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Makena Drug Compounding Lawsuit Against FDA Gets New Life

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On January 7, 2014, a three-judge panel of the United States Circuit Court for the District of Columbia unanimously vacated the dismissal of claims against the U.S. Food and Drug Administration ("FDA") and others by K-V Pharmaceutical Company ("K-V") and its subsidiary, Ther-Rx Corporation ("Ther-Rx").[1] K-V and Ther-Rx had sued claiming federal regulators unlawfully allowed pharmacies to compound[2] a cheaper alternative to the synthetic progesterone drug Makena. The United States District Court for the District of Columbia dismissed the suit in 2012 but was directed to reconsider its ruling last week in light of a 2013 D.C. Circuit decision addressing the reviewability of agency enforcement discretion, like the FDA's.

The claims and contours of the Makena action test the limits of the FDA's use of discretion to enforce drug importation and compounding rules. Its outcome, coupled with recently enacted compounding legislation, will carry important implications for different players in the pharmaceutical industry. We discuss below.

1. The run-up to the case of K-V Pharm. Co. v. U.S. Food & Drug Admin.

K-V is a pharmaceutical manufacturer focusing on women's healthcare.[3] In February 2011, the FDA approved K-V's new drug application for Makena (hydroxyprogesterone caproate), an injectable hormone medication used to reduce the risk of preterm birth in at-risk women.[4] Before 2011, a compounded version of Makena's active pharmaceutical ingredient ("API"), commonly known as "17P," had been made available to patients whose physicians requested the drug from a pharmacist.[5] Once approved, Makena obtained seven years of exclusivity under the Orphan Drug Act.[6, 7]

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[1] *K-V Pharm. Co. v. U.S. Food & Drug Admin.*, No. 12-5349, 2014 WL 68499, at *1 (D.C. Cir. Jan. 7, 2014).

[2] "Drug compounding is a process by which a pharmacist or doctor combines, mixes, or alters ingredients to create a medication tailored to the needs of an individual patient. Compounding is typically used to prepare medications that are not commercially available, such as medication for a patient who is allergic to an ingredient in a mass-produced product." *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 360-61 (2002).

[3] *See* http://www.kvpharmaceutical.com/about_us_landing.aspx.

[4] *See* 2/4/11 "FDA approves drug to reduce risk of preterm birth in at-risk pregnant women," http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm242234.htm.

[5] *See* 7/5/12 Complaint for Declaratory and Injunctive Relief, No.: 1:12-cv-01105-ABJ (ECF No. 1) ("K-V Complaint") at ¶ 2.

[6] *See* 3/30/11 "FDA Statement on Makena," http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm249025.htm.

[7] The 1983 Orphan Drug Act was enacted with the goal of promoting the development and expediting the approval of so-called "orphan drugs" - those prescribed to treat a "rare disease or condition." *See* 21 U.S.C. § 360bb. A "rare disease or condition" includes "any disease or condition which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will be recovered from sales in the United States of such drug." *See* 21 U.S.C. § 360bb(a)(2). The law sought to accomplish these twin purposes by "reducing the overall financial cost of development, while enhancing the developer's ability to recover that cost through sale of the drug," including "by granting the manufacturer seven years of exclusive marketing rights for such drug for such

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Apparently in response to negative media coverage and resulting pressure from members of Congress over Makena's high list price, the FDA announced in March 2011 that

> [i]n order to support access to this important drug, at this time and under this unique situation, FDA does not intend to take enforcement action against pharmacies that compound hydroxyprogesterone caproate based on a valid prescription for an individually identified patient unless the compounded products are unsafe, of substandard quality, or are not being compounded in accordance with appropriate standards for compounding sterile products.[8]

