



JONES DAY
COMMENTARY

DO COMPOUNDING PHARMACIES “LIVE IN SIN”?

THE FDA’S ASSERTION OF ENFORCEMENT AUTHORITY OVER PHARMACY COMPOUNDING, AND TWO COURTS’ EFFORTS TO BLESS THE PRACTICE

Pharmacy compounding, as the Food and Drug Administration (“FDA”) explains, “is an age-old practice in which pharmacists combine ... ingredients to create unique medications that meet specific needs of individual patients.” The FDA has recognized that “pharmacy compounding is a vital service that helps many people.”¹ Congress expressly recognized and regulated the practice by adding §503A to the Food, Drug, and Cosmetic Act. But the fundamental legal questions about compounding still have no definitive answer.

Is pharmacy compounding even legal? The FDA’s position is oddly ambiguous. The relevant FDA guidance document states that §503A “is now invalid,” and the Courts of Appeals are split on this point. The FDA warns that certain perceived abuses are subject to enforcement action, but the guidance document is pointedly silent regarding the legality of compounding as it is traditionally practiced. The FDA’s implied

position, and the stance it has taken in recent litigation, is that although even traditional forms of compounding are illegal, the FDA will exercise its discretion and will refrain from enforcing against most compounding.

In response, pharmacists have complained to the courts that “it remains no small burden ... to ‘live in sin’—their livelihood having no greater assurance than the FDA’s good graces.”² Two recent court rulings have accepted this argument: the Fifth Circuit’s 2005 decision in *Medical Center Pharmacy*, and *Franck’s*, a September 2011 opinion from the Middle District of Florida. These two opinions, although approaching the analysis quite differently, have found common ground. Both hold that the FDA has authority to curb abuses. But these two courts also took the view that traditional compounding practices are legal, and that the livelihoods of compounding pharmacies do not depend upon the FDA’s tolerance of “sin.”

PHARMACY COMPOUNDING AND THE FIRST 50 YEARS OF THE FOOD, DRUG, AND COSMETIC ACT

The practice of pharmacy compounding, by all accounts, is both ancient and ubiquitous. Pharmacies have compounded drugs with mortars and pestles—the tools that have become their symbols—for centuries, if not longer. In the 19th century, the vast majority of prescriptions were filled through compounding. Pharmacists continued to fill most prescriptions through compounding until well after the 1938 enactment of the Food, Drug, and Cosmetic Act (the “Act,” or “FDCA”).³

Today, pharmaceutical manufacturers produce, in final form, the vast majority of medications. However, compounding remains widespread. The FDA views compounding as vital, particularly for people “who are allergic to inactive ingredients in FDA-approved medicines, and others who need medications that are not available commercially.” The FDA likewise recognizes that “compounded medications are also prescribed for children who may be unable to swallow pills, need diluted dosages of a drug made for adults, or are simply unwilling to take bad-tasting medicine.”⁴ Walgreens, the nation’s largest pharmacy chain, advertises compounding services on its web site, claiming essentially the same benefits.

The FDCA prohibits the sale of “new drugs” without the approval of the FDA. Multiple courts have found the literal definition of “new drugs” to be sufficiently broad to encompass medicines resulting from pharmacy compounding. While pharmacies in theory could seek approval for compounded products, “because obtaining FDA approval for a new drug is a costly process, requiring FDA approval of all drug products compounded by pharmacies for the particular needs of an individual patient would, as a practical matter, eliminate the practice of compounding.”⁵

The original 1938 Act left unanswered the question of whether the prohibition of unapproved drugs was intended to ban compounding. Indeed, the original Act does not mention pharmacy compounding in any context. According to the Fifth Circuit, “[f]or roughly fifty years following the FDCA’s enactment, the compounding question lay dormant, without dispute and without answer.”⁶ Most states regulate compounding as part of their oversight of pharmacies.

