**ORAL ARGUMENT NOT YET SCHEDULED**
Nos. 15-5021 and 15-5022 (consolidated)

**IN THE UNITED STATES COURT OF APPEALS**
**FOR THE DISTRICT OF COLUMBIA CIRCUIT**

TAKEDA PHARMACEUTICALS U.S.A., INC., and
ELLIOTT ASSOCIATES, L.P., ELLIOTT INTERNATIONAL, L.P.,
and KNOLLWOOD INVESTMENTS, L.P.,

*Plaintiffs-Appellants*,

v.

SYLVIA MATHEWS BURWELL, in her official capacity as Secretary,
U.S. 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-Appellees.*

HIKMA PHARMACEUTICALS PLC and
WEST-WARD PHARMACEUTICALS CORP.,

*Intervenor-Defendants-Appellees.*

On Appeal From The United States District Court For The District Of Columbia
Case Nos. 14-cv-1668 (KBJ) and 14-cv-1850 (KBJ)

# OPENING BRIEF FOR APPELLANTS ELLIOTT ASSOCIATES, L.P., ELLIOTT INTERNATIONAL, L.P., AND KNOLLWOOD INVESTMENTS, L.P.

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## CERTIFICATE AS TO PARTIES, RULINGS, AND RELATED CASES

Pursuant to D.C. Circuit Rule 28(a)(1), Plaintiffs-Appellants state as follows:

**(A) Parties and Amici:**

The parties in this Court's Case Nos. 15-5021 and 15-5022 are Plaintiff-Appellant Takeda Pharmaceuticals U.S.A., Inc. ("Takeda"); Plaintiffs-Appellants Elliott Associates, L.P., Elliott International, L.P., and Knollwood Investments, L.P. (together, the "Elliott Appellants"); Defendant-Appellee Sylvia Mathews Burwell, in her official capacity as Secretary, United States Department of Health and Human Services; Defendant-Appellee Margaret Hamburg, M.D., in her official capacity as Commissioner of Food and Drugs, Food and Drug Administration ("FDA"); Intervenors-Defendants-Appellees Hikma Pharmaceuticals PLC and West-Ward Pharmaceuticals Corp. (together, "Hikma"); and Pharmaceutical Research and Manufacturers of America (PhRMA), as amicus curiae in support of Appellants.

**(B) Rulings Under Review:**

The Elliott Appellants seek review of the following orders of the district court (Jackson, J.): (1) the Order entered on January 9, 2015 denying the Elliott Appellants' Motion for Summary Judgment and granting Appellees' and Intervenors-Defendants-Appellees' Cross-Motions for Summary Judgment (Case No. 14-

cv-1668, D.E.68); (2) the Memorandum Opinion entered on January 12, 2015 (Case No. 14-cv-1668, D.E. 74; Case No. 14-cv-1850, D.E. 16); (3) the Order entered on January 15, 2015 dismissing Takeda's complaint (Case No. 14-cv-1668, D.E. 77); and (4) all other orders and rulings adverse to the Elliott Appellants in these consolidated cases.

**(C) Related Cases:**

Several of Takeda's U.S. patents, to which this lawsuit contends Hikma was required to certify, are the subject of patent infringement litigation pending in the Federal Circuit as *Takeda Pharmaceuticals U.S.A., Inc. v. Hikma Americas Inc.*, Nos. 15-1139 and 15-1142 (Fed. Cir.). There are no other related cases.

/s/ Michael A. Sitzman
Michael A. Sitzman

## RULE 26.1 DISCLOSURE STATEMENT

Pursuant to Federal Rule of Appellate Procedure 26.1 and this Court's Rule 26.1, the Elliott Appellants state as follows:

Elliott Associates, L.P. is a Delaware limited partnership that has no publicly held parent, and no publicly held entity controls or owns 10% or more of Elliott Associates, L.P.

Elliott International, L.P. is a Cayman Islands limited partnership that has no publicly held parent, and no publicly held entity controls or owns 10% or more of Elliott International, L.P.

Knollwood Investments, L.P. is a Delaware limited partnership that has no publicly held parent, and no publicly held entity controls or owns 10% or more of Knollwood Investments, L.P.

The Elliott Appellants 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® use patents remain in force.

/s/ Michael A. Sitzman
Michael A. Sitzman

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## GLOSSARY

| | |
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| ANDA | Abbreviated New Drug Application |
| APA | Administrative Procedure Act |
| FDA | Food and Drug Administration |
| FDCA | Food, Drug, and Cosmetic Act |
| NDA | New Drug Application |
| RLD | Reference-Listed Drug |

## INTRODUCTION

This is an action under the Administrative Procedure Act to set aside FDA's approval of Hikma's new drug application for "Mitigare" for failing to comply with the Food, Drug, and Cosmetic Act and FDA regulations requiring Hikma to certify that Mitigare would not infringe Takeda's patents. Six years ago, FDA approved Colcrys®—Takeda's novel single-ingredient, 0.6 mg colchicine drug product for the prophylaxis of gout flares. Takeda holds several patents covering the use of colchicine for the prophylaxis of gout flares (the "Colcrys® use patents"). Looking to seize this market with a generic equivalent and circumvent the Colcrys® use patents, Hikma filed an application under Section 505(b)(2) of the FDCA for a single-ingredient, 0.6 mg colchicine drug product for the prophylaxis of gout flares called Mitigare. The only change Hikma made was to put Mitigare in a capsule instead of a tablet, like Colcrys®.

Section 505(b)(2) of the FDCA provides a shortcut for applicants seeking to avoid the expensive safety and efficacy studies required for new drug applications. But that shortcut comes with obligations: Under Section 505(b)(2) and FDA's implementing regulations, Hikma was required to certify that Mitigare would not infringe Takeda's patents and notify Takeda of that certification—an act that would expose Hikma to patent infringement litigation and an automatic 30-month stay of its application. Hikma failed to honor the statutory quid pro quo and provide the

required certification; FDA therefore should have denied the application as incomplete.

Instead, FDA approved Hikma's application without a certification. Worse, the district court upheld FDA's tortured reading of the statute, ignoring the incontrovertible fact that Hikma sought approval for a use of colchicine covered by Takeda's patents, and dismissed in a footnote FDA's binding regulation requiring patent certifications in these precise circumstances. That was error: Section 505(b)(2) and FDA's regulation are not rendered legal nullities by the trivial difference between tablets and capsules.

