IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

K-V PHARMACEUTICAL COMPANY,
2280 Schuetz Road
St. Louis, MO 63146,

and

THER-Rx CORPORATION,
2280 Schuetz Road
St. Louis, MO 63146,

Plaintiffs,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION,
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002,

UNITED STATES DEPARTMENT OF HEALTH & HUMAN SERVICES,
200 Independence Avenue, S.W.
Washington, D.C. 20201,

MARGARET A. HAMBURG, M.D.,
Commissioner of Food and Drugs,
U.S. Food and Drug Administration,
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002,

and

KATHLEEN SEBELIUS,
Secretary of Health and Human Services,
U.S. Department of Health & Human Services,
200 Independence Avenue, S.W.
Washington, D.C. 20201,

Defendants.

Case No. _____

PLAINTIFFS' MOTION FOR TEMPORARY RESTRAINING ORDER AND PRELIMINARY INJUNCTION

Plaintiffs, K-V Pharmaceutical Company and Ther-Rx Corporation (collectively, "KV"), by undersigned counsel, respectfully move under Federal Rule of Civil Procedure 65 for a temporary restraining order and a preliminary injunction against Defendants – (1) the United States Food and Drug Administration ("FDA"), (2) the United States Department of Health and Human Services ("DHHS"), (3) Margaret A. Hamburg, M.D., Commissioner of Food and Drugs, and (4) Kathleen Sebelius, Secretary of Health and Human Services – for the reasons set forth in the accompanying memorandum.

Plaintiffs request a temporary restraining order:

1. Declaring that:

(a) FDA's March 30, 2011 Statement and its June 15, 2012 statement and the policy of non-enforcement against the compounding of 17P not customized to meet the special needs of patients who have the condition for which Makena is indicated but for whom Makena is medically inappropriate, which those statements set forth and maintain, are unlawful, in that they violate 21 U.S.C. §§ 360cc(a), 353a, and 355(a).

(b) FDA's allowance of the importation of unapproved active pharmaceutical ingredient ("API") for compounded 17P not so customized violates 21 U.S.C. § 381(a).

(c) FDA has a duty under 21 U.S.C. § 360cc(a) to protect Makena from the kind of approval of non-customized compounded 17P that FDA's March 30, 2011 Statement announced and FDA's June 15, 2012 statement maintains and the unlawful competition that has resulted from those statements; and that, to the extent that FDA's CPG 460.200 fails to make protection of orphan drug exclusivity a significant factor in case evaluation, it is unlawful.

(d) Because FDA's March 30, 2011 Statement approved, invited, and called forth the unlawful competition with Makena by compounded 17P not customized to meet the

special needs of patients who have the condition for which Makena is indicated but for whom Makena is medically inappropriate, FDA has a duty to terminate that unlawful competition forthwith.

2. Ordering that:

(a) Defendants immediately suspend FDA's March 30, 2011 Statement and June 15, 2012 statement, announce that those statements are suspended, and not maintain or implement the policy of non-enforcement as to non-customized compounding of 17P set forth and maintained in those statements.

(b) Defendants cease and desist from permitting the importation into the United States of unapproved API for compounded 17P.

(c) Within two (2) business days, Defendants issue a new public statement communicating (i) their intent to enforce, in appropriate cases and with priority to compounding that is regular or in inordinate amounts, 21 U.S.C. §§ 360cc(a), 353a and 355(a) against compounders of 17P not customized to meet the special needs of patients who have the condition for which Makena is indicated but for whom Makena is medically inappropriate, and (ii) that shipments of unlawful compounded 17P not so customized must cease immediately.

(d) Within ten (10) business days, Defendants report to the Court, under seal if and to the extent necessary and with a redacted version publicly filed, the actions they have taken to terminate shipments of unlawful compounded 17P not customized to meet the special needs of patients who have the condition for which Makena is indicated but for whom Makena is medically inappropriate.

Plaintiffs request a preliminary injunction:

1. Declaring that:

(a) The distribution in interstate commerce of compounded 17P beyond the scope of the traditional practice of pharmacy, *i.e.*, the distribution in interstate commerce of a compounded version of 17P that is not customized for an individual patient who has the condition for which Makena is indicated but for whom Makena is medically inappropriate, is unlawful.

(b) FDA's March 30, 2011 Statement, and FDA's June 15, 2012 statement, and the policy of non-enforcement against compounded 17P not so customized, which those statements set forth and maintain, are unlawful, in that they violate 21 U.S.C. §§ 360cc(a), 353a, 355(a), and 331(d), and are not a lawful exercise of enforcement discretion; and therefore the Statement and policy are arbitrary, capricious, an abuse of discretion, otherwise not in accordance with law, in excess of statutory jurisdiction, authority, or limitation, short of statutory right, and without observance of procedure required by law.

(c) Defendants have a duty under 21 U.S.C. § 360cc(a) to protect Makena from the kind of approval of non-customized compounded 17P that FDA's March 30, 2011 Statement announced and FDA's June 15, 2012 statement maintains and the unlawful competition that has resulted from those statements; and that, to the extent that FDA's CPG 460.200 fails to make protection of orphan drug exclusivity a significant factor in case evaluation, it is unlawful.

(d) 21 U.S.C. 360cc(a) requires Defendants to enforce 21 U.S.C. § 355(a), in light of 21 U.S.C. § 353a, to the extent necessary to protect an orphan drug's exclusivity.

(e) Because FDA's March 30, 2011 Statement approved, invited, and called forth the unlawful competition with Makena by compounded 17P not so customized, Defendants have a duty to terminate that unlawful competition forthwith.

(f) FDA cannot make findings as to access to or availability of an approved orphan drug, *e.g.*, Makena, without complying with the procedural and substantive provisions of 21 U.S.C. § 360cc(b) and 21 C.F.R. § 316.36 (2012); 5 U.S.C. § 558(c); and the Due Process Clause of the Fifth Amendment to the U.S. Constitution.

(g) In considering (i) whether the holder of an approved application for an orphan drug, *e.g.*, Makena, can assure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated an orphan drug, or (ii) whether such persons otherwise have adequate access to the drug, FDA may not consider the list price, or any other price, or the cost, of the drug.

(h) The foreign-manufactured active pharmaceutical ingredient ("API") for compounded 17P appears to be— and is— an unapproved new drug under 21 U.S.C. § 355.

(i) Such API for compounded 17P cannot lawfully be introduced or delivered for introduction into interstate commerce or lawfully be imported into the United States.

(j) Since March 30, 2011 and continuing to the present, Defendants have been, and are, allowing the import of such API for compounded 17P, and that such allowance has been and is arbitrary, capricious, an abuse of discretion, and otherwise not in accordance with law.

(k) FDA's March 30, 2011 Statement announcing implicitly that FDA would allow such imports was and is arbitrary, capricious, an abuse of discretion, and otherwise not in accordance with law.

2. Ordering that:

(a) Defendants withdraw FDA's March 30, 2011 Statement and June 15, 2012 statement, announce that those statements are withdrawn, and not maintain or implement the policy of non-enforcement as to non-customized compounding of 17P set forth in the March 30, 2011 Statement.

(b) Defendants take sufficient enforcement actions to stop the unlawful competition with Makena by compounded 17P not customized to meet the special needs of patients who have the condition for which Makena is indicated but for whom Makena is medically inappropriate.

(c) Defendants report to the Court quarterly for one year and semi-annually for the following two years, under seal if and to the extent necessary and with a redacted version publicly filed, the actions they have taken to terminate shipments of non-customized compounded 17P.

(d) Defendants not permit the entry into the United States, and not release into domestic commerce any future shipments, of foreign-manufactured API for use in compounding non-customized 17P, except such API that is from an establishment that is identified in an approved NDA for hydroxyprogesterone caproate injection, and that is in compliance with that approved NDA.

(e) Defendants DHHS and Secretary Sebelius take all actions necessary and appropriate to implement the relief awarded by the Court, including, but not limited to, withdrawal of CMS's March 30, 2011 statement relating to payment for 17P.

Because the requested temporary restraining order and preliminary injunction present no risk of monetary damage to Defendants, no bond is necessary pursuant to Rule 65(c) of the Federal Rules of Civil Procedure.

Plaintiffs request pursuant to LCvR 65.1(d) that the Court schedule the hearing on this motion for a preliminary injunction as soon as practicable, but in any event no later than July 26, 2012.

Undersigned counsel certifies that, pursuant to LCvR 7(m) and LCvR 65.1(a), draft copies of the Complaint and Memorandum in Support of Motion for Temporary and Preliminary Relief in this action were provided on Monday, July 2, to Gerald C. Kell, Senior Trial Counsel, Consumer Protection Branch of the U.S. Department of Justice, Civil Division; William B. Schultz, Acting General Counsel, Office of the General Counsel, Department of Health and Human Services; and Paige H. Taylor, Senior Counsel, Food and Drug Administration. Counsel further certifies that, on Tuesday, July 3, he conferred with Mr. Kell and informed him that KV intended to initiate the lawsuit on Thursday, July 5. Counsel informed Mr. Kell that KV intended to request a hearing on its motion for a temporary restraining order on July 9 or 10, and invited Mr. Kell to meet undersigned counsel at the Courthouse on Thursday, July 5, to present Defendants' position. Counsel will provide Mr. Kell and Ms. Taylor with copies of this motion and all related pleadings and papers as set forth in the attached certificate of service. Undersigned counsel further certifies that he was unable to obtain consent to the proposed relief in his conference with Mr. Kell.

This motion is supported by the attached Memorandum in Support of Motion for Temporary and Preliminary Relief; the supporting declarations of Scott Goedeke, Michael Jozwiakowski, Thomas McHugh, and Patrick Ronan and exhibits thereto; and arguments to be

made at a hearing. Proposed Orders for a temporary restraining order and a preliminary injunction accompany this motion.

Dated: July 5, 2012

Respectfully submitted,

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KATHLEEN SEBELIUS,
Secretary of Health and Human Services,
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Defendants.

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PLAINTIFFS' MEMORANDUM IN SUPPORT OF MOTION FOR TEMPORARY AND PRELIMINARY RELIEF

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Torpharm, Inc. v. FDA, No. 03-2401, 2004 U.S. Dist. LEXIS 524 (D.D.C. Jan. 8, 2004) 23

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21 C.F.R. § 316.36(a)(2) 21

21 C.F.R. § 316.36(a)-(b) (2012) 21

21 C.F.R. pt. 320 (2012) 3

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Orphan Drug Regulations, 57 Fed. Reg. 62,076 (Dec. 29, 1992) (final rule) ... 4, 22, 22-23, 44-45

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OTHER AUTHORITIES

Sheldon T. Bradshaw, Kyle Sampson, & Brian J. Wesoloski, *Did FDA Apply a Remedy Worse Than the Disease In Refusing To Clear the Market of Unapproved Versions of Makena?*, Food & Drug Pol'y Forum 4 (June 8, 2011) 24

Brief for the Petitioners, *Thompson v. W. States Med. Ctr.*, 535 U.S. 357 (2002) (No. 01-344) ..... *passim*

John L. Chollet & Michael J. Jozwiakowski, *Quality investigation of hydroxyprogesterone caproate active pharmaceutical ingredient and injection*, 38 Drug Dev. & Indus. Pharmacy 540 (2012) 17, 18

Doctors Rail Against Pregnancy Drug's Cost, Dallas Morning News (Mar. 19, 2011) 13

eCompounding Pharmacy, *Find a Local Compounding Pharmacy Near You* 15

Kevin Kinkade, Mo. Bd. of Pharmacy, *Pharmacy Compounding: Report on Quality Assurance Initiatives in the State of Missouri and Issues Impacting Customer Protection* (2005) 9

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TABLE OF ABBREVIATIONS

17P	Compounded versions of hydroxyprogesterone caproate injection
APA	Administrative Procedure Act
API	Active Pharmaceutical Ingredient
CMS	Centers for Medicare & Medicaid Services
DHHS	United States Department of Health and Human Services
FDA	Food and Drug Administration
FDCA	Federal Food, Drug, and Cosmetic Act
HPC	Hydroxyprogesterone Caproate
NDA	New Drug Application
NIH	National Institutes of Health
ODA	Orphan Drug Act

STATEMENT

I. INTRODUCTION.

In 1983, in the Orphan Drug Act ("ODA"), which amended the Federal Food, Drug, and Cosmetic Act ("FDCA"), Congress recognized that the markets for drugs designed to treat rare diseases or conditions are too small for drug manufacturers to recoup the extensive costs involved in securing approval from the Food and Drug Administration ("FDA") and complying with post-approval requirements. Accordingly, the ODA provides incentives to induce manufacturers to develop, obtain FDA approval of, and market "orphan drugs" that are effective and safe to treat these diseases and conditions. The most important such incentive is seven years of market exclusivity, during which a manufacturer has the right to be the exclusive marketer of such a drug for the rare disease or condition for which it was approved.

Plaintiffs, K-V Pharmaceutical Company and its wholly-owned subsidiary, Ther-Rx Corporation (together, "KV"), responded to that incentive by investing or committing over a quarter of a billion dollars to acquire, develop, and market Makena® (hydroxyprogesterone caproate ("HPC" or "17P") injection[1]), a sterile injectable drug administered weekly for up to 21 weeks to pregnant women with a history of preterm birth to reduce the risk of another preterm birth. FDA classified Makena as an orphan drug in 2007, approved it on February 3, 2011, and on February 11, 2011 stated that it is "entitled to seven years of orphan-drug exclusive approval." *See* Declaration of Scott Goedeke ("Goedeke Decl.") ¶ 4 & Ex. 1.

