IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

ELLIOTT ASSOCIATES, L.P., ELLIOTT INTERNATIONAL, L.P., and KNOLLWOOD INVESTMENTS, L.P.,

Plaintiffs,

v.

SYLVIA MATHEWS BURWELL, in her official capacity as SECRETARY, UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES,

and

MARGARET HAMBURG, M.D., in her official capacity as COMMISSIONER OF FOOD AND DRUGS, FOOD AND DRUG ADMINISTRATION,

Defendants.

Civil Action No. 1:14-cv-1850 (KBJ)

PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT

COME NOW PLAINTIFFS Elliott Associates, L.P., Elliott International, L.P., and Knollwood Investments, L.P. and pursuant to Federal Rule of Civil Procedure 56 and Local Civil Rule 7(h) and (n) hereby respectfully move this Court to enter summary judgment for Plaintiffs on all claims. This motion is supported by the Memorandum of Points and Authorities, the Declaration of Matthew D. McGill, and supporting exhibits filed concurrently herewith.

Dated: November 17, 2014

/s/ Matthew D. McGill

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CERTIFICATE OF SERVICE

I hereby certify that on this 17th day of November 2014, I caused a copy of the foregoing Plaintiffs' Motion For Summary Judgment, and the accompanying Plaintiffs' Memorandum Of Points And Authorities In Support Of Their Motion For Summary Judgment and Declaration of Matthew D. McGill In Support Of Plaintiffs' Motion For Summary Judgment, to be served upon all parties via this Court's Electronic Case Filing system.

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PLAINTIFFS' MEMORANDUM OF POINTS AND AUTHORITIES IN SUPPORT OF THEIR MOTION FOR SUMMARY JUDGMENT

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INTRODUCTION

This is an action under the Administrative Procedure Act to set aside the unlawful approval of a new drug application for Mitigare, a single-ingredient 0.6 mg colchicine capsule for the prophylaxis of gout flares. In approving that application, the Food and Drug Administration ("FDA") failed to comply with the statutory provisions governing that application—and failed to require the applicant, Hikma Pharmaceuticals LLC ("Hikma"), to comply with them either. As a result, both FDA and Hikma circumvented the statutory requirement that Hikma provide notice of its application to Takeda Pharmaceuticals U.S.A., Inc. ("Takeda"), the holder of several patents covering the use of colchicine for the prophylaxis of gout flares. Because Takeda had no prior notice of Hikma's confidential application when FDA suddenly approved it on September 26, 2014, Takeda was unable to assert its patents in sufficient time to invoke a 30-month stay of approval and prevent Mitigare from entering the market and eroding sales of Takeda's patented colchicine product, Colcrys®. And because Plaintiffs Elliott Associates, L.P., Elliott International, L.P., and Knollwood Investments, L.P., (collectively, "Plaintiffs") own or benefit from a contractual right in the Colcrys® patents and the right to receive royalties from the sales of Colcrys® during the life of those patents, Plaintiffs have suffered and will continue to suffer injury as a result of FDA's unlawful approval.

FDA's approval of Mitigare was unlawful, arbitrary, and capricious for at least two independent reasons.

First, FDA's approval of Mitigare without requiring Hikma to certify that it was not infringing the Colcrys® patents covering the use of colchicine for the prophylaxis of gout flares violates the plain text of Section 505(b)(2) of the Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 355(b)(2). Section 505(b)(2) explicitly requires an applicant to certify that each patent claiming a use for the drug for which the applicant is seeking approval is either expired, invalid,

or will not be infringed. *Id.* § 355(b)(2)(A). FDA's repository of patents, known as the Orange Book, lists *four patents* owned by Takeda as claiming a "[m]ethod of using colchicine for the prophylaxis of gout flares"—exactly the use for which Hikma sought approval—yet FDA did not require Hikma to certify to those "controlling use patents," as Congress labeled them.[1] And as a result, FDA deprived Takeda of the right to file a patent infringement lawsuit that would have automatically stayed FDA action on Hikma's application for 30 months, during which time Plaintiffs and Takeda could have pursued administrative remedies, and Takeda would not have been forced to defend its patents on a motion for preliminary injunction.[2] FDA's decision to approve Hikma's 505(b)(2) application without complying with the patent certification process was in excess of statutory authority and without observance of procedure required by law.

Second, FDA's approval of Hikma's 505(b)(2) application without requiring a certification to the Colcrys® patents was also arbitrary and capricious. An agency acts arbitrarily and capriciously when it departs from established policy without notice, comment, or reasoned justification—and FDA has done exactly that. Without any prior notice, FDA unreasonably departed from longstanding policy, and violated its own regulation, by:

- failing to require Hikma to certify to patents listed in the Orange Book as claiming the indication for which Hikma was seeking approval;

[1] H.R. Rep. No. 98-857, pt. 1 at 32 (1984) (attached as Exhibit L to Declaration of Matthew D. McGill) [hereinafter House Report].

[2] Ordinarily a patent is entitled to a presumption of validity, 35 U.S.C. § 282, and invalidity must be demonstrated by clear and convincing evidence. *Microsoft Corp. v. i4i Ltd. P'ship*, 131 S. Ct. 2238, 2242 (2011). On a motion for preliminary injunction, these burdens are reversed, and the patentee must establish a substantial likelihood of success on infringement. *See, e.g.*, *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1355-56 (Fed. Cir. 2001). By unlawfully granting approval, FDA stripped the Colcrys® patents of the presumption to which they were entitled.

- failing to prevent Hikma from using the 505(b)(2) pathway to circumvent patent certification requirements that would have applied had Hikma filed an Abbreviated New Drug Application ("ANDA") under Section 505(j) of the FDCA;
- failing to require Hikma to reference the safety and efficacy studies for Colcrys®, the drug most similar to Mitigare, and instead to rely on studies for the unpatented drug Col-Probenecid, which differs from Mitigare in (i) concentration, (ii) approved indication, (iii) active ingredients, and (iv) dosage form; and
- violating its regulation requiring a patent certification where a Section 505(b)(2) applicant seeks approval for an indication claimed by a listed method-of-use patent.

This is not Hikma's first attempt to engineer a stealth approval of Mitigare. FDA has been on notice of Hikma's maneuvering since at least 2011, when FDA rejected Hikma's unlawful attempt to use Section 505(b)(2) to obtain approval of an exact "duplicate" of Colcrys® without certifying to its patents.[3] At that point, Hikma had three options. It could have submitted a comprehensive New Drug Application under Section 505(b)(1), but that would have cost millions of dollars and taken years to complete. It also could have sought approval as a generic "duplicate" of a previously approved drug product, but that would have required Hikma to submit an ANDA under Section 505(j) that relied on Colcrys® as the Reference Listed Drug and contained a certification to the Colcrys® patents.

Hikma chose the third option: It "changed" its product from tablet to capsule and tried Section 505(b)(2) again. But that blatant end-run was no more lawful than Hikma's first, failed attempt. Under settled FDA policy, Hikma was not allowed to use Section 505(b)(2) as an end-

[3] Ltr. from Janet Woodcock, Dir., Ctr. for Drug Evaluation & Research, FDA, to Gary L. Vernon, Sidley Austin LLP 11-12, Docket No. FDA-2010-P-0614 (May 25, 2011) (attached as Exhibit A to Declaration of Matthew D. McGill) [hereinafter Colchicine CP Response].

run around the Colcrys® patents. Hikma was required to reference the "most similar alternative" drug—Colcrys®—and certify to its patents. Section 505(b)(2) is available when an applicant seeks "approval of a *change to an approved drug* that would not be permitted under section 505(j)."[4] Here, it is obvious that the previously "approved drug" was Colcrys® and the "change" was simply from tablet to capsule. Yet, inexplicably, FDA allowed Hikma to pretend that the previously "approved drug" was Col-Probenecid—a drug that differs from Mitigare in four different respects—and the "change[s]" were in the concentration of the active moiety, the composition of the active moieties, the approved indication, and the dosage form. In other words, FDA allowed Hikma to pretend that a 0.6 mg colchicine capsule approved for prophylaxis of gout flares has more in common with (i) a combination tablet of 500 mg of probenecid and 0.5 mg of colchicine indicated for chronic gouty arthritis, than it does with (ii) a 0.6 mg tablet of colchicine indicated for prophylaxis of gout flares. Why did Hikma rely on this dissimilar drug as its reference? Because Col-Probenecid (unlike Colcrys®) has no patents. As a result of FDA's willingness to violate its own policies, Hikma avoided certifying to any patents and kept its infringing product secret from the world until after it was approved.

FDA's action is a textbook example of unprincipled agency decisionmaking and is exactly what the APA was enacted to remedy. FDA's approval of Mitigare should be declared unlawful and set aside.

STATEMENT OF FACTS

This case presents a challenge to FDA final action that violates the plain text of the Hatch-Waxman Amendments to the FDCA and FDA's own longstanding administrative policies.

[4] *See* FDA, *Draft Guidance for Industry: Applications Covered by Section 505(b)(2)*, at 3 (1999), *available at* http://www.fda.gov/downloads/Drugs/Guidances/ucm079345.pdf (emphasis added). A copy of this guidance is provided as Exhibit B to the Declaration of Matthew D. McGill.