If not reversed, the district court's judgment will fundamentally upset the balance embodied in the patent certification requirement: protection of intellectual property rights for innovators' drugs in exchange for a regulatory shortcut for non-infringing copies. The Elliott Appellants (through their affiliates) made a sizeable investment in the substantial efforts to obtain FDA approval for the safe and effective use of Colcrys® and in return received valuable contractual rights. The district court's crabbed interpretation of the certification requirement undermines those contractual rights and destroys the benefits afforded to an innovator that risked tens of millions of dollars and committed years of diligence to improving the safety profile of a dangerous drug.[1]

[1] Colchicine, the sole active ingredient in both Colcrys® and Mitigare, was

The district court's judgment should be reversed and FDA's approval of Mitigare should be set aside.

## JURISDICTIONAL STATEMENT

The district court had jurisdiction pursuant to 28 U.S.C. §§ 1331, 1361, and 2201-2202. The case arises under the Food Drug and Cosmetic Act, 21 U.S.C. § 301 *et seq.*, and the Administrative Procedure Act, 5 U.S.C. §§ 701-706. The district court entered final judgment in favor of the Appellees and Intervenors-Defendants-Appellees on January 15, 2015. JA98.

This Court has jurisdiction over this appeal from the final decision of the district court pursuant to 28 U.S.C. § 1291. The Elliott Appellants timely appealed on January 20, 2015. JA17 (ECF 83).

## STATUTES AND REGULATIONS

The text of relevant statutes and regulations is set out in the Addendum to this brief.

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found by FDA to have led to 169 deaths prior to the paradigm shift in dosing methodology brought about by the invention of Colcrys®. JA127. In fact, Colcrys® was so revolutionary that FDA effectively removed all forms of generic colchicine from the market, deeming them unsafe, shortly after approving Colcrys®. *See* JA36-37.

## STATEMENT OF ISSUES PRESENTED

FDA's regulations require that a 505(b)(2) applicant "shall submit an applicable certification" to another party's method-of-use patents when "the labeling of the drug product for which the applicant is seeking approval includes an indication that … is claimed by a use patent." 21 C.F.R. § 314.50(i)(1)(iii)(B). Section 505(b)(2) of the FDCA, the statute implemented by those regulations, provides that an applicant must certify "with respect to *each patent* which claims the drug for which such investigations were conducted or *which claims a use for such drug for which the applicant is seeking approval under this subsection*." 21 U.S.C. § 355(b)(2)(A) (emphases added). The issues presented are:

**1.** Whether FDA's approval of Mitigare without requiring certification to Takeda's Colcrys® use patents was arbitrary and capricious because Mitigare's label "include[d] an indication"—use of colchicine for prophylaxis of gout flares—"claimed by" several of those patents.

**2.** Whether FDA's approval of Mitigare without requiring certification to Takeda's Colcrys® use patents was arbitrary and capricious because those patents "claim[ed] a use for" colchicine, the "drug for which [Hikma] [was] seeking approval under" Section 505(b)(2).

## STATEMENT OF THE CASE

### A. Statutory Background

The FDCA prohibits any person from selling a drug product in interstate commerce without FDA approval. 21 U.S.C. § 355(a). A drug manufacturer may seek FDA approval through one of three pathways:

*First*, innovators of novel drug products must file with FDA a New Drug Application 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 identify "the patent number and the expiration date" of any method-of-use patent that it owns "which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted." 21 U.S.C. § 355(b)(1)(G). The applicant must also draft and submit a short "use code" describing the claimed method of use. 21 C.F.R. § 314.53(c)(2)(ii)(P). FDA lists this patent information in a publication known as the "Orange Book," which serves as a reference to copiers looking to identify potentially relevant intellectual property. *See id.* § 314.53(e); *see also, e.g.*, *Dey Pharma, LP v. Sunovion Pharm. Inc.*, 677 F.3d 1158, 1159-60 (Fed. Cir. 2012). 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 July 2015).

*Second*, a generic drug manufacturer 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.*

*Third*, a manufacturer may seek to market a new drug product differing only slightly from a previously approved drug, such as a different dosage amount or a different indication. For these drugs, 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 prior applicants and on published studies and literature (rather than solely the 505(b)(2) applicant's studies) to establish the safety and efficacy of the new, slightly different drug product.

Critically, just like an ANDA applicant, a 505(b)(2) applicant must certify that its proposed drug will not infringe the patents claiming *either* the drug which was the subject of studies relied upon by the applicant *or* a use for the drug for which the applicant seeks approval. *See* 21 U.S.C. § 355(b)(2)(A). A 505(b)(2) applicant must also provide notice of that certification to the patent-holder. *See id.* § 355(b)(3); 21 C.F.R. § 314.52. FDA's implementing regulation provides:

> If the labeling of the drug product for which the applicant is seeking approval includes an indication that, according to the [Orange Book] 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) (emphasis added).

The patent certification and notice provisions for ANDAs and 505(b)(2) applications are essential to the statutory scheme created by the Hatch-Waxman Amendments to the FDCA, Pub. L. No. 98-417, 98 Stat. 1585, 1593-94 (1984). "Congress 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). A 505(b)(2) applicant, for example, can "avoid the costly and time-consuming studies required for a pioneer drug" by relying on extant literature for other drugs. *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 676 (1990). Meanwhile, "[t]o induce" innovators like Takeda "to make the 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), Congress provided them a period of exclusivity to sell their patent-protected drug products and the ability to defend their patents *before* copies or generic drugs are brought to the market. If a patent-holder who receives notice that its patents are implicated in a 505(b)(2) application files a suit for infringement within 45 days of receiving the notice, FDA may not approve the 505(b)(2) application for 30 months unless a court orders otherwise. 21 U.S.C. § 355(c)(3)(C).

### 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. JA107, JA454, JA483. In July 2009, FDA approved a 505(b)(2) application 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 to be used for the treatment of acute gout flares. JA34, JA107, JA476-77, JA503. Several months later, FDA approved a second indication for the use of Colcrys® for the prophylaxis of gout flares. JA479.

In its applications, Mutual relied on published literature, a previously approved listed drug product, and its own clinical trials. JA476-79. 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 further obtained patents directed to colchicine and the use of colchicine for various treatments. Seventeen of these patents are listed in FDA's Orange Book entry for Colcrys®. *See* JA506-07. And four of those patents—the Colcrys® use patents—are listed in the Orange Book and described with a use code as claiming a "[m]ethod of using colchicine for the prophylaxis of gout flares." JA515 (use code U-1020); *see also* JA506-07 (referencing U.S. Patent No. 7,619,004; U.S. Patent No. 7,820,681; U.S. Patent No. 8,907,655 (the "'655 patent"); and U.S. Patent No. 8,440,722 (the "'722 patent") with use code U-1020). Thus, manufacturers who submit ANDAs or 505(b)(2) applications for a method of using colchicine for the prophylaxis of gout flares *must* certify that their proposed products will not infringe the Colcrys® use patents. Several drug manufacturers did just that, filing ANDAs for generic Colcrys® products and certifying to Takeda's patents as required by 21 U.S.C. § 355(j)(2)(A)(vii). As contemplated by the statute, Takeda was thus afforded the opportunity to file pre-approval infringement lawsuits (and did so).[2]

[2] *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).

