Congressional Research Service

FDA's Authority to Regulate Drug Compounding: A Legal Analysis

Jennifer Staman
Legislative Attorney

October 17, 2012

Congressional Research Service
7-5700
www.crs.gov
R40503

CRS Report for Congress
Prepared for Members and Committees of Congress

Summary

In light of the recent meningitis outbreak, believed to have been caused by a contaminated compounded steroid injection, the regulation of drug compounding has received significant attention. Compounding is traditionally defined as a process of combining, mixing, or altering ingredients in order to create a medication for a particular patient. However, as in the case of the pharmacy that produced the steroid medication, concerns have been raised about compounding pharmacies producing drugs on a larger scale, something more akin to drug manufacturing. While drug compounding has historically been regulated primarily by states through their regulation of pharmacies, recent questions have been raised about the extent to which the Federal Food, Drug, and Cosmetic Act (FFDCA) governs this practice, and what authority the U.S. Food and Drug Administration (FDA) has to regulate a compounded drug as a "new drug," subject to approval by the FDA, as well as other requirements.

In 1997, Congress enacted the FDA Modernization Act of 1997 (FDAMA), which was a comprehensive revision of the FFDCA. Section 127 of FDAMA added Section 503A to the FFDCA, which excepted compounded drugs from various "new drug" requirements, conditioned upon the compounded drugs meeting a variety of restrictions. One of the restrictions in Section 503A of the FFDCA was that drug providers were prohibited from soliciting or advertising particular compounded drugs. These speech restrictions were challenged on First Amendment grounds and were struck down by the Supreme Court in *Thompson v. Western States Medical Center*. Following this decision, there was controversy over the current status of compounded drugs under the FFDCA and whether the remaining provisions of Section 503A remain good law, an issue that the Supreme Court did not address in *Western States*. The two circuits that addressed this issue took different positions. While the Ninth Circuit in *Western States* determined that Section 503A was struck down in its entirety, the Fifth Circuit in *Medical Center Pharmacy v. Mukasey* found that the lawful provisions of Section 503A are still in effect. Accordingly, these cases have created an interesting scenario of non-uniform enforcement throughout the U.S. In the Fifth Circuit, compounded drugs are specifically exempted from new-drug, adulteration, and misbranding requirements of the FFDCA if certain criteria are met; while in the Ninth Circuit (and, according to the FDA, the rest of the United States), compounded drugs are subject to these requirements, but the FDA may exercise discretion in taking action against an entity that violates these provisions. This report provides a brief historical overview of the FDA's regulation of drug compounding and addresses these conflicting decisions. The report will also address the FDA's current authority to regulate compounded drugs under the FFDCA in light of these decisions.

Contents

Background 1
Thompson v. Western States Medical Center 3
2002 FDA Compliance Policy Guide 5
Medical Center Pharmacy v. Mukasey 6
Issues with Current FDA Authority to Regulate Drug Compounding 8

Contacts

Author Contact Information 11

Background

Under its traditional definition, drug compounding is a process in which a pharmacist combines, mixes, or alters various drug ingredients to create a medication for an individual patient in response to a practitioner's prescription.[1] It is generally used to prepare medications that are not typically commercially available, such as a drug in a lower dosage for a child, or a drug without a dye or a preservative in response to a patient allergy.[2] Compounding is considered a conventional component of the practice of pharmacy and has historically been regulated at the state level.[3]

The Federal Food, Drug, and Cosmetic Act (FFDCA), as amended, establishes certain minimum standards for the manufacturing, marketing, and distribution of drugs, and authorizes the FDA to ensure that drugs and other products marketed in the United States are safe and effective for their intended uses.[4] The act prohibits any person from introducing a "new drug" into interstate commerce unless it is approved by the FDA. A "new drug" is defined by the act as "[a]ny drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug is not generally recognized … as safe and effective for use under the condition prescribed, recommended, or suggested in the labeling thereof."[5] In order to be determined to be safe and effective, new drugs are subject to a lengthy approval process, which is supervised by the FDA. The FFDCA also contains requirements preventing drugs from being adulterated[6] or misbranded.[7] Until 1997 with the enactment of the FDA Modernization Act of 1997 (FDAMA, discussed below),[8] Congress had not explicitly addressed whether compounded drugs had to meet these requirements of the FFDCA.[9]

---

[1] *See* Western States Medical Center v. Shalala, 238 F.3d 1090, 1092 (9th Cir. 2001).

