UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

K-V PHARMACEUTICAL COMPANY, *et al.*,	)	
Plaintiff,	)	
v.	)	No. 1:12-cv-01105-ABJ
UNITED STATES FOOD AND DRUG ADMINISTRATION, *et al.*,	)	
Defendants.	)	

MEMORANDUM IN SUPPORT OF DEFENDANTS' MOTION TO DISMISS AND IN OPPOSITION TO PLAINTIFFS' MOTION FOR INJUNCTIVE RELIEF

K-V Pharmaceutical Co. and its subsidiary Ther-Rx Corp., sponsors of the drug Makena, seek declaratory and injunctive relief primarily to compel the United States Food and Drug Administration (FDA) to "take sufficient enforcement actions to stop the unlawful competition with Makena" from pharmacies that are compounding 17-hydroxyprogesterone caproate (17-HPC), the active ingredient in Makena. Plaintiffs claim entitlement to this extraordinary form of relief because FDA issued a statement on March 30, 2011[1] expressing the agency's intent to exercise enforcement discretion, under certain conditions, related to the compounding of 17-HPC. In a press release issued shortly before filing this suit (but not in their Complaint), Plaintiffs aptly described FDA's March 2011 statement as "outdated" because it has been updated and superseded by an FDA statement issued on June 15, 2012 and by Questions and Answers (Q&As) the agency posted on its website on June 29, 2012. The June 2012 statement and Q&As advise pharmacies that FDA is currently applying its normal enforcement policies to the compounding of 17-HPC, that compounding of that drug should not exceed the scope of traditional pharmacy practice, and that FDA may take enforcement action against pharmacies that compound large volumes of drugs that are essentially copies of commercially available products and for which there does not appear to be a medical need for individual patients to whom the drug is dispensed.

Plaintiffs' Complaint should be dismissed. Their claims are not justiciable. To establish standing, Plaintiffs must allege an injury that is likely to be redressed by the relief they seek.

[1] Plaintiffs cite and refer to the March 2011 statement, as well as several subsequent statements by FDA, in their Complaint and Motion. Copies are attached as follows: "FDA Statement on Makena" (Mar. 30, 2011), Exhibit 1; "FDA Statement on Makena" (Nov. 8, 2011), Exhibit 2; "Updated FDA Statement on Compounded Versions of hydroxyprogesterone caproate (the active ingredient in Makena)" (June 15, 2012), Exhibit 3; "Questions and Answers on Updated FDA Statement on Compounded Versions of hydroxyprogesterone caproate (the

Plaintiffs cannot satisfy the redressability requirement because the declaratory and injunctive relief they seek, including an order compelling FDA to take enforcement actions and to refuse import entries of 17-HPC active pharmaceutical ingredient (API),[2] either is unavailable as a matter of law or is not likely to redress their injury.

Even if Plaintiffs can establish standing, FDA's March 2011 statement is not subject to judicial review under the Administrative Procedure Act (APA) because FDA's decisions not to take enforcement action are committed to the agency's discretion under *Heckler v. Chaney*, 470 U.S. 821 (1985). Moreover, the conduct alleged - a statement expressing an intent to exercise enforcement discretion - does not state a violation of any of the sections of the Federal Food, Drug, and Cosmetic Act (FDCA) cited by Plaintiffs. Finally, this Court should refuse to grant the requested mandatory injunction. FDA's testing of samples of compounded 17-HPC and the active ingredient failed to reveal any major safety concern. Forcing FDA to reject its enforcement priorities in favor of Plaintiffs' commercial interests would be both inappropriate and contrary to the public interest.

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active ingredient in Makena)" (June 29, 2012), Exhibit 4.

[2] In this brief, we refer to API and "bulk drug substance" interchangeably. An API is "any substance or mixture of substances intended to be used in the manufacture of a drug product and that, when used in the production of a drug, becomes an active ingredient in the drug product. Such substances are intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease or to affect the structure and function of the body." *See* FDA CPG 7356.002F, "Active Pharmaceutical Ingredient Process Inspection" (*available at* http://www.fda.gov/downloads/ICECI/ ComplianceManuals/CompliancePrograManual/ucm125420.pdf).

REGULATORY AND FACTUAL BACKGROUND

I. Statutory Framework

A. The Federal Food, Drug, and Cosmetic Act

Under the FDCA's comprehensive scheme for regulating drug manufacturing, labeling, and marketing, it is unlawful to distribute any "new drug" intended for human use without FDA approval. 21 U.S.C. §§ 331(d), 355(a). The FDCA defines "new drug" as "[a]ny drug (except a new animal drug . . .)"[3] that "is not generally recognized . . . as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof." *Id*. § 321(p)(1). To obtain FDA approval to market a "new drug" for human use, the sponsor must show that the drug is both safe and effective for its intended uses. 21 U.S.C. §§ 355(a), (b).

The FDCA also imposes standards for manufacturing (known as "current good manufacturing practice") to ensure that drugs are safe, effective, pure, and potent. 21 U.S.C. § 351(a)(2)(B). In addition, it requires the labeling of drugs to provide "adequate directions for use," which includes information about drug contents, uses, and effects; drugs that are not properly labeled are "misbranded." *Id*. § 352. The FDCA prohibits the manufacture and distribution of adulterated or misbranded drugs in interstate commerce. *Id*. § 331(a) - (c), (k).

B. Compounded Drugs

Compounding is "a process by which a pharmacist or doctor combines, mixes, or alters ingredients to create a medication tailored to the needs of an individual patient. Compounding is typically used to prepare medications that are not commercially available, such as medication for a patient who is allergic to an ingredient in a mass-produced product." *Thompson v. W. States*

[3] The FDCA contains separate provisions for drugs used in animals, which are not at issue in this case.

Med. Ctr., 535 U.S. 357, 360 (2002); *see also Med. Ctr. Pharmacy v. Mukasey*, 536 F.3d 383, 387 (5th Cir. 2008). Under certain conditions, compounding provides an important public health benefit. *W. States*, 535 U.S. at 369 ("The Government . . . has an important interest . . . in permitting the continuation of the practice of compounding so that patients with particular needs may obtain medications suited to those needs."); Pls.' Br. at 4-5 (discussing how for some patients "it may be medically necessary for a patient to take a 'compounded' version of a drug").

The FDCA's "new drug" definition encompasses drugs compounded by pharmacists and physicians. *Med. Ctr.*, 536 F.3d at 394. In 1992, FDA issued a Compliance Policy Guide ("CPG"), which explained its enforcement policy toward pharmacists engaged in compounding drugs for human use. *Id.* at 390; Pls.' Br. Ex. A. In the CPG, FDA explained that although compounding can serve important public health purposes, "an increasing number of establishments with retail pharmacy licenses are engaged in manufacturing, distributing, and promoting unapproved new drugs for human use in a manner that is clearly outside the bounds of traditional pharmacy practice and that violates the Act." *Id.* at 2. To address these concerns, the 1992 CPG identified a number of factors that FDA took into account when determining whether to initiate an enforcement action. *Id.* at 4-6.

1. Section 353a

Congress amended the FDCA through the Food and Drug Administration Modernization Act of 1997 ("FDAMA"), Pub. L. No. 105-115, 111 Stat. 2296. Section 127(a) of FDAMA, codified at 21 U.S.C. § 353a, specifically addresses "Pharmacy compounding" of human drugs. Under section 353a, compounded drugs are explicitly exempt from three requirements of the FDCA: (i) "current good manufacturing practice," 21 U.S.C. § 351(a)(2)(B); (ii) "adequate directions for use" in labeling, *id*. § 352(f)(1); and (iii) premarket approval for human use, *id*. §

355. But those exemptions apply only when certain statutorily prescribed criteria are satisfied.[4] *Med. Ctr.*, 536 F.3d at 394.

The criteria in section 353a include restrictions on the advertising and promotion of compounded drugs. *See id*. § 353a(a), (c). In 1998, seven pharmacies challenged those restrictions as an impermissible regulation of commercial speech. The Ninth Circuit held that those provisions are unconstitutional and cannot be severed from the rest of section 353a, causing all of section 353a to be invalid. *W. States Med. Ctr. v. Shalala*, 238 F.3d 1090 (9th Cir. 2001). The Supreme Court affirmed the Ninth Circuit's ruling that section 353a's advertising and soliciting restrictions were unconstitutional, but the Court did not rule on the severability of those restrictions. *W. States*, 535 U.S. at 360.

2. FDA's 2002 Compounding CPG

After the Supreme Court invalidated the advertising provisions of section 353a, FDA issued a revised CPG on compounding human drugs. *See* CPG Sec. 460.200, "Pharmacy Compounding" (May 2002) (*available at* http://www.fda.gov/downloads/AboutFDA/ CentersOffices /CDER/UCM118050.pdf). Like the 1992 CPG, FDA's revised CPG sets forth a

[4] For example, a licensed pharmacist or physician must compound "for an identified individual patient" based on a "valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient." 21 U.S.C. § 353a(a). The pharmacist or physician may use bulk drug substances that comply with the standards in an applicable United States Pharmacopoeia (USP) or National Formulary (NF) monograph, that are components of drugs approved by the Secretary of HHS, or that appear on a list developed through rulemaking. *Id.* § 353a(b)(1)(A). Also, the pharmacist or physician may not compound "regularly or in inordinate amounts (*as defined by the Secretary*) any drug products that are essentially copies of a commercially available drug product." *Id*. § 353a(b)(1)(D) (emphasis added). But for purpose of that criterion, "the term 'essentially a copy of a commercially available drug product' does not include a drug product in which there is a change, made for an identified individual patient, which produces for that patient a significant difference, as determined by the prescribing practitioner, between the compounded drug and the comparable commercially available drug

non-exhaustive list of factors that the agency considers in determining whether to recommend enforcement action to the Department of Justice (DOJ). *Id.*[5]

In 2006, various pharmacies challenged FDA's regulation of compounded drugs, arguing that such drugs are not "new drugs" within the meaning of the FDCA. The Fifth Circuit held that compounded drugs are, in fact, "new drugs." *Med. Ctr.*, 536 F.3d at 394. The court concluded, however, that the restrictions on commercial speech held unconstitutional in *Western States* could be severed from the rest of section 353a and that the remainder of section 353a is valid and remains in force. *Id*. at 404.

The decisions of the Fifth and Ninth Circuits directly conflict on whether the non-advertising provisions of section 353a are valid and in effect. After the *Medical Center* opinion, FDA posted the following statement on its website: "FDA and [DOJ] are currently evaluating the Fifth Circuit's opinion. In the meantime, FDA will follow the court's decision in the Fifth Circuit and with respect to the plaintiffs covered by the decision. Elsewhere, the agency will continue to follow the enforcement approach reflected in the [2002 Compounding CPG]." *See* "Medical Center v. Mukasey" (*available at* http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm134919.htm).