### C. FDA Approval Of Mitigare

Hikma, unlike multiple of its competitors, did not follow the statutory procedures when it sought approval of its Colcrys® duplicate. Hikma's U.S. manufacturer, West-Ward Pharmaceutical Corp., submitted a 505(b)(2) application in 2010 for a single-ingredient oral colchicine tablet for the prophylaxis of gout flares—a copy 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® must be submitted as an ANDA, not a 505(b)(2) application. *See* JA472-73. FDA confirmed that Mutual was correct: "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 must proceed as an ANDA under 21 U.S.C. § 355(j). *See* JA483.

Undaunted, Hikma filed another application for a single-ingredient, 0.6 mg colchicine product indicated for the prophylaxis of gout flares—Mitigare. *See* JA517. But rather than submit an ANDA, Hikma reformulated Mitigare as a *capsule*, not a tablet, and filed another 505(b)(2) application. *See id.* For the safety and efficacy studies supporting its 505(b)(2) application, Hikma purported to rely upon studies conducted for an unpatented combination drug, Col-Probenecid, not Colcrys®. Col-Probenecid, which was approved more than 35 years ago for the treatment of chronic gouty arthritis, JA25; JA384, is a substantially different drug

product than Mitigare (and Colcrys®), with different active ingredients, different concentrations, a different dosage form, and a different indication. Col-Probenecid is not even approved for the "prophylaxis of gout." Despite Takeda's 17 Orange Book–listed patents for Colcrys®—four of which are listed for a "[m]ethod of using colchicine for the prophylaxis of gout"—Hikma did not file a certification to those patents as required by Section 505(b)(2)(A). *See* JA44; *see also* JA113-14.

Without warning or notice to Takeda, FDA approved Hikma's Mitigare application on September 26, 2014, and Hikma publicly announced the approval four days later. *See* JA44, JA522. Had FDA required Hikma to certify to the Colcrys® use patents, Takeda could have sued Hikma for patent infringement based upon the certification, triggering the statutory 30-month stay of any FDA approval of the Mitigare application. Indeed, just days after learning of FDA's unlawful approval of Mitigare, Takeda sued Hikma in federal court for infringement of the '722 and '655 patents. JA45, JA524-41.

### D. The Elliott Appellants Bring Suit Under The APA

FDA's unlawful approval of Mitigare and failure to enforce the FDCA's patent certification requirements significantly injured the Elliott Appellants and will continue to do so unless set aside. According to Hikma's reporting, annual sales of colchicine in the United States are nearly $700 million. *See* JA522. The Elliott Appellants are the record-holder and economic beneficiaries of a contractual "con-

tingent value right" to receive a percentage of royalties from sales of Colcrys® in the United States while the Colcrys® use patents remain in force. JA449-50, JA460. The contingent value right arises from a substantial investment that Elliott Associates, L.P. made in the corporate parent of Mutual, without which FDA's approval of Colcrys® may not have been possible. *See* JA460. Mitigare competes directly with Colcrys®, and reduced sales of Colcrys® deprive the Elliott Appellants of royalties from sales of this important product. *See* JA447.

The Elliott Appellants accordingly filed suit in the district court in November 2014 seeking to set aside FDA's unlawful approval of Mitigare without requiring Hikma to certify to the Colcrys® use patents. *See* JA445-66. The Elliott Appellants argued that because the Colcrys® use patents are listed in the Orange Book as claiming the exact same indication as Mitigare, FDA's approval of the drug violated not only the FDCA, but also FDA's own regulation providing its authoritative interpretation of the statute. The district court consolidated that action with Takeda's suit seeking the same relief on different grounds. The parties filed cross-motions for summary judgment, and the district court denied Takeda's and the Elliott Appellants' motions, instead granting summary judgment for FDA and Hikma. *See* JA22-23.

The district court concluded that Section 505(b)(2) "clear[ly]" requires an applicant to certify "only … to the product patents or the method-of-use patents

that are associated with the reference listed drug (i.e., the drug product on whose investigations the 505(b)(2) applicant relies)." JA75. Because Hikma had purported to rely upon Col-Probenecid (despite its many differences from Mitigare), the district court concluded, the FDCA did not require it to certify to the Colcrys® use patents. The district court addressed the Elliott Appellants' argument that FDA's own authoritative regulation required certification to the Colcrys® use patents in only a footnote. *See* JA84-85 n.25.

This appeal followed.

## STANDARD OF REVIEW

Under the APA, courts must "hold unlawful and set aside agency action, findings, and conclusions found to be … (A) arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2). Because the district court reviewed FDA's action "under the APA," this Court "review[s] the administrative action directly, according no particular deference to the judgment of the District Court." *Holland v. Nat'l Mining Ass'n*, 309 F.3d 808, 814 (D.C. Cir. 2002).

"It is axiomatic … that an agency is bound by its own regulations." *Nat'l Envtl. Dev. Ass'n's Clean Air Project v. EPA*, 752 F.3d 999, 1009 (D.C. Cir. 2014) (internal quotation marks omitted). "Thus, an agency action may be set aside as

arbitrary and capricious if the agency fails to comply with its own regulations." *Id.* (internal quotation marks omitted).

Likewise, courts must set aside an agency's action that violates a federal statute. The familiar *Chevron* framework guides the analysis. If "Congress has directly spoken to the precise question at issue," "that is the end of the matter." *Chevron U.S.A. Inc. v. NRDC, Inc.*, 467 U.S. 837, 842-43 (1984). If, on the other hand, a court determines after "employing traditional tools of statutory construction" that the statute is ambiguous, "the question for the court is whether the agency's answer is based on a permissible construction of the statute." *Id.* at 843 & n.9. That deference, however, is reserved for "authoritative statutory interpretations." *BNSF Ry. Co. v. Surface Transp. Bd.*, 748 F.3d 1295, 1300 (D.C. Cir. 2014); *see also Cent. Laborers' Pension Fund v. Heinz*, 541 U.S. 739, 748 (2004) (neither "unreasoned statement[s]" nor "longstanding agency practice" can "trump a formal regulation with the procedural history necessary to take on the force of law").

