REPORT 9 OF THE REPORT OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH (A-13)
Pharmacy Compounding
(Reference Committee E)

EXECUTIVE SUMMARY

Objective. To provide an overview of contemporary issues in pharmacy compounding and recommend amendments to existing AMA policy on this topic.

Methods. English-language reports were selected from a PubMed and Google Scholar search from 2000 to May 2013, using the terms "pharmac*" in combination with "drug compounding/standards," "legislation/regulation," "oversight," and "epidemiology." Additional articles were identified by manual review of the references cited in these publications. Further information was obtained from the Internet sites of the U.S. Food and Drug Administration (FDA), American Society of Health-System Pharmacists (ASHP), National Association of Boards of Pharmacy (NABP), and Centers for Disease Control and Prevention (CDC). Information also was derived from an invitational meeting on pharmacy compounding organized by ASHP, the Pew Charitable Trusts' Drug Safety Project, and the American Hospital Association.

Results. Several different surveys have identified serious quality issues with compounded drugs. Since 2001 at least 20 pharmacy compounding errors have been associated with 1,022 adverse events, including 80 deaths, usually because of contamination of sterile products. Current compounding practices include traditional compounding of a product for an individual patient pursuant to a prescription, anticipatory compounding whereby products are compounded in batches prior to receipt of a specific patient prescription, and batch product used to supply hospitals as well as physician practices in the absence of a patient prescription. Some entities (recently referred to as compounding "manufacturers") operate in a fashion to compound various products in bulk for marketing and distribution into interstate commerce. Many hospitals outsource a significant portion of their sterile compounding needs. Compounding standards have been developed by the United States Pharmacopeia for both sterile and nonsterile products, and state-based accreditation of compounding pharmacies has been offered since 2006. Because of conflicting court decisions, some uncertainty exists regarding the reach of federal oversight by the FDA.

Conclusion. The use of compounded products is deeply embedded in the U.S. healthcare system. While traditional compounding pharmacies licensed and regulated by states continue to provide important patient-specific services, the overall practice of pharmacy compounding has evolved into an industrial-scale national business. A need exists to establish a clear boundary between traditional compounders and compounding manufacturers and to clarify specific areas of jurisdiction for the FDA and state boards of pharmacy. Because of the extensive array of current pharmacy compounding practices, and dependence of the healthcare system on such products, changes to the current system must be accomplished in a stepwise manner and in a way that does not otherwise jeopardize patient care. In the absence of a suitable FDA-approved product, allowances also should be made for the conduct of compounding practices that can supply products needed to manage urgent and emergent care scenarios in a safe manner.

REPORT OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH

CSAPH Report 9-A-13

Subject: Pharmacy Compounding

Presented by: Sandra A. Fryhofer, MD, Chair

Referred to: Reference Committee E
(Lawrence K. Monahan, MD, Chair)

INTRODUCTION

Definition and Practice

Pharmacy compounding involves the preparation of customized medications that are not commercially available for individual patients with specialized medical needs.[1] Traditional pharmacy compounding involves the act of combining, mixing, or altering ingredients to prepare a customized medication for an individual patient upon receipt of a valid prescription for the compounded product. Driven by medical needs, cost issues, physician preferences, and in some cases drug shortages, the compounding industry has evolved over the past 20 years to include high capacity, industrialized practices involving batch production. Such products often enter interstate commerce and are delivered to health care settings in the absence of a specific patient prescription.

Patient Harm from Pharmacy Compounding

Several different surveys conducted by the U.S. Food and Drug Administration (FDA) and state boards of pharmacy have identified serious quality issues with compounded drugs, most commonly clinically significant potency variations, but also lack of appropriate sterility testing.[2-11] Although the recent nationwide epidemic of fungal meningitis attributed to contaminated, preservative-free, compounded methylprednisolone injections focused attention on compounding practices, patient harm, including fatalities from compounded medications, is not new.[12] The Pew Charitable Trusts' Drug Safety Project has compiled a historical list of illnesses and deaths associated with compounded medications (also see testimony provided by FDA Commissioner Margaret Hamburg, MD, on this topic).[13,14] According to Pew, since 2001 at least 20 pharmacy compounding errors have been associated with 1,022 adverse events, including 80 deaths. Contamination of sterile products was the most common compounding error, though some incidents were the result of miscalculations and mistakes in filling prescriptions. Examples include bacterial contamination of steroid injections and parenteral nutrition products, contaminated cardioplegia solutions or ophthalmic drug products, and superpotent intravenous colchicine solutions.[2] Recently, an outbreak of fungal endophthalmitis after intravitreal injection of repackaged bevacizumab (Avastin®) and triamcinolone was reported affecting 8 patients who suffered loss of visual acuity.[15]