Under political pressure resulting in part from press reports about Makena's initial list price, FDA on March 30, 2011 destroyed Makena's market exclusivity by issuing a public state-

[1] HCP, the active pharmaceutical ingredient ("API") in Makena and in compounded versions of HPC, is also known as "17P." For convenience, we use the term "17P" only in reference to the compounded versions.

ment encouraging distribution of unapproved "compounded" versions of 17P by announcing a policy of non-enforcement against those unlawful drugs. FDA statements on June 15 and 29, 2012 did not announce an intent to enforce against those drugs. Without a major change in the marketplace for Makena very soon, KV cannot survive. This lawsuit seeks relief from the ongoing injury of unlawful competition that is destroying KV. As explained *infra*, that relief would also benefit patients by restoring to them the protection of the FDCA's drug-approval process.

II. THE FEDERAL FOOD, DRUG, AND COSMETIC ACT.

Since 1938, the FDCA has prohibited the introduction of any "new drug" into interstate commerce without FDA approval. FDCA §§ 505(a), 301(d), 21 U.S.C. §§ 355(a), 331(d).[2] The

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[2] The original Section 355 was enacted in Public Law No. 75-717, § 505, 52 Stat. 1040, 1052-53 (1938). The FDCA, as amended, is codified at 21 U.S.C. §§ 301-399d.

The term "drug" means "(A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clause (A), (B), or (C)." FDCA § 201(g)(1), 21 U.S.C. § 321(g)(1). The term "[c]omponent" means "any ingredient intended for use in the manufacture of a drug product . . . ." 21 C.F.R. § 210.3(b)(3) (2012). The term "[d]rug product" means "a finished dosage form, for example, tablet, capsule, solution, etc., that contains an active drug ingredient generally, but not necessarily, in association with inactive ingredients. . . ." 21 C.F.R. § 210.3(b)(4) (2012). Under these definitions, compounded 17P is a "drug" and a "drug product." The term ''new drug'' means

> (1) Any drug . . . the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof . . . ; or
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> (2) Any drug . . . the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.

process to develop a new drug and obtain FDA approval is lengthy and expensive. In addition to studies to show effectiveness and safety, the process includes development of a controlled and reliable manufacturing process and the drafting of labeling adequate to guide prescribing. FDCA § 505(b)(1)(D), (F), 21 U.S.C. § 355(b)(1)(D), (F). FDA may impose conditions on the approval of a new drug; *e.g.*, it may require more studies of the drug. FDCA § 505(*o*), 21 U.S.C. § 355(*o*). A manufacturer of an approved drug is also subject to many post-approval requirements. *See, e.g.*, 21 C.F.R. pts. 210, 211, §§ 314.70, 314.80, 314.81, 314.97, 314.98, 314.540, 314.630 (2012). Even a generic drug is subject to approval and post-approval requirements. *See* FDCA § 505(j), 21 U.S.C. § 355(j); 21 C.F.R. § 314.105(c), pts. 211, 320 (2012).[3]

III. ORPHAN DRUGS AND THE ORPHAN DRUG ACT.

Historically, as Congress found in 1983, "because so few individuals are affected by any one rare disease or condition, a pharmaceutical company which develops an orphan drug may reasonably expect the drug to generate relatively small sales in comparison to the cost of developing the drug and consequently to incur a financial loss."[4] Therefore, the ODA provides incentives for development of orphan drugs. *See* FDCA §§ 525, 527, 21 U.S.C. §§ 360aa, 360cc; ODA §§ 4, 5, 96 Stat. at 2053, 2056 (codified as amended at 26 U.S.C. § 45C, 21 U.S.C. § 360ee); Orphan Drug Regulations, 56 Fed. Reg. 3338, 3338 (Jan. 29, 1991) (proposed rule).

The ODA's most important incentive is a period of market exclusivity, which Congress believed essential to inducing orphan drug development. *E.g.*, H.R. Rep. No. 97-840(I), at 11

FDCA § 201(p), 21 U.S.C. § 321(p). Any compounded version of 17P is a "new drug."

[3] Pharmacies have certain exemptions under FDCA §§ 503(b)(2) (adequate directions for use), 510(g)(1) (registration with FDA), 704(a)(2)(A) (scope of FDA inspection), 21 U.S.C. §§ 353(b)(2), 360(g)(1), 374(a)(2).

[4] Orphan Drug Act, Pub. L. No. 97-414, § 1(b)(4), 96 Stat. 2049, 2049 (1983). The ODA, as amended, is codified at 21 U.S.C. §§ 360aa-360ee.

(1982), *reprinted in* 1982 U.S.C.C.A.N. 3577, 3583; Orphan Drug Regulations, 57 Fed. Reg. 62,076, 62,077 (Dec. 29, 1992) (final rule) ("the major incentive of the Orphan Drug Act"). The act grants seven years of market exclusivity to the first sponsor of an approved orphan drug, and thereby gives the sponsor a chance to recoup its costs and make a profit. *See* 21 U.S.C. § 360cc(a). This market exclusivity is intended to function much like a product patent. *See Genentech, Inc. v. Bowen*, 676 F. Supp. 301, 302-06 (D.D.C. 1987).[5]

The holder of orphan drug exclusivity must be able to supply sufficient quantities of the drug. 21 U.S.C. § 360cc(b). *See infra* note 43. When deciding whether an exclusivity holder can supply sufficient quantities, FDA must give the holder (i) notice of its concern about drug supply, and (ii) an opportunity to respond. 21 U.S.C. § 360cc(b); 21 C.F.R. § 316.36 (2012). In this context, access to an orphan drugs is solely a matter of quantities available. *See* 56 Fed. Reg. at 3343.[6] FDA agrees that it has no authority to consider an orphan drug's price in assessing access to it. 57 Fed. Reg. at 62,079, 62,084.[7]

IV. COMPOUNDING AND THE FOOD AND DRUG ADMINISTRATION MODERNIZATION ACT.

Some patients need customized medications. For example, a patient may be unable to take an FDA-approved drug because of an allergy to an inactive ingredient or because the dosage form (*e.g.*, a tablet) is inappropriate for that patient. In such cases, it may be medically necessary

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[5] *See also Baker Norton Pharm., Inc. v. FDA*, 132 F. Supp. 2d 30, 31 (D.D.C. 2001); Rare Diseases Orphan Product Development Act of 2002, Pub. L. No. 107-281, § 2(a)(5)-(6), 116 Stat. 1992, 1992-93 (2002) ("tremendous success" of ODA).

[6] FDA has not asserted—and there is no factual basis for it to assert, Declaration of Scott Goedeke ("Goedeke Decl.") ¶¶ 8-10, 25— that there has been, is, or is likely to be, any shortfall in supply from KV to meet all market demand for HPC injection.

[7] A statement by FDA in a *Federal Register* preamble has the status of an advisory opinion binding on FDA unless FDA repudiates it or a court overrules it. 21 C.F.R. § 10.85(d)(1), (e) (2012).

for a patient to take a "compounded" version of a drug, which is customized for that patient and is not reviewed by FDA. "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." *Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 360-61 (2002). "Compounding is typically used to prepare medications that are not commercially available . . . ." *Id.* at 361.

Although compounding to meet the special needs of individual patients is a traditional part of the practice of pharmacy,[8] the commercial manufacturing of drugs and FDA's regulatory control have greatly limited its scope. The FDCA of 1938 made compounding unlawful: under 21 U.S.C. § 321(p), quoted *supra* note 2, a compounded drug is a "new drug," and 21 U.S.C. § 355(a) prohibits the distribution of a new drug without FDA approval. *See* Thompson Br. 4-5. Compounders of drugs customized for individual patients, however, cannot recover the costs of obtaining FDA approval. *W. States*, 535 U.S. at 369-70.

Because access to customized drugs sometimes is medically necessary, FDA has allowed it in limited circumstances: when no commercially available drug is medically appropriate for a particular patient. FDA has "recognized that compounding can serve an important public purpose for which the health benefits outweigh the risks if the compounding is performed in response to a valid prescription in order to meet the medical needs of an individual patient for whom commercially available drugs are inadequate." Thompson Br. 5 (emphasis added).

In the 1980s and early 1990s, FDA saw examples of "pharmacies" exceeding the scope of traditional compounding by distributing nationwide "compounded" drugs produced on a com-

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[8] *See, e.g.*, *W. States*, 535 U.S. at 360-61; *Prof'ls & Patients for Customized Care v. Shalala*, 56 F.3d 592, 593 (5th Cir. 1995); Brief for Petitioners at 33, *Thompson v. W. States Med. Ctr.*, 535 U.S. 357 (2002) (No. 01-344) ("Thompson Br."), *available at* http://www.justice.gov/osg/briefs/2001/3mer/2mer/2001-0344.mer.aa.pdf.

mercial scale without FDA approval.[9] In 1992, FDA issued an enforcement policy, under which FDA would continue to defer to state pharmacy boards to regulate traditional compounding, but would enforce the FDCA to halt "compounding" that was really manufacturing. CPG 7132.16.

In 1997, Congress confirmed the important, but limited, role of traditional compounding in the Food and Drug Administration Modernization Act, which added to the FDCA Section 503A, 21 U.S.C. § 353a.[10] Section 353a makes traditional customized compounded drugs lawful by exempting them from the FDCA's new-drug-approval requirements and certain other requirements, if the compounding pharmacist complies with certain restrictions designed to preserve the limited scope of traditional compounding and to exclude drug manufacturing.[11]

First, a pharmacist may dispense a compounded drug only if a physician has determined that "a compounded product is necessary for the identified patient." 21 U.S.C. § 353a(a); *see also* H.R. Rep. No. 105-399, at 94; S. Rep. No. 105-43, at 67-68. Second, a pharmacist must not compound "regularly or in inordinate amounts" drugs that "are essentially copies of a commercially available drug product." 21 U.S.C. § 353a(b)(1)(D). Third, a pharmacist must not compound a drug before receiving a prescription, unless there is a pre-existing relationship among the pharmacist, a doctor, and a patient as to that drug, in which case the drug may be made in "limited quantities" for that patient before receipt of the prescription. *Id.* § 353a(a). Fourth, the

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[9] *See* FDA, Compliance Policy Guide § 7132.16, at 2 (Mar. 16, 1992) ("CPG 7132.16") (Exhibit A hereto), (superseded by Compliance Policy Guide § 460.200 (May 29, 2002) ("CPG 460.200"), *available at* http://www.fda.gov/OHRMS/DOCKETS/98fr/02D-0242_gdl0001.pdf.). "Drug manufacturing is the large scale production of a drug product, typically for a substantial market." Thompson Br. 34.

[10] Pub. L. No. 105-115, § 127, 111 Stat. 2296, 2328-30 (1997).

[11] *See* H.R. Rep. No. 105-399, at 94 (1997) (Conf. Rep.) ("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."); *see also* S. Rep. No. 105-43, at 67 (1997) (expressing similar intent).

total quantity of compounded drugs that a pharmacy distributes out-of-state must not exceed five percent of the pharmacy's total prescription orders.[12] Fifth, a pharmacist may compound drugs only from proper ingredients. *Id.* § 353a(b)(1)(A)-(C). Sixth and seventh, a pharmacist must not solicit prescriptions and must not "advertise or promote the compounding of any particular drug." *Id.* § 353a(a), (c). *See W. States*, 535 U.S. at 364-65.

In *Western States*, the Court held that the sixth and seventh restrictions violated the First Amendment. *Id.* at 372-74. The Ninth Circuit had held that the other five restrictions are not severable from the sixth and seventh, and thus do not survive to authorize traditional compounding. *W. States Med. Ctr. v. Shalala*, 238 F.3d 1090, 1096-97 (9th Cir. 2001), *aff'd on other grounds*, 535 U.S. 357 (2002). The Supreme Court did not rule on severability. 535 U.S. at 360, 366.[13] Later, the Fifth Circuit—agreeing with the district court, *Med. Ctr. Pharm. v. Gonzales*, 451 F. Supp. 2d 854, 861-63 (W.D. Tex. 2006), held that the other five restrictions are severable and do remain in force. *Med. Ctr. Pharmacy v. Mukasey*, 536 F.3d 383, 401-06 (5th Cir. 2008).

V. FDA'S PAST ENFORCEMENT PRACTICE AND THE DANGERS OF UNREGULATED COMPOUNDING.

By distinguishing between (i) traditional patient-by-patient compounding to meet special needs and (ii) manufacturing in the guise of compounding, Section 353a codifies FDA's long-standing enforcement policy, reflected in CPG 7132.16. *W. States*, 535 U.S. at 364; Thompson Br. 6, 13-14, 29-30. It is unlawful to compound drugs that are "copies or near copies of FDA-approved drug products," and that are "compounded without a medical need for their variation

[12] 21 U.S.C. § 353a(b)(3)(B)(ii). As an alternative to the five percent cap, FDA may enter into a memorandum of understanding with a State to develop other criteria to prevent inordinate sales of compounded drugs. 21 U.S.C. § 353a(b)(3)(B)(i).

[13] The demise of Section 353a in its entirety, rather than just its unconstitutional parts, would restore to FDA the degree of enforcement discretion the statute removed. Presumably, that is why the Solicitor General did not seek *certiorari* on that issue.

from the FDA-approved, commercially-available drugs with which they compete."[14] FDA has brought court actions against such compounding. *See, e.g.*, *United States v. Sene X Eleemosynary Corp.*, 479 F. Supp. 970, 979 (S.D. Fla. 1979) (at FDA's request, enjoining pharmacy from distributing drug that pharmacy was "compounding and dispensing . . . on a routine basis" in violation of the FDCA's new-drug, adulteration, and misbranding provisions); *Cedars N. Towers Pharmacy, Inc. v. United States*, No. 77-4695, 1978 U.S. Dist. LEXIS 15829, at *6 (S.D. Fla. Aug. 28, 1978) ("Bulk compounding of drugs at wholesale prices with nationwide distribution is not the type of activity intended to be exempt from registration [as a drug manufacturer]."). In 2006, FDA warned Wedgewood Pharmacy, which currently is a major compounder of 17P, Goedeke Decl. ¶ 29, that it was unlawfully compounding numerous commercially available products, and compounding a number of drugs—including 17P—"regularly and in sufficient quantities," so that its operations were inconsistent with any permissible compounding practice.[15]

Similarly, FDA's current guidance on compounding (issued after the Supreme Court's decision in *Western States*) advises that "the scope and nature of a pharmacy's activities [may] raise the kinds of concerns normally associated with a drug manufacturer and result in significant

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[14] FDA Warning Letter NYK 2008-06 (Jan. 10, 2008), *available at* http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm155170.htm. *See also, e.g.*, FDA Warning Letter CIN-07-28792-06 (Dec. 1, 2006) (declaring that compounder's products were impermissible copies of commercially available products), *available at* http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2006/ucm076191.htm; FDA Warning Letter 2005-NOL-06 (Dec. 9, 2004) (same), *available at* http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2004/ucm146702.htm; FDA Warning Letter CIN-06-27353-15 (Aug. 9, 2006) (concluding that a compounder engaged in unlawful drug manufacturing by compounding copies of commercially available drugs without showing "any legitimate medical need for . . . insignificant differences in formulation"), *available at* http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2006/ucm076025.htm.