[2] Western States Medical Center et al. v. Shalala, 69 F. Supp. 2d 1288, 1292 (D. Nev. 1999). *See also* Statement of Steven K. Galson, Acting Director, Center for Drug Evaluation and Research, U.S. Food and Drug Administration, before the Senate Committee on Health, Education, Labor and Pensions, Hearing on "Federal and State Role in Pharmacy Compounding and Reconstitution: Exploring the Right Mix to Protect Patients," (October 23, 2003).

[3] It should be noted that drugs may be compounded for animal use. *See, e.g.,* Medical Center Pharmacy v. Mukasey, 536 F.3d 383, 406-409 (5th Cir. 2008); United States v. Algon Chemical, Inc., 879 F.2d 1154 (3rd Cir. 1989). The statutes, regulations, and FDA policies governing compounding for animals differ from those governing drug compounding for humans. This report will only address federal law as it relates to drug compounding for human use.

[4] 21 U.S.C. §301 *et seq.* The FFDCA regulates several other products besides drugs, including certain foods, cosmetics, and dietary supplements.

[5] 21 U.S.C. §321(p). Exceptions are made for certain "grandfathered" drugs used prior to the FFDCA, as well as drugs intended only for investigational use.

[6] Under the FFDCA, a drug may be deemed adulterated if "the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this Act … as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess." See 21 U.S.C. §351 for a complete definition. FDA regulations set forth various standards for good manufacturing practices, including standards relating to personnel, facilities, and drug product containers. 21 C.F.R. §211.1 *et seq.*

[7] The FDA approves drugs for specific uses that are reflected in their labeling. A drug may be deemed to be misbranded if, among other possibilities, the labeling is false or misleading or if its labeling does not bear "adequate directions for use." 21 U.S.C. §352.

[8] Food and Drug Administration Modernization Act, P.L. 105-115, 111 Stat. 2296 (November 21, 1997).

[9] It should be noted that the FFDCA explicitly addresses compounded drugs in at least two notable areas. First, under Section 510(g) of the FFDCA, pharmacies are exempt from registering as drug manufacturers under the act if the pharmacies maintain establishments "in conformance with any applicable local laws regulating the practice of pharmacy and medicine and which are regularly engaged in dispensing prescription drugs or devices, upon (continued...)

For approximately the first 50 years of the FFDCA, pharmacists compounded drugs without getting FDA approval for these drugs, and regulation of drug compounding was left to the states.[10] The reason for this, in large part, is because it is widely recognized that compounded drugs could not meet the FFDCA's drug approval requirements because compounded drugs are traditionally made in small amounts for an individual patient (e.g., safety and efficacy trials are impracticable, and compounding pharmacies cannot afford testing for the new drug approval process to meet the needs of individual patients).[11]

Thus, the question of whether the FDA could regulate compounded drugs was generally not disputed until around the early 1990s when the FDA became concerned that some pharmacists were engaged in large-scale bulk compounding that was, in the FDA's view, more akin to drug manufacturing and an attempt to avoid the FFDCA's new drug requirements.[12] In response to these perceived abuses, the FDA issued a Compliance Policy Guide in 1992 addressing its position regarding its authority to regulate compounding.[13] The FDA declared "that while retail pharmacies ... are exempted from certain requirements of the [FFDCA], they are not the subject of any general exemption from the new drug, adulteration, or misbranding provisions" of the FFDCA.[14] While the FDA also indicated that its guidance was not intended to affect a pharmacist's traditional role of compounding drugs extemporaneously in reasonable quantities and pursuant to a valid prescription, the FDA warned that it "may, in the exercise of its enforcement discretion, initiate federal enforcement actions … when the scope and nature of a pharmacy's activity raises the kind of concerns normally associated with a manufacturer." The 1992 Compliance Policy Guide set forth certain factors the FDA would consider in determining whether to exercise enforcement discretion against a compounding pharmacy whose activities raise concerns similar to those of drug manufacturers, including soliciting business to compound specific drug products, using commercial scale manufacturing or testing equipment to compound

(...continued)

prescriptions of practitioners licensed to administer such drugs or devices to patients under the care of such practitioners in the course of their professional practice, and which do not manufacture, prepare, propagate, compound, or process drugs or devices for sale other than in the regular course of their business of dispensing or selling drugs or devices at retail." 21 U.S.C. §360(g)(1). In other words, this provision appears to recognize that traditional compounding by pharmacists is not manufacturing. Richard R. Abood, PHARMACY PRACTICE AND THE LAW, Fifth Ed. (2008). Second, similar language limits the types of pharmacy records that the FDA may review during an inspection. See 21 U.S.C. §374.

[10] *See Western States*, 535 U.S. at 362.