In October 2011, K-V provided information to the FDA that it claimed raised concerns about the potency and purity of the APIs in samples of compounded 17P.[9] In a June 2012 press release, the FDA said that "the analysis of this limited sample of compounded hydroxyprogesterone caproate products and APIs did not identify any major safety problems."[10] It nonetheless cautioned that "[c]ompounding large volumes of drugs that are copies of FDA-approved drugs circumvents important public health requirements," and that "it is applying its normal enforcement policies for compounded drugs to compounded hydroxyprogesterone caproate."[11]

A month later, K-V and Ther-Rx filed a four-count complaint in federal court seeking a panoply of declaratory and injunctive relief based on the FDA's alleged unwillingness to pursue compounders of 17P.[12] The failure to do so, they claimed, violated the Administrative Procedure Act ("APA") and several provisions of the Federal Food, Drug, and Cosmetic Act ("FDCA").[13] In particular, they alleged the government's "policy of non-enforcement" against the import of 17P's APIs and its compounding were "effectively approving, inviting, encouraging, and permitting . . . direct nationwide competition between an entire class of unapproved compounded drug products . . . and an approved orphan drug product."[14]

2. The district court dismisses the case citing the FDA's "enforcement discretion"

On September 6, 2012, the United States District Court for the District of Columbia dismissed K-V and Ther-Rx's complaint, relying primarily on the United States Supreme Court's 1985 decision in *Heckler v. Chaney*.[15] In *Chaney* - which, coincidentally, involved a challenge to the FDA's enforcement discretion - the Court held that an agency's refusal to take an investigative or enforcement action is presumptively unreviewable under the APA.[16] "[A]n agency's decision not to take enforcement action should be presumed immune from judicial review under § 701(a)(2) [of the APA]. For good reasons, such a decision has

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[rare] disease or condition." *See Genentech, Inc. v. Bowen*, 676 F. Supp. 301, 303 (D.D.C. 1987) (brackets in original; internal quotations omitted).

[8] *See* footnote 5, *supra*.

[9] See 11/8/11 "FDA Statement on Makena," http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm279098.htm.

[10] *See* 6/15/12 "Updated FDA Statement on Compounded Versions of hydroxyprogesterone caproate (the active ingredient in Makena)," http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm308546.htm.

[11] *See id*.

[12] *See* K-V Complaint at ¶ 1.

[13] *K-V Pharm. Co. v. U.S. Food & Drug Admin.*, 889 F.Supp.2d 119, 123 (D.D.C. 2012), *reversed and remanded by K-V Pharm. Co. v. U.S. Food & Drug Admin.*, 2014 WL 68499, at *1.

[14] *See* K-V Complaint at ¶¶ 15; 22.

[15] 470 U.S. 821 (1985).

[16] *See id*. at 832.

traditionally been committed to agency discretion, and we believe that the Congress enacting the APA did not intend to alter that tradition."[17]

The APA's presumption of unreviewability, however, is a rebuttal one. "[T]he presumption may be rebutted where the substantive statute has provided guidelines for the agency to follow in exercising its enforcement powers."[18] Where "the agency has consciously and expressly adopted a general policy that is so extreme as to amount to an abdication of its statutory responsibilities," that, too, "might indicate that such decisions were not committed to agency discretion."[19] This reflected the judgment by Congress not to "set agencies free to disregard legislative direction in the statutory scheme that the agency administers."[20]

The D.C. federal district court determined that "plaintiffs' claims . . . fall squarely within the *Chaney* presumption of unreviewability," and that "this case is fundamentally an effort to get the Court to direct and oversee the FDA's enforcement activities, and that it cannot do."[21] The FDA's March statement, it held, was not tantamount to a statement of a general enforcement policy capable of judicial review because of, among other things, its consideration of the individual circumstances surrounding the compounding of 17P.[22] That made it "the sort of ad hoc, context-bound nonenforcement pronouncement that . . . would inherently implicate an agency's unreviewable enforcement discretion."[23]