## SUMMARY OF ARGUMENT

**1.** FDA's approval of Mitigare without requiring certification to the Colcrys® use patents was arbitrary and capricious because it violated FDA's own binding regulation. 21 C.F.R. § 314.50(i)(1)(iii)(B) requires a 505(b)(2) applicant to file "an applicable certification" if "the labeling of the drug product for which the applicant is seeking approval includes an indication that" according to the Orange

Book "is claimed by a use patent." Mitigare's label contained an indication for "prophylaxis of gout flares." Takeda's Colcrys® use patents are listed in the Orange Book as claiming that very indication. FDA's binding regulation accordingly required Hikma to certify whichever of the following was "applicable": that Takeda had not submitted patent information to FDA, that the patents were expired, or that they were "invalid, unenforceable, or will not be infringed." 21 C.F.R. § 314.50(i)(1)(i). Hikma filed no certification, and FDA's acquiescence was an unlawful violation of its own regulation.

**2.** FDA's approval of Mitigare without requiring certification to the Colcrys® use patents also violated Section 505(b)(2) itself. The plain language of the statute requires a 505(b)(2) applicant to certify to "each patent … which claims a use for *such drug for which the applicant is seeking approval under this subsection*." 21 U.S.C. § 355(b)(2)(A) (emphasis added). The Colcrys® use patents claim the use of colchicine for prophylaxis of gout flares, the precise use of colchicine for which Hikma sought approval. The statute's legislative history reinforces its straightforward meaning: "the applicant must certify" with respect to "all product patents which claim the listed drug and *all use patents which claim an indication for the drug for which the applicant is seeking approval*." H.R. Rep. No. 98-857, pt. 1, at 32 (1984) (emphasis added). This clear requirement codifies the basic underpinnings of the Hatch-Waxman amendments to the FDCA: 505(b)(2)

applicants may rely upon the work of others to bring generic drugs to market far more quickly than would be possible if they were required to perform full safety and efficacy studies. In exchange, innovators who perform expensive safety and efficacy studies and receive patents for their contributions have an opportunity to litigate claims of infringement *before* infringing drugs reach the market and erode sales of innovators' drugs. Because Congress spoke precisely to this issue, the Court should resolve this case at *Chevron*'s first step. Even at *Chevron*'s second step, the only interpretation of Section 505(b)(2) worthy of deference is FDA's binding regulation that required Hikma to certify to the Colcrys® use patents.

## ARGUMENT

### I. FDA's Approval Of Mitigare Was Arbitrary, Capricious, And Contrary To Law Because FDA's Binding Regulation Required Hikma To Certify To The Colcrys® Use Patents

FDA's regulations concerning 505(b)(2) applications provide that "[i]f the labeling of the drug product for which the applicant is seeking approval includes an indication that, according to the [Orange Book] 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). Thus, if a 505(b)(2) applicant's label includes an indication already claimed by a use patent, the regulation mandates ("shall submit") a certification. Paragraph (i)(1)(i), in turn, sets forth the four "applicable" patent certifications: (1) that no patent exists;

(2) that the patent expired; (3) that the applicant will wait until the patent expires; or "(4) [t]hat the patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted." *Id.* § 314.50(i)(1)(i).

Hikma sought FDA approval of the drug product colchicine for the prophylaxis of gout. Hikma's label included a single indication: "MITIGARE™ is indicated for prophylaxis of gout flares in adults." JA625. That exact same "indication" is, according to the Orange Book, "claimed by [Takeda's] use patent[s]" for Colcrys®. 21 C.F.R. § 314.50(i)(1)(iii)(B); *see* JA506, JA515. Yet despite the straightforward applicability of this regulation, Hikma never certified to any of the Colcrys® use patents, and FDA approved Mitigare without ever requiring Hikma to do so. The result is equally straightforward: FDA violated its regulation, and its action was arbitrary and capricious as a matter of law. *See, e.g.*, *Nat'l Envtl. Dev.*, 752 F.3d at 1009.

The district court all but ignored FDA's departure from its regulation, addressing this issue in a passing footnote. *See* JA84-85 n.25. According to the district court, "FDA has long maintained that the only 'applicable' patent certifications are those that are made in relation to product or use patents that claim the reference listed drug." *Id.* Thus, it reasoned, the regulation required Hikma to certify

to product and use patents for only Col-Probenecid, upon whose studies Hikma purported to rely.

The district court cited no authority (or even the interpretations in which FDA has "long maintained" this position) for its strained interpretation of the word "applicable," and its reading of the regulation is flawed in at least two ways.[3] First, the plain meaning of the word "applicable" in this context is that, where the applicant's label contains an indication that is claimed in an existing method-of-use patent, the applicant must select *which* of the "circumstances" enumerated in paragraph (i)(1)(i) "applies": that the patent has not been submitted to FDA; that the patent has expired; that the applicant will wait until the patent has expired; or that the patent is invalid, unenforceable, or will not be infringed. 21 C.F.R. § 314.50(i)(1)(i)(A). Paragraph (iii)(B) requires that the applicant "*shall submit* an applicable certification," *id.* § 314.50(i)(1)(iii)(B) (emphasis added), but the district

[3] The district court also erroneously suggested that 21 C.F.R. § 314.50(i)(1)(iii)(B) "concerns proper labeling" rather than the issues in this case. JA84-85 n.25. But FDA may approve a new drug only "under 'the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof.'" *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. 2466, 2471 (2013) (quoting 21 U.S.C. § 355(d)). Thus, it is the approved label that provides the indication for the drug at issue. The cited regulations have nothing to do with "proper labeling." The titles of the section and subsection of the regulation—"Patent certification[s]" required in 505(b)(2) applications with respect to "Method of use patent[s]"—make clear that the regulation addresses the precise questions at issue here. 21 C.F.R. § 314.50(i) & (i)(1)(iii); *cf. id.* 21 C.F.R. § 314.50(c)(2)(i) (addressing labeling requirements).

court's strained interpretation of the word "applicable" eliminates the mandatory ("shall") requirement. Thus, the issue that FDA (and the district court) should have confronted was which of the four "applicable" certifications Hikma was required to file, not whether a certification was required at all.