[11] Statement of Steven K. Galson, Acting Director, Center for Drug Evaluation and Research, U.S. Food and Drug Administration, before the Senate Committee on Health, Education, Labor and Pensions, Hearing on "Federal and State Role in Pharmacy Compounding and Reconstitution: Exploring the Right Mix to Protect Patients," (October 23, 2003). *See also* Thompson v. Western States, 535 U.S. 357, 369 (2002) ("…it would not make sense to require compounded drugs created to meet the unique needs of patients to undergo the testing required for the new drug approval process. Pharmacists do not make enough money from small-scale compounding to make safety and efficacy testing of their compounded drugs economically feasible, so requiring such testing would force pharmacists to stop providing compounded drugs.")

[12] *Medical Center Pharmacy*, 536 F.3d at 389. The FDA's concern over the practice of compounding has also been, in large part, due to certain patient injuries caused by compounded drugs. The Agency has asserted that it knows of more than 200 adverse events involving 71 compounded products since 1990, including certain instances with "devastating repercussions." *See*, U.S. Food and Drug Administration, The Special Risks of Pharmacy Compounding, *available at* http://www.fda.gov/consumer/updates/compounding053107.html.

[13] Compliance Policy Guide No. 7132.16 (March 1992).

[14] *Id.*, as cited in *Western States*, 535 U.S. at 362. It should also be noted that prior to the enactment of FDAMA, courts found that compounded drugs were new drugs. *See, e.g.*, Prof'ls & Patients for Customized Care v. Shalala, 56 F.3d 592, 593 n.3 (5th Cir. 1995).

drug products, and compounding (on a regular basis or in excessive amounts) drug products that are commercially available in the market place and that are essentially generic copies of commercially available, FDA-approved drug products.[15]

In order to "clarify the status of pharmacy compounding under Federal law,"[16] Congress added Section 503A (21 U.S.C. §353a) to the FFDCA as part of the FDA Modernization Act of 1997 (FDAMA), which specifically addressed the FDA's role in the regulation of drug compounding. Section 503A of the FFDCA, as added by FDAMA, exempts compounded drugs from FFDCA requirements regarding drug adulteration, misbranding, and new drug approval, provided that certain conditions are satisfied.[17] Among these requirements, a drug product must be compounded by a licensed pharmacist or physician for an indentified individual patient based on a valid prescription.[18] The compounded drug must comply with standards of an applicable U.S. Pharmacopoeia, or made from FDA-approved drug ingredients, meet certain manufacturing criteria, and the drug compounded must not be one that appears on a list of drugs (published by the Secretary) of drug products that have been withdrawn or removed from the market because the product, or components of the product have been found to be unsafe or not effective.[19] Further, the drug provider compounding the drug may not "compound regularly or in inordinate amounts … any drug products that are essentially copies of a commercially available drug product."[20]

Section 503A of the FFDCA also provided that the exemptions from the FFDCA's new drug and other requirements only applied to drug products compounded based on a valid prescription that was not solicited.[21] Further, the section states that a drug may be compounded and subject to the exemptions only if the pharmacy, licensed pharmacist, or licensed physician does not advertise or promote the compounding of any particular drug.[22] In November of 1998, just days after the provision became effective, several compounding pharmacies challenged the restrictions on solicitation and advertising as being an impermissible regulation of speech under the First Amendment.

Thompson v. Western States Medical Center[23]

In *Western States*, a group of licensed pharmacies brought an action against the Secretary of Health and Human Services (HHS) and the Commissioner of the FDA, claiming that FDAMA's restrictions on solicitation and advertising violated the pharmacies' rights to free speech under the

[15] Compliance Guide 7132.16, as cited in *Medical Center Pharmacy*, 536 F.3d at 391.

[16] Compliance Policy Guide 460.200 (May 2002); *see also* H.Rept. 105-399 at 94, which addresses section 503A of the FFDCA ("It is the intent of the conferees to ensure continued availability of compounded drug products as a component of individualized therapy, while limiting the scope of compounding so as to prevent manufacturing under the guise of compounding. Section 503A establishes parameters under which compounding is appropriate and lawful.").

[17] *See* Section 127 of P.L. 105-115.

[18] 21 U.S.C. §353(a)

[19] 21 U.S.C. §353a(b)(1).

[20] 21 U.S.C. §353a(b)(1)(D).

[21] 21 U.S.C. §353a(a).

[22] 21 U.S.C. §353a(c).

[23] Thompson v. Western States Medical Center, 535 U.S. 357 (2002).

First Amendment.[24] The district court evaluated whether the provisions were an impermissible government regulation of commercial speech[25] under the factors articulated in *Central Hudson Gas and & Electric v. Pub. Service Comm'n of New York*,[26] and granted the pharmacies summary judgment on the basis that the provision was indeed a violation of the First Amendment.