Since the Fifth Circuit's 2008 decision in *Medical Center*, because there is uncertainty about whether section 353a would be applied in courts outside the Ninth Circuit, when

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product." *Id.* § 353a(b)(2).

[5] These factors include compounding drugs in anticipation of receiving prescriptions (except in very limited amounts), using commercial-scale equipment for compounding, compounding drugs that were withdrawn or removed from the market for safety reasons, compounding drugs that are essentially copies of commercially available drugs where there is no documentation of the medical need for the particular variation of the compound for the particular patient, and compounding finished drugs from bulk active ingredients that are not components of FDA-approved drugs without an FDA-sanctioned investigational new drug

considering advisory actions (such as issuing a Warning Letter) and enforcement actions (such as a seizure or injunction) based on violations of 21 U.S.C. §§ 351(a)(2)(B), 352(f)(1), and/or 355, FDA carefully assesses the compounder's conduct under *both* the 2002 Compounding CPG and section 353a before taking action. *See, e.g.*, Warning Letter to J&F Int'l Inc. (dated Apr. 9, 2010) (*available at* http://www.fda.gov/ICECI/EnforcementActions/WarningLetters /2010/ucm208772.htm).[6] Moreover, in light of the complexity of taking enforcement action during this circuit split, FDA is generally prioritizing enforcement actions related to compounded drugs using a risk-based approach, giving the highest enforcement priority to compounded products that are causing harm or that amount to health fraud. *See* Exs. 1&3.

C. Orphan Drugs

Drugs that are intended to treat rare diseases or conditions are referred to as "orphan drugs." Congress amended the FDCA through the Orphan Drug Act (ODA), Pub. L. No. 97-414, 96 Stat. 2049 (codified, as amended, at 21 U.S.C. §§ 360aa to 360ee), to provide special benefits to a sponsor of drug product (including a biological drug or antibiotic) to treat a rare disease or condition.[7] Among other benefits, the sponsor of the orphan drug may obtain tax credits for the costs of clinical research and a waiver of filing fees under the Prescription Drug User Fee Act (PDUFA). 26 U.S.C. §§ 45C, 280C; 21 U.S.C. § 379h(k).

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application. CPG 460.200.

[6] By comparison, all of the Warning Letters Plaintiffs cite (*see* Pls.' Br. at 8 n.14) were issued prior to the *Medical Center* decision.

[7] The term "rare disease or condition" is defined to mean any disease or condition that either affects less than 200,000 persons in the United States, or affects more than 200,000 persons in the United States and for which there is no reasonable expectation that the cost of developing and making available the drug for such disease or condition in the United States will be recovered from sales of such drug in the United States. 21 U.S.C. § 360bb(a)(2).

In addition, once FDA approves a new drug application (NDA) filed under 21 U.S.C. § 355, or issues a biologics license application (BLA) under the Public Health Service Act (PHSA), 42 U.S.C. § 262, for a drug designated for the rare disease or condition, the agency "may not approve" another sponsor's NDA, abbreviated new drug application (ANDA), or BLA "for such drug for such disease or condition . . . until the expiration of seven years from the date of the approval of the approved application, or the issuance of the license." 21 U.S.C. § 360cc(a). This exclusivity provision, by its plain language, does not guarantee a drug protection from competition. It applies only to bar FDA from approving certain NDAs, ANDAs, and BLAs. It does not bar FDA from approving another sponsor's NDA or BLA for the same drug for a different indication, nor does it prevent FDA from approving another sponsor's NDA or BLA for a different drug for the same indication. *Id.*[8] This provision makes no mention of compounded drug products.

II. Factual Background

A. 17-HPC and Approval of Makena

17-HPC was originally approved in 1956, to treat habitual and recurrent abortion, threatened abortion, and post-partum pains, and was marketed under the name Delalutin, by

[8] The Secretary may approve another sponsor's NDA or BLA for the same drug for the same indication if the sponsor of the orphan-designated drug consents or if "the Secretary finds, after providing the holder notice and opportunity for the submission of views, that in such [seven year] period the holder of the approved application or of the license cannot 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 . . . ." 21 U.S.C. § 360cc(b).

In addition, FDA can grant orphan-designation to another sponsor with a drug that is chemically the same as and for the same indication as an approved orphan drug if the second sponsor can make a plausible showing that it may be able to produce a clinically superior drug product. 21 C.F.R. § 316.20(a). If clinical superiority is shown, FDA can approve the subsequent sponsor's drug for the same indication in spite of orphan exclusivity on the ground that it is not "the same drug." 21 C.F.R. §§ 316.3(b)(3), 316.3(b)(13).

Squibb Corporation. FDA approved Delalutin for additional indications in 1972. In 2000, after Bristol-Myers Squibb, Squibb Corporation's successor in interest, notified FDA that Delalutin was no longer being marketed in the United States and requested that its applications be withdrawn, FDA withdrew approval of the Delalutin NDAs. 75 Fed. Reg. 36419, 36420 (June 25, 2010). Following withdrawal of the NDAs, 17-HPC was available in this country only through compounding pharmacies. Armstrong, J., "Unintended Consequences — The Cost of Preventing Preterm Births after FDA Approval of a Branded Version of 17OHP," New Eng. J. Med. 2011; 364:1689-1691 (available at http://www.nejm.org/doi/full/10.1056/NEJMp1102796).

On January 25, 2007, FDA designated 17-HPC an orphan drug for the prevention of pre-term birth in singleton pregnancies. Compl. ¶ 51; Jozwiakowski Decl. Ex. 1 (Dkt. No. 2-3). Through a series of corporate transfers, ownership of the orphan designation and the Makena NDA were ultimately owned by K-V. Compl. ¶¶ 12, 54-55, 66. Although the compounded doses of 17-HPC were available for approximately $10-20 per dose, Plaintiffs set the initial list price for a dose of Makena at more than $1,500. Compl. ¶¶ 68, 71. Makena is administered by weekly injection, with an average course of treatment of 16 weeks. Jozwiakowski Decl. ¶ 3. Thus, the original list price for a course of treatment of Makena was "up to $30,000." Compl. ¶ 73. After Makena was approved, Plaintiffs sent a letter to compounding pharmacies in which they purported to speak for FDA, stating that because FDA had approved Makena, compounded 17-HPC caproate injection should no longer be made by compounding pharmacies and suggesting that FDA would take action against further compounding of the drug. Ex. 1.

Plaintiffs' decision to set the list price for Makena at roughly 100 times the price of the compounded version of the product that had been available for many years sparked news stories, Congressional interest, and inquiries to FDA. *See, e.g.*, Goedeke Decl. (Dkt. No. 2-2) Ex. 8

(news article quoting an obstetrician-gynecologist, "'I've been using the compounded pharmacy version for years. Five doses cost a woman only $36.99.' He said he feared many women would find the drug too costly now, particularly those who are uninsured."); *id.* Ex. 10 at 9 (questions to the Commissioner of Food and Drugs during congressional hearing).

B. FDA's March 30, 2011 Statement

On March 30, 2011, FDA issued a brief statement regarding Makena. Ex. 1. The agency noted that 17-HPC had been available through compounding for many years and that the agency had "exercised enforcement discretion with respect to most products made through traditional pharmacy compounding," including 17-HPC. *Id.* The agency emphasized that "Because Makena is a sterile injectable, where there is a risk of contamination, greater assurance of safety is provided by an approved product." FDA explained that it "prioritizes enforcement actions related to compounded drugs using a risk-based approach, giving the highest enforcement priority to pharmacies that compound products that are causing harm or that amount to health fraud." The statement further explained:

> FDA understands that the manufacturer of Makena, KV Pharmaceuticals, has sent letters to pharmacists indicating that FDA will no longer exercise enforcement discretion with regard to compounded versions of Makena. This is not correct.
>
> 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. As always, FDA may at any time revisit a decision to exercise enforcement discretion.

Id.

C. FDA's November 8, 2011 Statement

In October 2011, Plaintiffs provided FDA with the results of an investigation that the company had commissioned. Ex. 2; Jozwiakowski Dec. ¶ 35. Plaintiffs' investigation involved testing samples of compounded 17-HPC products as well as bulk 17-HPC API. *Id.* FDA promptly and carefully reviewed the data Plaintiffs submitted and then issued a statement announcing that, although FDA had not validated or otherwise confirmed the analyses provided by Plaintiffs, the information submitted showed that "there is variability in the purity and potency of both the bulk APIs and compounded hydroxyprogesterone caproate products that were tested." Ex. 2. FDA further stated that the agency was conducting its own investigation, including testing of compounded products and 17-HPC API, and would also conduct an on-site review of the laboratory analyses provided by Plaintiffs. *Id.*

FDA reminded physicians and patients in the meantime that "before approving the Makena new drug application, FDA reviewed manufacturing information, such as the source of the API used by its manufacturer, proposed manufacturing processes, and the firm's adherence to current good manufacturing practice." *Id.* FDA then reiterated what it said in its March 2011 statement: "as with other approved drugs, greater assurance of safety and effectiveness is generally provided by the approved product than by a compounded product." *Id.*

D. FDA's June 15, 2012 Statement and June 29, 2012 Q&As

On June 15, 2012, FDA issued a statement, "Updated FDA Statement on Compounded Versions of hydroxyprogesterone caproate (the active ingredient in Makena)." Ex. 3. FDA's June 2012 statement summarized the results of its investigation. *Id.* After testing samples of 17-HPC APIs and compounded 17-HPC and also re-testing the retained samples of compounded 17-HPC from Plaintiffs' investigation, FDA concluded that its investigation did not identify any

major safety problems. Ex. 3; Jozwiakowski Decl. ¶ 36. The agency explained that "[a]lthough the analysis of this limited sample of compounded hydroxyprogesterone caproate products and APIs did not identify any major safety problems, approved drug products, such as Makena, provide a greater assurance of safety and effectiveness than do compounded products. Before approving the Makena NDA, FDA reviewed manufacturing information, such as the source of the API used by its manufacturer, proposed manufacturing processes, and the firm's adherence to current good manufacturing practice." *Id.* The agency stressed that, by comparison, the "drugs that pharmacists compound (including compounded hydroxyprogesterone caproate) are not FDA approved, which means they do not undergo premarket review nor do they have an FDA finding of safety and efficacy." *Id.*

FDA also addressed the issue of pharmacy compounding of copies of Makena:

> Compounding large volumes of drugs that are copies of FDA-approved drugs circumvents important public health requirements, including the [FDCA's] drug approval provisions. Consumers and health professionals rely on the Act's evidence-based drug approval process to ensure that drugs are safe and effective. For that reason, *one factor that the agency considers in determining whether a drug may be compounded is whether the prescribing practitioner has determined that a compounded product is necessary for the particular patient and would provide a significant difference for the patient as compared to the FDA-approved commercially available drug product*.

