

[REDACTED]

From: [REDACTED]
Sent: Monday, May 21, 2007 9:30 AM
To: Anderson, Kathleen R
Cc: Nasr, Samia
Subject: Inspection Request, Ameridose

Attachments: Ameridose_IR_sn.doc; Ameridose medwatch.pdf

Kathy,
Attached is an inspection request for Ameridose pharmacy for your review and edits. We received a Medwatch alleging the firm is a manufacturer of injectable products and not a pharmacy (attached). Ameridose is registered with the FDA.
Thank you, [REDACTED]



Ameridose_IR_sn.d
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Ameridose
medwatch.pdf

[REDACTED]
Staff Fellow
Division of New Drugs, Labeling and Compliance
Food and Drug Administration
[REDACTED]



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

Date: May 21, 2007
r
From: [REDACTED] Staff Fellow
Compounding Team
Division of New Drugs and Labeling Compliance, HFD-317

Through: Kathleen R. Anderson _____
Deputy Director
Division of New Drugs and Labeling Compliance, HFD-310

Subject: Inspection Request

Firm: Ameridose
50 Fountain Street
Framingham, MA 01702

To: Michael R. Kravchuk, Director
Investigations Branch, New England District Office, HFR-NE250 .

CC: Gail T. Costello, District Director
New England District Office, HFR-NE200

This memo requests an inspection of Ameridose, to obtain current information about the firm's compounding practices, especially as they relate to the compounding of injectable medications. Please conduct an inspection jointly with the Massachusetts State Board of Pharmacy. During this inspection, please obtain information that is responsive to the questions referenced below and obtain documentation (including official documentary samples) to support regulatory action.

The Agency received a report through its MedWatch system (see attachment) alleging Ameridose is engaged in the manufacture of unapproved intravenous solutions that are not dispensed pursuant to a prescription (attached). According to the firm's website (www.ameridose.com), the facility is registered with the FDA.

Please note the FDA-482, Notice of Inspection, was recently updated to include the exemptions available for pharmacies that meet certain criteria. To assure that a pharmacy is made aware of the inspection provisions of the FDCA, and what exemptions might apply to its operations, **it is important to use the internet version of the FDA-482 for pharmacy facilities. This form is located at the following URL: <http://intranet.fda.gov/omp/forms/internal/Form%20FDA%20482.pdf>**.

Background

FDA regards traditional pharmacy compounding as the combining, mixing, or altering of ingredients by a pharmacist in response to a physician's prescription to create a medication tailored to the needs of an individual patient. See *Thompson v. Western States Med. Ctr.*, 535 U.S. 357, 360-61 (2002). Traditional compounding typically is used to prepare medications that are not commercially available, such as medication for a patient who is allergic to an ingredient in a mass-produced product, or diluted dosages for children.

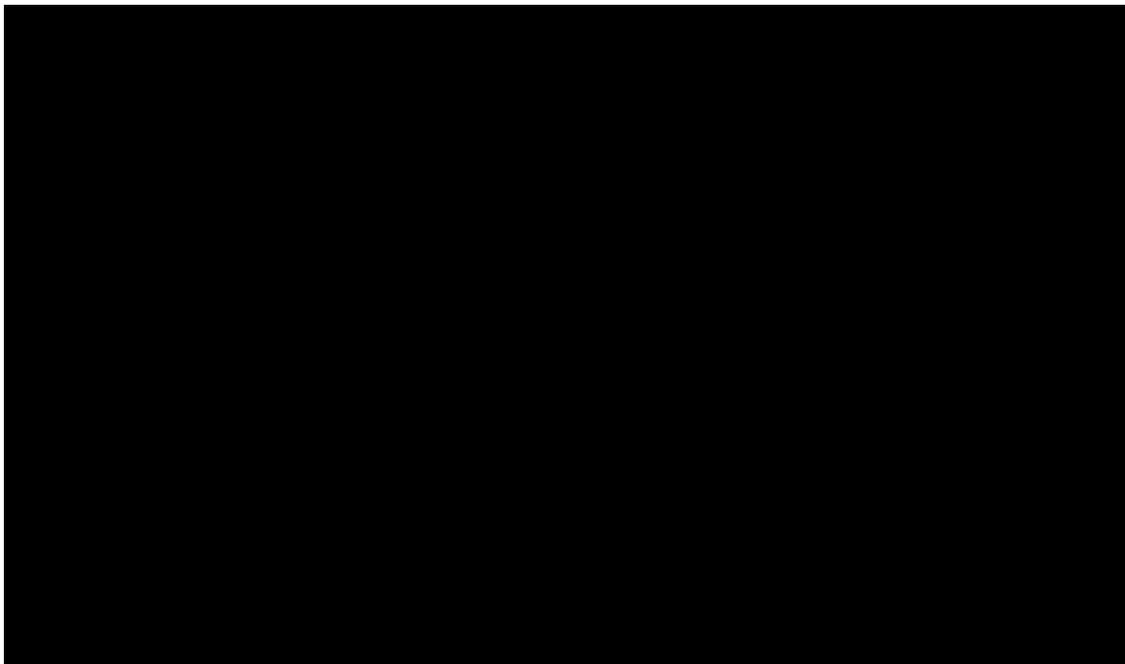
All compounded prescription drugs are "new drugs" within the meaning of the FDCA. When a pharmacist compounds a prescription drug, by definition, he or she creates a new drug under federal law because the compounded product is not "generally recognized, among experts . . . as safe and effective." See 21 U.S.C. §§ 321(p); *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, Inc.*, 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."); *Weinberger v. Hynson, Westcott & Dunning*, 412 U.S. 619, 629-30 (1973) (explaining the definition of "new drug"). Under the FDCA, a new drug -- including a compounded new drug -- may not be legally manufactured or sold in the United States unless it has been pre-approved by FDA as safe and effective for its intended uses. See 21 U.S.C. §§ 321(g) and (p), 352, 353(b), and 355. In virtually every instance, the drugs that pharmacists compound have not been so approved.