In evaluating whether the other provisions of Section 503A remained intact, the district court found that there is "no question" that the other sections could be severed[27] from the remaining sections.[28] The court explained that the modification of the statute did not prevent it from operating as law, based on the numerous other requirements that must be met in the production and distribution of compounded drugs. The Ninth Circuit Court of Appeals affirmed the district court's holding that the speech provisions of section 503A were unconstitutional, but also reversed in part, holding that the compounding provisions were not severable from the rest of the section.[29]

In discussing the severability issue, the court explained that the solicitation and advertising provisions were an essential component in balancing the preservation of compounded drugs alongside the desire to prevent pharmacists and others from engaging in drug manufacturing. The court pointed to legislative history that, in its opinion, demonstrated an intent to strike this balance.[30] The court further indicated that the legislative record demonstrated that Congress meant to exempt compounding pharmacists from FFDCA requirements only in return for a prohibition on the promotion of specific compounded drugs. The court also dismissed the applicability of the existing severability clause in the FFDCA[31] as not indicative of a presumption

---

[24] Western States Medical Center, et al. v. Shalala, 69 F. Supp. 2d 1288 (D. Nev. 1999).

[25] The First Amendment to the United States Constitution provides that "Congress shall make no law ... abridging the freedom of speech, or of the press.... " Despite its absolute language, it provides no protection to some types of speech and only limited protection to others. One type of speech to which it applies only limited protection is commercial speech, which is "speech that proposes a commercial transaction." Board of Trustees of the State University of New York v. Fox, 492 U.S. 469, 482 (1989). Commercial speech may be banned if it advertises an illegal product or service, and, unlike fully protected speech, may be banned if it is unfair or deceptive. For a more general discussion of First Amendment jurisprudence regarding freedom of speech, see CRS Report 95-815, *Freedom of Speech and Press: Exceptions to the First Amendment*, by Kathleen Ann Ruane.

[26] 447 U.S. 557 (1980). For commercial speech, the Supreme Court has prescribed the four-prong Central Hudson test to determine its constitutionality. This test asks initially (1) whether the commercial speech at issue is protected by the First Amendment (that is, whether it concerns a lawful activity and is not misleading) and (2) whether the asserted governmental interest in restricting it is substantial. "If both inquiries yield positive answers," then to be constitutional the restriction must (3) "directly advance[ ] the governmental interest asserted," and (4) be "not more extensive than is necessary to serve that interest." *Id.* at 566 (1980).

[27] When one section of a law is held unconstitutional, courts are faced with determining whether the remainder of the statute is "severable," i.e., it remains valid, or whether the whole statute is nullified. In general, courts examine whether the statute can fully operate without the unconstitutional provision in the manner that Congress intended. *See infra* notes 54-58 and accompanying text.

[28] *Western States*, 69 F. Supp. 2d at 1309-10.

[29] Western States Medical Center v. Shalala, 238 F.3d 1090 (9th Cir. 2001).

[30] For example, the Ninth Circuit cited a House report explaining that FDAMA was designed to "ensure continued availability of compounded drug products as a component of individualized drug therapy, while limiting the scope of compounding so as to prevent manufacturing under the guise of compounding." H.Rept. 105-399, as cited in Western States, 238 F.3d at 1097.

[31] Section 901 of the FFDCA provides, "If any provision of this Act [21 U.S.C. §§301 *et. seq.*] is declared unconstitutional, or the applicability thereof to any person or circumstances is held invalid, the constitutionality of the remainder of the Act ... and the applicability thereof to other persons and circumstances shall not be affected thereby." 21 U.S.C. §391.

that Congress intended for unoffending provisions of FDAMA to remain valid. The court explained that because Congress approved the severability clause before FDAMA's passage, there was no indication of whether the clause was to only apply to the original FFDCA, or to the FFDCA as amended by FDAMA.

In its brief requesting Supreme Court review on the First Amendment issue, the government indicated its acquiescence with the court of appeals' conclusion that, if the solicitation and advertising provisions in Sections 503A(a) and (c) are unconstitutional, they are not severable from the other provisions of Section 503A. Accordingly, the government did not seek review of that holding.[32] The Supreme Court later affirmed the lower court rulings that the speech restrictions were unconstitutional, but because neither party petitioned for certiorari on the severability issue, the Court articulated that it "had no occasion" to review that portion of the court of appeals' decision.[33]

2002 FDA Compliance Policy Guide

Western States did not address the FDA's authority to regulate drug compounding in the absence of the FDAMA provision. Because (at least in part) of the confusion about the extent of the FDA's authority to regulate compounding remaining after this decision, the FDA issued a Compliance Policy Guide in 2002, largely similar to the compliance guide issued in 1992.[34] The FDA stated that because the Supreme Court did not rule on the severability issue, the Court "therefore left in place" the Ninth Circuit holding that the other provisions of Section 503A were not severable, and the section was therefore invalid. Accordingly, the FDA determined that it needed to issue guidance to the compounding industry regarding the factors the agency would consider in exercising enforcement discretion with regard to pharmacy compounding.