A. Statutory Background

The Hatch-Waxman Amendments to the FDCA, Pub. L. 98-417, 98 Stat. 1585, 1593-94 (1984), "sought to strike a balance between incentives, on the one hand, for innovation, and on the other, for quickly getting lower-cost generic drugs to market." *Teva Pharm. Indus. Ltd. v. Crawford*, 410 F.3d 51, 54 (D.C. Cir. 2005). Because development of a new drug product is notoriously "expensive and time-consuming," *Pfizer Inc. v. Shalala*, 182 F.3d 975, 976 (D.C. Cir. 1999), effective incentives for innovation necessarily include statutory protections for the substantial "investments necessary to research and develop new drug products," *Mylan Pharm., Inc. v. FDA*, 454 F.3d 270, 272 (4th Cir. 2006) (internal quotation marks omitted). Having funded those substantial investments here, Plaintiffs bring this action to enforce the statutory protections that Congress has guaranteed.

Under the FDCA, a manufacturer may not sell a new therapeutic drug in interstate commerce without FDA approval. 21 U.S.C. § 355(a). Innovators of novel drug products must file with FDA a New Drug Application ("NDA") containing detailed information about the drug's safety and efficacy (21 U.S.C. § 355(b)(1)) and proposed method of use (21 C.F.R. § 314.53(b)-(c)). The NDA applicant must also identify "the patent number and the expiration date" of any method of use patent "with respect to which a claim of patent infringement could reasonably be asserted." 21 U.S.C. § 355(b)(1)(G). These reporting requirements "encourage broad disclosure and do not require NDA applicants to make an extrajudicial determination of actual infringement." *Bayer Schering Pharma AG v. Lupin, Ltd.*, 676 F.3d 1316, 1325 (Fed. Cir. 2012). FDA lists this patent information in a publication officially known as the *Approved Drug Products with Therapeutic Equivalence Evaluations* and more commonly known as the "Orange Book," which serves as a reference to copiers looking to identify potentially relevant intellectual property. *See Organon, Inc. v. Teva Pharm., Inc.*, 244 F. Supp. 2d 370, 374 n.6 (D.N.J. 2002).

The current version of the Orange Book is available on the FDA website. *See* FDA, Orange Book, http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm (last updated Sept. 2014). For patents claiming a method of using the new drug, FDA also requires innovators to draft and submit a short "use code" describing the claimed method of use that FDA publishes in the Orange Book. 21 C.F.R. § 314.53(c)(2)(ii)(P), (e).

Generic manufacturers seeking to market a duplicate copy of an innovator's proprietary drug can file with FDA an Abbreviated New Drug Application, or ANDA. 21 U.S.C. § 355(j). The ANDA seeks to rely on the innovator's safety and efficacy data by showing that the generic drug "has the same active ingredients as, and is biologically equivalent to, the brand-name drug." *Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 132 S. Ct. 1670, 1676 (2012) (citing 21 U.S.C. § 355(j)(2)(A)(ii), (iv)). The brand-name drug on which the generic applicant relies is known as a Reference Listed Drug, or RLD. Because FDA cannot approve a generic drug that would infringe an innovator's patent, a generic company must include with its ANDA a certification "that its proposed generic drug will not infringe the brand's patents." *Id.* With regard to method-of-use patents, FDA relies exclusively on the innovator's use code when determining whether to approve a proposed generic product. *See id.* at 1677.

A third approval pathway is available where a new prescription drug differs only slightly from a previously approved drug, as is the case, for example, where a new drug has a different dosage form than the previously approved drug. In those cases, the manufacturer may submit a type of NDA governed by Section 505(b)(2) of the FDCA. *See* 21 U.S.C. § 355(b)(2); 21 C.F.R. § 314.54(a). These so-called 505(b)(2) applications allow manufacturers to rely on previous investigations conducted by a prior drug applicant and on published studies and literature—rather than solely the applicant's studies—to establish the safety and efficacy of the new

prescription drug. As with ANDA applicants, a 505(b)(2) applicant must include with its application a certification that its proposed drug will not infringe the patents claiming the drug which was the subject of studies relied upon by the applicant or claiming a use for the drug for which the applicant seeks approval. *See* 21 U.S.C. § 355(b)(2)(A). Moreover, applicants who file a 505(b)(2) certification must also provide notice of that certification to the patent-holder. *See* 21 U.S.C. § 355(b)(3); 21 C.F.R. § 314.52.

These patent certifications and notice provisions are a crucial component of effectuating Congress's intent to spur innovation by granting pioneers statutory exclusivity rights and the ability to defend their patents *before* copies or generic drugs hit the market. Specifically, if a patent-holder who receives notice that their patents are implicated in a 505(b)(2) drug application files a suit for infringement within 45 days of the notice, FDA may *not* approve the 505(b)(2) application for *thirty months*, unless a court orders otherwise. 21 U.S.C. § 355(c)(3)(C). As with ANDAs, FDA relies on use codes to determine whether to approve a 505(b)(2) application that implicates method-of-use patents. *See* 21 C.F.R. § 314.53(c)(2)(ii); *see also Caraco*, 132 S. Ct. at 1684 ("Use codes are pivotal to the FDA's implementation of the Hatch–Waxman Amendments . . . .").

B. Colcrys® (colchicine) 0.6 mg Oral Tablets

Takeda's Colcrys® is the only single-ingredient colchicine product that FDA has designated as an RLD. *See* Colchicine CP Response 12; *see also* McGill Decl., Exhibit C. In July of 2009, FDA approved two 505(b)(2) applications filed by Mutual Pharmaceutical Company ("Mutual")—the company that developed Colcrys® and later was indirectly acquired by Takeda—for Colcrys® oral tablets in 0.6 mg strength: One for the treatment of familial Mediterranean fever (FMF) and another for the treatment of acute gout flares. Colchicine CP Response 5-6; *see also* McGill Decl., Exhibit D. A few months later, FDA approved Mutual's

505(b)(2) application for the use of Colcrys® for the prophylaxis of gout flares. Colchicine CP Response 8.

In its applications, Mutual relied on published literature, a previously-approved listed drug product, and its own clinical trials. Colchicine CP Response 5-8. Before Mutual's applications, FDA had not approved a single-ingredient colchicine product for any indication. As a result of Mutual's work, colchicine was approved for new indications that had not been previously approved for any colchicine product. Mutual thus received numerous patents directed to colchicine and the use of colchicine for various treatments (along with seven years of exclusivity under the Orphan Drug Act for the use in connection with treating FMF and three years of exclusivity for conducting other, additional studies). Seventeen of these patents are listed in FDA's Orange Book for Colcrys®. *See* McGill Decl., Exhibit E. Four of the listed patents—the Colcrys® patents—claim the use of colchicine for the prophylaxis of gout and list in the Orange Book as their use code a "[m]ethod of using colchicine for the prophylaxis of gout flares." *See* McGill Decl., Exhibit E (referencing U.S. Patent No. 7,619,004; U.S. Patent No. 7,820,681; U.S. Patent No. 8,097,655 (the "'655 patent") and; U.S. Patent No. 8,440,722 (the "'722 patent")); McGill Decl., Exhibit H. Thus, any manufacturers who submit ANDAs or 505(b)(2) applications citing to Colcrys® as the RLD or who seek approval for a method of using colchicine for the prophylaxis of gout must certify that their proposed products will not infringe the Colcrys® patents.

C. FDA Approval Of Mitigare

In the fall of 2010, public reports stated that Hikma's U.S. manufacturer, West-Ward Pharmaceutical Corp., had submitted a 505(b)(2) application for a single-ingredient oral colchicine tablet for the prophylaxis of gout flares—a duplicate of Colcrys®. When Mutual did not receive notice of a patent certification, it filed a Citizens Petition with FDA requesting

confirmation that any duplicate version of Colcrys® would need to be submitted as an ANDA, rather than a 505(b)(2) application. *See* Colchicine CP Response 1-2.

In its response, FDA granted Mutual's request and confirmed that West-Ward had inappropriately submitted a 505(b)(2) application for approval of a duplicate version of Colcrys®.[5] *See* Colchicine CP Response 2-3. Specifically, FDA determined that "a marketing application for a colchicine tablet, 0.6 mg, with a proposed indication already approved for Colcrys® is a 'duplicate' of a listed drug and is required to be submitted under section 505(j)" as an ANDA, rather than 505(b)(2). *Id.* at 12. It then explained that "[t]he 505(b)(2) pathway is intended" not for duplicates of listed drugs, but rather "for products that differ from a listed drug," citing its regulation for applications that seek approval of modifications of listed drugs such as "a new indication or new dosage form." *Id.* at 13 (citing 21 C.F.R. § 314.54). Regardless of the pathway used, however, FDA explained that "[b]oth 505(b)(2) and ANDA applicants . . . are required to submit an appropriate patent certification or statement for each patent that claims the listed drug *or a method of using the drug for which the applicant is seeking approval*." *Id.* at 10-11 (emphasis added).