Accordingly, the U.S. Supreme Court observed that “[f]or approximately the first 50 years after the enactment of the FDCA, the FDA generally left regulation of compounding to the States.”⁷

The first mention of compounding in the Act arrived with the Drug Amendments of 1962. As part of an extensive overhaul of the Act, the Drug Amendments required manufacturers and others to register their establishments and broadened the ability of the FDA to conduct site inspections. The Amendments, however, exempted “pharmacies ... which do not ... compound, or process drugs for sale other than in the regular course of their business of dispensing or selling drugs at retail.” These provisions remain in effect, at sections 510(g)(1) and 704(a)(2)(A) of the Act.

THE FDA’S CONCERNS ABOUT COMPOUNDING, AND RECENT ENFORCEMENT ACTIVITY

Beginning in the 1990s, and continuing to the present, the FDA has become increasingly concerned about the dangers it perceives from compounding. These concerns fall roughly into two categories. First, some companies allegedly engage in the large-scale production of drugs under the guise of compounding. Such companies, in the FDA’s eyes, are acting like manufacturers, but often without complying with the regulations requiring good manufacturing practices. This can cast doubt upon the purity and quality of the drugs, and a 2006 study performed by the FDA found that one third of the compounded drugs sampled “failed analytical testing using rigorously defensible testing methodology.”⁸ The FDA considers a company to be an illegal manufacturer, rather than a traditional compounder, if it produces drugs in large volumes without having first received prescriptions for the drugs, or if it produces drugs that are substantially identical to approved drugs (and hence the compounding does not further the goal of creating custom-tailored products for patients who cannot use available approved drugs).

The FDA’s second principal concern is that since very few compounded drugs are within the scope of an approved new drug application, the FDA has not verified the safety and efficacy of most compounded medicines. These concerns are enhanced where the FDA comes to believe that

particular drugs are dangerous as compounded, or are ineffective for their promoted uses. Thus, in recent years, FDA enforcement has often focused on removing specific compounded drugs from the market. In 2008, for example, the FDA launched a major campaign against “bio-identical hormone replacement therapy” (“BHRT”), alleging that compounders of BHRT products were making unsubstantiated claims that BHRT was a superior treatment for menopausal hormone therapy, Alzheimer’s disease, stroke, and cancer. Other enforcement campaigns in the past five years have targeted products made for “lipo-dissolve” treatments, topical anesthetic creams, inhalation drugs, and domperidone.

When discussing its enforcement policies—at least regarding drugs for human use—the FDA is always careful to state that it is not targeting “traditional” pharmacy compounding, meaning small-scale activity in response to physician prescriptions. (The FDA’s policy toward the compounding of animal drugs is in some respects stricter, as discussed below.) Nevertheless, the FDA has declared that the entire practice of compounding is “under FDA scrutiny.” The FDA publishes an article for consumers titled “The Special Risks of Pharmacy Compounding” and publishes posters warning that compounded drugs can “present risks to patients” and “can expose many patients to health risks associated with unsafe or ineffective drugs.”⁹

THE ENACTMENT AND SUDDEN DEMISE OF FEDERAL LEGISLATION REGULATING PHARMACY COMPOUNDING, AND THE FDA’S ASSERTION OF UNBOUNDED ENFORCEMENT DISCRETION

In 1997, Congress amended the FDCA to add a new §503A, titled “Pharmacy Compounding.” Section 503A exempted compounded drugs from key portions of the Act: the prohibition against selling unapproved new (human) drugs, the requirement to comply with “good manufacturing practices” regulations, and certain labeling requirements.

Section 503A also reflects many of the FDA’s concerns about the practice of compounding. To qualify for the exemption, the drug must be provided in response to a physician’s prescription, and the drug must be compounded by a licensed

pharmacist or physician who does not “regularly or in inordinate amounts” compound copies of commercially available drugs. Section 503A limits which drug substances can be used for compounding, and the FDA can prohibit the use of dangerous substances. Lastly, the physician prescription must be “unsolicited,” and the pharmacy must not advertise or promote the compounding of any particular drug.