The FDA indicated that it did not intend the Compliance Policy Guide to regulate traditional compounding practices (i.e., pharmacists who extemporaneously compound reasonable quantities of drugs upon receipt of a valid prescription for an identified patient). In addition, the FDA noted that it would continue to defer to the state authorities regarding "less significant violations" of the FFDCA. However, the FDA explained its concern with pharmacies that were not compounding in the regular course of business, but were manufacturing large quantities of drug products without a prescription for them. The FDA explained that 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, it determined that it should seriously consider enforcement action. The FDA set out nine acts it would consider in pursuing an enforcement action:

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

[32] Thompson v. Western States Med. Ctr., 2001 U.S. Briefs 344, 11 (August 24, 2001)

[33] Western States, 535 U.S. at 365.

[34] Food and Drug Administration, Compliance Policy Guides Manual §460.200, Pharmacy Compounding (May 2002), available at http://www.fda.gov/ora/compliance_ref/cpg/cpgdrg/cpg460-200.html#BACKGROUND.

3. Compounding finished drugs from bulk active ingredients that are not components of FDA-approved drugs, without an FDA sanctioned investigational new drug application
4. Receiving, storing, or using drug substances without first obtaining written assurance from the supplier that each lot has been made in an FDA-registered facility
5. Receiving, storing, or using drug components not guaranteed 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 other 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
9. Failing to operate in conformance with applicable state law regulating the practice of pharmacy.

The FDA indicated that the list of acts was not exhaustive, and that other factors may be appropriate to consider in enforcement actions.

Medical Center Pharmacy v. Mukasey

In September 2004, 10 licensed pharmacies specializing in drug compounding brought suit challenging FDA's authority to regulate compounded drugs.[35] In *Medical Center Pharmacy v. Ashcroft* (later changed to *Medical Center Pharmacy v. Gonzalez* and then *Medical Center Pharmacy v. Mukasey*), plaintiffs sought, among other things, a declaration that drugs compounded by licensed pharmacists were not "new drugs" per se under the FFDCA. The district court granted summary judgment on the pharmacies' claim, finding that compounded drugs were "implicitly exempt" from the new-drug requirements.[36] The court, relying on language of the Supreme Court from *Western States*, reasoned that if compounded drugs were not exempt from the new-drug requirements, the drugs would have to undergo the new-drug approval process, which would be impracticable. The court indicated that the FDA's 2002 Compliance Policy Guide, which exempts traditional compounding from the scope of the guidance, and instead focuses on the regulation of pharmacies that manufacture drugs "under the guise of compounding," provided additional support for the position that traditional compounding was not subject to the new-drug approval requirements. The court also opined that the remainder of Section 503A was severable following *Western States*. The court explained that it was not bound by the Ninth Circuit, and that the severability statute in the FFDCA is "clear and unambiguous."[37]

[35] Medical Center Pharmacy, et al. v. Gonzales, et al., 451 F. Supp. 2d 854 (W.D. Tex.)(2006).

[36] *Id.* at 858.

[37] *Id.* at 864.

On appeal, the Fifth Circuit disagreed with the district court, finding that compounded drugs are "new drugs" and are subject to the drug approval, adulteration, and misbranding requirements.[38] However, in light of the fact that the provisions of 503A were severable, the court found that compounded drugs are subject to a "limited exemption" from the those requirements if the drugs are compounded in accordance with the non-speech provisions of that section. The court based its holding in part on the definition of "new drug," under the FFDCA. Given that a compounded drug is created by mixing or combining an approved drug with something else to create a "concoction" that has not been previously approved for use, a compounded drug was, based on the plain language of the statute, a new drug.[39] Further, given that the FFDCA contains certain exceptions to the new drug definition (e.g., for "grandfathered" drugs), the court found meaning in the lack of an exemption to the new-drug definition for drugs created by compounding.