Three years later, without notice to Takeda, FDA approved Hikma's single-ingredient colchicine product, Mitigare, as a 0.6 mg capsule indicated for the prophylaxis of gout flares. *See* McGill Decl., Exhibit I. Rather than resubmit Mitigare as an ANDA, as FDA had recommended, Hikma repackaged Mitigare as a capsule, rather than a tablet, and filed another 505(b)(2) application. It was this new application that the FDA approved on September 26, 2014. Hikma publicly announced the approval on September 30, 2014. *See* McGill Decl., Exhibit J.

[5] FDA also admitted that it had erroneously told Hikma that publicly-available literature establishes that colchicine is safe and effective, and that Col-Probenecid may be used as an RLD in a 505(b)(2) application seeking approval for a duplicate of Colcrys®. Colchicine CP Response 16.

Despite owning 17 Orange Book-listed patents for Colcrys®—four of which are for a "[m]ethod of using colchicine for the prophylaxis of gout"—Takeda never received notice of a patent certification, as required under Section 505(b)(2)(A). Had FDA required Hikma to certify to the Colcrys® patents, Takeda undoubtedly would have sued Hikma for patent infringement, thus triggering the 30-month stay of any FDA approval of Hikma's application. Indeed, just four days after learning of FDA's unlawful approval of Hikma's product, Takeda sued Hikma in federal Court for infringement of the '722 and '655 patents. *See* McGill Decl., Exhibit K.

D. Plaintiffs' Interest

FDA's approval of Mitigare without requiring Hikma to provide a patent certification or public notice has directly and substantially impacted Plaintiffs.

Plaintiffs are the record holder and economic beneficiaries of a contingent value right to receive royalties from the sale of Colcrys® in the United States so long as the Colcrys® patents remain in force. Verified Compl. ¶¶ 15-17, 56. The contingent value right arises from a substantial investment made by Plaintiff Elliott Associates, L.P. in the corporate parent of Mutual, the company that developed Colcrys® and obtained 17 patents for its innovation. *See id.* ¶ 16. Capital investments such as these are commonplace and frequently necessary in the development of innovative and life-improving drugs, an endeavor that involves notoriously "large research and development costs." *Baker Norton Pharm., Inc. v. FDA*, 132 F. Supp. 2d 30, 31 (D.D.C. 2001).[6] Indeed, as a result of its investment and Mutual's innovation, FDA granted Orphan Drug status to Colcrys® for FMF. When Takeda acquired Mutual's parent, Elliott Associates, L.P. negotiated and received the contingent value right in consideration for its investment stake in Mutual's parent. *See* Verified Compl. ¶ 56.

[6] *See also* Matthew Herper, The Truly Staggering Cost Of Inventing New Drugs, *Forbes* (Feb. 10, 2012), http://www.forbes.com/sites/matthewherper/2012/02/10/the-truly-staggering-cost-of-inventing-new-drugs/ (costs of developing a new drug can be "as much as $11 billion").

The value of the contingent value right is substantial. According to Hikma's own reporting, sales of colchicine in the United States are nearly $700 million annually. *See* McGill Decl., Exhibit J. Thus, over the life of the Colcrys® patents, the value of the contingent value right may be hundreds of millions of dollars. FDA's unlawful approval of Mitigare, if not set aside, will greatly diminish or destroy the value of Plaintiffs' contingent value right. Verified Compl. ¶ 23.

STANDARD OF REVIEW

In this APA action, the Court reviews FDA's administrative determination as a legal question, applying on summary judgment the same standards that would govern a Rule 12(b)(6) motion to dismiss. *Depomed, Inc. v. U.S. Dep't of Health & Human Servs.*, --- F. Supp. 2d ----, 2014 WL 4457225, at *7 (D.D.C. Sept. 5, 2014). "'[W]hen a party seeks review of agency action under the APA, the district judge sits as an appellate tribunal,' and '[t]he entire case on review is a question of law.'" *Id.* (quoting *Am. Bioscience, Inc. v. Thompson*, 269 F.3d 1077, 1083 (D.C. Cir. 2001)) (some internal quotation marks omitted); *accord Marshall Cnty. Health Care Auth. v. Shalala*, 988 F.2d 1221, 1226 (D.C. Cir. 1993).

In reviewing a final agency action, courts do not defer to an agency's interpretation of a statute when "Congress has directly spoken to the precise question at issue." *Chevron, USA, Inc. v. NRDC, Inc.*, 467 U.S. 837, 842-43 (1984). Under the familiar two-step analysis, an agency's violation of a clear congressional command must be set aside at *Chevron*'s step one. *See Depomed*, --- F. Supp. 2d ----, 2014 WL 4457225, at *9 (finding "no need to proceed beyond *Chevron*'s step one" where FDA violated the "plain language of the Orphan Drug Act"). "'If the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress.'" *Id.* at *8 (quoting *Chevron*, 467 U.S. at 842-43). And even if the statutory text can be deemed ambiguous, an agency's

action may be set aside at *Chevron*'s step two if the action "'is arbitrary or capricious in substance, or manifestly contrary to the statute.'" *Id.* (quoting *Mayo Found. For Med. Educ. & Research v. United States*, 131 S. Ct. 704, 711 (2011)).

Nor is administrative deference appropriate where the "agency's interpretation conflicts with a prior interpretation, or when it appears that the interpretation is nothing more than a convenient litigating position, or a *post hoc* rationalizatio[n] advanced by an agency seeking to defend past agency action against attack." *Christopher v. SmithKline Beecham Corp.*, 132 S. Ct. 2156, 2166 (2012) (internal citations and quotation marks omitted; alteration in original). An agency's action is arbitrary and capricious when the agency fails to provide a "reasoned explanation for the agency's apparent departure from [its own] precedent." *Friedman v. Sebelius*, 686 F.3d 813, 828 (D.C. Cir. 2012).

SUMMARY OF ARGUMENT

FDA's approval of Hikma's application for Mitigare must be set aside for two independent reasons.

First, the approval of Hikma's 505(b)(2) application for Mitigare violated the plain text of the FDCA's patent certification requirement. Section 505(b)(2)(A) requires that Hikma certify with respect to any patents listed in the Orange Book that "claim[] a use for such drug for which [Hikma] is seeking approval." The four Colcrys® patents are listed in the Orange Book as claiming a "method of using colchicine for the prophylaxis of gout flares"—precisely the drug and use for which Hikma sought and obtained approval—but FDA failed to require that Hikma certify to those patents. Consequently, Takeda was blocked from suing Hikma for patent infringement under the Hatch-Waxman Amendments, and Plaintiffs were unable to pursue administrative remedies during the statutory 30-month stay. In view of the plain text of Section 505(b)(2), as confirmed by its legislative history and the overall statutory scheme, FDA violated

the "unambiguously expressed intent of Congress," *Depomed*, --- F. Supp. 2d ----, 2014 WL 4457225, at *8 (internal quotation marks omitted), and its approval of Hikma's application must be set aside at *Chevron*'s step one. *See* 5 U.S.C. § 706(2)(C). And even if the statute could be deemed ambiguous using traditional tools of construction (which it cannot), FDA's action here is due no deference because it is in violation of their own regulations—which set forth the same interpretation of the statute as advanced by Plaintiffs here—and is manifestly contrary to the statute, therefore failing at *Chevron*'s step two.

Second, in approving Hikma's 505(b)(2) application, FDA arbitrarily and capriciously violated its own longstanding policies without notice or reasoned justification. FDA long has required applicants to certify to patents listed in the Orange Book as claiming the indication for which the applicant was seeking approval—but FDA inexplicably failed to do so here. FDA also has long prevented applicants from using the 505(b)(2) pathway to circumvent certification requirements that would apply in the ANDA context—but FDA again failed to do so here. And FDA long has required 505(b)(2) applicants to rely on the safety and efficacy studies for the previously approved drug most similar to the applicant's drug—but, once again, FDA failed to do so here. In addition, FDA violated its own regulation expressly directing that a 505(b)(2) applicant file a patent certification in exactly the circumstances presented here. Each of these unreasonable departures from longstanding policy and agency regulations is arbitrary and capricious, and further requires that FDA's approval of Mitigare be set aside. *See* 5 U.S.C. § 706(2)(A).

ARGUMENT

I. FDA Violated Congress's Express Command And Clear Intent By Approving Mitigare Without Requiring Hikma To Certify To The Colcrys® Patents

This Court's "review of an agency's procedural compliance with statutory norms is an exacting one." *Natural Res. Def. Council, Inc. v. SEC*, 606 F.2d 1031, 1048 (D.C. Cir. 1979). When an agency acts or interprets a statute "contrary to clear congressional intent," courts owe the agency's interpretation no deference. *Chevron*, 467 U.S. at 843 & n.9; *see also Depomed*, --- F. Supp. 2d ----, 2014 WL 4457225, at *9. Here, the plain text of the Hatch-Waxman Amendments, as confirmed by its detailed legislative history, overall structure, and FDA's own regulations, make abundantly clear that Hikma, in applying for approval of Mitigare, was required to certify to the listed Colcrys® patents. FDA's approval of Hikma's application without these certifications was in excess of its statutory authority and must be vacated under the APA.