Second, the district court's interpretation reads paragraph (i)(1)(iii)(B) completely out of the regulation. If paragraph (i)(1)(iii)(B) simply applied the same criteria as paragraph (i)(1)(i) under the same circumstances, it would serve absolutely no role in the regulatory scheme. This Court should not accept an interpretation that would "render the pertinent regulation a *nullity*." *Sec'y of Labor v. Twentymile Coal Co.*, 411 F.3d 256, 261 (D.C. Cir. 2005); *accord, e.g.*, *Rainsong Co. v. FERC*, 151 F.3d 1231, 1234 (9th Cir. 1998) ("in the construction of administrative regulations … it is presumed that every phrase serves a legitimate purpose") (quotation marks omitted).

Contrary to the district court's opinion, the plain language of paragraph (i)(1)(iii)(B) requires certification with respect to *any* use patent claiming the indication that appears on the labeling of the drug product for which approval is sought—in this case, the use of colchicine for the prophylaxis of gout. The word "applicable" does not specify which *use patents* are relevant; rather, it refers to the words that directly follow it—the "applicable *certification under paragraph (i)(1)(i)*." Thus, the regulation requires one of the four types of certifications—as

listed in clauses (1) through (4) of paragraph (i)(1)(i)—to be made regarding use patents covered by paragraph (i)(1)(iii)(B), not merely the patents for which those certifications are already required under (i)(1)(i). This interpretation of paragraph (i)(1)(iii)(B) is the only one that gives all of its words—indeed any of them—substantive effect.

The subsections of 21 C.F.R. § 314.50(i)(1) are cumulative and complementary; each addresses a particular circumstance. Subsection (i)(A) provides the basic certification requirements, including the four types of available certifications and a representation that notice will be provided to each patent owner. Each of the subsequent subsections begins with the word "[i]f" followed by some specified circumstance. Subsection (i)(B) applies "if" the RLD is a licensed generic drug. Subsection (ii) applies "if" there are no relevant patents for the RLD. Subsection (iii)(A) applies "if" the RLD's method-of-use patents and the label differ. Finally, subsection (iii)(B) applies "[i]f the labeling of the drug product for which the applicant is seeking approval includes an indication that … is claimed by a use patent." *See generally* 21 C.F.R. § 314.50(i)(1)(i)-(iii). FDA cannot pick and choose the provisions it "deem[s] suitable" to comply with—or the regulations it chooses to enforce—in any "given case." *Schering Corp. v. Shalala*, 995 F.2d 1103, 1105 (D.C. Cir. 1993) (per curiam) (quotation marks omitted). Through its erroneous interpretation of the regulation, the district court permitted FDA to do just that.

FDA's binding regulation unambiguously required Hikma to certify to the Colcrys® use patents, which claimed the same indication for prophylaxis of gout flares that appears on the Mitigare label. FDA approved Mitigare without requiring Hikma to satisfy that requirement. "'Although it is within the power of [an] agency to amend or repeal its own regulations, [an] agency is not free to ignore or violate its regulations while they remain in effect.'" *Nat'l Envtl. Dev.*, 752 F.3d at 1009 (quoting *U.S. Lines, Inc. v. Fed. Mar. Comm'n*, 584 F.2d 519, 526 n.20 (D.C. Cir. 1978)). FDA's violation of its regulation was arbitrary and capricious, and this Court should set aside FDA's unlawful action.

## II. FDA's Approval Of Mitigare Was Arbitrary, Capricious, And Contrary To Law Because Section 505(b)(2) Required Hikma To Certify To The Colcrys® Use Patents

FDA's violation of its own binding regulation is sufficient for this Court to set aside its approval of Mitigare as arbitrary and capricious. FDA's action also violated the plain language of Section 505(b)(2) itself. That is an independent ground for this Court to hold FDA's action unlawful.

Judicial "review of an agency's procedural compliance with statutory norms is an exacting one." *NRDC, Inc. v. SEC*, 606 F.2d 1031, 1048 (D.C. Cir. 1979). Because Congress clearly "prescrib[ed] a precise course of conduct other than the one chosen by the agency," this Court's analysis ends at *Chevron*'s first step. *Vill. of Barrington, Ill. v. Surface Transp. Bd.*, 636 F.3d 650, 659 (D.C. Cir. 2011).

Even if the Court concludes that Section 505(b)(2) is ambiguous, the Court may "defer to the agency's permissible interpretation, but only if the agency has offered a reasoned explanation for why it chose that interpretation." *Id.* at 660. In this case, the *only* reasoned interpretation of Section 505(b)(2) FDA has *ever* offered is the one it put forth in its binding regulation, discussed above. FDA's unreasoned change in position in this litigation merits no deference, so even at *Chevron*'s second step, FDA's approval of Mitigare must fall.

### A. Section 505(b)(2)(A) Clearly Required Certification To The Colcrys® Use Patents

FDA approved Mitigare without requiring Hikma to certify to the Colcrys® use patents because Hikma purported to rely upon a different drug, Col-Probenecid, in its application. In the district court, FDA argued that the FDCA required Hikma to certify to method-of-use patents only for Col-Probenecid (of which there were none). The "traditional tools of statutory construction"—the statute's plain text, legislative history, and overall structure and purpose—all confirm the "clear congressional intent" (*Chevron*, 467 U.S. at 843 n.9) to require certification to "*each patent* … which claims a use for *such drug for which the applicant is seeking approval under this subsection*," not merely the RLD. 21 U.S.C. § 355(b)(2)(A) (emphases added).

### 1. Text

As explained above, Section 505(b)(2) of the FDCA allows a new drug applicant to prove a drug's safety and efficacy by relying on existing drug investigations that "were not conducted by or for the applicant." 21 U.S.C. § 355(b)(2). "[H]aving done that, a § 505(b)(2) applicant can avoid preclinical and certain human studies necessary in full NDA applications." *Ethypharm S.A. Fr. v. Abbott Labs.*, 707 F.3d 223, 227 (3d Cir. 2013).

To benefit from this accelerated pathway, a 505(b)(2) applicant must certify to each patent listed in the Orange Book "[1] which claims the drug for which such investigations were conducted or [2] 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. Because four Colcrys® use patents are listed in the Orange Book for using that drug, colchicine, "for the prophylaxis of gout flares," Hikma was required to include with its 505(b)(2) application a certification that the Colcrys® use patents were either expired (they were not) or else invalid or not infringed. Hikma failed to make that certification, and FDA's approval of the Mitigare application violated the plain text of the FDCA.