[15] *See* FDA Warning Letter 06-NWJ-03 (Oct. 31, 2006), *available at* http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2006/ucm076147.htm.

violations of the new drug, adulteration, or misbranding provisions of the Act." CPG 460.200, at 3. It also states: "FDA will consider whether there is documentation of the medical need for the particular variation of the compound for the particular patient." *Id.* at 4. Except as to 17P, FDA has restricted compounding to its traditional narrow scope. *See, e.g.*, Thompson Br. 2-7. [16]

These statutory and regulatory restrictions on unapproved compounded drugs serve important patient-safety goals because only approved drugs have been shown to be effective and safe in clinical trials, are manufactured under strict FDA-approved controls, have FDA-approved labeling, and are subject to FDA's post-approval requirements and oversight. FDA does not review traditional compounding, and manufacturers purporting to be compounders sometimes resist FDA oversight.[17] Wedgewood Pharmacy, for example, resisted an FDA inspection – even after FDA had obtained a warrant. *Wedgewood Vill. Pharmacy, Inc. v. United States*, 421 F.3d 263 (3d Cir. 2005). That difficulty, however, does not justify across-the-board non-enforcement.

"Literature in pharmacy is replete with incidents where consumers have been harmed or large scale compounding practices made the dispensing of sub-standard products of major significance."[18] "[P]roblems with the quality of compounded drugs occur throughout the country. . . . From 1990 to 2005, FDA learned of at least 240 serious illnesses and deaths associated with

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[16] *United States v. Franck's Lab, Inc.*, 816 F. Supp. 2d 1209 (M.D. Fla. 2011), *appeal docketed*, No. 11-15350 (11th Cir. Nov. 16, 2011), held that FDA lacks authority to regulate traditional compounding of animal drugs customized for individual non-food-producing animals. The instant case involves human drugs, which are subject to different statutory provisions.

[17] *Federal and State Role in Pharmacy Compounding and Reconstitution: Exploring the Right Mix To Protect Patients, Hearing Before the S. Comm. on Health, Education, Labor, and Pensions*, 108th Cong. 40 (2003) (statement of Steven K. Galson, M.D., M.P.H., Deputy Dir. & Acting Dir., Ctr. for Drug Evaluation & Research, FDA) ("Galson Testimony"), *available at* http://www.pharmwatch.org/comp/hearing.pdf.

[18] Kevin Kinkade, Mo. Bd. of Pharmacy, *Pharmacy Compounding: Report on Quality Assurance Initiatives in the State of Missouri and Issues Impacting Customer Protection* 2 (2005), *available at* http://pr.mo.gov/boards/pharmacy/Pharmacy-Compounding-Report-FY-2005.pdf.

improperly compounded products. Because pharmacists are not required to report adverse events to FDA, there may be additional deaths and injuries of which the agency is unaware."[19]

VI. THE DEVELOPMENT AND APPROVAL OF MAKENA.

Preterm birth—birth prior to 37 weeks of gestational age—is the leading cause of neonatal mortality in industrialized countries, and is a major cause of early childhood mortality and morbidity.[20] As FDA has recognized, the medical need for an approved drug product to reduce the risk of preterm birth was particularly acute because of "the public health importance of reducing the incidence of preterm birth and its attendant morbidity and mortality."[21]

On May 6, 2006, KV's predecessor submitted to FDA a new drug application ("NDA") for approval of Makena to prevent preterm birth in singleton pregnancies.[22] The NDA relied in part on two clinical studies by the National Institutes of Health ("NIH"), which were published in 2003 and 2007.[23] Although compounded 17P was available, Goedeke Decl. ¶ 5, FDA designated

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[19] FDA, *2006 Limited FDA Survey of Compounded Drug Products* 2 (2006), *available at* http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm204237.htm. *See also* FDA, The Special Risks of Pharmacy Compounding (May 31, 2007), *available at* http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/ucm107839.pdf.

[20] Declaration of Michael Jozwiakowski ("Jozwiakowski Decl.") ¶ 2.

[21] FDA, *17α-Alpha Hydroxyprogesterone Caproate for Prevention of Preterm Birth, Overview of FDA Background Document* 9 (Aug. 2, 2006), *available at* http://www.fda.gov/ohrms/dockets/ac/06/briefing/2006-4227B1-02-01-FDA-Background.pdf.

[22] *See* Declaration of Thomas McHugh ("McHugh Decl.") ¶ 3. The history of ownership of Makena (formerly known as "Gestiva") is summarized in *id.* ¶¶ 4, 7.

[23] *See id.* ¶ 5. KV has had no free ride on the NIH studies. KV paid full value for the rights to Makena, and that value reflected the developmental status of and the anticipated revenues from the drug, not who had paid for the two studies. The cost of those studies is a very small percentage of KV's total cost for Makena. *Id.* ¶ 10. Reliance on NIH studies is not unusual; many vital drugs are available partly because pharmaceutical companies were able to build on research funded by NIH. Jozwiakowski Decl. ¶ 7. Indeed, a grant program for clinical testing of orphan drugs exists under 21 U.S.C. § 360ee. Congress expanded the program in the Rare Diseases Orphan Product Development Act of 2002, Pub. L. No. 107-281, § 3, 116 Stat. 1992, 1993.

the NDA for Priority Review, Jozwiakowski Decl. ¶ 4. "A *Priority Review* designation is given to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists."[24] Thus, FDA considered Makena potentially a "major" advance on compounded 17P and/or considered compounded 17P inadequate therapy. On January 25, 2007, FDA designated Makena an orphan drug. Jozwiakowski Decl. ¶ 4.

During the ensuing four years of FDA review, FDA required significant additional information to assure that Makena is effective and safe, including additional animal studies; information on chemistry, manufacturing and controls, and on product purity and potency; and additional studies. McHugh Decl. ¶ 6. FDA also required KV to sponsor two major, multi-year post-approval human studies costing tens of millions of dollars.[25] By the time of approval, KV had spent or committed more than $276 million for Makena, including $77-79 million for research and clinical trials. McHugh Decl. ¶¶ 8(b)-9. On February 3, 2011, FDA approved Makena to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. Approval Letter, *supra* note 25. Eight days later, FDA confirmed Makena's orphan drug exclusivity. Goedeke Decl., Ex. 1.

FDA Commissioner Margaret Hamburg, M.D., hailed FDA's approval of Makena: "I

Nothing in the statute suggests that benefit from a federal expenditure justifies destroying an approved orphan drug's market exclusivity.

[24] FDA, *Fast Track, Accelerated Approval and Priority Review, Accelerating Availability of New Drugs for Patients with Serious Diseases*, *available at* http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/SpeedingAccesstoImportantNewTherapies/ucm128291.htm (last updated May 28, 2010); *see also* FDA, Manual of Policies and Procedures § 6020.3, at 2 (2012) (describing priority review), *available at* http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/ ucm082000.pdf.

[25] McHugh Decl. ¶ 6; Letter from Julie Beitz, FDA, Office of Drug Evaluation III, to Robb Hesley, Hologic, Inc., re Accelerated Approval for NDA 021945 (Feb. 3, 2011) ("Approval Letter"), *available at* http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2011/021945s000ltr.pdf.

think it is important and an advance that we have an FDA-approved drug to prevent pre-term pregnancy and all of its consequent serious medical concerns for both mother and infant. And while the drug has been available through compounding, . . . compounding as a practice has been associated with serious health risks, contamination . . . ."[26] The March of Dimes also welcomed the approval.[27] Plainly, these parties did not regard compounded 17P as satisfactory.

VII. CONTROVERSY GENERATED BY MEDIA REPORTS ON MAKENA'S PRICE.

Weeks after FDA approved Makena, news media reported that its initial list price would be $1,500 per injection, *i.e.*, up to about $30,000 for a course of treatment, a significant increase over the cost of compounded 17P. A drug's "list price," however, is a pre-negotiation price. It does not reflect what patients, Medicaid, or private insurers ultimately pay for a drug. It is standard industry practice for both public and private payers to negotiate substantial price reductions and rebates to reach a mutually agreeable net effective price. Goedeke Decl. ¶ 12.

An orphan drug necessarily is expensive, as compared to other approved drugs and to compounded drugs, because (i) it must meet the same standards for approval, and so the costs of developing it and gaining approval are not necessarily less than those for drugs for larger patient populations; but (ii), due to the smallness of an orphan drug's patient population, recovery of those costs and any profit must be drawn from fewer patients; and (iii) compounders do not incur the costs of obtaining FDA approval and complying with FDA's post-approval requirements.[28]

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[26] *FY 2012 FDA Budget: Hearing Before the Subcomm. on Agriculture, Rural Development, Food and Drug Administration, and Related Agencies of the S. Comm. on Appropriations*, 112th Cong. 10 (Mar. 17, 2011) (Lexis/Nexis) ("2012 FDA Budget Hearing") (Exhibit B hereto).

[27] *See, e.g.*, March of Dimes, *March of Dimes Welcomes FDA Approval of Progesterone Injections* (Feb. 4, 2011), *available at* http://www.marchofdimes.com/news/feb4_2011.html.

[28] Goedeke Decl. ¶¶ 21, 23. Some orphan drugs have a list price of more than $200,000 annually. *Id.* ¶ 21. *See also id.* ¶ 22.

Moreover, many press reports failed to note KV's programs to ensure that women who cannot afford Makena can obtain it. Even before FDA's March 30, 2011 Statement, KV had announced that it would provide the drug free to uninsured women with household income below a certain amount, and at substantial discounts to other women on the basis of need.[29] Under Makena's current patient-assistance programs, an uninsured patient with an annual gross household income below $60,000 is not required to pay anything for Makena; and an uninsured woman with annual gross household income of $115,000 pays $20 per injection. Insured patients, too, can benefit. About 85% of all patients pay $20 or less per injection. Goedeke Decl. ¶¶ 14-16.

In response to the media reports and resulting public clamor, FDA initially confirmed that it has no authority to regulate the price of Makena or any other drug, and that compounding copies of an approved drug regularly or in inordinate amounts is prohibited.[30] Nonetheless, political pressures mounted to do "something" to bring down the supposed price of the drug.[31]

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[29] Goedeke Decl. ¶ 11; Press Release, KV, K-V Pharmaceutical Company Announces Comprehensive Patient Assistance Program for Makena™ (Mar. 8, 2011), *available at* http://www.kvpharmaceutical.com/news_center_article.aspx?articleid=339. After FDA issued its Statement, KV, through Ther-Rx Corporation, publicly announced additional price reductions. *See* Press Release, Ther-Rx Corporation, Ther-Rx Corporation Takes Action to Further Ensure High-Risk Women Are Able to Access FDA-Approved Makena™ (Apr. 1, 2011), *available at* http://www.kvpharmaceutical.com/news_center_article.aspx?articleid=341.

[30] *Doctors Rail Against Pregnancy Drug's Cost*, Dallas Morning News, at Briefing 1 (Mar. 19, 2011) (quoting FDA spokesperson, Jeff Ventura), Goedeke Decl., Ex. 8.

[31] Senator Sherrod Brown of Ohio—a member of the Appropriations Subcommittee with jurisdiction over FDA—sent to KV a public letter urging KV to reconsider the price of Makena. Letter from Sen. Sherrod Brown to Greg Divis, CEO, KV (Mar. 10, 2011), *available at* http://brown.senate.gov/imo/media/doc/Makena%20Letter.pdf. At a March 17, 2011 hearing on FDA's FY 2012 budget, Senator Brown said to Commissioner Hamburg: "it's so important that we figure out something to do here." 2012 FDA Budget Hearing 10. He added: "I'm just looking for FDA to take leadership with HHS in finding a way, a strategy to pass quickly to get this company to price its drug more reasonably for American women." *Id.* at 11. Shortly thereafter, the Chairman and five other Members of the House Committee on Energy and Commerce, which has legislative jurisdiction over FDA, requested that FDA make its staff available to explain FDA's decision to approve Makena. Letter from Rep. Fred Upton *et al.* to Hon. Margaret A.

VIII. FDA'S MARCH 30, 2011 STATEMENT AND ITS CONSEQUENCES.

On March 30, 2011, FDA issued a "Statement on Makena" (the "Statement"). It ended:

> In 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.[32]

The words "to support access" make clear that FDA is calling forth violations of the FDCA and withholding enforcement to drive down the price of HPC injection. There is no factual basis for concern about supplies of Makena.[33] Moreover, FDA's Statement fails to mention the limitations on compounding in Section 353a and in FDA's own CPG 460.200, discussed *infra* pp. 27-28. The Statement also does not mention (i) the factual circumstances of any particular compounders, (ii) any need to prioritize use of FDA's enforcement resources, or (iii) any written notice or warning FDA will send to compounders of 17P. The Statement also does not subject compounders of 17P to any of the approval or post-approval requirements that apply to Makena

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Hamburg, M.D. (Mar. 25, 2011), *available at* http://republicans.energycommerce.house.gov/Media/file/Letters/112th/032511FDA.pdf. *See also* McHugh Decl. ¶ 12 & n.1. Senator Brown brought additional pressure on FDA and CMS before March 30, 2011. *See* a page on Senator Brown's website: http://www.brown.senate.gov/search/?q=makena&access=p&as_dt=i&as_epq=&as_eq=&as_lq=&as_occt=any&as_oq=&as_q=&as_sitesearch=&client=brown&sntsp=0&filter=0&getfields=&lr=&num=15&numgm=3&oe=UTF8&output=xml_no_dtd&partialfields=&proxycustom=&proxyreload=0&proxystylesheet=default_frontend&requiredfields=&sitesearch=&sort=date%3AD%3AS%3Ad1&start=0&ud=1.