A. The Plain Text of Section 505(b)(2) Requires That Hikma Certify To The Colcrys® Patents

1. FDA purported to approve Hikma's application under Section 505(b)(2) of the FDCA, which allows new drug applicants to prove a drug's safety and effectiveness by relying on existing drug investigations that "were not conducted by or for the applicant." *See* 21 U.S.C. § 355(b)(2). Sometimes known as "Paper NDAs"—because they may rely on published drug studies rather than original clinical research—505(b)(2) applications commonly are viewed as a potential alternative to the ANDA approval process for generic "duplicates" of existing drugs. *See Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 676-77 (1990). In light of the close parallel between the 505(b)(2) and ANDA approval pathways, the drafters of the Hatch-Waxman Amendments made clear that Section 505(b)(2) demands the "same" procedural compliance required of ANDA applicants, and may not be used to "circumvent" innovators' listed patents by

filing "sham Paper NDA's" calculated to avoid the patent certification requirement. House Report 33. Thus, "as when filing an ANDA application, a § 505(b)(2) applicant must certify whether its drug will infringe any patents listed in the Orange Book." *Ethypharm S.A. France v. Abbott Labs.*, 707 F.3d 223, 227 (3d Cir. 2013).

Under Section 505(b)(2)(A), an applicant seeking approval for a new drug must certify to each patent listed in the Orange Book "which claims a use for such drug for which the applicant is seeking approval." 21 U.S.C. § 355(b)(2)(A). Here, Hikma sought approval of Mitigare, a single-ingredient colchicine product, for the prophylaxis of gout flares. McGill Decl., Exhibit F; McGill Decl., Exhibit I. There are four patents listed in the Orange Book for a "method of using colchicine for the prophylaxis of gout"—the Colcrys® patents. *See* McGill Decl., Exhibit E; Exhibit H. Accordingly, Hikma was required to include with its application a certification that the Colcrys® patents were either expired (which they were not) or not infringed or invalid. Because Hikma failed to make that certification, FDA's approval of the Mitigare application violated the plain text of the FDCA.

2. No plausible reading of Section 505(b)(2) supports FDA's action. In its briefs in the Takeda action, FDA argues that there was no obligation to certify to the Colcrys® patents because Hikma did not rely on Colcrys® for its safety and efficacy studies, but instead on an unpatented drug known as Col-Probenecid, which (unlike Colcrys®) is a drug product with different active ingredients, different concentration of those ingredients, and approved for a different indication: "the treatment of chronic gouty arthritis when complicated by frequent, recurrent, acute attacks of gout." *See* McGill Decl., Exhibit G; McGill Decl., Exhibit M; Def.'s Opp. to Mot. for Temporary Restraining Order and/or Preliminary Injunction 7, *Takeda Pharm. U.S.A., Inc. v. Burwell*, No. 14-cv-1668 (D.D.C. Oct. 17, 2014), ECF No. 15. Hikma did not

seek approval for an approved indication of a colchicine/probenecid combination (Col-Probenecid); it sought approval for an approved indication of a single-ingredient colchicine drug (Colcrys®). Thus, any method-of-use patents listed for Col-Probenecid (of which there were none) would have been completely irrelevant under the second clause of Section 505(b)(2)(A). In contrast, the Colcrys® method-of-use patents that claimed the precise use of colchicine for which Hikma was seeking approval were dead on.

In seeking to justify FDA's lawless action, Hikma has suggested that the phrase "such drug" in Section 505(b)(2)(A) does not refer to the drug "for which the applicant is seeking approval" (*i.e.*, colchicine), but instead to the "drug for which such investigations were conducted," (*i.e.*, the colchicine/probenecid combination). *See, e.g.*, Hikma Pharm. PLC & West-Ward Pharm. Corp.'s Supp. Br. Opp. Permanent Injunction 13, *Takeda Pharm. U.S.A., Inc. v. Burwell*, No. 14-cv-1668 (D.D.C. Nov. 14, 2014), ECF No. 45. Assuming that to be FDA's unexpressed rationale, FDA is rewriting the statute and is conflating two separate certification requirements in Section 505(b)(2)(A). The first is to each patent "which claims the drug for which such investigations were conducted," the product patents. The second is to each patent "which claims a use for such drug for which the applicant is seeking approval," the method of use patents, or as Congress calls them, "controlling use patents." *See* House Report 32. The focus in the latter instance is on the uses for the drug for which the applicant is seeking approval, not the investigations upon which the applicant relies. Here, there can be no dispute that Hikma was seeking approval for the use of colchicine for the prophylaxis of gout—and Takeda had "controlling use patents" covering the use of colchicine for the prophylaxis of gout. FDA has endorsed this reading in this very litigation. In Takeda's parallel APA lawsuit, FDA explained that a 505(b)(2) applicant "must submit" a certification "for each patent that claims the listed

drug or a method of using *the drug for which the applicant is seeking approval*, and for which information is required to be filed under section 355(b)(1) or 355(c)(2) of the FDCA." *See* Def.'s Opp. to Mot. for a Temporary Restraining Order and/or Preliminary Injunction 5-6, *Takeda Pharm. v. Burwell*, No. 14-cv-1668 (D.D.C. Oct. 17, 2014), ECF No. 15 (emphasis added).

FDA's reading of Section 505(b)(2)(A) not only contravenes the plain statutory text, but it also renders key portions of the statute meaningless and superfluous. *See TRW Inc. v. Andrews*, 534 U.S. 19, 31 (2001) ("It is a cardinal principle of statutory construction that a statute ought, upon the whole, to be so construed that, if it can be prevented, no clause, sentence, or word shall be superfluous, void, or insignificant.") (internal quotation marks omitted). By reading the phrase "such drug" in the second certification requirement ("which claims a use for such drug for which the applicant is seeking approval") to refer only to patents claiming the "drug for which such investigations were conducted," FDA is rendering the latter phrase "for which the applicant is seeking approval," meaningless. In the case at bar, for example, Hikma was not seeking approval of a combination colchicine/probenecid drug, but it relied upon that drug for its investigations. If the combination colchicine/probenecid drug is substituted in for "such drug," as FDA reads the statute, then "for which the applicant is seeking approval" becomes meaningless. In effect, FDA's reading inserts a hard stop after the word "drug" and deletes the language that follows. But that is not the statute that Congress enacted. Instead, Section 505(b)(2)(A) makes unmistakably clear that Congress expected applicants to certify to patents claiming a use for "such drug *for which the applicant is seeking approval*." 21 U.S.C. § 355(b)(2)(A) (emphasis added).

FDA's interpretation is inconsistent with usage elsewhere in the statute. Where Congress wished to refer back to a drug previously mentioned, and to no other drug, it simply used the phrase "such drug" in isolation without any further modification or explanation. For example, Section 505(b)(1) requires the applicant to identify "any patent which claims the drug for which the applicant submitted the application or which claims a method of using *such drug*," with no further modification or explanation. 21 U.S.C. § 355(b)(1) (emphasis added). So, too, in Section 505(a). *See* 21 U.S.C. § 355(a) (forbidding the sale of a new drug in commerce unless there is effective regulatory approval "with respect to such drug"). In contrast, by modifying the phrase "such drug" in Section 505(b)(2)(A) with the additional phrase "for which the applicant is seeking approval," Congress unambiguously conveyed that it was requiring certification to any patents claiming a use for the *applicant's* drug—not those claiming a use for any other drug on which the applicant happens to be relying to prove safety and efficacy. The drug for which Hikma sought approval is colchicine, and Colcrys® is listed in the Orange Book as having patents for a use of colchicine—the prophylaxis of gout flares—that is *identical* to the use for which Hikma is seeking approval. Hikma therefore was required to certify to the Colcrys® patents.[7]

Subparagraph 505(b)(2)(B) makes doubly clear that subparagraph 505(b)(2)(A) necessarily requires applicants to certify to patents claiming uses "for which the applicant is seeking approval"—thereby ruling out any reading that would render that phrase superfluous. Under subparagraph (B), if the applicant is *not* seeking approval for the patented use, then the

[7] Even if FDA's reading could somehow be squared with the statute as a whole—and it cannot—it is at odds with the ordinary usage of "such." The primary definition of "such" is "of a kind or character about to be indicated, suggested, or exemplified," as in "will do ~ things as counsel an immigrant on buying a second-hand car." *Webster's Third New International Dictionary* 2283 (1976). Here, the character of "such drug" to be indicated is "for which the applicant is seeking approval." Accordingly, a plain reading of Section 505(b)(2) is entirely consistent with the ordinary usage of "such."

applicant is required to file a so-called "carve-out" statement to that effect. *See* 21 U.S.C. § 355(b)(2)(B). In other words, subparagraph (B) provides a pathway for the applicant to carve the patented use out of its label if—and only if—the applicant is not seeking approval for that patented use. This carve-out provision would be entirely unnecessary if subparagraph (A) did not otherwise require the applicant to certify to patents claiming an approved use for the drug "for which the applicant is seeking approval." *Id.* § 355(b)(2)(A). Absent any need to certify under subparagraph (A), there would be no need to provide for a carve-out exception under subparagraph (B).