The pharmacies in *Medical Center Pharmacy* had argued that including compounded drugs under the new drug definition would, in effect, extinguish the practice of traditional compounding. The court also acknowledged the idea that interpreting the new-drug definition so as to include compounding did appear inconsistent with the idea that compounding should be able to persist and not be subject to the rigorous requirements of new drug approval. However, the court pointed out that these issues can be reconciled. Under the court's reasoning, even if compounded drugs are effectively made unlawful by the new drug definition and approval requirements, pharmacists could still continue compounding because the FDA has the ability exercise enforcement discretion and can decline enforcement of "minor violations."[40] In other words, the FDA would be in a position, as it did historically, to use this discretion and not enforce new drug requirements on compounded drugs. While the court expressed some reluctance to rely on the FDA's discretion in its enforcement of drug compounding, the court still found that because the FDA has demonstrated willingness to accommodate traditional compounding, pharmacies would still be able to compound drugs even if they were deemed new drugs.

The Fifth Circuit also pointed to the enactment of FDAMA as evidence that Congress intended that the new-drug provision apply to drugs created by pharmacy compounding.[41] However, in order to rely on FDAMA as justification for why compounded drugs could be considered new drugs under the FFDCA, the court evaluated whether the statute was still valid in light of the *Western States* decision. The court examined the severability clause in the FFDCA and found, contrary to the Ninth Circuit, that the severability clause applied to Section 503A. The court explained that if Congress did not want the FFDCA's severability clause to apply to Section 503A, it would have specifically said so. Further, the court did not see the free speech provisions as so central to the purpose of FDAMA that Congress would not have passed the statute without them. The Fifth Circuit also stated that the remaining requirements were sufficient to accomplish the goal of protecting access to compounded drugs while preventing pharmacies from engaging in large-scale drug manufacturing.[42] The court also disagreed with the Ninth Circuit in finding that

[38] Medical Center Pharmacy v. Mukasey, 536 F.3d 383 (5th Cir. 2008).

[39] *Id.* at 394-95.

[40] *Id.* at 398-99.

[41] *Id.* at 400.

[42] The Fifth Circuit also pointed to the Supreme Court's evaluation of the advertising provision in *Western States*:

> Several non-speech-related means of drawing a line between compounding and large-scale manufacturing might be possible here.... It might even be sufficient to rely solely on the non-speech-related provisions of FDAMA, such as the requirement that compounding only be conducted in response to a prescription or a history of receiving a prescription, 21 U.S.C. § 353a(a), and the limitation on the percentage of a pharmacy's total sales that out-of-state sales of

(continued...)

the legislative history to FDAMA was "inconclusive" as to whether Congress would not have enacted FDAMA without the speech provisions of Section 503A.[43]

Issues with Current FDA Authority to Regulate Drug Compounding

As discussed above, the *Western States* and *Medical Center Pharmacy* cases directly conflict on the question of whether the non-speech provisions of Section 503A are severable and thus, whether the remaining sections of the statute are still in effect. Based on these two decisions, the FDA has determined that it will apply the non-advertising provisions of Section 503A of the FFDCA to entities that are located within the jurisdiction of the Fifth Circuit (Texas, Louisiana, and Mississippi) as well as to the plaintiffs that brought the *Medical Center* case.[44] In all other locations, the FDA will continue to apply the enforcement policy articulated in the 2002 Compliance Policy Guide. In other words, the current situation presents an interesting scenario of non-uniform enforcement throughout the United States. In the Fifth Circuit, compounded drugs are specifically exempted from adulteration, misbranding, and new drug provisions of the FFDCA, subject to meeting certain criteria; while in the Ninth Circuit (and, according to the FDA, the rest of the United States), compounded drugs are subject to these provisions, but the FDA may exercise discretion in taking action against a pharmacy that violates them.

The parties in *Medical Center Pharmacy* did not petition the Supreme Court for review, and thus, uncertainty remains about the FDA's authority to regulate compounded drugs as new drugs. Courts may still evaluate the FDA's position that compounded drugs are new drugs, or, relatedly, whether the non-speech provisions of Section 503A of the FFDCA that include an exemption for these drugs remain intact. If these types of challenges were to occur outside of the Fifth or Ninth Circuits, a court could rely upon, but would be under no obligation to follow, the *Western States/Medical Center Pharmacy* precedent. Unless a future case on these issues reaches the Supreme Court, the question of how the FDA may regulate compounded drugs may not be settled unless Congress takes legislative action.

Under the current drug compounding regime outside of the Fifth Circuit, some have expressed concern that the FDA's 2002 Compliance Policy Guide creates confusion regarding when FDA

(...continued)

> compounded drugs may represent, § 353a(b)(3)(B).... *Nowhere in the legislative history of FDAMA or petitioners' briefs is there any explanation of why the Government believed forbidding advertising was a necessary as opposed to merely convenient means of achieving its interests.* Medical Ctr. Pharm. v. Mukasey, 536 F.3d at 404 n.43 (citing *Western States*, 535 U.S. at 372-73.) (emphasis added).