Id. (emphasis added).

In contrast to the March 30, 2011 statement that FDA was exercising enforcement discretion related to compounding of 17-HPC in certain circumstances, the June 15, 2012 statement "emphasize[d] that [FDA] is applying its *normal enforcement policies for compounded drugs to compounded hydroxyprogesterone caproate*." *Id.* (emphasis added). FDA also warned compounding pharmacies that "[t]he compounding of any drug, including hydroxyprogesterone

caproate, *should not exceed the scope of traditional pharmacy compounding*." *Id.* (emphasis added).

K-V issued its own press release in response to FDA's June 15, 2012 statement. Among other things, K-V trumpeted FDA's statement that it is "applying its normal enforcement policies for compounded drugs to compounded [17-HPC]" as "*a reversal of [FDA's] March 30, 2011 statement*." K-V Press Release, "FDA and CMS Issue Important Updates on Makena," (June 18, 2012) (*available at* http://www.kvph.com/news_center_article.aspx?articleid=359) (emphasis added). K-V's President and CEO stated, "We believe the announcements from [FDA and Centers for Medicare & Medicaid Services (CMS)] are a *clear signal that the compounding of hydroxyprogesterone caproate should not exceed the sc* http://www.kvph.com/news_center_article.aspx?articleid=359*ope of traditional pharmacy compounding . . . .*" *Id.* (emphasis added).

On June 29, 2011, FDA added the Q&As to its webpage. *See* Ronan Decl. ¶ 13 (Dkt No. 2-5); Ex. 4. Among other things, the Q&As stated:

- "FDA does not consider compounding large volumes of copies, or what are essentially copies, of any approved commercially-available drug to fall within the scope of traditional pharmacy practice. One factor that the agency considers in determining whether a drug may be compounded is whether the prescribing practitioner has determined that a compounded product is necessary for the particular patient and would provide a significant difference for the patient as compared to the FDA-approved commercially available drug product."

- "The FDA may take enforcement action against pharmacies that compound large volumes of drugs that are essentially copies of commercially available products and for which there does not appear to be a medical need for individual patients to whom the drug is dispensed."

- "A risk-based approach to enforcement relates to how the FDA generally prioritizes its enforcement efforts. The FDA's June 15, 2012 statement should *not* be interpreted to mean that the FDA will take enforcement action only if the agency identifies a particular safety problem. We reiterate that the compounding of any drug, including hydroxyprogesterone caproate, should not exceed the scope of traditional pharmacy compounding."

Id. (emphasis in original).

Plaintiffs issued a press release in response to FDA's posting of the Q&As. *See* K-V Press Release, "FDA Issues Further Guidance About Makena," (July 2, 2012) (http://www.kvph.com/news_center_article.aspx?articleid=362). In that press release, Plaintiffs quoted FDA's Q&As extensively and described FDA's March 30, 2011 statement as "outdated." *Id.*

ARGUMENT[9]

I. Plaintiffs Lack Standing Because They Have Not Alleged Redressable Injuries

For Plaintiffs to establish constitutional standing, a jurisdictional requirement, they "must show an injury in fact that is fairly traceable to the challenged conduct and that will likely be redressed by a favorable decision on the merits." *Rempfer v. Sharfstein*, 583 F.3d 860, 868 (D.C. Cir. 2009). Plaintiffs cannot meet their burden on this third standing prong because the relief they seek is unavailable as a matter of law and, even if granted, Plaintiffs' belief that enforcement actions will redress their alleged injury is, at best, highly speculative. *Judicial Watch, Inc. v. Nat'l Archives and Records Admin.,* Civ. No. 10-1834 (ABJ), 2012 U.S. Dist. LEXIS 26684 *29 (D.D.C. Mar. 1, 2012) ("An injury is not redressable where the 'only apparent avenue of redress for plaintiffs' claimed injuries . . . is unavailable.'") (quoting *Newdow v. Roberts*, 603 F.3d 1002, 1003 (D.C. Cir. 2010)).

[9] In support of this motion, Defendants reference certain factual materials for the Court to consider in addition to the Complaint. The Court may consider such materials in ruling on challenges to subject matter jurisdiction under Fed. R. Civ. P. 12(b)(1). *See Coal. for Underground Expansion v. Mineta*, 333 F.3d 193, 198 (D.C. Cir. 2003); *Herbert v. Nat'l Acad. of Scis.*, 974 F.2d 192, 197 (D.C. Cir. 1992). When ruling on a Rule 12(b)(6) motion, the Court may examine the Complaint, any documents either attached to or incorporated in the Complaint, items in the record of the case, and of which the court may take judicial notice. *See Stewart v. Nat'l Educ. Ass'n*, 471 F.3d 169 (D.C. Cir. 2006).

Plaintiffs allege that more than 100 pharmacies are compounding 17-HPC, and, in their prayer for relief, they ask this Court to compel FDA to "take sufficient enforcement actions to stop the unlawful competition with Makena by compounded [17-HPC] not customized to meet the special needs of patients . . . ." Pls. Br. at 6; Compl. at 42; Goedeke Dec. ¶ 31. Plaintiffs also ask the Court to order FDA to "report to the Court" periodically for three years about "the actions they have taken to terminate shipments of non-customized [17-HPC]," and also to halt shipments of foreign-manufactured 17-HPC API. Compl. at 42.

Plaintiffs' requests that this Court supervise FDA's enforcement activities are extraordinary and improper because, as discussed below (pp 18-21), FDA's non-enforcement decisions are committed to the agency's discretion. *See Heckler v. Chaney*, 470 U.S. 831, 837-38; *Judicial Watch*, 2012 U.S. Dist. LEXIS 26684 *39 (where court could not order relief plaintiff sought because the "enforcement tools provided to the defendant under [the statute] are committed to the agency's sole discretion," plaintiff lacked standing); *see Block v. SEC*, 50 F.3d 1078, 1084 (D.C. Cir. 1995) ("the agency alone, and neither a private party nor a court, is charged with the allocation of enforcement resources."); *Coker v. Sullivan*, 902 F.2d 84, 89 (D.C. Cir. 1990) ("This court should not steer the Department's resources and shape its priorities when we lack knowledge of the matters competing for the Department's attention."); *see also Norton v. S. Utah Wilderness Alliance*, 542 U.S. 55, 64 (2004) (under 5 U.S.C. § 706(1), court can only compel agency to take "a discrete agency action that it is *required* to take").

Plaintiffs are, in effect, asking the Court to assume the role of FDA's "director of enforcement," a task for which it is ill-suited. *Chaney*, 470 U.S. at 831-32 ("The agency is far better equipped than the courts to deal with the many variables involved in the proper ordering of its priorities."). To meet Plaintiffs' demands, the Court must order FDA to disregard not only its

own risk-based approach for prioritizing inspection and enforcement resources regarding compounding generally but also, consequently, its priorities for other unrelated enforcement activities: more time spent on pharmacies compounding 17-HPC means less time spent pursuing enforcement actions in other areas. *Sierra Club v. Whitman*, 268 F.3d 898, 903 (9th Cir. 2001) (EPA "must be able to choose which violations are most egregious. It would be unwise for the judiciary . . . to attempt to set the priorities for the EPA's enforcement decisions.").

Even if this Court were inclined to order *FDA* to *take* enforcement actions, as Plaintiffs request, it could not do so because actions to enforce the FDCA under 21 U.S.C. §§ 332, 333, & 334, are brought in the name of the United States, 21 U.S.C. § 337(a), by DOJ.[10] DOJ is not a party to this suit. Moreover, even if DOJ authorized and the government successfully litigated several enforcement actions against some of the 100 pharmacies allegedly compounding 17-HPC, Plaintiffs apparently further assume and speculate that all other pharmacies would promptly stop compounding 17-HPC and/or that the remaining pharmacies that remain undeterred would not increase their production to take up the slack created by those pharmacies that were deterred. Thus, redress of Plaintiffs' injury through the requested injunctive relief depends on tiers of speculation.[11]

In addition, the declaratory relief Plaintiffs seek regarding the now concededly outdated March 2011 statement and the enforcement actions they seek would provide, at most, indirect and speculative relief. Plaintiffs claim that "KV's survival as a going concern *is primarily dependent* on KV's ability to obtain relief from FDA's March 30, 2011 Statement and the policy

[10] DOJ authorization is not required for FDA to refuse an import entry, however.

[11] Plaintiffs' request can also be viewed as a thinly disguised effort for a private party to enforce the FDCA. It is settled law that only the FDA and DOJ can enforce the FDCA. *See Ellis v. C.R. Bard, Inc.*, 311 F.3d 1272, 1284 n.10 (11th Cir. 2002) (citing cases).

it sets forth, and the *resulting actions by CMS and state Medicaid agencies . . . .*" Compl. ¶ 95 (emphasis added). FDA's March 2011 statement has already been superseded by an updated statement and Q&As, which explain the agency is applying its normal enforcement policies to 17-HPC compounding, that the compounding of 17-HPC should not exceed the scope of traditional pharmacy compounding, that "FDA does not consider compounding large volumes of copies, or what are essentially copies, of any approved commercially-available drug to fall within the scope of traditional pharmacy practice," and that "FDA may take enforcement action against pharmacies that compound large volumes of drugs that are essentially copies of commercially available products and for which there does not appear to be a medical need for individual patients to whom the drug is dispensed." Exs. 3 & 4. CMS also has issued an updated Informational Bulletin on June 15, 2012 (Ex. 5). The Bulletin explains that "States may, under appropriate circumstances, cover APIs . . . if such coverage is consistent with the State plan," but also "remind[s] States of their responsibility to cover FDA approved products, such as Makena, that qualify as covered outpatient drugs under the Medicaid drug rebate program" and that "[a]ny prior authorization procedures for such drugs must be administered in accordance with Section 1927(d) of the Social Security Act, without imposing unreasonable conditions." *Id.*

Despite this change of landscape, according to Plaintiffs, state Medicaid organizations have not changed their behavior. In their most recent Press Release, Plaintiffs claim that some payers deny access to Makena by maintaining "unreasonable coverage policies" that "disregard" the most recent statements by FDA and CMS. K-V Press Release, "FDA Issues Further Guidance About Makena" (July 2, 2012) (*available at* http://www.kvph.com/news_center_article.aspx?articleid=362) (emphasis added); *see also* Goedeke Dec. ¶ 43. Plaintiffs have failed to show that payers are likely to change their

reimbursement policies should this Court declare that FDA's March 2011 statement was not a lawful exercise of enforcement discretion because this statement has already been superseded.[12] As a result, they have failed to establish standing. *Lujan v. Defenders of Wildlife*, 504 U.S. 555, 562 (1992) (plaintiff bears the burden of showing that entities not before the court will make choices "in such manner as to . . . permit redressability of injury.").

For all of these reasons, Plaintiffs have failed to allege a justiciable claim.