This last set of restrictions proved troublesome. A group of compounding pharmacies immediately filed suit, alleging that the advertising restrictions violated pharmacies’ First Amendment rights. The Ninth Circuit agreed and struck down the entirety of §503A.¹⁰ The Supreme Court affirmed that the advertising restrictions are unconstitutional but explicitly did not decide whether the remainder of §503A can be severed. *Thompson v. Western States Medical Center*, 535 U.S. 357 (2002).

While the *Western States* decision was pending, the FDA had begun implementing §503A. The FDA promulgated regulations prohibiting the use of a long list of drug products and established a standing Pharmacy Compounding Advisory Committee.¹¹ But after the *Western States* decision, the FDA stated that “all of section 503A is now invalid.” Although the FDA never withdrew the regulations it had enacted under §503A, the Pharmacy Compounding Advisory Committee stopped meeting, and the FDA did not update the regulation listing prohibited drug products.

The FDA’s position, stated as recently as 2010, is that “[b]ecause compounded drugs are ‘new drugs’ under the FDCA that are unapproved, the statute generally prohibits their introduction into interstate commerce.”¹² The FDA has issued a nonbinding guidance document setting out when it will “consider exercising its enforcement discretion regarding pharmacy compounding.” Generally, the FDA does not plan to bring enforcement proceedings against “traditional” compounding. But notwithstanding §503A, which exempts compliant pharmacies from certain code provisions, the guidance warns that the FDA can charge pharmacists with violating those same code provisions.

The FDA views its authority to enforce as being broader than the power delegated under §503A and the resulting

regulations. For example, enforcement proceedings are likely against pharmacies that compound using any of the drug products listed in the guidance's appendix. This list is similar to the list that had been promulgated through notice-and-comment rulemaking, but the guidance lists drugs that are not named in the formal regulation. Furthermore, drugs that have been at the center of recent FDA enforcement campaigns, including BHRT and domperidone, do not appear in either the guidance or the regulation.

MEDICAL CENTER PHARMACY AND THE PHARMACIES THAT WOULD NOT “LIVE IN SIN”

Following the *Western States* decision, a group of compounding pharmacies brought a suit challenging the FDA's authority to regulate compounded drugs as “new drugs” or “new animal drugs.” The pharmacy plaintiffs argued that they did not “live in sin.” They asserted that even though §503A had been struck down, compounding remained legal, and pharmacies' right to compound drugs did not depend upon the FDA's favorable exercise of discretion. See *Medical Center Pharmacy v. Mukasey*, 536 F.3d 383 (5th Cir. 2008).

The peril of “living in sin” is by no means trivial. The FDA's enforcement policy does not bind the FDA, and it is subject to change at any time without warning. Furthermore, selling unapproved “new drugs” is a crime, punishable by imprisonment.

The pharmacies' arguments were well received by the Fifth Circuit, although the resulting victory was less sweeping than the pharmacies had hoped. The *Medical Center Pharmacy* court viewed the enactment of §503A as making the case “easy.” Breaking with the Ninth Circuit, the Fifth Circuit held that the unconstitutional restrictions on advertising are severable from the remainder of §503A, which remains in effect. Thus, although compounded drugs are “new drugs” under the FDCA, compounding is legal. As long as pharmacies comply with the requirements set out in §503A (apart from the restrictions on advertising), the compounded drugs are exempt from the rules specified in §503A, including the prohibition against the sale of unapproved new drugs.