Action of the AMA House of Delegates 2013 Annual Meeting: Recommendations in Report 9 of the Council on Science and Public Health Adopted as Amended, and Remainder of Report Filed.

Given the evolution of the pharmacy compounding industry, the current reliance of the healthcare system in this country on compounded drug products, and the accumulation of patient harm, the Council believes a clear need exists for more effective and appropriate oversight. This report also is responsive to American Medical Association (AMA) Policy D-120.949, "Ensuring the Safe and Appropriate Use of Compounded Medications," which directs the AMA to monitor ongoing federal and state evaluations and investigations of the practices of compounding pharmacies, encourage the development of regulations that ensure safe compounding practices that meet patient and physician needs, and report back on efforts to establish the necessary and appropriate regulatory oversight of compounding pharmacy practices. Accordingly, this report provides an overview of contemporary issues in pharmacy compounding and recommends amendments to existing AMA policy on this topic.

METHODS

English-language reports were selected from a PubMed and Google Scholar search from 2000 to May 2013, using the terms "pharmac*" in combination with "drug compounding/standards," "legislation/regulation," "oversight," and "epidemiology." Additional articles were identified by manual review of the references cited in these publications. Further information was obtained from the Internet sites of the U.S. Food and Drug Administration (FDA), American Society of Health-System Pharmacists (ASHP), National Association of Boards of Pharmacy (NABP), and Centers for Disease Control and Prevention (CDC). Information also was derived from an invitational meeting on pharmacy compounding organized by ASHP, the Pew Charitable Trusts' Drug Safety Project, and the American Hospital Association.

CURRENT PHARMACY COMPOUNDING PRACTICES

In contrast to FDA-approved drugs, pharmacy compounded products are not evaluated for safety and efficacy, can be exempt from current good manufacturing practice requirements (cGMP), and lack standard product labels and instructions for safe use. Compounding pharmacies also are not required to report adverse events to the FDA. Nevertheless, despite the fact that all compounded products are viewed by the FDA as "unapproved drugs," their availability has become an integral part of the daily practice of medicine and pharmacy in this country. The current "market" for pharmacy compounding comprises a diverse array of practices, some of which overlap, as follows:

Traditional Compounding

Tradition compounding is the practice of compounding a product for an individual patient pursuant to a valid prescription for the compounded product.

Anticipatory Compounding

Anticipatory compounding is the practice of compounding a product in batches before the receipt of a valid patient-specific prescription, often based on historical patterns of use. This practice should be distinguished from compounding in batches to fill orders from hospitals or other health care providers without any prescription. The latter practice, which usually relies on the use of specific vendors, comprises a portion of a hospital's typical outsourcing activities (see below) and the provision of readily available "office stock" for clinicians.

Hospital Pharmacy-Based Compounding

Hospital pharmacies accomplish their own compounding of sterile infusions, solutions, injections, and pre-loaded syringes, as well as certain oral or topical products.

Hospital Outsourcing of Sterile Compounding Services.

Hospitals (as well as ambulatory clinics, surgical centers, and skilled nursing facilities) outsource orders for sterile compounded products. A portion of this practice is patient-specific, but most is done without a patient-specific prescription. Patient-specific compounded products are important in infectious disease, cardiology, immunosuppression, pain management, chemotherapy, fluid and electrolyte balance, required dilutions (e.g., pediatrics), allergy products, treatment of ocular diseases (topical, intravitreal, intraocular), pulmonary disease (inhalations), and certain irrigations. The typical scope of outsourcing includes pre-filled syringes (dilutions) for the operating room, epidural injections, opioid-based solutions for infusion pumps, pediatric electrolytes, concentrates (e.g., opioid and cardioplegia solutions), oxytocin infusions, some repackaged products, and products that may be unavailable due to drug shortages. The product array is driven to some degree by physician preferences. The trend toward increased outsourcing is based on sterility and quality assurance concerns, the need for standardization and availability of critical medications, pharmacy workload constraints, and lack of adequate facilities in-house.