B. The Legislative History Evinces Clear Congressional Intent That 505(b)(2) Applicants Certify To All Patents Claiming A Use Of The Drug For Which Approval Is Sought

An agency's interpretation of a statute must be rejected at *Chevron*'s step one if it "'appears from the statute or its legislative history'" that the interpretation "'is not one that Congress would have sanctioned.'" *Chevron*, 467 U.S. at 845 (quoting *United States v. Shimer*, 367 U.S. 374, 382-83 (1961)). Here, the legislative history confirms that FDA's interpretation is contrary to the statute and FDA's approval of Hikma's application must be set aside.[8]

In reporting on the Hatch-Waxman Amendments, the House Committee on Energy and Commerce spoke with extraordinary foresight and precision to virtually the identical situation presented here. In its Report, the Committee explained that under Section 505(b)(2), "the applicant must certify" with respect to "all product patents which claim the listed drug and all

[8] *See also FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 145-48 (2000) (analyzing legislative history in the first step of the *Chevron* analysis); *Dole v. United Steelworkers of Am.*, 494 U.S. 26, 41-43, 42 n.9 (1990) (same); *I.N.S. v. Cardoza-Fonseca*, 480 U.S. 421, 449 (1987) (determining the intention of Congress using legislative history as one of the "ordinary canons of statutory construction"); *Sierra Club v. EPA*, 551 F.3d 1019, 1027 (D.C. Cir. 2008) ("[T]he court must . . . 'exhaust the traditional tools of statutory construction, including examining the statute's legislative history to shed new light on congressional intent.'") (quoting *Am. Bankers Ass'n v. Nat'l Credit Union Admin.*, 271 F.3d 262, 267 (D.C. Cir. 2001)); *Succar v. Ashcroft*, 394 F.3d 8, 31 (1st Cir. 2005) (analysis of legislative history at the first step of a *Chevron* analysis "is permissible and even may be required"); *Depomed*, 2014 WL 4457225, at *8 (acknowledging that legislative history is a traditional tool of statutory construction).

use patents which claim *an indication for the drug for which the applicant is seeking approval*" in a 505(b)(2) application. House Report 32.[9] The Committee referred to the latter category of patents as "controlling use patent[s]"—those that "claim an indication for the drug for which the applicant is seeking approval." *Id.* Here, Takeda's Colcrys® patents are the "controlling use patents" discussed in the Committee's Report: Each is listed in the Orange Book as claiming the *same* indication (prophylaxis of gout flares) for the *same* drug (colchicine) for which Hikma sought approval. These are exactly the circumstances in which the Hatch-Waxman drafters explained "the applicant must certify" to the listed patents. *Id.* (emphasis added).

The Committee further explained that "in some instances the applicant will have to make multiple certifications with respect to . . . controlling use patents." House Report 32. For example, the Committee explained, when a 505(b)(2) application seeks approval for any already-listed drug (like colchicine) that has multiple indications, a 505(b)(2) application "must also state, when applicable, that the applicant is not seeking approval for an indication which is claimed by any use patent for which it has not made a certification." *Id.* at 33. Thus, where approval is sought for an indication that *is* claimed by one or more listed use patents—such as the Colcrys® patents—the legislative history confirms that applicants must make a certification with respect to those use patents. And even where there may be multiple listed patents claiming the indication for which the applicant is seeking approval, "[t]he Committee intends that the applicant make the appropriate certification for *each* . . . controlling use patent." House Report 32 (emphasis added). Here, Hikma did not certify, and FDA allowed Hikma to circumvent this requirement.

[9] The statutory language discussed in the Committee's Report is identical to the language enacted. *Compare* House Report 7, *with* 21 U.S.C. § 355(b)(2)(A).

The Court need go no further in the legislative history to conclude that the statutory certification requirement should have been enforced here. But if there could be any doubt, the Committee further made clear that those submitting applications under Section 505(b)(2) must "make *the same* certifications regarding patents as mandated in the filing of ANDA's." House Report 32 (emphasis added). To underscore this point, the Committee warned that applicants must make a "good faith effort" to meet the certification requirements and should not "be permitted to circumvent this notice requ[ir]ement by filing sham Paper NDA's." *Id.* at 33. Yet that is precisely what FDA allowed Hikma to do: Circumvent Takeda's statutory notice and patent rights by submitting a "sham" NDA that went to all possible lengths to avoid certifying to the Colcrys® "controlling use patents." *Id.* at 32. Indeed, Hikma baldly *admits* that circumvention of the Colcrys® patents was its goal. *See* McGill Decl., Exhibit O, at 42-43, 47, 64-66, 72 (FDA, the Court, and Hikma all recognizing that Hikma's application was intended to "avoid" or "work around" Colcrys® patents "on purpose"); *see also* Mem. Order 6, *Takeda Pharm. v. West-Ward Pharm.*, No. 14-cv-1268 (D. Del. Oct. 9, 2014), ECF No. 21 (finding that "Hikma has effectively side-stepped the ANDA regime in an effort to get its generic product to market without appropriate legal underpinnings"); Redacted Reply Supp. Mot. Temp. Restraining Order or Prelim. Injunction 10, 12, *Takeda Pharm. v. Burwell*, No. 14-cv-1668 (D.D.C. Oct. 20, 2014), ECF No. 21 (citing administrative record). Hikma's actions are the very definition of a "sham paper NDA[]." House Report 33.

Previously, when Hikma sought approval for a "duplicate" tablet of Colcrys®, FDA determined that Hikma was required to file an ANDA "citing Colcrys® as the basis for ANDA submission" and making the requisite certifications to the Colcrys® patents. *See* Colchicine CP Response 12. Had Hikma taken that advice, Takeda could have asserted its patents and allowed

a federal court to resolve any issues of patent infringement *before* Hikma launched, as Congress intended. Hikma's 505(b)(2) application for a "change" from tablet to capsule without certifying to the Colcrys® patents therefore contravened clearly expressed congressional intent, and FDA's inexplicable approval of that "sham" must be set aside so that Hikma can return to the agency and at last comply with its statutory obligations.

C. The Statutory Scheme Also Requires That Hikma Certify To The Colcrys® Patents

"Statutory construction is a holistic endeavor" requiring consideration of the entire "statutory scheme." *Koons Buick Pontiac GMC, Inc. v. Nigh*, 543 U.S. 50, 60 (2004) (internal quotation marks omitted). Even where a statutory provision "may seem ambiguous in isolation," it "is often clarified by the remainder of the statutory scheme . . . because only one of the permissible meanings produces a substantive effect that is compatible with the rest of the law." *Id.* (internal quotation marks omitted). It is therefore a "fundamental canon of statutory construction that the words of a statute must be read in their context and with a view to their place in the overall statutory scheme." *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133 (2000) (citation omitted). The FDCA in particular must be interpreted in view of its "overriding purpose" to "give the Act the most harmonious, comprehensive meaning possible in light of the legislative policy," rather than "impute to Congress a purpose to paralyze with one hand what it sought to promote with the other." *Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609, 630-32 (1973) (internal quotation marks omitted).

No less than the express statutory text, the overall structure and purpose of the Hatch-Waxman Amendments make clear that Congress intended for applicants like Hikma to certify to patents like those listed for Colcrys®. *See Caraco*, 132 S. Ct. at 1680 (interpreting Section 505 by "consider[ing] statutory text and context together"); *Eli Lilly*, 496 U.S. at 669 (arriving at an

interpretation by examining "the structure of the [Hatch-Waxman] Act taken as a whole"); *see also Util. Air Regulatory Grp. v. EPA*, 134 S. Ct. 2427, 2442 (2014) ("[A]n agency interpretation that is inconsistent with the design and structure of the statute as a whole does not merit deference.") (internal citation and quotation marks omitted).

Under the FDCA, quite sensibly, "FDA cannot authorize a generic drug that would infringe a patent." *Caraco*, 132 S. Ct. at 1676."[10] The Hatch-Waxman Amendments therefore "direct brand manufacturers to file information about their patents" and "provide a description of any method-of-use patent[s]" they own—the so-called use code—for publication in the Orange Book. *Id.* Other companies must then consult the Orange Book to determine if any proposed new drug would implicate an innovator's listed patents. *See id.* And because FDA "lacks both the expertise and the authority to review patent claims" (*id.* at 1676-77 (internal quotation marks and alterations omitted)), the statute requires drug applicants to provide good-faith certifications with respect to any listed patents that *may* be implicated by a 505(b)(2) application and provide notice to relevant patent holders. 21 U.S.C. § 355(b)(2)(A), (b)(3).

The statutory certification is not confined to narrow circumstances where the listed patents indisputably *would* be infringed by the applicant's drug. Rather, as the House Report explains, Congress was concerned with identifying instances in which "a claim of patent infringement *could reasonably* be asserted." House Report 31 (emphasis added). Consistent with this purpose, drug applicants may certify that the listed patents "will not be infringed." 21 U.S.C. § 355(b)(2)(A)(iv). If the patent holder disagrees, it will file a lawsuit within 45 days, thus triggering "a substantial statutory benefit" (*Pfizer*, 182 F.3d at 979)—an automatic 30-month stay of FDA action on the pending application while a federal court resolves the

[10] Patents are a limited property right providing incentives to innovate, *see* U.S. Const. art. I, § 8, cl. 8, and FDA similarly is charged with "advancing the public health by helping to speed innovations," FDA, What We Do (last updated Aug. 5, 2014), http://www.fda.gov/aboutfda/whatwedo/.

infringement question. 21 U.S.C. § 355(c)(3)(C). In all of this, FDA's role is purely "ministerial" (*Caraco*, 132 S. Ct. at 1677 & n.2): Its job is merely to require a patent certification whenever an applicant seeks approval for a drug indication already covered by a listed use code.