II. Plaintiffs' Complaint Should be Dismissed Because FDA's "Non-enforcement Decisions" are Discretionary and Unreviewable.

A. Non-enforcement Decisions Are Presumptively Unreviewable

Plaintiffs seek review under the APA, 5 U.S.C. § 706. The judicial review provisions of the APA, 5 U.S.C. §§ 701-06, establish a cause of action for parties adversely affected either by agency actions or by an agency's failure to act. *Heckler v. Chaney*, 470 U.S. 821, 828 (1985). But the APA explicitly excludes from judicial review those agency actions that are "committed to agency discretion by law." 5 U.S.C. § 701(a). That exclusion applies, *inter alia*, when the statute at issue "is drawn so that a court would have no meaningful standard against which to judge the agency's exercise of discretion," *Chaney*, 470 U.S. at 830. Agency actions in these circumstances are unreviewable because "'the courts have no legal norms pursuant to which to evaluate the challenged action, and thus no concrete limitations to impose on the agency's

[12] Plaintiffs also ask this Court to order two forms of relief not supported by the allegations in their Complaint. First, Plaintiffs ask the Court to order the Department of Health and Human Services and Secretary Sebelius to "withdraw[] CMS's March 30, 2011 statement relating to payment for [17-HPC]." Compl. at 43. As noted, CMS already issued an updated statement, *see* Ex. 5, and thus there is no effective relief that can be ordered regarding the outdated CMS statement. Moreover, Plaintiffs have not alleged that the current or former CMS statements are contrary to that the statutes and regulations applicable to that agency. Thus, Plaintiffs have not alleged a basis for requiring CMS to withdraw its March 30, 2011 statement. Second, Plaintiffs seek an extension of their orphan drug exclusivity for Makena. Compl. at 42.

exercise of discretion.'" *Sec'y of Labor v. Twentymile Coal Co*., 456 F.3d 151, 156 (D.C. Cir. 2006) (quoting *Drake v. FAA*, 291 F.3d 59, 70 (D.C. Cir. 2002)).

To determine whether a matter has been committed to agency discretion, courts "'consider both the nature of the administrative action at issue and the language and structure of the statute that supplies the applicable legal standards for reviewing that action.'" *Twentymile Coal*, 456 F.3d at 156 (quoting *Drake*, 291 F.3d at 70). Where, as here, the challenged action involves an agency's decision not to take enforcement action, the action is presumptively unreviewable. *See Lincoln v. Vigil*, 508 U.S. 182, 191 (1993); *Chaney*, 470 U.S. at 831-32; *Sierra Club and Valley Watch, Inc. v. Jackson*, 648 F.3d 848, 855 (D.C. Cir. 2011); *Kisser v. Cisneros*, 14 F.3d 615, 620 (D.C. Cir. 1994). The presumption that an agency's non-enforcement decisions are not subject to judicial review "may be rebutted where the relevant statute supplies meaningful standards to cabin the agency's otherwise plenary discretion." *Drake*, 291 F.3d at 71; *see Chaney*, 470 U.S. at 832-33 ("the presumption may be rebutted where the substantive statute has provided guidelines for the agency to follow in exercising its enforcement powers."). On the other hand, if the statute in question does not "give any indication that violators must be pursued in every case, or that one particular enforcement strategy must be chosen over another" and if it provides no meaningful guidelines defining the limits of the agency's discretion, then enforcement is committed to the agency's discretion. *Sierra Club*, 648 F.3d at 855 (quoting *Ass'n of Irritated Residents v. EPA*, 494 F.3d 1027, 1033 (D.C. Cir. 2007) (citing *Chaney*, 470 U.S. at 834-35)).

However, as we show below, FDA did not violate the Orphan Drug Act.

B. *Heckler v. Chaney* and Its Progeny Establish that FDA's Non-enforcement Decisions Are Not Subject to Judicial Review Because the FDA's Enforcement Provisions Do Not Provide "Law to Apply."

The Supreme Court has held that the enforcement provisions of the FDCA do not provide "law to apply" to overcome this presumption of unreviewability. In *Heckler v. Chaney*, prison inmates sentenced to death by lethal injection filed a citizen petition with FDA, alleging that the use of certain drugs to execute prisoners violated the provisions of the FDCA prohibiting interstate distribution of an approved drug for an unapproved use, 21 U.S.C. § 355(a), and a misbranded drug, 21 U.S.C. § 352(f)(1). 470 U.S. at 823–24. The inmates requested, among other things, that FDA take investigatory and enforcement action to prevent the States from using the drugs at issue in administering the death penalty. *Id.* at 824. FDA denied the petition, relying on its inherent enforcement discretion to decline to pursue the requested investigative and enforcement action. *Id.* at 824.

The Supreme Court held that an agency's refusal to take enforcement steps is "presumptively unreviewable," *id.* at 832, and that, in the FDCA, Congress had neither indicated an intent to circumscribe agency enforcement discretion nor provided meaningful standards for defining the limits of that discretion. *Id.* at 835. The FDCA's injunction provision, 21 U.S.C. § 332, "gives no indication of when an injunction should be sought," and the seizure provision, 21 U.S.C. § 334, "is framed in the permissive—[the violative article] 'shall be liable to be proceeded against.'" *Id.* (quoting 21 U.S.C. § 334). As for the criminal provision, 21 U.S.C. § 333, the Court acknowledged its mandatory language ("Any person who violates a provision of section 301 *shall* be imprisoned . . . or fined . . . ." (emphasis added)), but found "no indication in case law or legislative history that" Congress intended to mandate criminal prosecution of every violator of the FDCA. *Id.* "Conclud[ing] that the presumption that agency decisions not to

institute proceedings are unreviewable under 5 U.S.C. § 701(a)(2) is not overcome by the enforcement provisions of the FDCA," *id.* at 837, the *Chaney* Court held that "FDA's decision . . . is therefore not subject to judicial review under the APA," *id.* at 837-38.

Relying on *Chaney*, the D.C. Circuit has repeatedly upheld FDA's discretion not to take enforcement action under the FDCA. *See Jerome Stevens Pharms., Inc. v. FDA*, 402 F.3d 1249, 1258 (D.C. Cir. 2005) ("Each of [the deadline extensions for submitting NDAs for marketed unapproved drugs] is an exercise of FDA's enforcement discretion, and [plaintiff] fails to demonstrate how 21 U.S.C. § 355 and 21 U.S.C. § 393 provide guidelines for the exercise of such discretion."); *Cutler v. Hayes*, 818 F.2d 879, 893 (D.C. Cir. 1987) ("The [FDCA] imposes no clear duty upon FDA to bring enforcement proceedings to effectuate either the safety or the efficacy requirements of the Act. . . . Congress has not given FDA an inflexible mandate to bring enforcement actions against all violators of the Act."); *Cmty. Nutrition Inst. v. Young*, 818 F.2d 943, 950 (D.C. Cir. 1987) ("[T]he gravamen of [plaintiffs'] complaint is that FDA failed to initiate enforcement proceedings. *But as the [Chaney] Court held . . . , FDA enjoys complete discretion not to employ the enforcement provisions of the [FDCA], and those decisions are not subject to judicial review*.") (emphasis added); *Schering Corp. v. Heckler*, 779 F.2d 683, 686 (D.C. Cir. 1985) ("The Court's decision in *Chaney* manifestly forecloses judicial review here in a case involving the same agency and the identical statute."); *cf. Int'l Ctr. for Tech. Assessment v. Thompson*, 421 F. Supp. 2d 1, 8 (D.D.C. 2006) ("FDA's determination not to take any enforcement actions in connection with the GloFish [new animal drug application] is discretionary and not subject to judicial review.").

C. Counts I -III Should be Dismissed Because Sections 355, 353a, and 360cc Do Not Provide "Law to Apply"

Plaintiffs claim that the presumption that non-enforcement decisions are unreviewable is overcome here because sections 355, 353a,[13] and 360cc[14] provide guidelines for the agency to apply in exercising its enforcement discretion. Pls.' Br. at 38. None of these sections reflects even a modest attempt by Congress to guide or limit FDA's enforcement discretion.

1. Section 355

Plaintiffs' reliance on section 355 (Compl. ¶¶ 114-16) can be rejected "summarily." *Chaney*, 470 U.S. at 835-36. As here, the *Chaney* plaintiffs claimed section 355's prohibition against "introduction of 'new drugs' absent agency approval" supplied the Court with 'law to apply'" to overcome the presumption of unreviewability of FDA's non-enforcement decision. *Id.* at 836. The Court dispensed with that argument quickly, holding that section 355 is "simply irrelevant to the agency's discretion to refuse to initiate proceedings." *Id.*; *Cutler v. Hayes*, 818 F.2d at 893 (the FDCA "imposes no clear duty upon FDA to bring enforcement proceedings to effectuate either the safety or the efficacy requirements of the Act."). Thus, section 355 does not aid Plaintiffs' argument.

2. Section 353a

As discussed above (pp 4-5), section 353a sets forth conditions under which licensed pharmacists or physicians may compound drugs for human use without having to comply with the FDCA's requirements for premarket approval of new drugs, labeling that bears adequate

[13] Plaintiffs contend that the advertising restrictions in section 353a found to be unconstitutional are severable and that the remaining provisions of section 353a are valid and in effect. Pls.' Br. at 32. For purposes of this memorandum, the government will assume that section 353a is in effect. But a court may have a different view in any enforcement action.

[14] Plaintiffs also rely on 21 U.S.C. § 381(a). We address section 381(a) separately

directions for use, and current good manufacturing practice. Although section 353a details many conditions for qualifying for these limited exemptions, it only indicates when a compounded drug *is not in violation* of the new drug and specified adulteration and misbranding provisions. If the compounded drug satisfies section 353a's conditions, enforcement and non-enforcement issues under the exempted sections do not arise. When a compounded drug does not comply with section 353a, however, FDA (and the courts) must refer to the substantive provisions (sections 352(f)(1) and 355) that the Supreme Court has already decided give no guidance as to the appropriate exercise of discretion. *Chaney*, 470 U.S. at 836; *see Sierra Club v. Larson*, 882 F.2d 128, 132 (D.C. Cir. 1989) ("The relevant question here is whether the [statute] provides standards for ascertaining when the [agency] should recommend that formal enforcement proceedings be commenced or when the Secretary is required to make a determination of compliance or non-compliance or to institute an enforcement action."). Thus, section 353a provides no "law to apply."

3. Section 360cc

Plaintiffs' reliance on section 360cc (Compl. ¶¶ 104-09) fares no better. Section 360cc outlines specific conditions under which FDA may not approve an application under section 355 or issue a license under the PHSA for the same drug (i.e., another sponsor's 17-HPC) for the same disease or condition (i.e., to reduce the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth). 21 U.S.C. § 360cc. Plaintiffs admit that FDA has not approved an application under section 355 or issued a license under the PHSA for 17-HPC, but claim that FDA's March 30, 2011 statement was "the functional equivalent of such an approval." Pls.' Br. at 21.