Extent of Outsourcing. A survey of acute care hospitals participating in Medicare by the Office of Inspector General found that 92% of such hospitals relied on compounded sterile products.[16] Although 25% of these hospitals also used higher risk compounded products (e.g., the use of nonsterile ingredients or devices with the intent of compounding sterile end products), such products comprised less than 1% of compounded sterile products that were used in 2012. Of the hospitals that used higher risk compounded sterile products in 2012, 85% purchased these products from outside sources.

Compounding "Manufacturers"

Although not strictly a defined class (as of yet), it is generally agreed that compounding "manufacturers" are entities which compound sterile products in bulk in the absence of a patient specific prescription. Batches are used for "off the shelf" marketing and distribution to supply clients such as hospitals, ambulatory care centers, clinics, skilled nursing facilities, and physician offices.

CURRENT COMPOUNDING STANDARDS

All states license pharmacists to compound, but states have varying degrees of regulation, oversight, and enforcement activities for compounding pharmacies. ASHP has published Technical Assistance Bulletins and Guidelines, for example, on the "Quality Assurance for Pharmacy-Prepared Sterile Products," and "Guidelines on Outsourcing Sterile Compounding Services."[17,18] Other resources and training for sterile compounding also exist, and various state pharmacy practice acts create their own regulatory frameworks.

United States Pharmacopeia Standards

The United States Pharmacopeia Convention (USP), publisher of the United States Pharmacopeia and the National Formulary (USP–NF), the official compendia for drugs

marketed in the United States, developed a set of enforceable compounding standards for practice. The primary USP standards on compounding are contained in two general chapters from USP-NF; <795> Pharmaceutical Compounding−Nonsterile Preparations and <797> Pharmaceutical Compounding−Sterile Preparations.[19,20] In addition to these chapters, USP develops monographs that delineate standards for active pharmaceutical ingredients that may be compounded. The general chapters on compounding are supported by several other general chapters in USP-NF that address calculations, quality assurance, sterility tests, dosage forms, etc. A compilation of all general chapters relevant to compounding is available from USP via subscription or purchase.

USP-NF General Chapter <797> first became effective in 2004. Revised in 2008, it is currently undergoing further revision. The chapter is intended to promote practices for compounded sterile products that prevent harm to patients that could result from microbial contamination, endotoxins, incorrect strength, or unintended chemical or physical contamination of such products. This chapter applies to all practice settings where compounded sterile products are prepared and stored and identifies three risk levels for sterile compounded products, as follows:

<u>High Risk.</u>

The highest risk is present when nonsterile ingredients or devices are used, and/or a product requires terminal sterilization. Examples include infusion pump solutions or epidural injections created from bulk powdered ingredients. High risk products should be used within 24 hours of preparation if stored at room temperature, or within 3 days if refrigerated, unless sterility testing is conducted to support extended labeling.

<u>Medium risk</u>

A medium risk for contamination would apply when multiple individual or small doses of sterile products are combined or pooled to prepare a compounded sterile product that will be administered either to multiple patients or to one patient on multiple occasions. Medium risk also exists when the compounding process includes complex aseptic manipulations or is of unusually long duration. One example is the compounding of total parenteral nutrition fluids (using manual or automated devices) during which there are multiple injections, detachments, and attachments of nutrient sources to a final sterile container. Another example would be filling the reservoirs of injection and infusion devices with more than three sterile drug products and evacuating air before the filled device is dispensed.

<u>Low risk</u>

The lowest risk for sterile compounding involves practices such as the single volume transfer of sterile dosage forms using sterile devices, or the simple aseptic measuring and transferring of ≤3 packages of sterile products to compound drug admixtures and nutritional solutions.

It should be noted that although Chapter <797> incorporates a number of core standards for training, facility design, labeling, and quality control and includes some suggested standard operating procedures for sterile compounding, it is not a substitute for, or equivalent to, cGMP required by the FDA for pharmaceutical manufacturers. The latter are process-directed and based on a system of specific standard operating procedures that the Agency evaluates for adherence to, within the manufacturer’s quality control system. The standards contained in

USP-NF General Chapter <797> are generally most applicable to the compounding of sterile products in small batches.