The district court erroneously concluded that Section 505(b)(2) requires certification "only with respect to patents that either claim the drug product … upon

which the applicant is relying (the reference listed drug), or that claim *a method of using the reference listed drug for which the applicant is seeking approval*." JA77 (emphasis added). First, the district court incorrectly assumed that "drug" must mean only "drug product" throughout Section 505(b)(2)(A). *See* JA78. In fact, FDA's own regulations acknowledge that *within Section 505(b)(2)(A)*, "drug" can mean both "the drug product or drug substance that is a component of the drug product." 21 C.F.R. § 314.50(i)(1)(i)(A).[4] Congress used the context surrounding the word "drug" to make clear which meaning applied: When Congress meant the RLD, it referred to the "drug for which investigations described in paragraph (1)(A) were conducted." 21 U.S.C. § 355(b)(2)(B); *see also id.* § 355(b)(2)(A) ("drug for which such investigations were conducted"). When Congress meant, instead, the drug substance (here, colchicine), it referred to the "drug for which the applicant is seeking approval." *Id.* § 355(b)(2)(A).

This careful use of language was necessary because—unlike in the ANDA context under 21 U.S.C. § 355(j) in which the RLD and the new drug are identical

[4] FDA amended its regulations to employ this expansive interpretation of the word "drug" in 1994, explaining that the change serves "to clarify the types of patents for which a certification should be made." 59 Fed. Reg. 50,338, 50,339 (Oct. 3, 1994). The amendment led to more listed patents to which copiers must certify, *see Andrx Pharm., Inc. v. Biovail Corp.*, 276 F.3d 1368, 1377 n.5 (Fed. Cir. 2002), and rendered cases decided under FDA's pre-1994 patent listing and certification requirements "of doubtful continuing validity," *Watson Pharm., Inc. v. Henney*, 194 F. Supp. 2d 442, 446 (D. Md. 2001).

and have the same active ingredients—Congress needed to account for *both* the RLD *and* the new, potentially different, drug for which the application was submitted. The district court's restriction of Section 505(b)(2)(A)'s scope to the RLD ignores Congress's careful drafting and encourages 505(b)(2) applicants to reference a drug that differs from the new drug in order to circumvent the patent certification requirements. Here, for example, even if Col-Probenecid *had* any method-of-use patents (it did not), they would have been completely irrelevant because Hikma sought approval of a single-ingredient colchicine drug, not a colchicine/probenecid combination. If Hikma had filed an ANDA for Col-Probenecid, then the district court's interpretation would have been correct, because the only relevant patents would have been those covering the product and use of Col-Probenecid. But Hikma was not looking for approval of a colchicine/probenecid combination for arthritis; it was seeking approval of colchicine for the prophylaxis of gout, and thus any patents covering the use of colchicine for the prophylaxis of gout would have to be addressed through the certification process.

Second, the district court's interpretation of the phrase "for which the applicant is seeking approval" as modifying not the word directly adjacent to it ("drug"), but rather the word "use" (*see* JA83), is untenable. Under the "nearest-reasonable-referent canon" of statutory interpretation, an adjectival phrase (here, "for which the applicant is seeking approval under this subsection") "normally ap-

plies only to the *nearest* reasonable referent." Antonin Scalia & Bryan A. Garner, *Reading Law: The Interpretation of Legal Texts* 152 (2012) (emphasis added). In Section 505(b)(2)(A), the nearest reasonable referent for that phrase is "drug," not "use." As a matter of normal English usage, it makes sense that such an adjectival phrase generally modifies the word nearest to it, not some other word in the sentence. *See id.* at 144-45, 152-53.

Congress's adherence to the nearest-reasonable-referent rule becomes clear in the following subsection. In Section 505(b)(2)(B) Congress first specified that it was addressing "the drug for which investigations described in paragraph (1)(A) were conducted" (the RLD) and then required the applicant to file a carve-out statement if the RLD has "a method of use patent which does not claim *a use for which the applicant is seeking approval*." 21 U.S.C. § 355(b)(2)(B) (emphasis added). The "for which" phrase clearly modifies "use," the referent adjacent to it. There is no reason why Congress would disregard this rule of usage in one subsection (i.e., (b)(2)(A)), and then go out of its way to follow it in the next subsection (i.e., (b)(2)(B)), as the district court's interpretation would require.

Third, the district court's interpretation of Section 505(b)(2)(A) renders 505(b)(2)(B) superfluous. Section 505(b)(2)(B) provides that if "the drug for which investigations … were conducted" (i.e., the RLD) has a listed method-of-use patent "which does not claim a use for which the applicant is seeking approval un-

der this subsection," the applicant must file "a statement that the method of use patent does not claim such a use." 21 U.S.C. § 355(b)(2)(B). But such a "carve-out" statement 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). Only the Elliott Appellants' interpretation of the statute gives meaning to all portions of Section 505(b)(2).

**2. Legislative History**

An agency's interpretation of a statute must be rejected at *Chevron*'s first step 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 (citation omitted); *see also Sierra Club v. EPA*, 551 F.3d 1019, 1027 (D.C. Cir. 2008) (the Court must "exhaust the traditional tools of statutory construction, including examining the statute's legislative history" (internal quotation marks omitted)). In this instance, the House Committee on Energy and Commerce spoke with remarkable clarity to the precise issue presented.

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 use patents which claim an indication for the drug for which the applicant is seeking approval*." H.R. Rep. No. 98-857, pt. 1, at 32 (emphasis added).

The Committee referred to this latter category as "controlling use patent[s]." *Id.*[5] Each of the Colcrys® use patents 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—hence, they are "controlling use patents." Yet FDA ignored this express requirement and focused on the irrelevant *non-controlling* use patents for Col-Probenecid (of which there were none).

**3. Structure and Purpose**

Congress struck a careful balance between, on one hand, providing incentives for investment and innovation and, on the other hand, facilitating the entry of low-cost alternatives to name-brand drugs. The patent certification requirements, a critical part of that balance, are "designed to guard against infringement of patents relating to pioneer drugs." *Eli Lilly*, 496 U.S. at 676-77. The Hatch-Waxman Act allowed Hikma to seek approval of a single-ingredient colchicine product, but only if it certified to all patents in the Orange Book "with respect to which a claim of patent infringement could reasonably be asserted," 21 U.S.C. § 355(b)(1)(G), including Takeda's Colcrys® use patents. FDA's novel interpretation turns that care-

[5] The Committee further explained that "in some instances an applicant will have to make multiple certifications with respect to … controlling use patents," H.R. Rep. No. 98-857, pt. 1, at 32, such as where approval is sought for a drug like colchicine with multiple indications. Even where multiple controlling use patents exist for the indication for which the applicant seeks approval, "[t]he Committee intend[ed] that the applicant make the appropriate certification for each … controlling use patent." *Id.*

ful balance upside down by allowing new drug applicants to certify to only patents for drugs that are dissimilar to the applicants' drugs, thereby circumventing patents for drugs most similar to the applicants' drugs and undermining incentives for innovation. Prior to this case, FDA agreed with that understanding of the FDCA's delicate balance, as demonstrated in its binding regulation discussed in Part I, *supra*.