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below.

Section 360cc's language is plain, and it states only that FDA may not approve an application or a license under specific statutory provisions and under specific circumstances. Plaintiffs argue that failure to apply section 360cc beyond its plain language to FDA's admittedly outdated statement regarding exercise of enforcement discretion would be "contrary to congressional intent." Pls.' Br. at 22. Yet, the words Congress used in the statute provide the best evidence of Congressional intent. *See Barnhart v. Sigmon Coal Co*., 534 U.S. 438, 461-62 (2002) ("courts must presume that a legislature says in a statute what it means and means in a statute what it says there. When the words of a statute are unambiguous, then, the first canon is also the last: 'judicial inquiry is complete.'") (quoting *Conn. Nat'l Bank v. Germain*, 503 U.S. 249, 253-54 (1992)). Moreover, because "all legislation has 'purposes and policies,'" general statements about the policies underlying the cited provisions cannot provide guidelines to overcome the *Chaney* presumption. *Twentymile*, 456 F.3d at 158.

The D.C. Circuit rejected a similar invitation to take a "functional" approach to a different FDCA exclusivity provision in *Teva Pharm. Indus. Ltd. v. Crawford*, 410 F.3d 51 (D.C. Cir. 2005). Teva challenged FDA's response to a citizen petition requesting that FDA prohibit Pfizer, Inc., from marketing an "authorized generic"[15] version of its own pioneer drug gabapentin during the 180-day exclusivity period that the FDCA awarded to Teva as an incentive for being the first generic applicant to successfully challenge the patent on Pfizer's drug. Analogous to the Orphan Drug Act's exclusivity period, the 180-day exclusivity provision prohibited FDA from approving another generic version of the same drug. *Id.* at 52 (citing 21

[15] An authorized generic drug is the brand name drug that was approved (by FDA) in the brand name drug company's NDA, but it is marketed either by the NDA holder or another company (including by a generic drug company) with different packaging and labeling to look like and compete with generic drugs.

U.S.C. § 355(j)(5)(B)(iv)). Pfizer's authorized generic "competed directly with Teva's [generic gabapentin] during [Teva's] period of exclusivity." *Id.* at 53. Like Plaintiffs here, Teva argued that the court should adopt a "functional" interpretation of the exclusivity provision because a "literal interpretation cannot defeat statutory purpose." *Id.* at 53. The D.C. Circuit rejected the argument. The court found that the exclusivity provision's prohibition on FDA approving a second or later *ANDA* during the exclusivity period could not be read to limit "what the FDA may do in such a way as to prevent the holder of an approved *NDA*, which does not need to file an ANDA . . . from marketing a brand-generic product." *Id.* at 54 (emphasis added). So too here. Section 360cc, a section directed at FDA's approval authority, is entirely silent as to whether FDA should take enforcement action against compounded versions of the same drug, or for that matter, any unapproved versions of the same drug that may exist. In short, section 360cc, like section 355, does not "provide[] guidelines for the agency to follow in exercising its enforcement powers," and, therefore, does not rebut the presumption of unreviewability. *Chaney*, 470 U.S. at 833.

Because sections 355, 353a, and 360cc do not provide guidelines for the agency to follow in exercising its enforcement powers, FDA's non-enforcement decisions are not subject to judicial review. Thus, Counts I-III of the Complaint should be dismissed.

D. Count IV Should Be Dismissed Because Section 381(a) Does Not Provide "Law to Apply"

In Count IV, Plaintiffs claim that FDA has violated 21 U.S.C. § 381(a), a provision of the FDCA that addresses importation of various FDA-regulated products, including drugs. Section 381(a) states, in part: "If it appears from the examination of such samples or otherwise that . . . (3) such article is adulterated, misbranded, or in violation of . . . [21 U.S.C. § 355] . . .,

then such article shall be refused admission . . . ." 21 U.S.C. § 381(a). Relying on *Beaty v. FDA*, Civ. No. 11-289 (RJL), 2012 U.S. Dist. LEXIS 41397 (D.D.C. Mar. 27, 2012), *appeal docketed*, Cook v. FDA, No. 12-5176 (D. C. Cir. May 31, 2012), Plaintiffs argue that section 381(a)'s use of "shall be refused" *requires* FDA to "deny admission to a drug offered for import that appears to be adulterated, misbranded, or in violation of Section 355." Pls.' Br. at 35-36. *Beaty* involved importation of a finished drug product imported from an unregistered foreign manufacturer, 2012 U.S. Dist. LEXIS 41397, *8-10 & n.6. Thus, the *Beaty* court did not consider section 381(a)'s application to APIs from registered manufacturers intended for use in compounding, nor, as a result, the consequences for compounding under section 353a if such foreign-manufactured APIs must be refused admission at the border. That issue bears separate consideration because the relief Plaintiffs seek would halt all compounding of 17-HPC, even when performed in accordance with the conditions in section 353a, and thwart compounding from APIs generally.

1. Background

Before turning to Plaintiffs' legal argument regarding section 381(a), we address two preliminary matters. First, Plaintiffs argue that 17-HPC API used in compounding is a "new drug." *See* Compl. ¶ 119. This is true not just for 17-HPC API, but all APIs used in compounding. When an API is used to compound a drug product, it is a component of a drug and therefore itself a drug. 21 U.S.C. § 321(g)(1)(D). As Plaintiffs argue, a drug is a "new drug" unless it is generally recognized by qualified experts as safe and effective (GRAS/E) for the conditions prescribed, recommended, or suggested in its labeling, 21 U.S.C. § 321(p). APIs that appear to violate section 355 are subject to refusal of admission under section 381(a)(3).[16]

[16] An API that lacks adequate directions for its intended use also appears to be misbranded under 21 U.S.C. § 352(f)(1), unless it qualifies for an exemption to that

Second, FDA's decisions about *import entries*[17] for 17-HPC API are exercises of enforcement discretion under section 381(a) and are unrelated to the March 2011 statement. When FDA is presented with an import entry for an API that is labeled for use in compounding - whether 17-HPC *or any other drug* - FDA's import operations staff does not typically refuse the entry on the ground that it is an unapproved new drug in violation of section 355, provided that the API is one that *could be used* for compounding under the agency's 2002 Compounding CPG or section 353a.[18] 17-HPC API, for example, could be used for compounding in accordance with section 353a both because it is a bulk drug substance that is the subject of a USP monograph and because it is a component in a drug approved by the Secretary. *See* 21 U.S.C. § 353a(b)(1)(A)(i); Pharmacopeia of the United States of America, USP 35-NF 30 at 3455-56 (Nov. 1, 2011).[19]

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requirement. *See, e.g.*, 21 C.F.R. § 201.120; 21 C.F.R. § 201.122.

[17] A brief description of the import process may be found in footnote 1 of the *Beaty* decision, 2012 U.S. Dist. LEXIS 41397, *5-6.

[18] *See, e.g.*, FDA Import Alert #66-66, "APIs That Appear To Be Misbranded Under [21 U.S.C. 352(f)(1)] Because They Do Not Meet The Requirements For The Labeling Exemptions In 21 CFR 201.122", *available at* http://www.accessdata.fda.gov/cms_ia/importalert_202.html (providing that an API that appears to be misbranded under section 352(f)(1) may be released if the importer "can supply evidence establishing that the article is: 1. *intended for pharmacy compounding that meets the requirements of section [353a] of the Act*, including that the API: a. is accompanied by a valid certificate of analysis, b. is manufactured by an establishment registered under section 510 of the Act, and c. does not appear on a list of drugs identified in 21 CFR 216.24, that have been withdrawn or removed from the market for reasons of safety or effectiveness."); *compare* FDA Import Alert #61-07, "Detention Without Physical Examination of Domperidone", *available at* http://www.accessdata.fda.gov/cms_ia/importalert_166.html (providing guidance to the import staff that the drug domperidone is not appropriate for pharmacy compounding use, and thus may be detained without physical examination, because "this bulk active ingredient is not a component of an FDA approved drug….").

[19] Thus, FDA does not dispute that it has exercised case-by-case enforcement discretion related to import entries for 17-HPC for use in compounding, but denies Plaintiffs' speculation that the March 2011 statement is the basis for that discretion. Even Plaintiffs acknowledge the March 2011 statement does not speak to importation of 17-HPC API. Compl. ¶ 124 (alleging that the March 2011 statement announced "implicitly" that FDA would allow importation).

FDA exercises enforcement discretion regarding APIs for use in compounding (under certain conditions) because the agency - like Plaintiffs - recognizes that compounding under certain conditions provides an important public health benefit and because Congress expressly permitted compounding from bulk drug substances in section 353a. *See W. States*, 535 U.S. at 369 ("The Government . . . has an important interest . . . in permitting the continuation of the practice of compounding so that patients with particular needs may obtain medications suited to those needs."); Pls.' Br. at 4-5 (discussing how for some patients "it may be medically necessary for a patient to take a 'compounded' version of a drug"). Moreover, it is usually not possible to evaluate *at the border* whether the pharmacy that eventually receives the foreign-manufactured API will compound it consistent with all of the provisions of section 353a. For example, FDA's import staff *can* assess at the time an API is offered for importation for use in compounding whether it is a bulk drug substance that meets one or more the criteria in section 353a(b)(1)(A)(i)(I)-(III) (e.g., it is a component of an FDA-approved drug or is the subject of a USP monograph). But, under ordinary circumstances, FDA import staff *cannot* assess at the border whether, for example, the drug will be compounded by a licensed pharmacist or physician "for an identified individual patient based on . . . a valid prescription" and whether the drug, if compounded before receipt of the prescription, will only be compounded in limited quantities and based on the pharmacy's history of receiving valid prescription orders for compounding the drug. *See* 21 U.S.C. § 353a(a).

Neither the Complaint's half-hearted speculation (*id.*) nor their brief's fact-free argument (Pls.' Br. 35-36) are allegations of fact that must be presumed to be true for purposes of this motion. *See, e.g., O'Gilvie v. Corp. for Nat'l Cmty. Serv.*, 802 F. Supp. 2d 77, 82 (D.D.C. 2011) (conclusory allegations "need not be treated as true, and . . . are insufficient to defeat [a] motion to dismiss"); *Int'l Ctr. for Tech. Assessment*, 421 F. Supp. 2d at 9 (court "need not accept as true inferences unsupported by facts set out in the complaint").