State Boards of Pharmacy and USP Compounding Standards

As of January 2012, 18 state boards of pharmacy required compliance with USP <797>, 27 states and the District of Columbia have incorporated only selected portions or do not cite the chapter, but have regulations in place addressing sterile compounding or parenteral nutrition, and five states lack any mention of USP <797> and have no regulations on sterile compounding.[21]

REGULATION AND ACCREDITATION OF COMPOUNDING PHARMACIES

States

Compounding pharmacies are licensed and regulated by their respective state boards of pharmacy. As noted above, some states require adherence to USP standards, while others rely on their own regulatory standards.

In an effort to improve standards, the Pharmacy Compounding Accreditation Board (PCAB) was created in 2006 through the combined efforts of several national pharmacy organizations and USP.[22] The mission of PCAB is to promote high quality pharmacy compounding through a voluntary accreditation program that recognizes adherence to established principles, policies and standards. PCAB accreditation gives patients, prescribers, and payers a way to select a pharmacy that meets or exceeds USP's quality standards. PCAB accreditation means the pharmacy has independent, external validation that it meets nationally accepted quality assurance, quality control, and quality improvement standards. However, only about 200 compounding pharmacies are currently accredited out of an estimated total of 7,000. A searchable state-by-state listing of accredited compounding pharmacies is maintained on the PCAB website.

Federal

The FDA has long been concerned about pharmacy compounding practices that deviate from the traditional model. The FDA first issued a Compliance Policy Guide (CPG) in 1992 that described certain factors that the Agency would consider in its enforcement approach to pharmacies that were producing drugs and appeared to be functioning more as manufacturers. That CPG remained in effect until Congress enacted the Food and Drug Administration Modernization Act of 1997. This legislation added a new Section 503A to the Food Drug and Cosmetic (FD&C) Act addressing FDA's authority over compounded drugs.[23] In doing so, Section 503A exempted compounded products from new drug approval, cGMP requirements, and adequate directions for use requirements under certain circumstances, and set forth conditions that must be followed by pharmacies or physicians in order to quality for these exemptions. Among other things, the statute also included a requirement for a patient specific prescription for compounded products, prohibited advertising or promoting, and "compounding regularly or in inordinate amounts any drug products that are essentially copies of a commercially available drug product."

Before the law took effect, compounding pharmacies sued to block its implementation. In *Thompson v. Western States Medical Center* (535 U.S. 357, 2002), the United States Supreme Court held that congressional restriction of advertising and promotion by

compounding pharmacies was unconstitutional. However, the Court did not rule on whether that advertising and promotion provision was "severable" from the rest of Section 503A. Federal circuit courts of appeals' decisions on this question are split. The 9th Circuit (including several western states and territories) holds that the provisions are not severable and hence Section 503A is considered void in its entirety; the 5th Circuit (several southwestern states) holds that the provisions are severable, and hence the remainder of Section 503A remains valid and enforceable.

Accordingly, different federal law exists for FDA authority depending on where the compounding pharmacy is located. It should be noted that the FDA revised the CPG in 2002 after the decisions from the U.S. Supreme Court and Ninth Circuit, but before the decision of the Fifth Circuit, and without the advertising and interstate shipment provisions. The CPG articulates nine factors that the Agency would consider in their federal oversight capacity (see Appendix).[24] In weighing their determination, the FDA considers whether the prescribing practitioner has determined that a compounded product is necessary for the particular patient and would provide a significant difference, as compared with the FDA-approved commercially available drug product.

The FDA also can conduct "for-cause" inspections based on complaints. In the wake of the fungal meningitis outbreak, the FDA identified 31 compounding pharmacies engaging in sterile compounding practices for focused priority inspections.[14] Virtually all facilities had significant objectionable conditions and quality concerns and were issued form FDA-483.[25] This form does not constitute a final Agency determination of whether any condition is in violation of the FD&C Act, but the observations often serve as evidence of a violation of the Act and its implementing regulations. Some additional recalls of compounded products or safety alerts have subsequently occurred.