[32] Press Release, FDA, FDA Statement on Makena (Mar. 30, 2011), *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm249025.htm. FDA issued the statement just in time for Secretary Sebelius to refer to it when questioned by Senator Brown at an appropriations hearing on March 30, 2012. *See Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations for Fiscal Year 2012: Hearing Before the S. Comm. on Appropriations* 23-24 (Mar. 30, 2012), *available at* http://www.gpo.gov/fdsys/pkg/CHRG-112shrg19104442/pdf/CHRG-112shrg19104442.pdf.

[33] *See supra* note 6. Moreover, after FDA issued its Statement, KV reduced Makena's list price from $1,500 to $690 per injection. Goedeke Decl. ¶ 13.

and that KV must bear the cost of. On November 8, 2011, and June 15 and June 29, 2012, FDA issued further statements that reiterated that uncustomized compounding is unlawful, but did not announce any intent to take any kind of enforcement action against any compounder of 17P.[34]

In the United States, there are more than 1,000 compounders.[35] FDA's Statement approved and encouraged their nationwide distribution, during KV's exclusivity period and for Makena's approved indication, of unlimited quantities of uncustomized 17P, some of which are commercially manufactured in facilities not approved, or routinely inspected, by FDA. More than 100 are compounding 17P, and the largest are doing so in commercial quantities. Goedeke Decl. ¶ 31. These compounded versions have unknown compositions and manufacturing processes not approved by FDA, lack FDA-approved labeling to guide prescribers, are not subject to required reporting of adverse events, and are injected to treat a life-threatening condition.[36] Compounders' responses to FDA's Statement show that the Statement elicited violations of the FDCA that otherwise would not have occurred. Indeed, its very purpose was to elicit violations

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[34] Press Release, FDA, FDA Statement on Makena (Nov. 8, 2011) ("FDA Nov. 8, 2011 Statement"), *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm279098.htm; Press Release, FDA, Updated FDA Statement on Compounded Versions of hydroxyprogesterone caproate (the active ingredient in Makena) (June 15, 2012) ("FDA June 15, 2012 Statement"), *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm308546.htm; FDA, Questions and Answers on Updated FDA Statement on Compounded Versions of hydroxyprogesterone caproate (the active ingredient in Makena) (undated, but posted June 29, 2012), *available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm310215.htm.

[35] *See* eCompounding Pharmacy, *available at* http://www.ecompoundingpharmacy.com/ (last visited June 26, 2012). The number was derived by clicking on each jurisdiction and adding the numbers of compounders identified. A chain with multiple pharmacies was counted as one unit.

[36] FDA's Statement suggests that FDA may take enforcement action if it learns, after the fact, that "the compounded products are unsafe, of substandard quality, or are not being compounded in accordance with appropriate standards for compounding sterile products." *See supra* note 34. Thus, FDA's approach to these products is akin to the unsatisfactory situation that led Congress to include the drug-approval process in the FDCA in 1938: as to compounded 17P, FDA now has to catch-up with drug safety and quality problems the approval process is intended to prevent.

Compounders' responses to FDA's Statement show that the Statement elicited violations of the FDCA that otherwise would not have occurred. Indeed, its very purpose was to elicit violations so as "to support access." For example, Wedgewood Pharmacy, which sells compounded drugs from its 40,000-square-foot facility, noted that, although "[u]nder normal circumstances, compounding pharmacies must stop making a prescription drug when the same drug is manufactured as a commercial product," FDA had given a "green light" for compounding versions of 17P.[37] Because FDA called forth the unlawful uncustomized compounding, reminders that such compounding is unlawful—without a threat to enforce—do not change conduct sufficiently.

In addition, within hours of the release of FDA's Statement, as part of an obviously coordinated plan, the Centers for Medicare & Medicaid Services ("CMS") issued a statement that invited States and Medicaid payers to pay for 17P, and advised on how to do it.[38]

State Medicaid authorities have interpreted FDA's Statement as authorizing the substitution of compounded 17P for Makena; some States even compel the use of compounded 17P rather than Makena by Medicaid beneficiaries. Goedeke Decl. ¶ 33. For example, seven States require doctors prescribing Makena to demonstrate why a patient needs it rather than compounded 17P; Louisiana "urge[s] medical professionals to use [compounded 17P] in their patients for whom it is indicated." *Id.* ¶¶ 33-34 (alterations in original) (internal quotation marks omitted).

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[37] Goedeke Decl. ¶ 29 (alteration in original) (internal quotation marks omitted); Wedgewood Pharmacy, With FDA green light, Wedgewood Pharmacy continues to compound 17P (hydroxyprogesterone caproate) (Mar. 30, 2011), *available at* http://www.wedgewoodpharmacy.com/news/press-room/with-fda-green-light-wedgewood-pharmacy-continues-to-compound-17p-hydroxyprogesterone-caproate-.html.

[38] *See* Cindy Mann, CMS, *CMCS Informational Bulletin, Makena* (Mar. 30, 2011), *available at* http://www.cms.gov/CMCSBulletins/downloads/Makena-CMCS-Info-Bulletin-03-30-2011.pdf. A CMS statement also accompanied the FDA June 15, 2012 statement: CMS, CMCS Informational Bulletin (June 15, 2012), *available at* http://www.medicaid.gov/Federal-Policy-Guidance/Downloads/CIB-2-06-15-12.pdf.

Thus, the regulatory system has been turned upside down: in many States, the FDA-approved drug is now disfavored or off-limits, in comparison to unapproved versions; and Medicaid beneficiaries are subjected to the avoidable additional risks presented by compounded 17P. CMS's June 15, 2012 statement has not changed State Medicaid agencies' policies. *Id.* ¶ 43.

Never before has FDA publicly authorized and encouraged compounders to produce and distribute nationwide unapproved and uncustomized drugs to replace an FDA-approved drug.

IX. FDA'S UNLAWFUL ALLOWANCE OF UNLAWFUL IMPORTATION OF VERSIONS OF THE ACTIVE INGREDIENT FOR COMPOUNDED 17P.

A study commissioned by KV, but conducted independently, found that all of the API for compounded 17P that could be identified was manufactured in China, the country where drug manufacturing facilities exporting to the United States are least likely to be inspected by FDA.[39] The Chinese versions of API imported into the United States for compounding into 17P are not identified in any NDA approved by FDA.[40] FDA is allowing the import of these drugs in

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[39] Jozwiakowski Decl. ¶¶ 23, 25. "Perhaps the most serious challenge on the horizon for FDA is that growing access to the global marketplace will also expose Americans to a set of economically-motivated harms including counterfeiting, fraud, and other intentional adulterations. Recent, highly-public incidents involving adulterated heparin and melamine-tainted baby formula underscore how serious the potential danger can be . . . . The U.S. has seen a steady increase in the number of counterfeiting incidents." FDA, Pathway to Global Product Safety and Quality 16 (July 7, 2011) (footnote omitted), *available at* http://www.fda.gov/downloads/AboutFDA/CentersOffices/OC/GlobalProductPathway/UCM262528.pdf. "Despite . . . recent improvements, FDA does not—nor will it—have the resources to adequately keep pace with the pressures of globalization." *Id.* at 3. The adulterated heparin and melamine-tainted baby formula came from China. Statement of Deborah M. Autor, FDA Deputy Comm'r for Global Regulatory Operations & Policy, Before the S. Comm. on Health, Educ., Labor & Pensions 2, 6 (Sept. 14, 2011), *available at* http://help.senate.gov/imo/media/doc/Autor.pdf. The contaminated baby formula "fatally poison[ed] six babies and ma[de] 300,000 others gravely ill." *Id.* at 2.

[40] Jozwiakowski Decl. ¶ 23. The study's methods and results are described in John L. Chollet & Michael J. Jozwiakowski, *Quality investigation of hydroxyprogesterone caproate active pharmaceutical ingredient and injection*, 38 Drug Dev. & Indus. Pharmacy 540 (2012), *available at* http://informahealthcare.com/doi/pdf/10.3109/03639045.2012.662511.

furtherance of the policy set forth in the Statement. As explained *infra* at pages 35-36, the importation of such drugs is unlawful, and FDA's allowance of such importation is unlawful.

At KV's request, independent firms obtained and tested ten samples of Chinese API for 17P and 30 samples of 17P in finished dosage form. The majority of API samples failed at least one of the specifications FDA set for Makena (primarily, unknown impurities), and one contained no drug at all (instead, it was glucose). Jozwiakowski Decl. ¶ 27. The majority of samples of finished dosage form failed at least one of the specifications set by FDA for Makena, primarily due to unacceptable potency and/or impurities in this injectable drug. These findings are reported in an article by employees of KV in a peer-reviewed scientific journal. *See supra* note 40. FDA conducted its own study and testing of API for compounded 17P and of finished product, and reported that its findings did not raise safety concerns. FDA June 15, 2012 Statement. FDA's study, however, was conducted under unfavorable circumstances: the compounders had advance knowledge of it from their trade association. *See* Jozwiakowski Decl. ¶ 36.

X. KV IS BEING IRREPARABLY HARMED BY FDA'S STATEMENT.

The competition from compounders, resulting from FDA's Statement, has undercut, and continues to undercut, significantly KV's sales of Makena and related revenues. McHugh Decl. ¶¶ 15-20. KV cannot compete on price with compounders that do not bear the costs of compliance with the FDCA. *Id.* ¶ 14. Even at a reduced price, Makena is, by far, KV's most important drug; without the revenue from its market exclusivity, KV cannot survive. *Id.* ¶¶ 18-27.

About 90% of patients treated with HPC are receiving compounded 17P, not Makena. *Id.* ¶ 20. KV's weekly sales of Makena have not returned to the level reached in its first weeks of sale before FDA's Statement. *Id.* Since March 29, 2011, KV's share price has fallen by more than 90%. *Id.* ¶ 22. Under these circumstances, KV cannot generate enough cash for operating expenses and debt obligations. *Id.* ¶ 21. Unless FDA publicly signals that it will stop the unlaw-

ful competition by compounders of uncustomized 17P (and thereby give KV's creditors reason to believe that KV is likely to be able to meet its financial obligations if given more time), KV will not be able to attract new capital at a reasonable cost, and is likely to exhaust its working capital within three to six months and be forced to file for bankruptcy before then. *Id.* ¶ 26. Thus, FDA's Statement and policy are causing severe irreparable harm to KV.

XI. KV'S EFFORTS TO RESOLVE THIS MATTER WITH FDA HAVE FAILED.

After FDA issued its March 30, 2011 Statement, KV lowered its list price significantly and developed information on quality issues concerning compounded 17P, which it provided to FDA in October 2011, as acknowledged in FDA's November 8, 2011 Statement. Since then, KV has communicated with FDA frequently in an effort to persuade FDA to stop the unlawful compounding of uncustomized 17P. This week, KV's efforts to obtain relief from FDA, however, have finally proven unsuccessful. *See* Declaration of Patrick Ronan ¶ 13.

ARGUMENT

Before FDA issued its Statement, Makena had effective market exclusivity under the ODA. Compounded 17P could be substituted only for patients for whom Makena is medically inappropriate. After the Statement, as the conduct of compounders and Medicaid agencies shows, FDA is allowing compounded versions of 17P, made from unapproved Chinese API, to displace Makena, despite Makena's statutory exclusivity. FDA's Statement, issued in response to political pressure as to Makena's list price, and the policy it sets forth violate 21 U.S.C. § 360cc by approving and inviting widespread violations of 21 U.S.C. §§ 353a and 355(a), and also violate 21 U.S.C. § 381(a), and are not an exercise of legitimate enforcement discretion.

I. STANDARDS FOR INTERIM RELIEF.

In deciding a motion for a preliminary injunction, a district court must consider "four factors: (1) the movant's showing of a substantial likelihood of success on the merits, (2)

irreparable harm to the movant, (3) substantial harm to the nonmovant, and (4) public interest." *Davis v. Pension Benefit Guar. Corp.*, 571 F.3d 1288, 1291 (D.C. Cir. 2009). "If the movant makes an unusually strong showing on one of the factors, then it does not necessarily have to make as strong a showing on another factor." *Id.* at 1291-92. "[W]hen the other three factors strongly favor interim relief, a court may grant injunctive relief when the moving party has merely made out a 'substantial' case on the merits." *Sterling Commercial Credit—Mich., LLC v. Phoenix Indus. I, LLC*, 762 F. Supp. 2d 8, 12 (D.D.C. 2011).

Courts "consider[] the same factors in ruling on a motion for a temporary restraining order and a motion for a preliminary injunction." *Morgan Stanley DW Inc. v. Rothe*, 150 F. Supp. 2d 67, 72 (D.D.C. 2001); *see also Jacksonville Port Auth. v. Adams*, 556 F.2d 52, 56 (D.C. Cir. 1977); *Boehringer Ingelheim Corp. v. Shalala*, 993 F. Supp. 1, 1 (D.D.C. 1997). Some decisions have stated that a higher standard applies where a temporary restraining order would constitute affirmative relief changing the *status quo*. *See Judicial Watch, Inc. v. Dep't of Commerce*, 501 F. Supp. 2d 83, 91 (D.D.C. 2007) (requiring clear entitlement to relief or that extreme or very serious damage will result); *Farris v. Rice*, 453 F. Supp. 2d 76, 78-79 (D.D.C. 2006) (same).