These patent protections are integral to the "balance" that Congress struck between providing incentives for investment and innovation and facilitating the entry of low-cost alternatives to brand name drugs. *Teva Pharm.*, 410 F.3d at 54; *see also Mylan Pharm.*, 454 F.3d at 272. In striking that balance, Congress "incorporated an important new mechanism designed to guard against infringement of patents relating to pioneer drugs"—the certification requirement. *Eli Lilly*, 496 U.S. at 676-77. Similarly, Congress believed that the 30-month stay period was also necessary to "fairly balance[] the rights of a patent owner to prevent others from making, using, or selling its patented product and the rights of third parties to contest the validity of a patent or to market a product which they believe is not claimed by the patent." House Report 28.

Section 505(b)(2)'s certification requirement therefore seeks to ensure that innovators can protect their patent rights long before the need for a TRO restraining a potential infringer's threatened launch. Congress sought to provide patentees with timely notice of any applications for new drugs that are *most likely to infringe*. The entire statutory scheme surrounding patent certifications would make little sense if new drug applicants were required to certify only to patents for drugs that are *dissimilar* to the applicant's drug, while circumventing patents for drugs *most similar* to the applicant's drug. FDA itself has acknowledged that the Hatch-Waxman Amendments sought to "provide[] patent protection for the developer of pioneer new drugs by delaying the effective date of approval of an ANDA or 505(b)(2) application until *all*

relevant product and use patents for the pioneer drug have expired, or until the patent owner is notified of, and given an opportunity to litigate, a challenge to such patents." Abbreviated New Drug Application Regulations, 54 Fed. Reg. 28,872, 28,874 (proposed July 10, 1989) (emphasis added). Congress's "scheme will not work, of course, if the holder of the patent pertaining to the pioneer drug is disabled from establishing in court that there has been an act of infringement" by reason of the patent-holder never receiving the notification of the application because the applicant circumvented the statute's notification requirements. *Eli Lilly*, 496 U.S. at 678. That is why Congress sensibly determined that certification is required for all controlling use patents "claim[ing] a use" for "such drug for which the applicant is seeking approval" (21 U.S.C. § 355(b)(2)(A))—the very patents most likely to be implicated by the new drug application.

Here, FDA apparently would read Section 505(b)(2) to require Hikma to file a certification only if there were patents covering Col-Probenecid—a combination drug differing in significant respects from Mitigare and thus not at all likely to present any infringement issues. *See infra* at 32-33. Even if that reading were supported by the text (and it is not), it would limit the statutory patent protections to *less relevant* patents—an absurd construction of Section 505(b)(2) that clearly was not Congress's intent. Only an interpretation that requires certification to the most relevant patents is consistent with the "overriding purpose" and "legislative policy" of the Hatch-Waxman Act (*Weinberger*, 412 U.S. at 630-32), and only this interpretation "produces a substantive effect that is compatible with the rest of the law" (*Nigh*, 543 U.S. at 60). As is evident from the overall statutory structure of the FDCA, Congress intended the protections afforded by the certification and notice process to apply to the patents most likely to be infringed by a new drug—here, the Colcrys® patents.

D. FDA's Approval Of Mitigare Is Owed No Deference Because It Contravenes FDA's Own Regulations And Is Manifestly Contrary To The FDCA

Even if the statute's text, history, and overall scheme were all ambiguous (they are not), any FDA *post hoc* interpretation commands no deference because FDA's own regulations—the only reasoned decisionmaking that is due deference in this case—adopt the same interpretation of Section 505(b)(2) as Plaintiffs. *See Christopher*, 132 S. Ct. at 2166 (courts should not defer when an "agency's interpretation conflicts with a prior interpretation, or when it appears that the interpretation is nothing more than a convenient litigating position, or a *post hoc* rationalizatio[n] advanced by an agency seeking to defend past agency action against attack" (internal citations and quotation marks omitted; alteration in original)); *Bowen v. Georgetown Univ. Hosp.*, 488 U.S. 204, 213 (1988) ("We have never applied the principle of [*Chevron* deference] to agency litigating positions that are wholly unsupported by regulations, rulings, or administrative practice. . . . Deference to what appears to be nothing more than an agency's convenient litigating position would be entirely inappropriate."); *Yakubova v. Chertoff*, No. 06-cv-3203, 2006 WL 6589892, at *3 (E.D.N.Y. Nov. 2, 2006) (because agency's position in litigation "is contrary to its own regulations, deference is not appropriate" (citation omitted)).

Under FDA regulations addressing certifications to method-of-use patents in 505(b)(2) applications, "[i]f the labeling of the drug product for which the applicant is seeking approval includes an indication that, according to the patent information submitted under section 505(b) or (c) of the act and § 314.53 or in the opinion of the applicant, is claimed by a use patent, the applicant shall submit an applicable certification under paragraph (i)(1)(i) of this section." 21 C.F.R. § 314.50(i)(1)(iii)(B). Here, Hikma's label has one indication: "MITIGARE™ is indicated for prophylaxis of gout flares." McGill Decl., Exhibit N, at 1. According to the Orange Book, which publishes the patent information submitted under section 505(b) and (c),

this indication is claimed by the Colcrys use patent. *See* McGill Decl., Exhibit E (listing Colcrys® use patents for use code 1020); McGill Decl., Exhibit H (defining use code 1020 as "method for using colchine for the prophylaxis of gout flares"). There can be no question, therefore, that FDA's official interpretation of Section 505(b)(2)—in accordance with Plaintiffs' interpretation—required certification to the Colcrys® patents and that FDA violated its own regulations by accepting Hikma's application without those required certifications. Finally, FDA's approval decision should be given no deference but rather should be set aside because it was "manifestly contrary to the statute." *Chevron*, 467 U.S. at 844.

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Using the "traditional tools of statutory construction" (*Chevron*, 467 U.S. at 843 n.9), Congress's intent is clear: Section 505(b)(2)(A) requires Hikma to certify to the Colcrys® patents because each "claims a use for such drug for which [Hikma] is seeking approval." 21 U.S.C. § 355(b)(2)(A). FDA regulations confirm this reading, and any FDA interpretation that allows circumvention of the Colcrys® patents would not be "a permissible construction of the statute." *Chevron*, 467 U.S. at 843. Had Hikma certified to the Colcrys® patents, a federal court could have resolved the infringement question *before* FDA approved Hikma's application and Hikma was poised to launch. And during the statutory 30-month stay on FDA action, Plaintiffs could have sought administrative remedies—for example, by filing a Citizen Petition—and Takeda would not have been prejudiced in asserting its patents. FDA's unlawful decision to allow Hikma to circumvent the certification requirement robbed Plaintiffs of these rights and plainly exceeded the agency's statutory authority in violation of the APA. *See* 5 U.S.C. § 706(2)(C).

II. FDA Acted Arbitrarily And Capriciously In Departing From Its Longstanding Policy And Its Own Regulations Without Notice And Reasoned Justification

The APA also authorizes a court to set aside a final agency action that is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). An agency acts arbitrarily and capriciously when it "fail[s] to explain its departure from the agency's own precedents," *Friedman v. Sebelius*, 686 F.3d 813, 828 (D.C. Cir. 2012), or where its actions reflect a "want of reasoned decisionmaking," *Fox v. Clinton*, 684 F.3d 67, 80 (D.C. Cir. 2012). *See also, e.g.*, *Lone Mtn. Processing, Inc. v. Sec'y of Labor*, 709 F.3d 1161, 1164 (D.C. Cir. 2013) (finding action arbitrary and capricious where agency "failed to even mention or discuss, let alone distinguish" prior orders).

In approving Hikma's 505(b)(2) application without a certification to the Colcrys® patents, FDA departed from its longstanding policy in at least three respects. *First*, FDA failed to prevent Hikma from using the 505(b)(2) pathway as a means of circumventing patent certification requirements that would have applied had Hikma filed an ANDA under Section 505(j). *Second*, FDA failed to require Hikma to reference Colcrys®, the most similar analog to Mitigare, and instead to rely on studies for Col-Probenecid, which differs from Mitigare in four respects. *Third*, FDA failed to require Hikma to certify to patents listed in the Orange Book as claiming the precise indication for which Hikma was seeking approval. Compounding these departures, FDA also violated its own regulation requiring that a 505(b)(2) applicant submit a patent certification in precisely these circumstances. Each of these departures lacked prior warning or reasoned justification. And each was arbitrary and capricious in violation of the APA.