2. FDA's Decisions Under 21 U.S.C. § 381(a) Are Presumptively Unreviewable

FDA's decisions not to refuse admission to import entries of 17-HPC API are the very type of enforcement decisions that fall within the *Chaney* presumption of unreviewability. Before refusing admission to an import entry, the agency undertakes a multi-step process that includes gathering information to determine whether a product is subject to refusal and identifying apparent violations of the FDCA, and concludes with the articles being voluntarily reconditioned (e.g., relabeled), destroyed or exported. If an article "appears" to be in violation of the FDCA and FDA determines that refusal may be warranted, FDA first issues a notice that specifies the violation charged. *See* 21 C.F.R. § 1.94(a); FDA Regulatory Procedures Manual (RPM) Ch. 9-1 (*available at* http://www.fda.gov/ICECI/ComplianceManuals/RegulatoryProceduresManual/default.htm). After providing the owner or consignee an opportunity to be heard and after considering all of the evidence, including any written and/or oral testimony submitted, FDA determines whether to refuse admission to the article or release it. RPM Ch. 9-1. If an article is refused admission, the article must be destroyed unless it is exported within 90 days after receiving the notice of refusal, or within such additional time as permitted. 21 U.S.C. § 381(a). Thus, FDA's enforcement decisions not to refuse admission to imports under 21 U.S.C. § 381(a) are directly analogous to the plainly discretionary and non-reviewable enforcement decisions not to institute a seizure action under 21 U.S.C. § 334, an injunctive proceeding under 21 U.S.C. § 332, or a criminal prosecution under 21 U.S.C. § 333.[20] As such, they are presumptively unreviewable. *Chaney*, 470 U.S. at 831.

[20] In *Beaty v. FDA*, Civ. No. 11-289 (RJL), 2012 U.S. Dist. LEXIS 41397 (Mar. 27, 2012), Judge Leon found *Chaney* inapplicable to a decision not to refuse admission to an unapproved new drug because it does not "involve a decision whether to initiate enforcement

3. There is No "Law to Apply" to Overcome the *Chaney* Presumption of Unreviewability

Under section 381(a), a prerequisite to any enforcement action against 17-HPC API or any other API is an FDA determination that an article "appears" to be adulterated, misbranded, or in violation of section 355, based on an examination of samples or "otherwise." A long line of court decisions confirms that the use of the terms "appear[ ]" and "otherwise" in section 381(a) establishes Congress' intent to provide FDA with broad discretion in determining whether an article appears to violate the FDCA. *See, e.g., K & K Merch. Group v. Shalala*, Civ. No. 95-10082, 1996 WL 183023, at *8 (S.D.N.Y. Apr. 17, 1996) (noting "the wide discretionary power FDA enjoys to determine the factors regarding its decision to grant or refuse admission of imported goods"); *Seabrook Int'l Foods, Inc. v. Harris*, 501 F. Supp. 1086, 1090–1091 (D.D.C. 1980) ("use of the term 'appears' in the statute is a striking and clear indication of Congress' intent to forego formal procedural requirements."), *aff'd sub nom., Cont'l Seafoods, Inc. v. Schweiker*, 674 F.2d 38 (D.C. Cir. 1982). Plaintiffs offer no basis for eliminating the discretion,

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proceedings against a violator of the Act" and because "FDA was not required to prove that a violation of the [FDCA] had occurred." *Id*. at 26. *Chaney*, by its own terms, is not limited to decisions whether to initiate judicial enforcement proceedings, and the *Beaty* court did not cite a single case that has applied *Chaney* in such a limited way. Indeed, *Chaney* has been given broad application beyond decisions about whether to initiate judicial enforcement proceedings. *See, e.g., Balt. Gas and Elec. Co. v. FERC*, 252 F.3d 456, 458 (D.C. Cir. 2001) (decision to settle enforcement action); *California v. United States*, 104 F.3d 1086, 1094 (9th Cir. 1997) (Attorney General's failure to take into custody any alien convicted of an aggravated felony); *Coker v. Sullivan*, 902 F.2d 84, 88-89 (D.C. Cir. 1990) (failure to monitor and withhold funding from state aid programs); *Dubois v. Thomas*, 820 F.2d 943, 948-51 (8th Cir. 1987) (EPA's failure to either issue a compliance order (*i.e.*, an administrative action) or commence a civil action); *Falkowski v. EEOC*, 764 F.2d 907, 911 (D.C. Cir. 1985) (denial of an EEOC employee's request for counsel); *City of Seabrook v. Costle*, 659 F.2d 1371, 1375 (5th Cir. 1981) (failure to provide notifications specified in the Clean Air Act); *Kixmiller v. SEC*, 492 F.2d 641, 645 (D.C. Cir. 1974) (decision to refrain from an investigation); *K&K Merch. Group, Inc. v. Shalala*, No. 95 CIV. 10082 (RPP), 1996 WL 183023, at *8 (decision not to refuse admission to imported articles).

apparent in the first clause of the provision at issue and inherent in agency enforcement as recognized by *Chaney*, about whether to expend resources to commence the hearing process. But Plaintiffs insist that the agency is nonetheless under a mandatory obligation to not only commence an enforcement proceeding but also to culminate it in a refusal to authorize importation in all cases.

Moreover, courts do not read "shall" as mandatory when such a reading impinges upon administrative enforcement discretion. *See Wood v. Herman*, 104 F. Supp. 2d 43, 47 (D.D.C. 2000) ("While it is a recognized tenet of statutory construction that the word 'shall' is usually a command, this principle has not been applied in cases involving administrative enforcement decisions." (citation omitted)); *see also Dubois v. Thomas*, 820 F.2d at 946–47; *City of Seabrook*, 659 F.2d at 1375 n.3. Indeed, in *Heckler v. Chaney*, the Supreme Court refused to afford the word "shall" in the FDCA a mandatory meaning where that interpretation would have circumscribed the agency's discretion not to enforce particular provisions. 470 U.S. at 835.[21] Because "shall" is generally permissive in the administrative enforcement context, and because of the discretionary language ("appears" and "otherwise") included within section 381(a), we respectfully disagree with the *Beaty* court's conclusion that Congress intended "shall be refused" to impose a mandatory obligation on FDA. *See Beaty*, 2012 U.S. Dist. LEXIS 41397 *17-18.

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[21] Consistent with *Chaney*, various courts interpreting the import provisions of the FDCA specifically have interpreted the "shall" in "shall be refused admission" to be discretionary. *See K & K Merch. Group v. Shalala*, Civ. No. 95-10082, 1996 WL 183023, at *8 (finding that the unreviewable "discretionary determination" to allow importation of noncompliant electronic systems is "more akin to an exercise of prosecutorial discretion than to a statutorily mandated exemption," even though the import provision, 21 U.S.C. § 360mm(a), states that any noncompliant electronic product "shall be refused admission into the United States"); *see also United States v. Food, 2,998 Cases*, 64 F.3d 984, 987 n.11 (5th Cir. 1995) (rejecting plaintiff's argument that "the express language of § 381 mandates that adulterated

Even assuming *arguendo* that *Beaty* is correctly decided, it is distinguished from the case at bar, for two reasons. First, the *Beaty* decision found that the FDCA provided "substantial guidance as to when and how imported drugs must be reviewed." *Id.* at *27. In particular, the court explained that section 381(a) provides that FDA shall request samples of drugs imported from unregistered manufacturers. *Id.* The court then found "law to apply" because "the statute . . . mandates the *universal exclusion of foreign drugs from unregistered establishments that appear* misbranded, adulterated, or *unauthorized* . . . ." *Id.* at *28 (emphasis added). But to the extent that the second sentence in section 381(a) might establish any limit on FDA's ultimate determination whether to initiate refusal proceedings, that limit would have no application to this case. Here, Plaintiffs do not allege that the 17-HPC APIs they seek to exclude from this country are from *unregistered* facilities. *See, e.g.,* Compl. ¶ 5. Thus, one of the foundations underlying the *Beaty* court's conclusion is absent.

More importantly, *Beaty* did not have the opportunity to consider the mandatory or permissive nature of the "shall" in "shall be refused admission" in the context of APIs intended for compounding. In this context, it is clear that reading "shall" in section 381(a) as mandatory would frustrate Congress' purposes in enacting section 353a to expand the scope of permissible compounding from bulk drug substances, and produce absurd results.

Congress modeled portions of section 353a on the agency's 1992 CPG. *See W. States*, 535 U.S. at 364. Whereas that CPG (CPG 7132.16) took a narrow view regarding bulk drug substances used in compounding ("If a pharmacy compounds finished drugs from bulk active ingredient materials considered to be unapproved new drug substances, . . . such activity must be covered by" an investigational new drug application, Pls.' Br. Ex. A at 4), Congress significantly

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goods being imported or offered for import, as here, *shall* be refused admission).

expanded the permissible use of bulk drug substances in section 353a. Under section 353a, a pharmacy may compound from a bulk drug substance if the bulk drug substance complies with a USP or NF monograph, is a component of a drug approved by FDA, or is on a list that Congress authorized FDA to develop by regulation. *See* 21 U.S.C. § 353a(b)(1)(A)(i), 353a(d)(2). Congress' significant expansion of the permissible types of bulk drug substances for compounding reflects a clear intent that pharmacies be allowed to compound drugs from bulk drug substances under the terms of section 353a.

If Plaintiffs' reading of the *Beaty* decision were to be adopted and applied to APIs from registered manufacturers for use in compounding, FDA would be required to refuse entry to all foreign-manufactured APIs because they appear to be unapproved new drugs. It is not practical to argue that pharmacies could simply compound using only APIs that are manufactured in this country because approximately 80% of all API manufacturers registered with FDA are located outside this country. *See* FDA Special Report, "Pathway to Global Product Safety and Quality" at 2 (*available at* http://www.fda.gov/downloads/AboutFDA/CentersOffices /OfficeofGlobalRegulatoryOperationsandPolicy/GlobalProductPathway/UCM262528.pdf). Indeed, Plaintiffs experience in trying to obtain 17-HPC API for its investigation is illustrative: all of the APIs it located were manufactured in China. Compl. ¶¶ 5, 89). Thus, a declaration that 17-HPC API "cannot lawfully be . . . imported" because it is an unapproved "new drug" (Compl. at 41) would effectively prohibit *all* compounding of 17-HPC, even when fully compliant with section 353a.[22] Thus, it is clear that the *Beaty* decision is inapplicable to the case at bar. Otherwise, section 381(a) cannot be harmonized with section 353a.

[22] An inflexible reading of "shall" in section 381(a) also would lead to absurd results in other contexts. For example, requiring FDA to refuse admission to all unapproved new drugs

For all of these reasons, section 381(a) does not provide "law to apply" to deny the presumption of unreviewability to FDA's non-enforcement decisions regarding 17-HPC API.

E. Plaintiffs' Remaining Arguments Cannot Overcome the Presumption of Unreviewability

Plaintiffs offer several flawed arguments why the March 2011 statement should not be afforded a presumption of unreviewability. Notably, not one of these arguments finds fault with FDA's current (June 2012) statement, which Plaintiffs term a "reversal" of FDA's March 2011 statement. *See supra* at 13.