The district court reached a contrary interpretation of Section 505(b)(2) based on FDA's post hoc litigating position and rewriting of the Hatch-Waxman Act's quid pro quo. *See* JA81-82. "To facilitate the approval of generic drugs as soon as patents allow," *Caraco Pharm. Labs.*, 132 S. Ct. at 1676, the Hatch-Waxman Act and FDA regulations require brand-name manufacturers to identify any relevant patent information, including use codes and method-of-use patents. ANDA and 505(b)(2) applicants, in turn, must include one of the four parent certifications. *See* 21 U.S.C. § 355(b)(2)(A), (j)(2)(A)(vii). Thus, applicants receive an expedited approval pathway, and in return patent holders can litigate claims of patent infringement *before* the markets for their products are disrupted.

It is beyond question that an ANDA applicant seeking to market a duplicate of an already-approved drug must certify to use patents claiming the same indication as the new drug. It is unreasonable to think that Congress intended to permit a 505(b)(2) applicant like Hikma to dodge the patent certification requirement by

making a minor adjustment (here, by changing from tablet to capsule) and purporting to rely upon studies for a *different*, unpatented drug like Col-Probenecid. The FDCA's text, legislative history, and structure and purpose foreclose any possibility that Congress intended the perverse result FDA facilitated here.

### B. Even If The FDCA Were Ambiguous, FDA's Official Interpretation In Its Regulation Requires That Its Approval Of Mitigare Be Set Aside

Even if this Court finds Section 505(b)(2) ambiguous, FDA's approval of Mitigare still must be set aside. As discussed in Part I, *supra*, FDA issued its authoritative interpretation of Section 505(b)(2) through 21 C.F.R. § 314.50. As relevant here, FDA required that "[i]f the labeling of the drug product for which the applicant is seeking approval includes an indication that" according to the Orange Book "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).

*That* "authoritative statutory interpretation[]" is the one to which deference under *Chevron*'s second step (if any) is owed. *BNSF Ry.*, 748 F.3d at 1300. FDA's post hoc interpretation offered in this litigation to defend its unlawful approval of Mitigare merits no deference. *Am.'s Cmty. Bankers v. FDIC*, 200 F.3d 822, 835 (D.C. Cir. 2000) ("[*P*]*ost hoc* rationalizations cannot support an affirmance of an agency decision based on an otherwise invalid rationale."); *accord Christopher v. SmithKline Beecham Corp.*, 132 S. Ct. 2156, 2166-67 (2012). Both

the FDCA itself and FDA's official interpretation of the statute required Hikma to certify to the Colcrys® use patents, and FDA's approval of Mitigare must be set aside.

## CONCLUSION

For the foregoing reasons, the Court should reverse the decision below by holding unlawful and setting aside FDA's approval of Mitigare.

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Respectfully submitted,

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**CERTIFICATE OF COMPLIANCE**
**WITH TYPE-VOLUME LIMITATION, TYPEFACE REQUIREMENTS, AND TYPE STYLE REQUIREMENTS**

1. This brief complies with the type-volume requirement of Federal Rule of Appellate Procedure 32(a)(7), as well as this Court's per curiam Order dated July 1, 2015, because this brief contains 6,996 words, as determined by the word-count function of Microsoft Word 2003, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(a)(7)(B)(iii); and

2. This brief complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) and the type style requirements of Federal Rule of Appellate Procedure 32(a)(6) because this brief has been prepared in a proportionally spaced typeface using Microsoft Word 2003 in 14-point Times New Roman font.

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# Addendum

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**21 U.S.C. § 355**

**§ 355 New Drugs.**

**(a) Necessity of effective approval of application**

No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) of this section is effective with respect to such drug.

**(b) Filing application; contents**

(1) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof as the Secretary may require; (F) specimens of the labeling proposed to be used for such drug, and (G) any assessments required under section 355c of this title. The applicant shall file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary shall publish information submitted under the two preceding sentences. The Secretary shall, in consultation with the Director of the National Institutes of Health and with representatives of the drug manufacturing industry, review and develop guidance, as appropriate, on the inclusion of women and minorities in clinical trials required by clause (A).

(2) An application submitted under paragraph (1) for a drug for which the investigations described in clause (A) of such paragraph and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted shall also include—

(A) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug for which such investigations were conducted or which claims a use for such drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under paragraph (1) or subsection (c) of this section—

(i) that such patent information has not been filed,

(ii) that such patent has expired,

(iii) of the date on which such patent will expire, or

(iv) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(B) if with respect to the drug for which investigations described in paragraph (1)(A) were conducted information was filed under paragraph (1) or subsection (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

* * *

**21 C.F.R. § 314.50**

**§ 314.50 Content and format of an application.**

Applications and supplements to approved applications are required to be submitted in the form and contain the information, as appropriate for the particular submission, required under this section. Three copies of the application are required: An archival copy, a review copy, and a field copy. An application for a new chemical entity will generally contain an application form, an index, a summary, five or six technical sections, case report tabulations of patient data, case report forms, drug samples, and labeling, including, if applicable, any Medication Guide required under part 208 of this chapter. Other applications will generally contain only some of those items, and information will be limited to that needed to support the particular submission. These include an application of the type described in section 505(b)(2) of the act, an amendment, and a supplement. The application is required to contain reports of all investigations of the drug product sponsored by the applicant, and all other information about the drug pertinent to an evaluation of the application that is received or otherwise obtained by the applicant from any source. FDA will maintain guidance documents on the format and content of applications to assist applicants in their preparation.

* * *

(h) *Patent information.* The application is required to contain the patent information described under § 314.53.