A. FDA Arbitrarily And Capriciously Violated Its Policies Prohibiting 505(b)(2) Applicants From Circumventing The Patent Certification Requirement By Failing To Reference The Most Similar Listed Drug

The approval of Hikma's application departed sharply from FDA's longstanding policy prohibiting 505(b)(2) applicants from circumventing the FDCA's patent certification requirements, and its related policy of requiring applicants to reference the most similar listed drug. Worse, FDA provided no reasoned justification for those sudden and troubling departures. "'[A]n agency's unexplained departure from precedent *must* be overturned as arbitrary and capricious.'" *Eagle Broad. Grp., Ltd. v. FCC*, 563 F.3d 543, 551 (D.C. Cir. 2009) (emphasis added) (quoting *Comcast Corp. v. FCC*, 526 F.3d 763, 769 (D.C. Cir. 2008)); *see also Am. Bioscience, Inc. v. Thompson*, 269 F.3d 1077, 1084, 1085 (D.C. Cir. 2001) (FDA acted arbitrarily in departing from "longstanding policy" with "no forthright justification").

1. Prior to its approval of Hikma's application, FDA expressly prohibited applicants from using the 505(b)(2) pathway to shirk statutory obligations that apply to ANDA applicants. For example, FDA's response to the 2004 Fenofibrate Citizens Petition flatly rejected the type of circumvention that FDA blessed here.[11] In its response, FDA explained that the FDCA's patent certification provisions "ensure that the 505(b)(2) applicant does not use the 505(b)(2) process to end-run the patent protections that would have applied had an ANDA been permitted." *Id.* at 9. FDA provided the following example in the analogous ANDA context:

> [I]f a tablet and a capsule are approved for the same moiety with patents listed for the tablet and none listed for the capsule, an ANDA applicant seeking approval for a tablet should cite the approved tablet as the reference listed drug. It should not circumvent the patents on the tablet by citing the capsule as the reference listed drug and filing a suitability petition under section 505(j)(2)(C) of the Act and 21 CFR 314.93 seeking to change to a tablet dosage form.

[11] *See* Ltr. from Steven J. Galson, Acting Dir., Ctr. for Drug Evaluation and Research, FDA, to Donald O. Beers, Arnold & Porter LLP, and William F. Cavanaugh, Jr., Patterson, Belknap, Webb & Tyler LLP, Docket No. 2004P-0386/CP1 & RC1 (Nov. 30, 2004) (attached as Exhibit P to Declaration of Matthew D. McGill) [hereinafter Fenofibrate CP Response].

Id. at 9 n.13. This policy against allowing applicants to end-run the FDCA's certification provisions, FDA explained, "ensures that patent certification obligations for 505(b)(2) applications and for ANDAs are parallel." *Id.* at 10. FDA's policy tracked the legislative history explaining that the changes to Section 505(b)(2) "require an applicant filing a Paper NDA[] for a listed drug under section [505(b)(2)] to make the same certifications regarding patents as mandated in the filing of ANDA's under new subsection (j)." House Report 32.

FDA more recently reiterated its longstanding anti-circumvention policy in the 2013 Suboxone Citizen Petition Response.[12] There, FDA announced that it remained the agency's policy to prevent "applicants from using the 505(b)(2) pathway to avoid patent protections that would have applied had the application been submitted [as an ANDA] under section 505(j)." Suboxone CP Response 4. FDA also reaffirmed its prior admonition that, in the parallel ANDA context, an applicant may not end-run the certification requirement by using as its reference listed drug a less appropriate, unpatented drug in lieu of a more appropriate, patented drug. *See id.* at 8 (quoting Fenofibrate CP Response 9 n.13).

Despite this policy, an "end-run" is exactly what FDA allowed Hikma to do here. If Hikma sought approval for its Mitigare product by filing an ANDA under Section 505(j), it would have been required to reference Colcrys®, which is the RLD.[13] Hikma also could have filed a "suitability petition" to change the dosage form from tablet to capsule. A "suitability petition" allows an ANDA applicant to request permission to seek approval for a drug product

[12] *See* Ltr. from Janet Woodcock, Dir., Ctr. for Drug Evaluation & Research, FDA, to David B. Clissold, Hyman, Phelps & McNamara, P.C., Docket Nos. FDA-2011-P-0869 & FDA-2013-P-0995 (Sept. 18, 2013) (attached as Exhibit Q to Declaration of Matthew D. McGill) [hereinafter Suboxone CP Response].

[13] Several generic drug manufacturers did exactly that. Because those applicants were required to certify to Takeda's patents for colchicine, Takeda was afforded the opportunity to file pre-approval infringement lawsuits under the Hatch-Waxman Amendments. *See Takeda Pharm. U.S.A. Inc. v. Par Pharm. Cos.*, No. 13-cv-1524 (D. Del. filed Aug. 30, 2013); *Takeda Pharm. U.S.A. Inc. v. Amneal Pharm. LLC*, No. 13-cv-1729 (D. Del. filed Oct. 21, 2013); *Takeda Pharm. U.S.A. Inc. v. Watson Labs. Inc.*, No. 14-cv-268 (D. Del. filed Feb. 27, 2014). FDA did not allow those ANDA applicants to circumvent the patent certification requirement, as it allowed Hikma to do here.

"that is not the same as a listed drug with respect to certain characteristics," such as dosage form. McGill Decl., Exhibit R; *see also* 21 C.F.R. § 314.93(b). Had Hikma filed an ANDA and a suitability petition, FDA would have required Hikma to certify to the Colcrys® patents. *See* Fenofibrate CP Response 9 n.13 (ANDA applicant "should not circumvent the patents on the tablet by citing the capsule as the reference listed drug and filing a suitability petition under section 505(j)(2)(C) of the Act and 21 CFR 314.93 seeking to change to a tablet dosage form"). As FDA has explained, that approach is necessary in "ensur[ing] that patent certification obligations for 505(b)(2) applications and for ANDAs are parallel." *Id.* at 10. Instead, by allowing Hikma to use the 505(b)(2) pathway in a way that decidedly was ***not*** parallel to the ANDA pathway, FDA violated its own policy. The need for certification in the ANDA context is no different in the 505(b)(2) context, because 505(b)(2) applicants must "make the same certifications regarding patents as mandated in the filing of ANDA's." House Report 32.

FDA knows of and expressly referenced the Colcrys® patents in its 2011 response to the Citizens Petition filed by Mutual. *See* Colchicine CP Response at 8. In that response, FDA acknowledged that West-Ward had previously submitted an erroneous 505(b)(2) application seeking approval to market an exact copy of Colcrys® albeit without complying with the statutory requirements governing ANDA applications. *See id.* at 11-12, 17 (noting that Hikma's U.S. manufacturer sought approval for a "colchicine tablet, 0.6 mg, with a proposed indication already approved for Colcrys"). Hikma's response to that letter was to reformulate its product from tablet to capsule, so that it was no longer a "duplicate drug," and resubmit its 505(b)(2) application for a 0.6 mg single-ingredient colchicine product. Notwithstanding this superficial change, it is obvious that the reference drug is still Colcrys®. Hikma's actions plainly were calculated to circumvent Section 505(b)(2)'s certification requirement. Once again, FDA's

abrupt departure from its longstanding anti-circumvention policy—with no notice, comment, or reasoned justifications—"lacks any coherence" and must be set aside. *Tripoli Rocketry Ass'n, Inc. v. Bureau of Alcohol, Tobacco, Firearms, & Explosives*, 437 F.3d 75, 77 (D.C. Cir. 2006).

2. Relatedly, FDA also violated agency policy by allowing Hikma to avoid referencing the most similar drug with the most current safety and efficacy data. Under longstanding FDA policy, applicants do not have unfettered discretion to choose any prior drug as the reference listed drug. Many prior drugs simply are inappropriate as a point of reference because they involve different active ingredients or different indications. Safety and efficacy studies on aspirin for the treatment of headaches, for example, provide little if any insight into the safety and efficacy of colchicine for the prophylaxis of gout flares.

In its 2004 Fenofibrate Citizen Petition Response, FDA announced that 505(b)(2) applicants should reference the "drug . . . most similar to the drug for which approval is sought." *Id.* at 9-10 & n.13. FDA also sought to distinguish *Marion Merrell Dow, Inc. v. Hoechst-Roussel Pharmaceuticals, Inc.*, No. 93-5074, 1994 WL 424207 (D.N.J. May 5, 1994), on the ground that the applicant in that case "failed to certify to patents on [the] pharmaceutical equivalent." Fenofibrate CP Response 10 n.15. Where the applicant "has certified to the patents on the product that is most similar to its own," FDA explained, "there can be no argument" that the applicant "used the 505(b)(2) process to circumvent patent certification obligations." *Id.* at 10-11 n.15. Here, however, FDA allowed Hikma to use as its reference listed drug Col-Probenecid—an unpatented combination drug product indicated for the treatment of chronic gouty arthritis when complicated by frequent, recurrent, acute attacks of gout—while failing to require Hikma to reference Colcrys® and certify to Takeda's patents listed for the use of colchicine for the prophylaxis of gout flares. Col-Probenecid obviously is not the "drug . . . most

similar to the drug for which approval is sought." Fenofibrate CP Response 9-10 & n.13. Colcrys® is.