II. FDA'S STATEMENT AND POLICY VIOLATE THE ORPHAN DRUG ACT.

Subject to three limited exceptions, the ODA provides to the sponsor of an orphan drug a seven-year period of exclusive marketing:

> Protection for drugs for rare diseases or conditions
>
> (a) Exclusive approval, certification, or license
>
> Except as provided in subsection (b) of this section, if the Secretary—
>
> (1) approves an application filed pursuant to section 355 of this title . . .
>
> for a drug designated under section 360bb of this title for a rare disease or condition, the Secretary may not approve another application under section 355 of

> this title . . . for such drug for such disease or condition for a person who is not the holder of such approved application . . . until the expiration of seven years from the date of the approval of the approved application . . . .

FDCA § 527(a), 21 U.S.C. § 360cc(a) (emphases added). FDA's Statement does not rely on any of the exceptions to market exclusivity, so they are not at issue here.[41]

Although FDA has not formally approved an application for compounded 17P during KV's exclusivity period, its Statement is the functional equivalent of such an approval. It publicly announces, as a matter of general applicability and future effect, that FDA will permit unlimited market entry of compounded versions of 17P during KV's exclusivity period. Thereby, FDA is violating Section 360cc(a) by nullifying the substance of the exclusivity that Congress plainly intended a party in KV's position to have. "'The purpose of the seven year period is to allow the sponsor of the orphan drug to recoup the cost of development by capturing all revenues from the sale of the drug for the rare disease.'"[42] A literal reading of Section 360cc as protecting only against formal approval of other applications, and thus as permitting FDA to destroy the practical benefit of exclusivity by broadly withholding enforcement against the marketing of unapproved versions of the same drug for the same indication, thereby allowing them to "captur[e] . . . revenues from the sale of the drug" would "dramatically separate the statute from its intended pur-

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[41] The ODA's "7-year period of exclusive marketing," 21 C.F.R. § 316.2 (2012), can be curtailed only in three circumstances. FDA can approve another application for the same drug and use if FDA finds, after affording the sponsor notice and the opportunity to respond, that the sponsor cannot ensure "the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition for which the drug was designated," 21 U.S.C. § 360cc(b)(1); 21 C.F.R. § 316.36(a)-(b) (2012). The only other circumstances are where FDA revokes a drug's orphan designation, *see* 21 C.F.R. § 316.29(b) (2012), or where the exclusivity holder consents, 21 U.S.C. § 360cc(b)(2); 21 C.F.R. § 316.36(a)(2). Here, sufficient quantities of Makena are available, its orphan status is in effect, and KV has not consented to compounding of 17P.

[42] *Genentech, Inc. v. Bowen*, 676 F. Supp. at 304-05 (emphasis added) (quoting H.R. Rep. No. 99-153, at 3 (1985) (commenting on Orphan Drug Amendments of 1985, Pub. L. No. 99-91, § 2, 99 Stat. 387, 387 (1985), which broadened availability of exclusivity)).

pose," and should be rejected for that reason, *Lewis v. United States*, 523 U.S. 155, 160 (1998).

FDA's Statement and policy are contrary to congressional intent. Congress is presumed to legislate against the background of established caselaw. *Wash. Legal Found. v. U.S. Sentencing Comm'n*, 17 F.3d 1446, 1450 (D.C. Cir. 1994). When the ODA was enacted in 1983, the settled caselaw barred FDA from permitting the marketing of unapproved new drugs (apart, possibly, from traditional compounding, which is not at issue here). *See infra* pp. 34-35. Thus, Congress surely considered the text of Section 360cc(a) adequate to protect orphan drug exclusivity. FDA's Statement and policy defeat that exclusivity by endorsing for multiple versions of 17P a means of market entry barred by caselaw Congress relied on.

The "obvious legislative intent behind the Orphan Drug Act" is "to promote the development of orphan drugs." *Baker Norton*, 132 F. Supp. 2d at 38. "The financial incentive for companies to develop such drugs is provided by the period of market exclusivity, which would be undermined if other companies could develop drugs with the same active moiety but minor differences in inactive ingredients." *Id.*; *see also* H.R. Rep. No. 97-840(I), at 11 (1982), *reprinted in* 1982 U.S.C.C.A.N. 3577, 3583 (discussing importance of exclusivity).

No statute authorizes FDA to eviscerate KV's market exclusivity. "FDA has no authority over drug pricing or any authority to consider it in drug approval."[43] Section 360cc does not permit FDA to consider cost when deciding whether there is sufficient access to an orphan drug.[44]

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[43] 57 Fed. Reg. at 62,079.

[44] *Id.* at 62,084 ("A comment requested that the high cost of an orphan drug be considered evidence that 'sufficient quantities' of the drug are not available 'to meet the needs of persons with the disease or condition for which the drug was designated.' Such a finding would then allow for the approval of subsequent identical drugs. [¶] FDA does not have the authority under existing law to equate high cost with lack of sufficient quantities, even though cost may affect access to a drug. As Congress used the term, 'sufficient quantities' refers only [to] the presence of enough drug and the means of its administration to meet the needs of all in the United States

"Regardless of how serious the problem an administrative agency seeks to address . . . it may not exercise its authority 'in a manner that is inconsistent with the administrative structure that Congress enacted into law.'" *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 125 (2000) (citation omitted). Nor may FDA suddenly change the legal permissibility of uncustomized compounding so as to defeat orphan drug exclusivity. Indeed, a long line of precedents bars FDA from defeating the market-exclusivity incentives Congress provided in the FDCA.[45]

In *Ranbaxy*, the D.C. Circuit rejected an FDA policy that permitted a brand manufacturer to delist a patent after a generic manufacturer had submitted an application that challenged the patent. The policy thereby permitted the brand manufacturer to prevent the generic manufacturer from obtaining 180 days of market exclusivity. 469 F.3d at 125. The court stated:

> By thus reducing the certainty of receiving a period of marketing exclusivity, the FDA's delisting policy diminishes the incentive for a manufacturer of generic drugs to challenge a patent . . . . The FDA may not . . . change the incentive structure adopted by the Congress, for the agency is bound "not only by the ultimate purposes Congress has selected, but by the means it has deemed appropriate, and prescribed, for the pursuit of those purposes."

Id. at 126 (quoting *MCI Telecomms. Corp. v. AT&T Co.*, 512 U.S. 218, 231 n.4 (1994)). The

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with the disease or condition for which the drug was designated."); *see also id.* ("[T]he agency believes it lacks the authority to consider costs of drugs in rendering decisions under § 316.36.").

[45] *See, e.g.*, *Teva Pharm. USA, Inc. v. Sebelius*, 595 F.3d 1303, 1318 (D.C. Cir. 2010) (rejecting FDA decisions allowing brand drug manufacturers to delist patents in order to thwart awards of market exclusivity); *Ranbaxy Labs. Ltd. v. Leavitt*, 469 F.3d 120, 125 (D.C. Cir. 2006) (same, except that *Teva* considered an amendment to the FDCA that was not at issue in *Ranbaxy*); *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1069, 1076 (D.C. Cir. 1998) (rejecting FDA's extra-statutory "successful defense" requirement for market exclusivity); *Granutec, Inc. v. Shalala*, No. 97-1873, 1998 U.S. App. LEXIS 6685, at *21, *30 (4th Cir. Apr. 3, 1998) (per curiam) (unpublished) (same); *Inwood Labs., Inc. v. Young*, 723 F. Supp. 1523, 1527 (D.D.C. 1989) (concluding that FDA's interpretation would impermissibly "affect adversely the incentives that Congress sought to create in providing for 180 days of exclusivity"), *vacated as moot*, 43 F.3d 712 (D.C. Cir. 1989); *see also Torpharm, Inc. v. FDA*, No. 03-2401, 2004 U.S. Dist. LEXIS 524, at *2 (D.D.C. Jan. 8, 2004) (rejecting FDA's use of "shared 180-day exclusivity"); *cf. Purepac Pharm. Co. v. Friedman*, 162 F.3d 1201, 1204-05 (D.C. Cir. 1980) (upholding regulation that followed statutory requirements for exclusivity)..

court concluded that, "because [FDA's policy] diminishes the incentive the Congress gave manufacturers of generic drugs, [it] is inconsistent with the purpose of the Act." *Id.* Here, too, FDA has created a new way to defeat an FDCA exclusivity provision. As in *Ranbaxy*, FDA's Statement "reduc[es] the certainty of [a drug company] receiving a period of marketing exclusivity" Congress intended it to have, and therefore it "is inconsistent with the purpose of the Act."

Indeed, were FDA free to allow unapproved compounded drugs to defeat orphan drug exclusivity, all the exclusivity incentives in the FDCA would become less reliable and thus less effective, including those for orphan drugs in Section 360cc(a); for generic drugs in 21 U.S.C. § 355(j)(5)(B)(iv); for new drugs in §§ 355(c)(3)(E)(i)-(ii), 355(c)(3)(E)(iii) and (c)(3)(E)(iv); for pediatric drugs in § 355a(b)-(c); and for new animal drugs in §§ 360ccc-2, 360b(c)(2)(F)(i)-(v).[46]

When Congress enacted the ODA in 1983, FDA and the courts had interpreted the FDCA as not permitting compounded drugs to be freely substituted for approved drugs. See cases cited *supra* p. 8. Congress thus plainly did not intend for market exclusivity to be at the mercy of purported FDA discretion to allow unapproved, uncustomized compounded drugs to substitute for approved drugs having statutory exclusivity. The ODA's specific exceptions to exclusivity in Section 360cc(b)—none of which is invoked in FDA's Statement—confirm the opposite. *Expressio unius est exclusio alterius*. *E.g.*, *Leatherman v. Tarrant Cnty. Narcotics Intelligence & Coordination Unit*, 507 U.S. 163, 168 (1993).

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[46] Sheldon T. Bradshaw, Kyle Sampson, & Brian J. Wesoloski, *Did FDA Apply a Remedy Worse Than the Disease In Refusing To Clear the Market of Unapproved Versions of Makena?*, Food & Drug Pol'y Forum 4 (June 8, 2011) ("FDA's decision has the real potential to inhibit the development of new drugs, including orphan drugs. Indeed, the agency's decision is likely to have a chilling effect on companies considering the development of drugs that, but for FDA's intervention, would have to compete against cheap, unapproved versions of the same drug. FDA's actions almost certainly will have a negative impact on orphan drug research, which often is very expensive.") (Exhibit C hereto). Mr. Bradshaw is a former Chief Counsel of FDA; he and his co-authors have no connection to KV.

Finally, the equities here strongly favor KV because FDA's destruction of KV's orphan drug exclusivity for Makena is unfair to KV in at least three ways.

First, FDA is treating similarly situated parties differently: it is treating KV differently than all other holders of orphan drug exclusivity (some of whom have much higher list prices, *see* Goedeke Decl. ¶¶ 21-22), and there is no legally relevant distinction between KV's situation and those of other holders of such exclusivity. Such distinction in treatment is unlawful, *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 27-28 (D.D.C. 1997) (citing cases); and it is unfair.

Second, FDA has subjected KV to competition from compounders, who can undercut KV's price because, unlike KV, they do not need to recover the costs of obtaining FDA approval and of complying with FDA's post-approval requirements. FDA imposed on KV, as a condition of market entry for Makena, a requirement of expensive additional studies. McHugh Decl. ¶ 6. FDA has imposed on compounders of 17P no such requirement, as a condition of their market entry. Such competition is unfair. *Cf. Bracco*, 963 F. Supp. at 28-29.[47]

Third, on March 30, 2011, FDA destroyed KV's exclusivity without having afforded KV any process—not the "notice and opportunity for the submission of views" on the issue of access to the orphan drug required by 21 U.S.C. § 360cc(b)(1) and 21 C.F.R. § 316.36(a); not the similar process required by the Administrative Procedure Act ("APA"), 5 U.S.C. § 558(c), for

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[47] *See also* Thompson Br. 29 (citing *Weinberger v. Bentex Pharm., Inc.*, 412 U.S. 645, 653 (1973), for the proposition that "it would be 'inherently unfair' to require compliance by one manufacturer with the new drug approval requirements 'while his competitors marketing similar drugs remain free to violate the [FDCA]'" (footnote omitted)); *id.* at 35-36, 40; FDA, Questions and Answers About FDA's Enforcement Action Against Unapproved Quinine Products 5 (undated, but after Dec. 15, 2006) ("Quinine Q & As") ("Allowing continued marketing of unapproved drugs that compete against approved counterparts challenges the integrity of the drug approval system that is designed to avoid the risks associated with potentially unsafe and ineffective drugs, and puts companies that comply with the law at a disadvantage."), *available at* http://www.fda.gov/downloads/Drugs/GuidanceCompliance%20RegulatoryInformation/EnforcementActivitiesbyFDA/SelectedEnforcementActionsonUnapprovedDrugs/ucm119653.pdf.

revocation of a "license," which, under 5 U.S.C. § 551(8), includes "the whole or a part of an agency . . . approval";[48] and not the process required by the Due Process Clause before a property interest is effectively destroyed, *see, e.g.*, *Bell v. Burson*, 402 U.S. 535, 539 (1971); *Propert v. District of Columbia*, 948 F.2d 1327, 1331-32 (D.C. Cir. 1991).[49]

In sum, FDA's Statement and the policy it sets forth violate Section 360cc(a). Thus, they are "arbitrary, capricious, an abuse of discretion, [and] otherwise not in accordance with law" under 5 U.S.C. § 706(2)(A), "short of statutory right" under 5 U.S.C. § 706(2)(C), and "without observance of procedure required by law" under 5 U.S.C. § 706(2)(D).