RISK-BASED APPROACHES TO REGULATION AND OVERSIGHT

USP General Chapter <797> identifies categories of risk based on process (i.e., sterile-to-sterile or nonsterile-to-sterile, and the number of product manipulations required or need for end-product sterilization). The degree of risk is inherent with the product type. Manipulation of sterile FDA-approved products is much less risky than starting with nonsterile active pharmaceutical ingredients and attempting to compound a sterile injectable product.

Some risk factors are common to both patient specific and batch compounding such as facility characteristics, personnel training, level of standardization, verification mechanisms, and compliance with standard operating procedures. For patient-specific compounding, beyond use dating and storage outside of the pharmacy also need to be addressed. For sterile batch compounding, standard operating procedures, segregation of materials, batch sizes, in-process checks, and sterilization methods assume increasing importance. The larger the operation, the more closely these processes should be aligned with cGMP. Product quarantine, assurance of sterility, and recall mechanisms are necessary requirements for compounding manufacturers, not to mention assurance of batch potency. Product volume and whether the facility attempts to generate product beyond its capabilities or to fill a temporary gap created by commercial drug shortages represent other categories of risk. Finally, distribution, storage, and repackaging practices also are relevant.

CURRENT LEGISLATION

According to the National Conference of State Legislatures, several states have introduced bills related to the regulation of compounding pharmacies. One issue is potential limits on office-use dispensing, or the practice of physicians obtaining compounded products without a patient prescription to be used in an office setting. At the state level, interest is moving in the direction of regular inspections, composition of state boards to include the relevant expertise for addressing sterile compounding issues, and more widespread adoption of USP standards for sterile compounding.

In early May, bipartisan legislation intended to clarify oversight for pharmaceutical compounding was introduced in the Senate (S. 959−Pharmaceutical Compounding Quality and Accountability Act). This goal of this legislation is to establish a clear boundary between traditional compounders and compounding manufacturers, and establish uniform federal quality standards for compounding manufacturers. Compounding manufacturers are defined as entities that (1) compound a sterile product prior to or without receiving a prescription (or that repackage a drug using sterile, preservative-free single dose vials, or that pool any sterile drug product) and, (2) introduce such drugs into interstate commerce. Interstate shipment of sterile compounded products produced by a hospital pharmacy within a self-contained hospital system would be exempted from this definition, and would be regulated as traditional compounding. Compounding manufacturers would not be licensed as state pharmacies and would have to register with the FDA (for a fee), provide a list of their products, operate in compliance with cGMP, investigate and report adverse events, and properly label products.

The legislation also prohibits the compounding of certain categories of drugs. It also preserves the state's primary role in the oversight of traditional pharmacy compounding, and permits limited quantities of products derived from anticipatory compounding, although biologics would be excluded from this practice, except in narrow circumstances (i.e., pediatric use within a hospital setting). The AMA submitted formal comments on the draft legislation, but it is not clear at this time how quickly this bill will move or what the final elements will be.

AMA POLICY

Current AMA Policy H-120.945, "AMA Action on Non FDA-Approved Compounded Medications," recognizes that compounding pharmacies should comply with current USP-NF compounding monographs, when available, and recommends that they be required to conform with USP-NF General Chapters on pharmaceutical compounding to ensure the uniformity, quality, and safety of compounded medications. AMA policy also recognizes the value of the PCAB accreditation program and encourages all state boards of pharmacy to require compounding pharmacies in their states to obtain the PCAB™ Seal of Accreditation or, alternatively, to satisfy comparable standards that have been promulgated by the state in its laws and regulations governing pharmacy practice. Finally, AMA policy encourages state boards of pharmacy and the NABP to work with the FDA to identify and take appropriate enforcement action against entities that are "illegally" manufacturing medications under the guise of pharmacy compounding.

COMMENT

While traditional compounding pharmacies licensed and regulated by states continue to provide important patient-specific services, the overall practice of pharmacy compounding has evolved into an industrial-scale national business. A need exists to establish a clear boundary between traditional compounders and compounding manufacturers and to clarify specific areas of jurisdiction for the FDA and state boards of pharmacy. Because of the extensive array of current pharmacy compounding practices, and dependence of the healthcare system on such products, changes to the current system must be accomplished in a stepwise manner and in a way that does not otherwise jeopardize patient care. In the absence of a suitable FDA-approved product, allowances also must be made for compounding practices that can realistically supply products needed to manage urgent and emergency situations in individual patients.