FRANCK'S AND THE COMPOUNDING OF ANIMAL DRUGS

Drugs intended for animals, like human drugs, are also commonly compounded. Indeed, compounding may be more prevalent for animal drugs, since “for significant diseases there are no effective FDA-approved drugs.”¹³

Under the Animal Medicinal Drug Use Clarification Act of 1994,¹⁴ veterinarians are allowed to prescribe approved human and animal drugs “off-label”—to treat conditions in animals even in the absence of an FDA finding that the drug is safe and effective for that particular purpose. The FDA interprets this statute as allowing the compounding of animal drugs, and accordingly it promulgated regulations permitting the practice.¹⁵ The regulations, however, permit compounding only from drugs that are in their approved, final form. The regulations do not permit “compounding from bulk drugs.” (“Bulk” compounding does not refer to the amount of the drug substance used but means using the chemicals from which a finished product can be manufactured, rather than using final-form medicines.)

The omission of bulk drugs from the animal compounding regulation is significant. There does not appear to be any dispute that compounding from bulk drugs falls squarely within the “traditional” practice of compounding. Indeed, courts have found that it is more difficult, more dangerous, and more expensive to compound from finished products. Finished products typically are mixtures of active and inactive ingredients, and compounding from such a mixture requires a pharmacist to reverse engineer the finished product into its unfinished form, and then determine how to separate and recombine ingredients into the prescribed dosage, formulation, and strength. The FDA, in excluding bulk drugs from the animal drug compounding regulations, did not find that compounding from bulk drugs was unduly dangerous or in any respect inferior to compounding from finished products. The FDA's rationale was that in the 1994 amendments, Congress permitted only off-label uses of approved drugs, and therefore Congress did not authorize the use of bulk products.¹⁶ By contrast, §503A—which focuses on drugs compounded for humans—requires the use of bulk drug substances.

In any event, the FDA takes a firm position against the bulk compounding of animal drugs. The relevant guidance document flatly states that “the compounding of a new animal drug ... from bulk drug substances results in an adulterated new animal drug....”

The FDA began cracking down on bulk compounding in the late 1980s. Rather than proceed against the people performing the compounding (largely veterinarians, as well as pharmacies), the FDA obtained injunctions against their suppliers.¹⁷ In doing so, the FDA did not prove that compounding was illegal. Instead, the FDA used a wrinkle in the labeling regulations that effectively made it impossible for wholesalers to lawfully label bulk containers.¹⁸

In 2010, the FDA brought suit against a Florida pharmacy, *Franck's Lab*, seeking to enjoin the bulk compounding of animal medications. The FDA took “the bright-line position that any compounding of animal medications from bulk substances violates [the Act], even when conducted by a state-licensed pharmacist for an individual animal patient pursuant to a valid veterinary prescription.” The *Franck's* court found, through undisputed evidence, that compounding from bulk substances pursuant to a veterinary prescription qualifies as “traditional compounding,” and that the *Franck's* litigation was the FDA's first attempt to bar a pharmacy from engaging in bulk compounding for non-food-producing animals. The FDA's position, as paraphrased by the court, was that “state-licensed veterinarians and pharmacists have, with the FDA's blessing, been ‘living in sin’....”¹⁹

The *Franck's* court, like the Fifth Circuit in *Medical Center Pharmacy*, took a dim view of the notion that compounding pharmacies across the nation are “living in sin,” and found in favor of the pharmacy. But the holdings of the two courts are in conflict. *Medical Center Pharmacy* held that the compounding of animal drugs is lawful only if performed within the confines permitted by the Animal Medicinal Drug Use Clarification Act. But no statute or regulation expressly authorizes bulk compounding of animal drugs, and as a result, the *Franck's* court could not decide in the pharmacy's favor without a broader holding. *Franck's* thus held that Congress had never intended to prohibit traditional compounding, notwithstanding the literal language of the FDCA. To find

such a prohibition by implication from the broad scope of the statutory definition of “new animal drugs” would be akin to hiding an elephant in a mouse hole.

Franck's did hold that compounding created “new animal drugs,” that the FDA could distinguish between manufacturing and compounding, and that the FDA could regulate the former. But the FDA's authority is restricted to the power to curb abuses. By asserting authority to enjoin a pharmacy from traditional pharmacy compounding in compliance with state law, *Franck's* held, “the FDA overreaches.”