III. FDA'S STATEMENT AND POLICY VIOLATE FDCA § 353a.

Section 353a "establishes [the] parameters under which compounding is appropriate and lawful." H.R. Rep. No. 105-399, at 94 (1997) (Conf. Rep.); S. Rep. No. 105-43, at 67 (1997) (same). Congress's express intent was to "limit[] the scope of compounding so as to prevent manufacturing under the guise of compounding," while permitting the use of "compounded drug products as a component of individualized therapy." H.R. Rep. No. 105-399, at 94 (emphasis added); *see also* S. Rep. No. 105-43, at 67 (same); *Med. Ctr. Pharmacy*, 536 F.3d at 391 (same). Accordingly, Congress established seven independent limitations on compounding. *See supra* pp. 6-7. FDA's Statement blatantly disregards four of them.

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[48] The approval of Makena includes its approval as an orphan drug with market exclusivity.

[49] Market exclusivity confers a "first-mover advantage," which "is a valuable asset." *Teva*, 595 F.3d at 1311. FDA's regulations confirm that holders of an orphan-drug designation (to which, upon approval of the orphan drug, market exclusivity attaches) have a cognizable property interest in that designation. *See* 21 C.F.R. § 316.27 (2012) (describing process to change or assign ownership of an orphan-drug designation). A protected property interest can be destroyed as a practical matter even without a formal revocation of title to the interest. *See, e.g.*, *Stidham v. Peace Officer Standards & Training*, 265 F.3d 1144, 1153 (10th Cir. 2001); *Westborough Mall, Inc. v. City of Cape Girardeau*, 794 F.2d 330, 336-37 (8th Cir. 1986); *Reed v. Vill. of Shorewood*,

First, the Statement does not require compounders to confirm that a patient has a medical need for compounded 17P rather than Makena. To comply with Section 353a, compounders must have a valid prescription or notation confirming that the "compounded product is necessary for the identified patient," 21 U.S.C. § 353a(a). They must "be able to cite a legitimate medical need for the compounded product that would explain why a commercially available drug product would not be appropriate. . . . This medical need would not include compounding drugs that are essentially copies of commercially available drug products for largely economic reasons." S. Rep. No. 105-43, at 67-68.[50] FDA's Statement permits compounding for economic rather than medical reasons, a purpose for compounding Congress intended to remain prohibited.

Second, compounders must not "compound regularly or in inordinate amounts . . . any drug products that are essentially copies of a commercially available drug product." 21 U.S.C. § 353a(b)(1)(D); *see also* CPG 460.200, at 4 (explaining that "[c]ompounding drug products that are commercially available in the marketplace or that are essentially copies of commercially available FDA-approved drug products" is a manufacturing, not compounding, activity).[51] FDA's Statement includes no such limitation; rather, it encourages regular compounding of 17P,

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704 F.2d 943, 949 (7th Cir. 1983).

[50] *See also* CPG 460.200, at 4 (explaining that FDA "will consider whether there is documentation of the medical need for the particular variation of the compound for the particular patient" in deciding whether it is permissible for a pharmacy to "compound a small quantity of a drug that is only slightly different than an FDA-approved drug"); H.R. Rep. No. 105-399, at 94 (explaining need to medically justify compounding of versions of commercially available drug products, and stating that, "where it is readily apparent, based on the circumstances," that a purported difference between the commercially available drug and the compounded drug is "a mere pretext to allow compounding of products that are essentially copies of commercially available products, such compounding would be considered copying of commercially available products" and would be impermissible if "done regularly or in inordinate amounts").

[51] Although 21 U.S.C. § 353a(b)(1)(D) authorizes FDA to define "inordinate amounts," the Senate Report explains that "'[i]nordinate' quantities means amounts typically associated with ordinary commercial drug manufacturing." S. Rep. No. 105-43, at 68.

i.e., versions of Makena, an FDA-approved, commercially available drug product.

Third, pharmacists must receive a prescription before compounding a drug, or they must have a pre-existing relationship with a doctor and patient where there is a history of prescribing the compounded drug, in which case the compounded drug may be made in "limited quantities" in advance. 21 U.S.C. § 353a(a). FDA's Statement disregards this limitation.

Fourth, unless compounders operate in a State with a memorandum of understanding with FDA, they are prohibited from distributing compounded drugs out-of-state in quantities that "exceed 5 percent of the total prescription orders dispensed or distributed," 21 U.S.C. § 353a(b)(3)(B)(ii). FDA's Statement disregards this limitation.

By disregarding all these limitations, FDA's Statement essentially releases the entire 17P compounding industry from Section 353a's restrictions. The compounding FDA has unleashed is not small-scale or local, and is not restricted to patients for whom Makena is unsuited. It is nationwide compounding for the entire population of patients, directly contrary to Section 353a. In effect, for the unlimited future, FDA has abrogated Section 353a as to compounders of 17P.

Although *Western States* struck down part of Section 353a(a) and all of Section 353a(c), many factors warrant the conclusion that the other restrictions in Section 353a are severable from the two unconstitutional provisions, and so remain in force.

Severability is a matter of legislative intent. *United States v. Booker*, 543 U.S. 220, 246 (2005). The test is "what 'Congress would have intended' in light of the Court's constitutional holding." *Id.* (quoting *Denver Area Educ. Telecomms. Consortium, Inc. v. FCC*, 518 U.S. 727, 767 (1996) (plurality opinion)). A court "must retain those portions of the Act that are (1) constitutionally valid, [*Regan v. Time, Inc.*, 468 U.S. 641, 652-53, (1984)], (2) capable of 'functioning independently,' [*Alaska Airlines, Inc. v. Brock*, 480 U.S. 678, 684 (1987)], and (3) consistent

with Congress' basic objectives in enacting the statute, *Regan*, [468 U.S.] at 653." *Booker*, 543 U.S. at 258-59. Here, plainly, the other restrictions in Section 353a are constitutional, and each of them can function independently of the unconstitutional provisions. Finally, their independent functioning plainly is "consistent with Congress' basic objectives" in Section 353a.

That Section 353a codifies an FDA enforcement policy, *see supra* p. 7, shows that Congress's purpose was to make that policy statutory, by enacting an exemption for traditional compounding from certain FDCA provisions, so that (i) traditional compounders would not be engaging in unlawful conduct permissible only at FDA's discretion, and (ii) manufacturers could not benefit from the exemption. *See supra* note 11. Congress's intent was to "bring the legal status of compounding in line with FDA's longstanding enforcement policy of regulating only drug manufacturing, not ordinary pharmacy compounding." 143 Cong. Rec. S9839 (daily ed. Sept. 24, 1997) (statement of Sen. Kennedy).[52] The statute removed FDA's discretion (i) to treat traditional customized compounding as unlawful and (ii) to treat uncustomized compounding as lawful. The statute's very point is to substitute statutory standards for FDA discretion. There is no other reason to codify an enforcement policy.

In view of that objective, Congress plainly would have preferred Section 353a without its unconstitutional provisions to no Section 353a at all. Whether or not the other provisions of Section 353a remain in effect, the ban on compounders' advertising and solicitation of prescriptions has been lost. If the other provisions are unseverable, traditional compounding is unlawful and its continuation is at FDA's mercy. There is no reason to believe that Congress would have preferred that outcome. *See Med. Ctr. Pharmacy*, 536 F.3d at 404-05.

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[52] "Rather than leaving to the enforcement discretion of the FDA the determination of when compounding should be permitted, Congress chose to delineate in the FDCA itself the limited

Rather, Congress's intent to make traditional compounding lawful without doing so for unapproved manufacturing makes it necessary to have criteria that distinguish between them. The remainder of Section 353a states Congress's criteria to achieve that purpose, and they do achieve it.[53] Nullifying the entire statute does not. Additional reasons support this conclusion.

First, out of deference to the legislative authority of the Congress, the Supreme Court has made clear that there is a strong preference for severability. "Unless 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." *Alaska Airlines*, 480 U.S. at 684 (internal quotation marks omitted).[54] Thus, the burden is on the party opposing severability to show that the remaining provisions cannot operate as a law. FDA cannot make that showing here. Plainly, the remaining restrictions can operate as law.

Second, the FDCA has a "separability" clause, FDCA § 1001 (formerly § 901), 21 U.S.C. § 391, which creates a presumption of severability, *Alaska Airlines*, 480 U.S. at 686. That the

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circumstances under which pharmacy compounding would be exempt as a matter of law from certain requirements that apply to drug manufacturers." Thompson Br. 7; *see also id.* at 31.

[53] "Much like the advertising provision, those other requirements function to create permissible space for compounding pharmacists while limiting pharmacists' ability to engage in large-scale manufacturing. Severing the advertising requirement would leave those other considerable requirements intact, and they would continue to effect Congress's purpose." *Med. Ctr. Pharmacy*, 536 F.3d at 403; *id.* at 403 n.43 ("Indeed, the Supreme Court recognized this consequence in reaching its decision that [§ 353a's] advertising provision was more restrictive than necessary to advance the government's interests . . . ."). In *Western States*, the Supreme Court suggested that the remaining provisions may suffice for the statutory purpose. 535 U.S. at 372-73.

[54] *See also, e.g.*, *Ayotte v. Planned Parenthood of N. New Eng.*, 546 U.S. 320, 328-29 (2006) ("We prefer . . . to sever [a statute's] problematic portions while leaving the remainder intact . . . we try not to nullify more of a legislature's work than is necessary, for we know that '[a] ruling of unconstitutionality frustrates the intent of the elected representatives of the people.'" (alteration in original) (citations omitted) (quoting *Regan*, 468 U.S. at 652)); *INS v. Chadha*, 462 U.S. 919, 931-35 (1983); *Buckley v. Valeo*, 424 U.S. 1, 108 (1976) (per curiam); *United States v. Jackson*, 390 U.S. 570, 591 (1968); *Champlin Ref. Co. v. Corp. Comm'n*, 286 U.S. 210, 234 (1932).

clause existed before 1997 is inconsequential because, "whenever Congress passes a new statute, it acts aware of all previous statutes on the same subject," *Erlenbaugh v. United States*, 409 U.S. 239, 244 (1972). There is no reason to require Congress to re-enact a provision already present in the statute being amended in order for that provision to apply to the statute as amended.

Third, here, as in *Community for Creative Non-Violence v. Turner*, 893 F.2d 1387, 1394 (D.C. Cir. 1990), the unconstitutional provisions are "merely a subset of the category of restrictions," and "[t]he other provisions, with the exception of [the unconstitutional provisions,] are not contingent upon the [unconstitutional provisions] for their existence and viability." Therefore, "these provisions are severable." *Id.* On this same reasoning, in part, the Fifth Circuit has held these very provisions severable. *Med. Ctr. Pharmacy*, 536 F.3d at 404.

Finally, the Ninth Circuit's brief contrary analysis in *Western States*, 238 F.3d at 1096-98, is deeply flawed. First, it disregards the earlier acknowledgement that, "[w]ithout the advertising restrictions, other safeguards exist to protect the public," *id.* at 1095 (citing other restrictions in § 353a). Second, the court's reliance on the legislative history is misplaced. FDA Commissioner Kessler's testimony, quoted at *id.* at 1097, did not even mention advertising. Rather, he noted, correctly, that the then-pending bill, H.R. 3199, 104th Cong. § 18 (1996), lacked any "constraints on the volume of compounding," and so would encourage "large-scale manufacturing under the guise of pharmacy compounding." 238 F.3d at 1097 (internal quotation marks omitted). Plainly, Congress responded by adding the multiple restrictions in Section 353a, including those on volume, not just the two unconstitutional restrictions. The court's treatment of the advertising ban as the only response to that testimony, *id.*, is contrary to the facts. *See Med. Ctr. Pharmacy*, 536 F.3d at 404. Third, the court's view that the advertising ban is critical to the purpose stated in the Conference Report, 238 F.3d at 1097, is contrary to the Supreme

Court's view, *see W. States*, 535 U.S. at 372-73; *see also Med. Ctr. Pharmacy*, 536 F.3d at 403 ("[W]e do not see the advertising provision as so central to the purpose of [§ 353a] that Congress would not have passed the statute without it."). Fourth, the court's dismissal of the FDCA's severability clause on the ground that it was not part of the 1997 law is contrary to *Erlenbaugh*.

In sum, the remaining provisions of Section 353a are severable from the invalid ones.

Because FDA's Statement and policy disregard four requirements of Section 353a, the Statement and policy are contrary to Section 353a. Thus, they are "arbitrary, capricious, an abuse of discretion, [and] otherwise not in accordance with law" under 5 U.S.C. § 706(2)(A), and are "in excess of statutory jurisdiction, authority, or limitations" under 5 U.S.C. § 706(2)(C).

IV. FDA'S STATEMENT AND POLICY VIOLATE THE FDCA'S DRUG-APPROVAL REQUIREMENT.

FDA's Statement and policy violate the requirement in Sections 355(a) and 331(d) that new drugs be approved by FDA before they are distributed in the United States.

"A fundamental precept of drug and device regulation in this country is that these products must be proven safe and effective before they can be sold." *Brown & Williamson*, 529 U.S. at 133 (internal quotation marks omitted). "[T]he Government has every reason to want as many drugs as possible to be subject to [FDA's] approval process." *W. States*, 535 U.S. at 369. "Manufacturers of drugs that lack required approval . . . have not provided FDA with evidence demonstrating that their products are safe and effective, and so we [FDA] have an interest in taking steps to either encourage the manufacturers of these products to obtain the required evidence and comply with the approval provisions of the [FDCA] or remove the products from the market."[55] *See also* Thompson Br. 12, 23, 45.

[55] FDA, Guidance for FDA Staff and Industry: Marketed Unapproved Drugs – Compliance Policy Guide § 440.100[:] Marketed New Drugs Without Approved NDAs or ANDAs 3 (Sept. 19, 2011), *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatory

The FDCA is very clear: "No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application . . . is effective with respect to such drug." 21 U.S.C. § 355(a). "The following acts and the causing thereof are prohibited: . . . (d) The introduction or delivery for introduction into interstate commerce of any article in violation of section . . . 355 . . . of this title." 21 U.S.C. § 331.