First, the Court should reject Plaintiffs' efforts to cast the March 2011 statement as a "policy." Citing *Crowley Caribbean Transport, Inc. v. Pena*, 37 F.3d 671 (D.C. Cir. 1994), Plaintiffs claim that a declaration of a "non-enforcement policy [is] not accorded the deference"

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would mean that FDA could not exercise enforcement discretion regarding import entries of drugs that are medically necessary and in short supply in this country. *See, e.g.*, FDA News Release, "FDA Acts To Bolster Supply of Critically Needed Cancer Drugs" (Feb. 21, 2012) (*available at* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements /ucm292658.htm) (announcing the temporary importation of the unapproved new drug Lipodox through an exercise of the agency's enforcement discretion in response to the critical shortage of the cancer drug Doxil). Thus, FDA's efforts to protect the public health in response to drug shortages would be seriously undermined.

Plaintiffs' reading of the statute would also vitiate FDA's personal use importation policy. According to that policy, "FDA personnel may use their discretion to allow entry of shipments of violative FDA regulated products when the quantity and purpose are clearly for personal use, and the product does not present an unreasonable risk to the user." RPM § 9-2. In 2000 and again in 2003, Congress ratified FDA's exercise of enforcement discretion under the agency's personal use policy by enacting and amending 21 U.S.C. § 384. *See* The Medicine Equity and Drug Safety Act of 2000, Pub. L. No. 106-387, § 1(a), 114 Stat. 1549A-35 (adding § 384); The Medicare Prescription Drug, Improvement and Modernization Act of 2003, Pub. L No. 111-383, 117 Stat. 2066, 2464 (replacing § 384). In the current version of § 384(j), Congress declared that FDA should "focus enforcement on cases in which the importation by an individual poses a significant threat to public health" and "exercise discretion to permit individuals to make such importations" in certain circumstances. 21 U.S.C. § 384(j)(1). These provisions never took effect, however, because FDA never made the requisite certification that their implementation would "pose no additional risk to the public's health and safety" and would "result in a significant reduction in the cost of covered products to the American

given to a decision against enforcement in an individual case. Pls.' Br. at 37. *Crowley* does not support Plaintiffs' assertion that the March 2011 statement should not be afforded the presumption of unreviewability. The *Crowley* court stated that "an agency's statement of a *general enforcement policy* may be reviewable for *legal sufficiency* where the agency has expressed the policy as a *formal regulation* after the full rulemaking process . . . or has otherwise articulated it in some form of *universal policy statement* . . . ." 37 F.3d at 676 (emphasis added). The court further explained, "It is *conceivable* that a document announcing a particular non-enforcement decision would actually lay out a general policy delineating the boundary between enforcement and non-enforcement and purport to speak to a broad class of parties; such a communication *might qualify*" as a reviewable "general statement of policy," but not "in the ordinary case" where "the more reasonable inference when faced with a context-bound non-enforcement pronouncement is that the agency has addressed the issue in comparatively ad hoc terms inherently implicating its non-reviewable enforcement discretion." *Id.* at 677.

FDA's March 2011 statement was not issued through rulemaking or articulated as a "universal policy statement" related to a "broad class of parties." It applied to the "unique" circumstances of compounding one particular drug (17-HPC) that had been available through compounding for many years and had been the subject of a letter from Plaintiffs to pharmacies purporting to represent FDA's enforcement position. Ex. 1. Even then the March 30, 2011 statement applied only under certain limited conditions. *Id*. It plainly was a "context-bound non-enforcement pronouncement" (*see id.* ("at this time and in this unique situation")) that has consistently been afforded a presumption of unreviewability.[23]

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consumer." 21 U.S.C. § 384(l)(1).

[23] *Edison Elec. Inst. v. EPA*, 996 F.2d 326, 333 (D.C. Cir. 1993), and *Am. Horse Prot.*

Moreover, Plaintiffs' contention that the March 2011 statement is subject to review because it is a "policy" cannot be squared with *Chaney, Jerome Stevens Pharms., Inc. v. FDA*, 402 F.3d 1249, 1258 (D.C. Cir. 2005), and *Schering Corp. v. Heckler*, 779 F.2d 683 (D.C. Cir. 1985). In *Chaney*, FDA responded to a citizen petition pertaining to the distribution of several different kinds of drugs used for capital punishment. 470 U.S. at 823. Even though the petition response was both formal and public, the Court held that the agency's non-enforcement decision was presumptively unreviewable. *Id.* at 837-38. Likewise, in *Jerome Stevens*, FDA's exercise of enforcement discretion was held unreviewable even though it related to distribution of multiple manufacturers' versions of a particular type of unapproved new drug and was announced in several notices published in the Federal Register. And in *Schering*, even though the government had twice alleged in enforcement actions in federal court that a drug was unapproved and, thus, in violation of the FDCA, the government's entry into a settlement agreement, filed in court, in which FDA agreed not to seek further enforcement against the drug pending other events was held to be an unreviewable exercise of enforcement discretion. 779 F.2d at 686.[24]

Ass'n v. Lyng, 812 F.2d 1, 4 (D.C. Cir. 1987), likewise provide no support for Plaintiffs' suggestion that the March 2011 statement was a "policy" to which the *Chaney* presumption is inapplicable. In *Edison*, the D.C. Circuit concluded that an issue of statutory interpretation embodied in an EPA enforcement policy was subject to review. 996 F.2d at 333. The court considered *Chaney* inapplicable because, unlike here, the petitioners were "not challenging the manner in which EPA has chosen to exercise its enforcement discretion." *Id.* In *American Horse*, the court concluded that the presumption of unreviewability in *Chaney* did not bar a challenge to an agency's failure to institute rulemaking proceedings. 812 F.2d at 3.

[24] Plaintiffs devote only a footnote to their efforts to distinguish *Jerome Stevens* and *Schering*, and the purported distinction they claim is that the agency's exercise of enforcement discretion in those cases was for a limited period of time. (Pls.' Br. at 40-41, n. 61). But the exercise of enforcement discretion related to compounding of 17-HPC described in FDA's now admittedly "outdated" March 2011 statement was also of limited (and even shorter) duration than the three years in *Jerome Stevens* and the eighteen months in *Schering*.

Chaney, *Jerome Stevens*, and *Schering* similarly reject Plaintiffs argument that this Court should deny the presumption of unreviewability to the March 2011 statement because it is not merely the "failure to enforce against past conduct" but "in the form of a press release, it addresses *future* conduct . . . ." Pls.' Br. at 39 (emphasis in original). The citizen petition response at issue in *Chaney* announced FDA's intention to refrain from taking investigative and enforcement action to prevent *future* violations. *Chaney*, 470 U.S. at 824. Likewise, the Federal Register notices at issue in *Jerome Stevens* announced that all levothyroxine sodium drug products were unapproved new drugs that required NDAs, set a compliance date *three years* later, and then extended that deadline twice. *Jerome Stevens*, 402 F.3d at 1250-51. And in *Schering*, FDA bound itself "not to initiate any enforcement litigation against [the drug at issue or its manufacturer] for a period of 18 months" into the future or, possibly, longer. 779 F.2d at 685. Each of these announcements gave what Plaintiffs would consider "public approval" to the continued marketing of unapproved new drugs, yet the Supreme Court and the D.C. Circuit afforded the agency's actions a presumption of unreviewability and declined to review them. *Id.* at 1257-58.

Second, Plaintiffs contend that the "considerations that give rise to the presumption" set forth in *Chaney* do not apply here. Pls.' Br. 38. Notably, Plaintiffs fail to identify a single case in which a court refused to afford the presumption to a non-enforcement decision based on alleged inapplicability of these *Chaney* "considerations." This is not surprising because the *Chaney* court "of course only list[ed] the above concerns to facilitate understanding of [its] conclusion that an agency's decision not to take enforcement action should be presumed immune from judicial review." *Chaney*, 470 U.S. at 832.

Third, Plaintiffs claim the March 2011 statement is subject to review and unlawful

because it was "based on impermissible factors," specifically "pricing" and "political pressure." Pls.' Br. at 39. Again, Plaintiffs identify no decision where a court has reviewed an exercise of enforcement discretion based on such a theory. Instead, Plaintiffs rely on *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983), which explains the arbitrary and capricious standard for actions that *are* subject to review. It does not suggest application of that standard to decisions committed to agency discretion. Plaintiffs also rely on a Fourth Circuit opinion, but that decision reviewed a challenge to an agency's "final marketing power policy," not an exercise of enforcement discretion, and it relied on pre-*Chaney* decisions. *See Electricities of N.C., Inc. v. Se. Power Admin.*, 774 F.2d 1262, 1267 (4th Cir. 1985).

Fourth, Plaintiffs contend (Pls.' Br. at 40) that FDA's March 2011 statement falls within a footnote in the *Chaney* decision in which the Supreme Court reserved the question whether an agency's action may not be "committed to agency discretion" if "it could justifiably be found that the agency has 'consciously and expressly adopted a *general policy' that is so extreme* as to amount to an abdication of its statutory responsibilities." *Chaney*, 470 U.S. 833 n.4 (citing *Adams v. Richardson*, 480 F.2d 1159 (D.C. Cir. 1973) (en banc) (emphasis added)). Plaintiffs try to compare FDA's enforcement discretion statement to giving "affirmative aid to violators" noted in *Adams*. Pls.' Br. at 40. The analogy does not hold. The *Adams* court specifically distinguished situations in which an agency elects not to initiate enforcement proceedings from "actively supplying segregated institutions with federal funds, contrary to the expressed purposes of Congress." 480 F.2d at 1162. FDA temporarily exercised enforcement discretion (under certain conditions), but it did not fund pharmacy compounding of 17-HPC. *See also Cutler v. Hayes*, 818 F.2d at 893 (the FDCA "imposes no clear duty upon FDA to bring enforcement proceedings to effectuate either the safety or the efficacy requirements of the Act. . . . Hence,

appellants' argument that judicial intervention under *Adams v. Richardson* is warranted to compel agency enforcement of [FDCA] requirements is not persuasive."). Indeed, any pharmacy that compounded 17-HPC while FDA's March 2011 statement was current did so at its own expense and at its peril that FDA might prioritize an enforcement action against it if the compounding was not "based on a valid prescription for an individually identified patient" or if "the compounded products [were] unsafe, of substandard quality, or [were] not being compounded in accordance with appropriate standards for compounding sterile products." Ex. 1.