Nor is it plausible that Col-Probenecid was the "most appropriate" drug for Hikma to reference (*see* Suboxone CP Response 8) when Mitigare is a virtual duplicate of Colcrys®. Had FDA adhered to its longstanding policy of requiring 505(b)(2) applicants to use the "most similar" (or even the "most appropriate") listed drug as the reference, it could not have approved Hikma's admitted effort to circumvent the statutory certification requirement by referencing a two-ingredient, 0.5 mg, colchicine-probenecid tablet indicated for the treatment of gouty arthritis. Instead, FDA acted as a witting partner in Hikma's chicanery—even going so far as to meet with Hikma in 2011 to devise a scheme to subvert Takeda's patents. *See, e.g.*, Def.'s Opp. to Mot. for a Temporary Restraining Order and/or Preliminary Injunction, at FDA00118, *Takeda Pharm. v. Burwell.*, No. 14-cv-1668 (D.D.C. Oct. 17, 2014), ECF No. 15-1 (describing FDA's 2011 "agreement" with Hikma on its development plan). For this additional reason, FDA's approval of Mitigare must be set aside as arbitrary and capricious.

B. FDA Arbitrarily And Capriciously Violated Its Policy Requiring 505(b)(2) Applicants To Certify With Respect To Patents Claiming The Indication For Which Approval Is Sought

Not only does the statute require Hikma to certify to the method of use patents that claim a use for colchicine, but longstanding FDA policy makes clear that patents claiming the indication for which approval is sought must be addressed through the certification process.

A drug's "'indication' refers generally to what a drug does." *Caraco*, 132 S. Ct. at 1683 n.7; *see also* 21 C.F.R. § 201.57(c)(2). FDA's regulation governing the information that must be listed in the Orange Book uses the terms *indication* and *approved method of use* interchangeably, and thus "ties information about indications to patent coverage." *Caraco*, 132 S. Ct. at 1683 n.7. For example, FDA requires patent holders to provide for publication in the Orange Book "a

description of each approved method of use or indication and related patent claim of the patent being submitted"—a use code. 21 C.F.R. § 314.53(c)(2)(ii)(P)(1); *see also id.* § 314.53(c)(2)(ii)(P)(3) (requiring a "description of the patented method of use as required for publication"); *id.* 21 C.F.R. § 314.53(e) ("[F]or each use patent," FDA will publish "the approved indications or other conditions of use covered by a patent."). FDA has long understood the significance of information in the Orange Book about patents covering a drug's approved method of use being tied to that drug's approved indication—here, the prophylaxis of gout flares. *See Caraco*, 132 S. Ct. at 1683 n.7.

FDA's longstanding interpretation tying a patented method of use to the drug's indication makes perfect sense as a matter of well-reasoned agency policy. A patented method of use, after all, simply claims a particular way of using a drug to achieve a novel and useful therapeutic effect in patients. And that is similarly what FDA requires under the "Indications" section of a drug's label, which must state that "the drug is indicated for the treatment, prevention, mitigation, cure, or diagnosis of a recognized disease or condition, or of a manifestation of a recognized disease or condition, or for the relief of symptoms associated with a recognized disease or condition." 21 C.F.R. § 201.57(c)(2). It would be anomalous and contrary to the FDCA's text and purpose to allow an ANDA or 505(b)(2) applicant to seek approval for a particular indication, but not certify to the patents listed in the Orange Book as claiming the identical approved method of use. In fact, as explained in Section I.D, FDA's own regulations require patent certifications when "the labeling of the drug product for which the applicant is seeking approval includes an indication that . . . is claimed by a use patent" in the Orange Book. 21 C.F.R. § 314.50(i)(1)(iii)(B).

Hikma sought and obtained approval for a 0.6 mg single-ingredient colchicine capsule indicated for the prophylaxis of gout flares. Each of the four Colcrys® patents is listed in the Orange Book with the use code for a "[m]ethod of using colchicine for the prophylaxis of gout flares." *See* McGill Decl., Exhibit E (referencing U.S. Patent No. 7,619,004; U.S. Patent No. 7,820,681; U.S. Patent No. 8,097,655; U.S. Patent No. 8,440,722); McGill Decl., Exhibit H. Hikma could have sought approval for some new indication or some indication that was not covered by the Colcrys® patents. Hikma could have also challenged the Takeda use code as "sweep[ing] more broadly" than Takeda's method of use patents—an action that would require Hikma to bring a claim or counterclaim (publicly) in litigation. *Caraco*, 132 S. Ct. at 1683 n.7; *see also* 21 U.S.C. § 355(c)(3)(D)(ii) (allowing applicant to seek a judicial order to correct a use code). Hikma did neither. Instead it sought approval for an indication that was claimed by Takeda's method of use patents, which according to FDA policy, required Hikma to certify to those patents. Thus, FDA was barred under its longstanding policy from approving Hikma's application without the required certification.

Neither Takeda nor Plaintiffs received prior notice that FDA was considering departing from its longstanding policy on indications. Indeed, Plaintiffs negotiated and obtained their contingent value right in reliance on that established policy. Had FDA provided timely notice, Plaintiffs could have taken immediate action to protect their interests at the agency level—for example, by filing a Citizen Petition setting forth reasons why FDA's longstanding policy is compelled by the FDCA and its legislative history. Instead, FDA's abrupt about-face was announced after the fact, thereby denying the public a voice in the administrative proceedings and forcing Plaintiffs to file this lawsuit in the face of Hikma's impending, unlawful launch. *See, e.g.*, *In re Long-Distance Tel. Serv. Fed. Excise Tax Refund Litig.*, 751 F.3d 629, 637 (D.C.

Cir. 2014) ("Standing alone, a notice and comment violation establishes that the government's conduct was arbitrary and capricious."). FDA's unexplained departure from longstanding policy, made without prior notice and comment, is arbitrary and capricious. *See, e.g.*, *Nat'l Ass'n of Regulatory Util. Comm'rs v. U.S. Dep't of Energy*, 680 F.3d 819, 825 (D.C. Cir. 2012) ("an unexplained departure from long-standing Department policy" is "arbitrary and capricious").

C. FDA Arbitrarily And Capriciously Violated Its Own Regulation, Which Sets Forth The Same Interpretation Advanced By Plaintiffs Here

"It is 'axiomatic' . . . 'that an agency is bound by its own regulations.'" *Nat'l Envtl. Dev. Association's Clean Air Project v. EPA*, 752 F.3d 999 (D.C. Cir. 2014) (quoting *Panhandle E. Pipe Line Co. v. FERC*, 613 F.2d 1120, 1135 (D.C. Cir. 1979). An agency may, of course, amend or repeal its regulations (*see id.*)—but it is "'*not* free to ignore or violate its regulations while they remain in effect.'" *Id.* (quoting *U.S. Lines, Inc. v. Fed. Mar. Comm'n*, 584 F.2d 519, 526 n.20 (D.C. Cir. 1978)) (emphasis added). When an agency fails to comply with its own regulations, its action will be set aside as arbitrary and capricious. *Id.*; *see also Dithiocarbamate Task Force v. EPA*, 98 F.3d 1394, 1398-1402 (D.C. Cir. 1996).

As discussed above, *see supra* Part I.D., FDA's regulation governing the content of Rule 505(b)(2) applications plainly adopts the interpretation that Plaintiffs advance here. Specifically, if the labeling of the "drug product for which the applicant is seeking approval includes an indication that . . . is claimed by a use patent, *the applicant shall submit an applicable certification* under paragraph (i)(1)(i) of this section." 21 C.F.R. § 314.50(i)(1)(iii)(B) (emphasis added). FDA violated this regulation in approving Hikma's application for Mitigare without requiring a patent certification. Accordingly, FDA's action must be set aside as arbitrary and capricious.

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The Hatch-Waxman Amendments to the FDCA reflect an intricate balance between the rights of pharmaceutical innovators who market patented drug products and manufacturers who seek to sell competing drugs that would infringe the innovator's patents. At the fulcrum of that balance is the FDCA's certification provisions, which ensure that innovators and their investors have the means to protect their patents—and profits—before a generic competitor is already on the market. Those profits, in turn, supply the capital for further innovation and investment that fuels pharmaceutical research and improves healthcare for all patients. "Lesser profits" mean "less research on new drugs." *Glaxo Operations UK Ltd. v. Quigg*, 894 F.2d 392, 396 (Fed. Cir. 1990).

Plaintiffs' substantial investment in Mutual provided critical capital for drug development in exchange for valuable rights. And Plaintiffs negotiated that investment in the expectation that FDA would enforce the certification provisions of the FDCA (as it did in the 2011 Colchicine CP Response) and adhere to its longstanding policies prohibiting 505(b)(2) and ANDA applicants from deploying creative workarounds to circumvent Takeda's listed patents. FDA's unlawful approval of Mitigare, if not set aside, would blaze a pathway for similar tactics in the future, deter investment in drug innovation, and upset the balance that Congress struck in the FDCA.

CONCLUSION

For the foregoing reasons, Plaintiffs respectfully request that this motion for summary judgment be granted, and that the Court hold unlawful and set aside FDA's approval of Mitigare.

Respectfully Submitted,

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