CONCLUSION

Despite the recent efforts of courts to regularize the federal law of compounding, the law remains very much in flux. *Medical Center Pharmacy* did not resurrect §503A nationwide. Rather, the case created a circuit split, and the FDA's published position is that it will follow only *Medical Center Pharmacy* in the Fifth Circuit. The *Franck's* decision was issued by a district court, and it remains subject to appeal.

Franck's, if appealed, creates an important battlefield, and should be followed closely. The *Franck's* holding—if upheld—supports the conclusion that pharmacy compounding has always been legal and is not a sin permitted at the sufferance of federal regulators.

LAWYER CONTACTS

For further information, please contact your principal Firm representative or one of the lawyers listed below. General email messages may be sent using our “Contact Us” form, which can be found at www.jonesday.com.

Jonathan Berman

Washington
+1.202.879.3669
jberman@jonesday.com

Michael Sennett

Chicago
+1.312.269.4243
msennett@jonesday.com

ENDNOTES

- 1 FDA Consumer Health Information, *The Special Risks of Pharmacy Compounding* (May 31, 2007).
- 2 *Medical Center Pharmacy v. Mukasey*, 536 F.3d 383, 400 (5th Cir. 2005); accord *United States v. Franck's Lab, Inc.*, Case No. 5:10-cv-147-Oc-32TBS (M.D. Fla., Sept. 12, 2011).
- 3 Pastner, Bruce M.D., J.D., *Pharmacy Compounding of Bioidentical Hormone Replacement Therapy (BHRT): A Proposed New Approach to Justify FDA Regulation of These Prescription Drugs* at 9.
- 4 FDA Consumer Health Information, *The Special Risks of Pharmacy Compounding* (May 31, 2007).
- 5 *Thompson v. Western States*, 535 U.S. 357, 369 (2002).
- 6 *Medical Center Pharmacy*, 536 F.3d at 389.
- 7 *Western States*, 535 U.S. at 362. This did not mean, however, that the FDA had no role in regulating pharmacies. For example, in 1948, the Supreme Court upheld the conviction of a pharmacist who sold medicine in violation of federal labeling requirements. *United States v. Sullivan*, 332 U.S. 689 (1948).
- 8 <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm204237.htm>
- 9 <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm107836.htm>, <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm238590.htm>
- 10 *Western States Medical Center v. Shalala*, 238 F.3d 1090 (9th Cir. 2001).
- 11 21 C.F.R. §§ 14.100(c)(18), 216.24.
- 12 This language is taken from a warning letter that is highlighted on the FDA's web site. The FDA took a similar position before the Fifth Circuit while litigating *Medical Center Pharmacy*.
- 13 *United States v. 9/1 KG. Containers*, 854 F.2d 173, 174 (7th Cir. 1988).
- 14 Codified at §512(a)(4), (5) of the Food, Drug, and Cosmetic Act.
- 15 21 C.F.R. § 530.13.
- 16 61 Fed. Reg. 25108 (May 17, 1996); 61 Fed. Reg. 57740 (Nov. 7, 1996).
- 17 *United States v. Algon Chemical Inc.*, 879 F.2d 1154 (3rd Cir., 1989); *9/1 KG. Containers*, 854 F.2d 173 (7th Cir. 1988).
- 18 Generally, drugs must be labeled to provide patients with "adequate directions for use." FDCA, §502(f). There is an exception for bulk drugs that are shipped to manufacturers named in an approved application. 21 C.F.R. §201.122. However, compounders do not hold such approvals, and the courts held that compounders therefore do not qualify for the exception.
- 19 *United States v. Franck's Lab, Inc.*, Case No. 5:10-cv-147-Oc-32TBS (M.D. Fla., Sept. 12, 2011).