FDA has long recognized, however, that traditional pharmacy compounding serves an important public health function by meeting the specialized medical needs of individual patients for whom commercially available approved drugs are inadequate or inappropriate. Accordingly, FDA historically has not taken enforcement actions against pharmacies engaged in traditional pharmacy compounding. Rather, FDA has directed its enforcement resources against establishments that manufacture large quantities of unapproved new drugs under the guise of traditional compounding, or whose compounding practices pose a significant or immediate threat to the public health or to the integrity of the drug approval processes of the FDCA.

FDA's current enforcement policy with respect to compounding of human drugs is articulated in Compliance Policy Guide (CPG), section 460.200 ["Pharmacy Compounding"], issued by FDA's Center for Drug Evaluation and Research on June 7, 2002.

The CPG lists factors that the agency considers in deciding whether to exercise its enforcement discretion with respect to compounding. The factors listed in the CPG are not intended to be exhaustive and other factors may also be appropriate for consideration.

Inspection



The public health can be harmed when drug products are made without adequate processing controls to assure their safety, purity, potency, quality, and identity. The inspection should include a review of the systems that impact these factors, including drug quality, facilities, equipments, production, packaging, and labeling. A major concern involves the actual or potential contamination or cross-contamination of products with filth, objectionable microorganisms, spores, endotoxins, foreign chemicals, and/or physical matter.

During your inspection, please obtain information that is responsive to the following questions. It is critical that you document, in writing, the answers to the questions in the establishment inspection report (EIR). **Questions regarding sterile compounded products are only applicable if the pharmacy is compounding sterile products.** Please note that this is not an exhaustive or complete list of questions. Inspectional findings need to dictate what questions and answers are pertinent to the pharmacy's operation.

- 1) According to the Board of Pharmacy, does the pharmacy operate in conformance with applicable state law regulating the practice of pharmacy?
- 2) Is the pharmacy licensed in other states? Is the pharmacy distributing compounded products out of state? If so, to what states and how many prescriptions per year does it mail or distribute outside of the state?
- 3) What is the pharmacy's annual revenue? What is its annual revenue from compounded products?
- 4) Are written prescriptions/physician orders for identified individual patients received before dispensing compounded injectable products each time they are dispensed? If not, what is the volume (e.g., number of doses) distributed per year without prescriptions/physician orders?
- 5) Does the pharmacy compound drug products in anticipation of receiving prescriptions? If so, what drugs does the pharmacy compound in anticipation of receiving prescriptions, and in what volume (e.g., number of doses) per year?
- 6) What is the volume of the pharmacy's compounding? How many different compounded products does it produce? How many doses of each product does it compound on a daily and annual basis? How many total prescriptions for all compounded products does the pharmacy annually dispense?
- 7) How many prescriptions for compounded products does the pharmacy annually dispense? What dosage forms, strengths, and quantities of the products does the pharmacy compound?
- 8) Does the pharmacy compound copies or essentially copies of commercially available FDA-approved drug products (i.e., products that have the same active ingredient, dosage form, and strength)? If so, which commercially available drugs are being copied, and in what amounts (e.g., number of prescriptions per year)? Please obtain formulation information that will enable us to compare the compounded product formulations to FDA-approved formulations.
- 9) In certain circumstances, it may be appropriate for a pharmacist to compound a small quantity of a product that is only slightly different than a commercially available FDA-approved product (such as by removing a preservative or coloring agent for an individual patient with an allergy). In these circumstances, does the pharmacy have documentation from the health care practitioner that demonstrates the medical need for the particular variation of the compounded product for each individual patient?
- 10) Does the pharmacy compound any products that have been withdrawn or removed from the market for safety reasons? If so, please obtain documentation showing the types and amounts of compounded drugs.