[43] *See also* United States v. Bader, 2009 U.S. Dist. LEXIS 63490 (D. Colo. 2009), where a Tenth Circuit district court evaluated a motion for reconsideration over whether human growth hormone imported by a pharmacist was a "finished, consumer-usable" drug that was improperly smuggled and distributed under various federal criminal provisions, and the FFCDA, or whether it was used as an ingredient in a compounded drug under which the pharmacist may be able to escape liability. In discussing whether the pharmacist had engaged in drug compounding, because Bader was a party in the *Medical Center Pharmacy* case, the court found that the provisions of FDAMA were considered severable. The court, in granting the motion, found that the trial court would need to determine, among other things, whether the pharmacist's conduct violated the terms of FDAMA.

[44] *See, e.g.*, Letter from Alonza E. Cruse, Director, Los Angeles District, U.S. Food and Drug Administration, to Ari S. Schafer, Civic Center Pharmacy (December 16, 2008), *available at* http://www.fda.gov/foi/warning_letters/s7071c.pdf.

enforcement authority will be used.[45] It has been argued that the FDA Compliance Policy Guide lacks a clear description of the circumstances under which the agency will take action against pharmacies.[46] The FDA has countered that the guidance gives the agency flexibility in responding a wide variety of situations involving public health and safety issues.[47]

The FDA's authority to regulate compounded drugs is set forth in a guidance document. In contrast to agency rules, which have the force and effect of law, guidance documents are merely considered to be a general statement of policy.[48] These statements of policy are agency statements that "advise the public prospectively of the manner in which the agency proposes to exercise a discretionary power."[49] Congress has passed requirements specific to FDA guidance documents, which state that such documents "shall not create or confer any rights for or on any person, although they present the views of the Secretary on matters under the jurisdiction of the Food and Drug Administration."[50] Under regulations prescribing FDA good guidance practices, it is stated that guidance documents do not establish legally enforceable rights or responsibilities and do not legally bind the public or the FDA."[51] Accordingly, if a court were to evaluate the position the FDA takes in its 2002 Compliance Policy Guide, a court may choose not to defer to the FDA's position on when it may exercise enforcement discretion, or whether compounded drugs are "new drugs." However, in *Medical Center Pharmacy*, the Fifth Circuit evaluated the FDA's statutory interpretation that compounded drugs were new drugs under a standard that is more deferential to agency action, a standard that is typically reserved for products of formal agency process (e.g., notice and comment rulemaking).[52] It should be noted that the few courts that have evaluated the Compliance Policy Guide have found the guidance to be appropriate or reasonable.[53]

---

[45] U.S. Government Accountability Office, GAO-04-195T Prescription Drugs, State and Federal Oversight of Drug Compounding by Pharmacies, Testimony Before the Committee on Health, Education, Labor, and Pensions, U.S. Senate (October 2003) at 12.

[46] *Id.* According to GAO testimony, pharmacy associations pointed to terms in the guidance, such as "very limited quantities" and "commercial scale manufacturing or testing equipment" that are not defined, and observed that FDA also has the right to consider other factors in addition to those in the guidance without giving further clarification. *Id.* at 12.

[47] Government Accountability Office, note 45 *supra.*

[48] Jeffrey S. Lubbers, A GUIDE TO FEDERAL AGENCY RULEMAKING 94 (4th ed. 2006). Executive Order 13422 sets forth a definition of a guidance document. Executive Order 13422, Further Amendment to Executive Order 12866 on Regulatory Planning and Review, January 18, 2007, http://www.whitehouse.gov/news/releases/2007/01/20070118.html.

[49] Tom C. Clark, Attorney General, Attorney General's Manual on the Administrative Procedure Act, at 30 n.3 (1947), http://www.law.fsu.edu/library/admin/1947iii.html; see, e.g., Chamber of Commerce v. United States Department of Labor, 174 F.3d 206, 212 (D.C. Cir. 1999).

[50] 21 U.S.C. §371(h). The provisions on guidance documents were added in 1997 by FDAMA §405.

[51] 21 C.F.R. §10.115(d)(1).