Compounded versions of 17P are "new drugs."[56] Yet, FDA is allowing them to be mass-produced and broadly marketed without approval. "Compounding on that scale exposed significant numbers of people to the health and safety risks that had prompted enactment of the new drug approval requirements in the first place. Moreover, such compounding threaten[s] the integrity and efficacy of the new drug approval process by [reducing drug manufacturers' incentives to submit to it]." Thompson Br. 13; *see also id.* at 20-22, 27-29, 30-31.

Until March 30, 2011, FDA had interpreted the FDCA as prohibiting manufacturing under the guise of compounding, and had enforced that interpretation. *See* CPG 7132.16, at 3 (citing cases). Indeed, even before Congress enacted Section 353a, FDA had restricted com pounding to the production of small quantities of drugs for patients with special needs. *See*

Information/Guidances/ucm070290.pdf. This document states FDA's enforcement policy as to marketed unapproved drugs. Where a company newly obtains FDA approval of a drug that other companies have been marketing without approval, the policy allows only a limited grace period before FDA seeks to clear the market of the unapproved products, *id.* at 5-8, because the obtaining of FDA approval "benefits the public health by increasing the assurance that marketed drug products are safe and effective" and "because [the unapproved products] present a direct challenge to the drug approval system . . . ." *Id.* at 7. FDA "hopes" that the non-statutory "market exclusivity [created by FDA's removal of the unapproved products] will provide an incentive to firms to be the first to obtain approval to market a previously unapproved drug." *Id.* at 8 (footnote omitted). Thus, under FDA's policy, the benefits of the approval process outweigh the risk of monopoly pricing. KV was the first to obtain approval of HPC injection, but FDA is arbitrarily refusing to apply its general policy to KV, even though KV's statutory exclusivity gives FDA an added reason to stop the unlawful marketing of unapproved competing drugs.

[56] FDA argued successfully in *Medical Center Pharmacy* that all compounded drugs are new drugs. *See* 536 F.3d at 394-409. *See also supra* note 2.

supra pp. 4-9. Congress has never authorized FDA to allow the marketing of an entire class of unapproved compounded drugs beyond the scope of traditional customized compounding.

This Court has rejected attempts to allow the mass marketing of unapproved new drugs. *Cutler v. Kennedy*, 475 F. Supp. 838 (D.D.C. 1979), held invalid FDA regulations that allowed the marketing of drugs that had been found to be safe but whose effectiveness was undetermined. The Court noted that, "to protect drug consumers from the hazards of unsafe and ineffective drugs," *id.* at 848, the FDCA requires that drugs be generally recognized as safe and effective or that they be found by FDA to be safe and effective before they are marketed, and that to say that FDA has the authority to authorize the marketing of drugs that satisfy neither condition is "a frontal assault on the premarket licensing scheme of the [FDCA]" and "flies in the face of the statutory scheme," *id.* at 854. FDA's Statement is precisely such an assault. [57]

This Court enjoined FDA from applying a policy that allowed drugs chemically equivalent to approved drugs to be marketed without approved NDAs. *Hoffmann-LaRoche, Inc. v. Weinberger*, 425 F. Supp. 890, 894-95 (D.D.C. 1975). "[P]ermitting new drugs to be marketed without an approved [NDA] contravenes the clear statutory requirement of preclearance mandated by 21 U.S.C. [§] 355 (1970). The FDA's choice of policy is not within the intendment of the 1962 New Drug Amendments and the legislative scheme they embody." *Id.* at 894.

In *American Public Health Ass'n v. Veneman*, 349 F. Supp. 1311 (D.D.C. 1972), this

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[57] In *Chaney v. Heckler*, 718 F.2d 1174, 1187 n.35 (D.D.C. 1983), *rev'd*, 470 U.S. 821 (1985), the court stated: "Moreover the two FDCA cases that the District Court cites do not hold that courts cannot review FDA's complete refusal to investigate and regulate an entire class of drugs. . . . In *Cutler v. Kennedy,* 475 F. Supp. 838 (D.D.C. 1979), the court refused on equity grounds to require FDA to take certain drugs off the market. *Id.* at 856. To the extent dicta in *Cutler* supports the broader proposition that certain FDA duties are not mandatory, and that FDA's actions cannot be reviewed, we expressly disapprove it." The Supreme Court, in reversing, did not mention *Cutler*. The D.C. Circuit's comment does not affect the discussion of *Cutler* here.

Court held unlawful FDA practices that permitted the marketing of new drugs that had not been shown to satisfy the FDCA's standards for approval; and the Court rejected FDA's argument that such matters were within its discretion, *id.* at 1314. *See also United States v. Generix Drug Corp.*, 460 U.S. 453 (1983) (rejecting a proposed interpretation of the FDCA that would have permitted the marketing of unapproved generic versions of approved new drugs).

Because FDA's Statement and the policy it sets forth violate Section 355(a) and because FDA has no authority to authorize the introduction into interstate commerce of unapproved new drugs (outside traditional compounding), the Statement and policy are "arbitrary, capricious, an abuse of discretion, [and] otherwise not in accordance with law" under 5 U.S.C. § 706(2)(A) and are "in excess of statutory jurisdiction, authority, or limitations" under 5 U.S.C. § 706(2)(C).

V. FDA'S STATEMENT AND POLICY VIOLATE 21 U.S.C. § 381(a).

Section 801(a) of the FDCA, provides in relevant part:

> The Secretary of the Treasury shall deliver to the Secretary of Health and Human Services, upon his request, samples of . . . drugs . . . which are being imported or offered for import into the United States . . . . If it appears from the examination of such samples or otherwise that . . . such article is . . . in violation of section 355 of this title . . . then such article shall be refused admission . . . .

21 U.S.C. § 381(a) (emphasis added). In *Beaty v. FDA*, ___ F. Supp. 2d ___, No. 1:11-cv-00289-RJL, 2012 WL 1021048 (D.D.C. Mar. 27, 2012), this Court held that this statute requires FDA to deny admission to a drug offered for import that appears to be adulterated, misbranded, or in violation of Section 355. In addition to its textual analysis, *id.* at *5-6, the Court explained:

> The purpose of the FDCA is to promote public health and safety, which, in the context of imported drugs, requires the FDA to ensure that only drugs approved as safe and effective enter into the country. *See Wash. Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 69 (D.D.C. 1998) (vacated on other grounds) (finding that the purpose of the FDCA is to "ensur[e] that when a citizen takes a prescription drug, that individual has absolute assurance that the product is safe and effective").

Id. at *5 n.6 (alteration in original). The Court held that the text of Section 381(a) precludes any

enforcement discretion under *Heckler v. Chaney*, 470 U.S. 821 (1985), to allow import of drugs that even "appear" to be adulterated, misbranded, or in violation of Section 355(a). *Beaty*, 2012 WL 1021048, at *6-8. The same analysis applies here. The versions of API imported in order to compound 17P are unapproved new drugs whose importation violates Section 355(a).[58]

FDA's March 30, 2011 Statement has encouraged compounding of 17P, with no limitation to an approved source of API; and FDA has allowed the import of unapproved API. Here, as this Court held in *Beaty*: "[D]efendants have acted arbitrarily and capriciously, and have abused their discretion both by departing from FDA's own regulations and longstanding policies and by undermining the purpose of the FDCA," *Beaty*, 2012 WL 1021048, at *10.

VI. FDA'S STATEMENT AND POLICY ARE REVIEWABLE BECAUSE THEY ARE NOT A PROPER EXERCISE OF ENFORCEMENT DISCRETION.

Nothing in the FDCA precludes judicial review under 5 U.S.C. § 701(a)(1). Under 5 U.S.C. § 701(a)(2), agency action is unreviewable only where there is no law to apply. *Heckler v. Chaney*, 470 U.S. at 830; *Citizens to Preserve Overton Park, Inc. v. Volpe*, 401 U.S. 402, 410 (1971), *overruled on other grounds by Califano v. Sanders*, 430 U.S. 99 (1977). *Chaney* makes an agency's failure or refusal to take enforcement action presumptively unreviewable. 470 U.S. at 831. However, "the presumption may be rebutted where the substantive statute has provided

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[58] The relevant definitions are quoted *supra* in note 2. Under these definitions, compounded 17P is a "drug," a "drug product," and a "new drug," and API intended for use in compounding 17P is a component of compounded 17P, and therefore is a "drug" and a "new drug." Because compounded versions of 17P lack FDA approval, API for those compounded versions is an unapproved new drug. Sections 355(a) and 331(d), quoted *supra* at page 33, prohibit the introduction, and the delivery for introduction, into interstate commerce of an unapproved new drug.

FDA approves API for a finished drug product as part of the NDA for that product. *See* 21 C.F.R. §§ 314.3 (defining the term "[d]rug substance," which is an API), 314.50(d)(1)(i) (2012) (requiring in an NDA inclusion of a full description of the drug substance and the name and address of its manufacturer). Thus, that information is part of the NDA that FDA approves. If API whose manufacturer is not so identified in an approved NDA is offered for import into the

guidelines for the agency to follow in exercising its enforcement powers. Thus, in establishing this presumption in the APA, Congress did not set agencies free to disregard legislative direction in the statutory scheme that the agency administers." *Id.* at 832-33 (footnote omitted). Here, FDA's Statement is reviewable because it sets forth a general policy, not a decision in an individual case. Further, as shown *infra*, Sections 360cc(a), 353a, 355(a), and 381(a) provide guidelines and, thus, law to apply. Moreover, the policies that support the presumption do not apply here. FDA's Statement also is reviewable because it is based on impermissible factors. Finally, FDA's Statement and policy are not a mere failure or refusal to take enforcement action.

First, where an agency has spelled out a non-enforcement policy, its action is more readily reviewable because it "will generally present a clearer (and more easily reviewable) statement of its reasons for acting." *Crowley Caribbean Transp., Inc. v. Peña*, 37 F.3d 671, 677 (D.C. Cir. 1994); *see also, e.g.*, *Edison Elec. Inst. v. EPA*, 996 F.2d 326, 333 (D.C. Cir. 1993); *Am. Horse Prot. Ass'n v. Lyng*, 812 F.2d 1, 4 (D.C. Cir. 1987). That is so here.

Declarations of a non-enforcement policy are not accorded the deference given to "an agency's decision to decline enforcement in the context of an individual case," *Crowley*, 37 F.3d at 676. "There are ample reasons for distinguishing the two situations. By definition, expressions of broad enforcement policies are abstracted from the particular combinations of facts the agency would encounter in individual enforcement proceedings." *Id.* at 677. Moreover, "an agency's pronouncement of a broad policy against enforcement poses special risks that it 'has consciously and expressly adopted a general policy that is so extreme as to amount to an abdication of its statutory responsibilities.'" *Id.* (citation omitted). Here, FDA's Statement expresses a non-enforcement policy as to future conduct by a large class of drug manufacturers.

United States, it is "in violation of section 355" within the meaning of Section 381(a).

Under *Crowley* and similar cases, the Statement and policy are reviewable.

Second, here there is law to apply. Sections 360cc(a), 353a, 355(a), and 381(a), together, provide "guidelines for the agency to follow in exercising its enforcement powers," *Chaney*, 470 U.S. at 833, and "meaningful standard[s]" for a court to apply, *id.* at 830. Those provisions bar FDA from allowing the marketing of unapproved, uncustomized "compounded" drugs in violation of Sections 360cc(a) ("[FDA] may not approve"), 353a and 355(a);[59] and they bar FDA from allowing the import of unapproved drugs ("shall be refused admission"). Therefore, if the presumption against review applies, it is rebutted.

Third, the presumption does not even apply to FDA's general policy Statement here. *Chaney* identified five considerations that give rise to the presumption:

> [A]n agency decision not to enforce often involves a complicated balancing of a number of factors which are peculiarly within its expertise. Thus, the agency must not only assess whether a violation has occurred, but whether agency resources are best spent on this violation or another, whether the agency is likely to succeed if it acts, whether the particular enforcement action requested best fits the agency's overall policies, and, indeed, whether the agency has enough resources to undertake the action at all.

470 U.S. at 831. Also, "when an agency refuses to act it generally does not exercise its coercive power over an individual's liberty or property rights, and thus does not infringe upon areas that courts often are called upon to protect." *Id.* at 832 (emphasis omitted). In addition, non-enforcement is hard to review because mere inaction provides no focus for a court's analysis, whereas, "when an agency does act to enforce, that action itself provides a focus for judicial review . . . ." *Id.* (emphasis omitted).

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[59] By analogy to *Overton Park*, "the very existence of [Section 360cc] indicates that protection of [exclusivity] was to be given paramount importance." *Overton Park*, 401 U.S. at 412-13 (footnote omitted). That protection is "not to be lost unless there [are] truly unusual factors present in a particular case . . . ." *Id.* at 413.

None of those rationales applies here. FDA's Statement does not invoke any of the issues *Chaney* identified as indicative of enforcement discretion in individual cases. FDA is destroying KV's property right in market exclusivity for Makena. Its asserted rationale ("to support access") provides a clear focus for judicial review, *see, e.g.*, *Alliance for Bio-Integrity v. Shalala*, 116 F. Supp. 2d 166, 171 (D.D.C. 2000) (distinguishing between "policy choices . . . and individual nonenforcement decisions"). "[E]ven very broad discretion is not the same as unreviewable discretion." *Nat'l Treasury Emps. Union v. Horner*, 854 F.2d 490, 495 (D.C. Cir. 1988).