RECOMMENDATION

The Council recommends that the following statement be adopted and the remainder of the report be filed.

That Policy H-120.945, "AMA Action on Non FDA-Approved Compounded Medications," be amended to read as follows:

Our AMA: 1. recognizes that traditional compounding pharmacies must be subject to state board of pharmacy oversight and comply with current United States Pharmacopeia and National Formulary (USP-NF) compounding monographs, when available, and recommends that they be required to conform with USP-NF General Chapters on pharmaceutical compounding to ensure the uniformity, quality, and safety of compounded medications; 2. ~~recognizes the accreditation program of the Pharmacy Compounding Accreditation Board (PCAB™) and the PCAB™ Seal of Accreditation as a means to identify compounding pharmacies that adhere to quality and practice standards, including those set forth in the USP-NF, for the preparation of individualized medications for specific patients; 3~~. encourages all state boards of pharmacy to reference sterile compounding quality standards, including but not limited to those contained in United States Pharmacopeia Chapter <797>, as the standard for sterile compounding in their state ~~require compounding pharmacies in their states to obtain the PCAB™ Seal of Accreditation or, alternatively,~~ and to satisfy other relevant ~~comparable~~ standards that have been promulgated by the state in its laws and regulations governing pharmacy practice; ~~and 4~~. 3.supports the view that facilities (other than pharmacies within a health system that serve only other entities within that health system) that compound sterile drug products without receiving a prescription order prior to beginning compounding and introduce such compounded drugs into interstate commerce be recognized as compounding manufacturers subject to FDA oversight and regulation; 4. supports the view that allowances must be made for the conduct of compounding practices that can realistically supply compounded products needed to meet anticipated clinical needs, including urgent and emergency care scenarios in a safe manner; and, ~~4~~5. in the absence of new federal legislation affecting the oversight of compounding pharmacies, continues to encourage~~s~~ state boards of pharmacy and the National Association of Boards of Pharmacy (NABP), ~~the umbrella organization for state boards of pharmacy,~~ to work with the United States Food and Drug Administration (FDA) to identify and take appropriate enforcement action against entities that are illegally manufacturing medications under the guise of pharmacy compounding. (BOT Action in response to referred for decision Res. 521, A-06)
(Modify Current HOD Policy)

Fiscal note: Less than $500

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APPENDIX

Compliance Policy Guidance for FDA Staff and Industry
Sec. 460.200 Pharmacy Compounding-Policy

Generally, FDA will continue to defer to state authorities regarding less significant violations of the Act related to pharmacy compounding of human drugs. FDA anticipates that, in such cases, cooperative efforts between the states and the Agency will result in coordinated investigations, referrals, and follow-up actions by the states. However, when the scope and nature of a pharmacy's activities raise the kinds of concerns normally associated with a drug manufacturer and result in significant violations of the new drug, adulteration, or misbranding provisions of the Act, FDA has determined that it should seriously consider enforcement action. In determining whether to initiate such an action, the Agency will consider whether the pharmacy engages in any of the following acts:

1. Compounding of drugs in anticipation of receiving prescriptions, except in very limited quantities in relation to the amounts of drugs compounded after receiving valid prescriptions.

2. Compounding drugs that were withdrawn or removed from the market for safety reasons. Appendix A provides a list of such drugs that will be updated in the future, as appropriate.

3. Compounding 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.

4. Receiving, storing, or using drug substances without first obtaining written assurance from the supplier that each lot of the drug substance has been made in an FDA-registered facility.

5. Receiving, storing, or using drug components not guaranteed or otherwise determined to meet official compendia requirements.

6. Using commercial scale manufacturing or testing equipment for compounding drug products.

7. Compounding drugs for third parties who resell to individual patients or offering compounded drug products at wholesale to other state licensed persons or commercial entities for resale.

8. Compounding drug products that are commercially available in the marketplace or that are essentially copies of commercially available FDA-approved drug products. In certain circumstances, it may be appropriate for a pharmacist to compound a small quantity of a drug that is only slightly different than an FDA-approved drug that is commercially available. In these circumstances, FDA will consider whether there is documentation of the medical need for the particular variation of the compound for the particular patient.

9. Failing to operate in conformance with applicable state law regulating the practice of pharmacy.