[52] Under Supreme Court precedent, certain agency actions should be afforded deference by the courts. In *Chevron U.S.A. Inc. v. Natural Resources Defense Council*, 467 U.S. 837 (1984), the Supreme Court established a two-part test for judicial review of agency statutory interpretations. First, a reviewing court must determine "whether Congress has directly spoken to the precise question at issue." If it has, the agency must of course comply with clear congressional intent, and regulations to the contrary will be invalidated. Second, in instances where congressional intent is not clear and the statutory language is ambiguous, the courts will likely defer to any reasonable agency interpretation, even if another interpretation is more plausible. However, the Supreme Court in *Christensen v. Harris County*, 529 U.S. 576 (2000) and *United States v. Mead Corp.*, 533 U.S. 218 (2001) analyzed *Chevron's* application, ruling that *Chevron* deference applies only if an agency's interpretation is the product of a formal agency process, such as adjudication or notice-and-comment rulemaking, through which Congress has authorized the agency "to speak with the force of law." *Mead Corp.*, 533 U.S. at 229. Although a notice about the Compliance Policy Guide was published in the Federal Register and public comments were requested (in accordance with the FDA's good guidance practices), it would seem (continued...)

If a future court were to take up the issue of whether the non-speech provisions in Section 503A are severable, it is difficult to predict how a court would rule. Under Supreme Court severability precedent, "[u]nless it is evident that the Legislature would not have enacted those provisions which are within its power, independently of that which is not, the invalid part may be dropped if what is left is fully operative as a law."[54] Further, a key inquiry evaluating severability is whether without the unconstitutional provision, "the statute will function in a manner consistent with the intent of Congress."[55] The Court has also indicated "when Congress has explicitly provided for severance by including a severability clause in the statute ... the inclusion of such a clause creates a presumption that Congress did not intend the validity of the statute in question to depend on the validity of the constitutionally offensive provision."[56] The courts in both *Western States* and *Medical Center Pharmacy* relied on various statements in the legislative history of FDAMA as evidence of whether the solicitation and advertising provisions of FDAMA were integral to the rest of the statute. However, neither court was able to point to a statement that explicitly referenced the unconstitutional provisions of Section 503A and the intent behind them. In addition, as in these two cases, if courts in another jurisdiction were to review whether Section 503A is severable, a court would likely evaluate the severability clause of the FFDCA. A court could agree with the Ninth Circuit, finding that because the severability clause was enacted prior to FDAMA, it is not clear whether it was to apply to the amended portions of the FFDCA.[57] Alternatively, a court could side with the Fifth Circuit and hold that the severability clause kept Section 503A of the FFDCA intact, assuming that if Congress had not wanted the clause to apply, it would have said so.[58]

(...continued)

more likely that a court would not employ *Chevron* deference in evaluating the agency's interpretation as provided in the guidance document. But, as discussed above, courts still employ this deferential standard outside of this formal agency action. *See also* In re the Matter of Establishment Inspection of Wedgewood Pharmacy Inc., 270 F. Supp. 2d 525 (D.N.J. 2003) (court applies *Chevron* deference to 2002 Compliance Policy Guide).

[53] *See, e.g.,* In the Matter of Establishment Inspection of Wedgewood Pharmacy, 421 F.3d 263 (3rd Cir. 2005)(court of appeals finds the guide "a reasonable basis under which to initiate an inspection under the FFDCA"). *See also* Schaerrer v. Stewart's Plaza Pharm., Inc., 79 P.3d 922, (Utah 2003)(In examining whether compounding pharmacy's conduct fell into category of "pharmacist" or "drug manufacturer," court states that "[w]hile the policy statements of the FDA are by no means binding on this court, they do provide meaningful guidance on a question that few, if any, courts in this country have yet considered."). It should also be noted that FDA regulations define a guidance document to include "documents that relate to: ... inspection and enforcement policies." 21 C.F.R. §10.115(b)(2). Thus, while not addressed in the *Wedgewood* case, given that the Compliance Policy Guide addressed when the FDA will exercise enforcement discretion on drug compounding, one could argue that the guide is an appropriate exercise of FDA authority.

[54] Alaska Airlines, Inc. v. Brock, 480 U.S. 678, 684 (1987)(quoting Buckley v. Valeo, 424 U.S. 1, 108 (1976) (per curiam), Champlin Refining Co. v. Corporation Comm'n of Oklahoma, 286 U.S. 210, 234 (1932).

[55] *Alaska Airlines*, 480 U.S. at 685.

[56] *Id.* at 686 (citing INS v. Chadha, 462 U.S. 919, 932 (1983); Champlin Refining Co. v. Corporation Comm'n of Oklahoma, 286 U.S. 210, 235 (1932).

[57] *Western States*, 238 F.3d at 1098-99.

[58] *Medical Center Pharmacy*, 536 F.3d at 401-402.

Author Contact Information

Jennifer Staman
Legislative Attorney
jstaman@crs.loc.gov, 7-2610