3. A Potential Silver Lining?

Ten months after K-V and Ther-Rx's loss in the D.C. district court, the D.C. Circuit took up the case of *Cook v. Food & Drug Admin.*,[24] which involved allegations by death row prisoners that the FDA had wrongly failed to refuse importation of unapproved and/or misbranded sodium thiopental, the first in a sequence of drugs used in the execution of state prisoners and currently an unapproved drug.[25] The FDA fell back on *Chaney*, arguing that its decision to release sodium thiopental shipments destined for correctional facilities was committed to agency discretion and thus was unreviewable under the APA.[26]

But the D.C. Circuit disagreed and decided review was appropriate. It recognized that "[t]he FDCA imposes mandatory duties upon the agency charged with its enforcement," *i.e.*, the FDA, including "precisely when the agency must determine whether a drug offered for import appears to violate the FDCA, and what the agency must do with such a drug"; namely, if and when the FDA must refuse admission to any drug that appears to violate the law's substantive prohibitions.[27] Accordingly, "[b]ecause these are clear statutory guidelines for the agency to follow in exercising its enforcement powers . . . the FDA's compliance with § 381(a) [was] subject to judicial review under the standards of the APA."[28] On the merits, the appeals court ruled that "[t]he FDA acted in derogation of [its] duties by permitting the importation of thiopental, a concededly misbranded and unapproved new drug, and by

[17] *See id*.
[18] *See id*. at 832-33.
[19] *See id*. at 833, n.4.
[20] *See Chaney*, 470 U.S. at 833.
[21] *K-V Pharm. Co.*, 889 F.Supp.2d at 133.
[22] *See id*. at 136.
[23] *See id*. at 137.
[24] 733 F.3d 1 (D.C. Cir. 2013).
[25] *See id*. at 3.
[26] *See id*. at 6-7.
[27] *See id*. at 7; 12.
[28] *See id*. at 10 (*citing Chaney*, 470 U.S. at 833) (internal quotations omitted).

declaring that it would not in the future sample and examine foreign shipments of the drug despite knowing they may have been prepared in an unregistered establishment."[29]

4. What Happens Next?

In an unpublished decision issued January 7, the D.C. Circuit remanded *K-V Pharm. Co.* for reconsideration in light of *Cook* and the Drug Quality and Security Act ("DQSA"),[30] enacted November 27, 2013.[31] *Cook*'s application of the FDA's duties under the FDCA's provisions governing importation would seem to make reviewable the FDA's decision to allow unapproved drug ingredients into the United States from at least some unregistered manufacturers/suppliers. Ultimately, though, whether and how *Cook* and the DQSA help K-V and Ther-Rx is anybody's guess. One way or another, resolution of the interplay between the APA and FDCA will further define the boundaries of the FDA's enforcement discretion in the important areas of drug compounding and importation. K&L Gates LLP will report on further developments as they unfold.

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[29] *See Cook*, 733 F.3d at 12.

[30] Pub. L. No. 113-54, 127 Stat. 587 (2013). The DQSA was the combination of compounding and supply chain security legislation originally proposed by the Senate Committee on Health Education, Labor, and Pensions and the House of Representatives. The DQSA consists of two independent acts - the Compounding Quality Act and the Drug Supply Chain Security Act. The first creates a voluntary compliance regime that allows compounding pharmacies to register with the FDA as "outsourcing facilities" and meet certain best practices requirements similar to drug manufacturers to be exempt from the FDCA's approval and labeling requirements. *See* "FDA Implementation of the Compounding Quality Act," http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/pharmacycompounding/ucm375804.htm. The second requires the FDA to implement an electronic, interoperable system to identify and trace certain prescription drugs as they are distributed in the United States, including through unique product identifiers on individual drug packages and product and transaction information at each sale with lot level information. *See* "Drug Supply Chain Security Act," http://www.fda.gov/drugs/drugsafety/drugintegrityandsupplychainsecurity/drugsupplychainsecurityact/default.htm.

[31] *K-V Pharm. Co.*, 2014 WL 68499, at *1.