Fourth, FDA's Statement and policy are reviewable (and unlawful) because they are based on impermissible factors: pricing, which FDA admits is irrelevant to its decision-making about drugs, *see supra* pp. 4, 22 & n.46, and political pressure. Agency action is arbitrary and capricious if it relies on factors Congress did not intend the agency to consider. *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983). "Even where an agency's action is committed to the agency's discretion, a court should hear a claim that an agency rested an action on considerations that Congress could not have intended to make relevant such as the political considerations alleged by plaintiffs." *Electricities of N.C., Inc. v. Se. Power Admin.*, 774 F.2d 1262, 1267-69 (4th Cir. 1985) (internal quotation marks omitted).

Fifth, FDA's Statement is not mere inaction, mere failure to enforce against past conduct. Rather, in the form of a press release, it addresses future conduct: it is a public approval of future uncustomized "compounding" of 17P, an affirmative public invitation, a "green light." Its purpose is to call forth supplies of 17P "to support access" to HPC. To that end, it must induce uncustomized "compounding" and prescribing of, and payment for, compounded 17P. FDA's Statement, with CMS's, actually stimulates violations of the FDCA that otherwise would not occur, and the flow of Medicaid and private money to pay for them. FDA's message to com

pounders is not "[G]o, and sin no more" (John 8:11), but, rather, "Start or continue sinning, in commercial quantities." CMS adds, in effect: "You'll be paid for doing so." Thus, this case is distinguished from *Chaney*, and is like *Cutler v. Kennedy* and *Hoffmann-LaRoche*.[60]

By approving in advance unlawful "compounding" of 17P, FDA's Statement, with CMS's statement (which relies on FDA's statement and encourages Medicaid payment for such 17P), gives active aid to violations of the FDCA. Thus, this case is like *Adams v. Richardson*, 480 F.2d 1159 (D.C. Cir. 1973) (en banc) (per curiam), preserved in *Chaney*, 470 U.S. at 833 n.4. There, the agency argued that its failure to enforce was an exercise of unreviewable discretion, but the court held its non-enforcement policy reviewable. The court noted the agency's affirmative aid to violators. *Adams*, 480 F.2d at 1162. In *Alliance to Save the Mattaponi v. United States Army Corps of Engineers*, 515 F. Supp. 2d 1 (D.D.C. 2007), noting that judicial review is available "where agency inaction is final action having the same impact as agency action," *id.* at 9, this Court held reviewable EPA's failure to veto the issuance of a permit because the failure was "essentially a decision (i.e., an action) to indirectly approve a permit," *id.* at 8.

FDA's encouragement of violations is a categorical abdication of its statutory duty to protect exclusivity under Section 360cc(a) and to enforce Sections 353a, 355(a), and 381(a). *See Sierra Club v. Thomas*, 828 F.2d 783, 793 (D.C. Cir. 1987); *Adams*, 480 F.2d at 1162; *Roane v. Holder*, 607 F. Supp. 2d 216, 225-27 (D.D.C. 2009); *Chiang v. Kempthorne*, 503 F. Supp. 2d 343, 351-52 (D.D.C. 2007); *see also Ringo v. Lombardi*, 706 F. Supp. 2d 952, 958-61 (W.D. Mo. 2010); *Roman v. Korson*, 918 F. Supp. 1108, 1114 (W.D. Mich. 1995).[61]

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[60] *Chaney* distinguished the facts it addressed ("refusal to [enforce]") from those in *Overton Park* ("an affirmative act of approval"). 470 U.S. at 831. FDA's Statement is an affirmative, albeit disguised, act of approval of compounded 17P. Therefore, this case is more like *Overton Park*.

[61] *Schering Corp. v. Heckler*, 779 F.2d 683 (D.C. Cir. 1985), and *Jerome Stevens Pharmaceuticals, Inc. v. FDA*, 402 F.3d 1249, 1257-58 (D.C. Cir. 2005), are distinguishable. *Schering* in-

In *Cutler v. Kennedy*, this Court reasoned that FDA was entitled to the equivalent of prosecutorial discretion, that the FDCA did not mandate enforcement, and that the violation at issue did not appear to be serious. 475 F. Supp. at 856. The Court specifically noted that FDCA § 309, 21 U.S.C. § 336, provides that FDA need not bring enforcement actions against all minor violations when it believes that the public interest would be adequately served by a written notice or warning. *Id.* Similarly, the court in *Cutler v. Hayes*, 818 F.2d 879, 892 (D.C. Cir. 1987), declined to order FDA to take enforcement action because the court found no enforcement mandate in the FDCA comparable to the mandate relied on in *Adams v. Richardson*, and FDA had taken 17 relevant enforcement actions. The court noted that FDA was entitled to assign enforcement actions designed to "prevent unnecessary consumer expense to a lower priority than that accorded one concerned with identifying and eliminating threats to human life." *Id.* at 894.

In contrast to those two cases, here there are statutory mandates for enforcement as a general policy (subject to the exercise of case-by-case discretion): Section 360cc(a), 353a, and 355(a) together restrict whatever discretion FDA has to permit the marketing of unapproved compounded versions of orphan drugs entitled to exclusivity under Section 360cc(a); and Section

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volved not a policy of non-enforcement, but a single-shot decision as to one company's product for a limited time until it came into compliance or was withdrawn. The court distinguished the former type of situation. *Schering*, 779 F.2d at 687. *Jerome Stevens* involved FDA actions that had effect only for a limited period until the drugs at issue came into compliance or were withdrawn. Those cases involved a limited deferral, rather than a refusal, of enforcement. Here, FDA is refusing broadly to perform its duty to protect statutory exclusivity against violations of Sections 353a and 355(a) that are unlimited as to time and involve many violators and versions of 17P; and the non-customized compounded products will never come into compliance.

Further, the summary application of *Chaney* in *Community Nutrition Institute v. Young*, 818 F.2d 943, 949-50 (D.C. Cir. 1987), has been superseded by the analysis in *Crowley*, 37 F.3d at 676-77, which was followed in, *e.g.*, *Ringo*, 706 F. Supp. 2d at 959-60; *Roane*, 607 F. Supp. 2d at 225-27; and *Chiang*, 503 F. Supp. 2d at 351. *See also OSG Bulk Ships, Inc. v. United States*, 132 F.3d 808, 812 (D.C. Cir. 1998) ("an agency's adoption of a general enforcement policy is subject to review"); *Nat'l Wildlife Fed'n v. EPA*, 980 F.2d 765, 772-74 (D.C. Cir. 1992).

381(a) precludes discretion to allow unlawful imports. Moreover, contrary to the situation in *Cutler v. Hayes*, here FDA has put the supposed economic interests of third-party payers and some patients above the medical interest of all patients in protecting the lives of their fetuses.[62]

The FDCA's "minor violations" provision, 21 U.S.C. § 336, does not support FDA's position here. The widespread marketing by many compounders of unapproved injectable drugs to treat a life-threatening condition, thereby imposing an avoidable elevated risk on thousands of pregnant women and their fetuses per year, Goedeke Decl. ¶ 8, is not a "minor" violation. FDA does not regard unapproved manufacturing in the guise of compounding as "minor." *See* CPG 460.200, at 2. Even as to a "minor" violation, Section 336 relieves FDA of the duty to take enforcement action only where FDA issues a written notice or warning. FDA has not done so here, and none of its statements mentions any plan to do so. Section 336 does not authorize FDA to invite and encourage violations (as it has done here) or even to treat them as acceptable.

Finally, although FDA's Statement asserts that FDA may take enforcement action if it learns after the fact that compounded 17P products have turned out to be "unsafe, of substandard quality, or are not being compounded in accordance with appropriate standards for compounding sterile products," *see supra* note 34, that approach abrogates the protections Congress intended Sections 353a and 355(a) to provide to patients, *cf. Hoffmann-LaRoche*, 425 F. Supp. at 892.

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[62] The statutory mandates here are analogous to the one held to trump FDA's claim of discretion in *Veneman*, 349 F. Supp. at 1315-16. There, FDA's failure to act against drugs unlawfully marketed was "agency action unlawfully withheld." *Id.* at 1316. The same conclusion applies here. Similarly, as this Court noted in *Mattaponi*, 515 F. Supp. 2d at 8 n.5, *Chaney* holds that Section 701(a)(2) applies where "the statute ('law') can be taken to have 'committed' the decisionmaking to the agency's judgment absolutely," 470 U.S. at 830. It cannot be that FDA has absolute

VII. KV IS ENTITLED TO TEMPORARY AND PRELIMINARY RELIEF.

The Court should grant the temporary and preliminary declaratory and injunctive relief requested at Complaint pages 38-42. Preliminary declaratory relief was granted under the All Writs Act in *Merrill Lynch, Pierce, Fenner & Smith Inc. v. Doe*, 868 F. Supp. 532 (S.D.N.Y. 1994). Here, such relief would be in aid of the Court's jurisdiction because it would increase the likelihood of KV's survival to maintain this action. Precedent for enjoining FDA from maintaining or implementing the policy set forth in the Statement is provided by *Hoffmann-LaRoche*, 425 F. Supp. at 894-95.[63] Precedent for ordering FDA not to permit import of unapproved API for compounded 17P is provided by the order entered in *Beaty* (attached hereto as Exhibit D).

For the foregoing reasons, KV has a clear likelihood of success on the merits: there never was a legitimate need "to support access" to HCP; FDA's Statement was and is indefensible.

Without interim relief, KV will suffer extreme and severe irreparable harm. As discussed in the McHugh Declaration at ¶¶ 18-27, KV depends almost entirely on sales of Makena to generate income, and without an immediate prospect of securing effective market exclusivity for Makena, KV cannot survive. Substantial loss of business and possible bankruptcy absent preliminary relief are irreparable harm. *Doran v. Salem Inn, Inc.*, 422 U.S. 922, 932 (1975); *see also, e.g.*, *Wis. Gas Co. v. FERC*, 758 F.2d 669, 674 (D.C. Cir. 1985) (per curiam); *Wash. Metro. Area Transit Comm'n v. Holiday Tours, Inc.*, 559 F.2d 841, 843 (D.C. Cir. 1977). Loss of the advantage of being the exclusive first marketer is, itself, irreparable harm. *Bracco*, 963 F. Supp. at 29.

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authority to nullify exclusivity under Section 360cc(a) by allowing all compounders of a particular drug to evade the limits in Section 353a and the approval requirement in Section 355(a).

[63] In *Cutler v. Kennedy*, this Court declined to order FDA to act against unlawfully marketed drugs, but stated that "FDA may not lawfully maintain" its unlawful policy; and it enjoined FDA from implementing it. 475 F. Supp. at 856.

Any harms to non-movants are insubstantial. The relief requested would not disrupt the activities of, or otherwise harm, the Defendants, who would apply lawful enforcement policies, and case-by-case discretion, to compounders of 17P. Those compounders have no legally protected interest in distributing unapproved products in violation of the FDCA. *See United States v. Diapulse Corp. of Am.*, 457 F.2d 25, 29 (2d Cir. 1972). KV's commitment to generous discounts, McHugh Decl. ¶ 14; Goedeke Decl. ¶ 20, would protect third-party payers.

Finally, the public interest strongly favors interim relief, for at least four reasons. First, such relief would serve the interests of patients. Without relief to KV, Makena may disappear. McHugh Decl. ¶ 16. There would then be no FDA-approved drug for Makena's indication. Makena treats the risk of preterm birth, which threatens the lives of fetuses. Such a drug should be reliably effective, sterile, and safe. *See* Commissioner Hamburg's statement, *supra* pp. 11-12.[64] Yet, 17P compounded from Chinese API is not reliable. *See supra* pp. 8-9, 17-18. In view of KV's financial-assistance program, the requested interim relief would also be consistent with patients' economic interests. *See* Goedeke Decl. ¶¶ 11-20; McHugh Decl. ¶ 14.

Second, there is a strong public interest in preserving the incentives for development of orphan drugs. "The financial incentive for companies to develop such drugs is provided by the period of market exclusivity . . . ." *Baker Norton*, 132 F. Supp. 2d at 38.[65] Allowing FDA to

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[64] "We also have seen drugs compounded that are essentially copies of commercially available products. [¶] Compounding pharmacies then sell these copies for less than the approved commercially available product. These appear to be compounded for economic reasons rather than genuine medical need. In such cases, we believe the consumer would be better served by the commercially available drug, which has been determined to be safe and effective and manufactured under rigorous good manufacturing practice requirements." Galson Testimony 39.

[65] "In debating the need for orphan drug exclusive marketing, Congress weighed the potential dangers of granting orphan drug exclusive marketing, which would limit competition, against the benefits to be gained by encouraging sponsors to develop drugs of marginal commercial value. In passing the law, Congress determined that the benefits exceeded the dangers. . . . It is clear

abrogate KV's exclusivity would be a disincentive to the development of new orphan drugs.

Third, "[p]reserving the effectiveness and integrity of the FDCA's new drug approval process is clearly an important governmental interest . . . ." *W. States*, 535 U.S. at 369.[66] Preventing uncustomized compounding of drugs would serve that interest.

Finally, the public interest would be served by requiring FDA to obey the law. *See, e.g.*, *Bracco*, 963 F. Supp. at 30.

CONCLUSION

For the foregoing reasons, KV meets even the heightened standard for affirmative temporary and preliminary relief, and its motion for such relief should be granted.

Respectfully submitted,

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Dated: July 5, 2012.

. . . that these incentives have been highly successful in contributing to the development and approval of orphan drugs that would not otherwise have been developed." 57 Fed. Reg. at 62,085.

[66] "Allowing continued marketing of these unapproved drugs also undermines the incentives needed to conduct the scientific studies to determine the safety and effectiveness of drugs, which benefits the public health." Quinine Q & As, *supra* note 49, at 5. *See also supra* note 57.

CERTIFICATE OF SERVICE

I hereby certify that on this 5th day of July, 2012, the foregoing Motion for Temporary Restraining Order and Preliminary Injunction, accompanied by the Memorandum in Support of Motion for Temporary and Preliminary Relief, the Declarations of Scott Goedeke, Michael Jozwiakowski, Thomas McHugh and Patrick Ronan (with attached exhibits), and Proposed Orders, were served:

Via hand-delivery on:

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