Finally, FDA has not "abdicated its statutory responsibilities." As reflected in all FDA's statements on the issue, FDA generally prioritizes "enforcement actions relating to compounded drugs using a risk-based approach, giving the highest enforcement priority to pharmacies that compound products that are causing harm or that amount to health fraud." *See* Exs. 1-3. When Plaintiffs brought information to FDA's attention suggesting variability in the potency and purity of compounded 17-HPC and 17-HPC API, FDA promptly conducted its own investigation and testing. Exs. 2&3; Compl. ¶ 5. As Plaintiffs acknowledge, FDA has made "repeated statements that Makena® offers greater assurance of safety and effectiveness than compounded 17P formulations." K-V Press Release, "FDA Issues Further Guidance About Makena" (July 2, 2012) (*available at* http://www.kvph.com/news_center_article.aspx?articleid=362), and FDA also warned compounding pharmacies that "[t]he compounding of any drug, including hydroxyprogesterone caproate, should not exceed the scope of traditional pharmacy compounding." Exs. 3&4. All of these actions have been consistent with the agency's enforcement priorities. *See Sierra Club v. Larson*, 882 F.2d at 133 (rejecting abdication of responsibility argument where agency conducted fact-finding investigation, drafted

recommendations, met with state officials; even though the government's actions did not satisfy plaintiff, they demonstrated that the government did not abdicate its statutory responsibilities).

Plaintiffs' "abdication" argument is, at bottom, a repackaged version of their arguments that there is "law to apply." But, as discussed in detail above, FDA does not have a "statutory duty to protect exclusivity under Section 360cc(a)" through enforcement actions and/or beyond its obligation not to approve another application under section 355 or license a biologic under the PHSA for the same drug for the same indication as Makena, and sections 353a, 355(a), and 381(a) do not individually or collectively operate to deny FDA's discretion over decisions not to enforce. Thus, Plaintiffs' "abdication" argument also misses the mark.

III. Counts I-III Should Be Dismissed Because They Do Not Allege A Violation of Sections 353a, 355, 360cc, or 381(a)

Even if this Court were to conclude that the presumption of unreviewability does not apply to FDA's March 2011 statement, the Complaint nevertheless should be dismissed because it does not allege conduct that violates sections 353a, 355, 360cc, or 381(a) of the FDCA.

A. Count I: Section 360cc

To allege that FDA's exercise of enforcement discretion, as articulated in the outdated March 2011 statement, violates section 360cc, Plaintiffs rewrite the statute. Plaintiffs claim that section 360cc "prohibits FDA, during the seven-year period of an approved orphan drug product's market exclusivity, from approving (*formally or in any other way*), *authorizing, inviting, encouraging, or generally permitting the introduction into interstate commerce of any compounded versions* of that same drug for the same orphan indication as to which the approved drug has been designated an orphan drug, *except where the compounded version is customized to meet the medical need of an individual patient for whom the approved product is not medically*

appropriate (and thus the approved orphan drug would not be used by that patient in any event)." Compl. ¶ 104 (emphasis added). But, of course, none of the italicized language is actually in the statute, which simply says:

> Except as provided in subsection (b) of this section, if the Secretary—
> (1) approves an application filed pursuant to section 355 of this title, or
> (2) issues a license under section 262 of title 42
>
> 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 or issue another license under section 262 of title 42 for such drug for such disease or condition for a person who is not the holder of such approved application or of such license until the expiration of seven years from the date of the approval of the approved application or the issuance of the license.

21 U.S.C. § 360cc.[25]

Plaintiffs admit that FDA "has not formally approved" another sponsor's application or license and, implicitly, that FDA's conduct was not prohibited by the "literal reading of" section 360cc. Pls.' Br. at 21. Thus, Plaintiffs use words like "effectively," "functional equivalent," and "de facto," *See* Compl. ¶¶ 15, 105; Pls.' Br. at 21, and argue that failure to apply section 360cc beyond its plain language to FDA's now-defunct statement regarding exercise of enforcement discretion would be "contrary to congressional intent." Pls.' Br. at 22. Yet, as discussed *supra*, the words Congress chose to use in the statute provide the best evidence of Congressional intent. *Barnhart*, 534 U.S. at 461-62.[26] Because the words of the statute are clear and, by Plaintiffs'

[25] Moreover, the words Plaintiffs ask this Court to read into the statute regarding *compounding* do not track section 353a.

[26] Because the statutory language is clear, there is no need to resort to the legislative history of the Orphan Drug Act. In any event, Plaintiffs do not identify any language from the legislative history in which Congress discussed enforcement against competition from unapproved drugs, compounded or otherwise. Plaintiffs imply that when Congress enacted the ODA in 1983, it did so against the backdrop of FDA "not permitting compounded drugs to be freely substituted for approved drugs." Pls.' Br. at 24. But the pre-1983 cases they cite (*id.* at 8, 24), *United States v. Sene X Eleemosynary Corp.*, 479 F. Supp. 970, 979 (S.D. Fla. 1979) and

own admission, they have not alleged a violation of the statute's plain language, Count I should be dismissed. *Barnhart*, 534 U.S. at 461 (courts' role is to "interpret the language of the statute enacted by Congress."); *see Teva*, 410 F.3d at 53.[27]

B. Count II: Section 353a

Plaintiffs allege that FDA's March 2011 statement of enforcement discretion also violated section 353a of the FDCA. As discussed, section 353a sets forth conditions under which FDA cannot apply 21 U.S.C. §§ 351(a)(2)(B), 352(f)(1), & 355 to human drugs compounded by licensed pharmacists or physicians. Drugs that do not meet the conditions in section 353a remain subject to those provisions.

Section 353a focuses on what the compounders, not Defendants, must do. The only provisions that mention the Secretary relate to preparing regulations (and completion of certain procedural steps before doing so) and developing a "standard memorandum of understanding for use by the States in complying with" the quantitative limits in 21 U.S.C. § 353a(b)(3)(B)(i). *See* 21 U.S.C. § 353a(b)(3), (d). Plaintiffs' claims are not related to any of these directions to Defendants, however. Because section 353a contains no commands to Defendants regarding enforcement, Plaintiffs' allegations do not state a violation of section 353a.

Cedar N. Towers Pharmacy, Inc. v. United States, No. 77-4695, 1978 U.S. Dist. LEXIS 15829 *5 (S.D. Fla. Aug. 28, 1978), involved pharmacies preparing and marketing *proprietary formulations* of drugs for various diseases. Plaintiffs have not cited a single enforcement action brought by FDA where the case was based *solely* on a pharmacy making copies of approved drugs.

[27] Plaintiffs also allege that the March 2011 statement failed to comply with the procedural requirements of the Due Process Clause of the Fifth Amendment to the U.S. Constitution. Compl. ¶¶ 10, 108. This claim rests entirely upon Plaintiffs' showing that FDA violated section 360cc(b), but, as discussed above, the March 2011 statement did not violate that section. Accordingly, Plaintiffs' Fifth Amendment claim fails as a matter of law.

C. Count III: Section 355

Plaintiffs claim FDA's March 2011 statement violates section 355 because, in their view, the statement "allow[s]" the marketing of "unapproved compounded drugs beyond the scope of traditional customized compounding," and, citing three pre-*Chaney* cases, argue that this Court "has rejected attempts to allow the mass marketing of unapproved new drugs." Pls.' Br. at 34. In contrast to the cases cited by Plaintiffs, FDA stated its intent to exercise enforcement discretion regarding the compounding of a single drug under certain conditions. It did not "formally authorize" the manufacture and distribution of multiple classes of unapproved new drugs. *Compare Cutler v. Kennedy*, 475 F. Supp. 838, 854-56 (D.D.C. 1979) (FDA could not "*formally authorize* the continued marketing of . . . drug products" that had been reviewed and not shown to be safe and effective) (emphasis added). More importantly, Plaintiffs' argument ignores holdings from the Supreme Court and the D.C. Circuit establishing beyond cavil that section 355 does not require FDA to initiate enforcement proceedings against every violator of the FDCA. *Chaney*, 470 U.S. at 836; *Cutler v. Hayes*, 818 F.2d at 893. Thus, Plaintiffs have not alleged conduct that violates section 355.

D. Count IV: Section 381(a)

Plaintiffs contend that section 381(a) *requires* FDA to refuse importation to drugs that "appear" to be unapproved new drugs, and thus FDA must refuse import entries for 17-HPC API. For the reasons discussed *supra*, the "shall" in "shall be refused admission" in section 381(a) is permissive and should not be interpreted as mandatory generally, and particularly in the context of APIs intended for compounding. *See supra* at 25-34.

For all of these reasons, Plaintiffs' Complaint should be dismissed even if this Court concludes that the *Chaney* presumption is somehow inapplicable to the March 2011 statement.

IV. Plaintiffs' Request for a Permanent Injunction Should be Denied

The standard for granting a permanent injunction requires the Court to consider four factors: (1) success on the merits; (2) whether the movant will suffer irreparable injury absent an injunction; (3) the balance of hardships between the parties; and (4) whether the public interest supports granting the requested injunction. *See Nichols v. Truscott*, 424 F. Supp. 2d 124, 143 (D.D.C. 2006). Unlike a preliminary injunction, actual success on the merits is required to obtain permanent injunctive relief. *Id.*

Plaintiffs have not shown success on the merits, and thus their request for injunctive (and declaratory) relief should be denied.[28] Even if Plaintiffs had shown success (or likelihood of success) on the merits, the injunctive relief they request - to compel FDA to "take sufficient enforcement actions" against pharmacies "to stop the unlawful competition with Makena" (Compl. at 42) - is extraordinary. Plaintiffs offer no precedent for it. *See* Pls. Br. at 43 (citing *Hoffman-LaRoche*, 425 F. Supp. at 894-95, as authority for enjoining FDA from implementing a policy, but that case did not compel FDA to take enforcement actions); *Cutler v. Kennedy*, 475 F. Supp. at 856 (refusing to order FDA to take enforcement action, court explained that FDA could not formally authorize the continued marketing of drug products that had been reviewed and not shown to be safe and effective, but "[i]nformally, of course, the FDA will be free to exercise its discretion to seek enforcement actions or not seek enforcement actions."); *see also supra* at 15.

Such injunctive relief would be harmful to the agency's ability to manage its enforcement resources and be contrary to the public interest. It is undisputed that the March 2011 statement is not FDA's current position. The agency is already applying its normal enforcement policies

[28] The Court instructed the parties that it is not necessary to brief the issue of irreparable harm. Minute Order, July 5, 2012.

toward pharmacies compounding 17-HPC. It will consider enforcement actions on a case-by-case basis, taking into account its priorities, assessment of the strength and legal risk of each case, and its available enforcement resources. The agency should not be compelled to reorder its public health priorities to accommodate Plaintiffs' concerns, particularly because, after investigation, FDA has not identified a major safety concern with the sampled compounded 17-HPC and the APIs used to make it. Ex. 3. Plaintiffs' request that this Court command and direct FDA's limited enforcement resources away from its risk-based approach is both harmful to FDA and contrary to the public interest.

CONCLUSION

For the foregoing reasons, Defendants' motion to dismiss should be granted and Plaintiffs' motion for injunctive relief should be denied.

Respectfully submitted,

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