- 11) Is the pharmacy offering compounded drug products at wholesale to other state licensed persons or commercial entities for resale? If so, please obtain documentation showing the types and amounts of compounded drugs.
- 12) Please describe/document the processes used to make the compounded products including the scale of production and any in-process controls. Does the firm adhere to its standard operating procedures concerning labeling, environmental testing, and product quality? What quantity of compounded products is on hand for sampling?
- 13) Does a quality assurance program exist? How does it monitor the facilities, equipment, and personnel to assure proper performance? What does the QA program do with a finding that does not meet specification?
- 14) Does the pharmacy have in place a system for handling patient complaints and adverse events? If yes, please describe the system. What complaints and adverse events are in this system? What complaints and adverse events associated with compounded injectable products are in the system?
- 15) How does the firm receive, generate, use, and examine labels and labeling to assure that they are accurate, complete, and suitable for use?
- 16) What labels and labeling are provided by the pharmacy to accompany the compounded products when it is dispensed to each patient? Please obtain copies of any and all labels, labeling, and other materials associated with dispensed compounded products.
- 17) What are the specific batch sizes that are prepared for each product and how often is each batch prepared?
- 18) Does the pharmacy compound drug products from bulk drug substances/active pharmaceutical ingredients (APIs) that are not components of FDA-approved products? If so, what are the bulk drug substances/APIs and what is the volume of drugs (e.g., number of doses or prescriptions per year) compounded from the bulk drug substances/APIs?
- 19) What are the names and addresses of the suppliers of the bulk drug substances/APIs used to compound products?
- 20) Are these bulk drug substances/APIs manufactured in FDA registered establishments? How does the firm assure the accuracy and quality of the bulk drug substances/APIs and are they guaranteed or otherwise determined to meet official compendia requirements? Is this verified, and if so, how?
- 21) Is the compounding area in the facility designed to prevent contamination or cross-contamination of products and to avoid unnecessary traffic and airflow disturbances? Are drug products and supplies stored under appropriate temperature, light, moisture, sanitation, and ventilation conditions? Is routine

environmental monitoring and documentation performed to prove that the compounding environment is properly maintained?

- 22) Does the pharmacy use industrial scale manufacturing equipments? If so, please identify these equipments.
- 23) Are equipments maintained, calibrated, serviced, cleaned, and monitored to assure that they are operating properly and within acceptable tolerance limits (e.g., water system, HVAC, autoclaves, filling equipment, scales/balances, etc)? Are cleaned equipments and utensils protected from contamination prior to use?
- 24) Are sterile products made in an environment that prevents contamination? Is this environment properly maintained? If the company compounds sterile products from non-sterile starting materials, what methods of sterilization are employed by the facility?
- 25) Do the mixing instructions on formula worksheets include the order of mixing, diluting, or manipulating the raw materials used to make the compounded products? What type of in-process or finished product testing is performed and at what frequency?
- 26) Are production personnel adequately trained to manipulate sterile products to reduce the potential for contamination? Are the movement of people, materials, and equipment minimized so as not to compromise the aseptic conditions in the class 100 area? Does the firm perform media fill runs?
- 27) How are the packaging materials chosen to prevent any type of physical or chemical interaction with the drug product? Do packaging materials preserve the sterility and strength of the finished preparation until it is administered?
- 28) How is the compounded products' beyond-use-date determined? Is it based on direct testing or extrapolation from reliable literature sources? Is there written justification to support the beyond-use-date?

If you have any questions please contact me at [REDACTED]

[REDACTED] PharmD, MPH

PAC Code: 56D015
FACTS Number:

CC:

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Draft: [REDACTED] 05/14/07

CATS #

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