas District Office, Attn: Edwin Ramos, Compliance Officer, 4040 North Central Expressway, Suite 300, Dallas, TX 75204. You should contact Mr. Ramos at 214-253-5218 to discuss the contents of this letter.

Sincerely yours,

Elaine R. Crosby

Elaine R. Crosby
Acting Director
Dallas District
U.S. Food and Drug Administration