(i) *Patent certification* —(1) *Contents.* A 505(b)(2) application is required to contain the following:

(i) *Patents claiming drug, drug product, or method of use.* (A) Except as provided in paragraph (i)(2) of this section, a certification with respect to each patent issued by the United States Patent and Trademark Office that, in the opinion of the applicant and to the best of its knowledge, claims a drug (the drug product or drug substance that is a component of the drug product) on which investigations that are relied upon by the applicant for approval of its application were conducted or that claims an approved use for such drug and for which information is required to be filed under section 505(b) and (c) of the act and § 314.53. For each such patent, the applicant shall provide the patent number and certify, in its opinion and to the best of its knowledge, one of the following circumstances:

(*1*) That the patent information has not been submitted to FDA. The applicant shall entitle such a certification "Paragraph I Certification";

(*2*) That the patent has expired. The applicant shall entitle such a certification "Paragraph II Certification";

(*3*) The date on which the patent will expire. The applicant shall entitle such a certification "Paragraph III Certification"; or

(*4*) That the patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted. The applicant shall entitle such a certification "Paragraph IV Certification". This certification shall be submitted in the following form:

I, ( *NAME OF APPLICANT* ), CERTIFY THAT PATENT NO. _____ ( *IS INVALID, UNENFORCEABLE, OR WILL NOT BE INFRINGED BY THE MANUFACTURE, USE, OR SALE OF* ) ( *NAME OF PROPOSED DRUG PRODUCT* ) FOR WHICH THIS APPLICATION IS SUBMITTED.

The certification shall be accompanied by a statement that the applicant will comply with the requirements under § 314.52(a) with respect to providing a notice to each owner of the patent or their representatives and to the holder of the approved application for the drug product which is claimed by the patent or a use of which is claimed by the patent and with the requirements under § 314.52(c) with respect to the content of the notice.

(B) If the drug on which investigations that are relied upon by the applicant were conducted is itself a licensed generic drug of a patented drug first approved under section 505(b) of the act, the appropriate patent certification under this section with respect to each patent that claims the first-approved patented drug or that claims an approved use for such a drug.

(ii) *No relevant patents.* If, in the opinion of the applicant and to the best of its knowledge, there are no patents described in paragraph (i)(1)(i) of this section, a certification in the following form:

IN THE OPINION AND TO THE BEST KNOWLEDGE OF ( *NAME OF APPLICANT* ), THERE ARE NO PATENTS THAT CLAIM THE DRUG OR DRUGS ON WHICH INVESTIGATIONS THAT ARE RELIED UPON IN THIS APPLICATION WERE CONDUCTED OR THAT CLAIM A USE OF SUCH DRUG OR DRUGS.

(iii) *Method of use patent.* (A) If information that is submitted under section 505(b) or (c) of the act and § 314.53 is for a method of use patent, and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent, a statement explaining that the method of use patent does not claim any of the proposed indications.

(B) If 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.

(2) *Method of manufacturing patent.* An applicant is not required to make a certification with respect to any patent that claims only a method of manufacturing the drug product for which the applicant is seeking approval.

(3) *Licensing agreements.* If a 505(b)(2) application is for a drug or method of using a drug claimed by a patent and the applicant has a licensing agreement with the patent owner, the applicant shall submit a certification under paragraph (i)(1)(i)(A)( *4* ) of this section ("Paragraph IV Certification") as to that patent and a statement that it has been granted a patent license. If the patent owner consents to an immediate effective date upon approval of the 505(b)(2) application, the application shall contain a written statement from the patent owner that it has a licensing agreement with the applicant and that it consents to an immediate effective date.

(4) *Late submission of patent information.* If a patent described in paragraph (i)(1)(i)(A) of this section is issued and the holder of the approved application for the patented drug does not submit the required information on the patent within 30 days of issuance of the patent, an applicant who submitted a 505(b)(2) application that, before the submission of the patent information, contained an appropriate patent certification is not required to submit an amended certification. An applicant whose 505(b)(2) application is filed after a late submission of patent information or whose 505(b)(2) application was previously filed but did not contain an appropriate patent certification at the time of the patent submission shall submit a certification under paragraph (i)(1)(i) or (i)(1)(ii) of this section or a statement under paragraph (i)(1)(iii) of this section as to that patent.

(5) *Disputed patent information.* If an applicant disputes the accuracy or relevance of patent information submitted to FDA, the applicant may seek a confirmation of the correctness of the patent information in accordance with the procedures under § 314.53(f). Unless the patent information is withdrawn or changed, the applicant must submit an appropriate certification for each relevant patent.

(6) *Amended certifications.* A certification submitted under paragraphs (i)(1)(i) through (i)(1)(iii) of this section may be amended at any time before the effective date of the approval of the application. An applicant shall submit an amended certification as an amendment to a pending application or by letter to an approved application. If an applicant with a pending application voluntarily makes a patent cer-

tification for an untimely filed patent, the applicant may withdraw the patent certification for the untimely filed patent. Once an amendment or letter for the change in certification has been submitted, the application will no longer be considered to be one containing the prior certification.

(i) *After finding of infringement.* An applicant who has submitted a certification under paragraph (i)(1)(i)(A)(*4*) of this section and is sued for patent infringement within 45 days of the receipt of notice sent under § 314.52 shall amend the certification if a final judgment in the action is entered finding the patent to be infringed unless the final judgment also finds the patent to be invalid. In the amended certification, the applicant shall certify under paragraph (i)(1)(i)(A)(*3*) of this section that the patent will expire on a specific date.

(ii) *After removal of a patent from the list.* If a patent is removed from the list, any applicant with a pending application (including a tentatively approved application with a delayed effective date) who has made a certification with respect to such patent shall amend its certification. The applicant shall certify under paragraph (i)(1)(ii) of this section that no patents described in paragraph (i)(1)(i) of this section claim the drug or, if other relevant patents claim the drug, shall amend the certification to refer only to those relevant patents. In the amendment, the applicant shall state the reason for the change in certification (that the patent is or has been removed from the list). A patent that is the subject of a lawsuit under § 314.107(c) shall not be removed from the list until FDA determines either that no delay in effective dates of approval is required under that section as a result of the lawsuit, that the patent has expired, or that any such period of delay in effective dates of approval is ended. An applicant shall submit an amended certification as an amendment to a pending application. Once an amendment for the change has been submitted, the application will no longer be considered to be one containing a certification under paragraph (i)(1)(i)(A)(*4*) of this section.

(iii) *Other amendments.* (A) Except as provided in paragraphs (i)(4) and (i)(6)(iii)(B) of this section, an applicant shall amend a submitted certification if, at any time before the effective date of the approval of the application, the applicant learns that the submitted certification is no longer accurate.

(B) An applicant is not required to amend a submitted certification when information on an otherwise applicable patent is submitted after the effective date of approval for the 505(b)(2) application.

* * *

## CERTIFICATE OF SERVICE

I hereby certify that on this 17th day of August, 2015, I caused the foregoing Opening Brief for Appellants Elliott Associates, L.P., Elliott International, L.P., and Knollwood Investments, L.P. to be electronically filed with the Clerk of the Court for the United States Court of Appeals for the District of Columbia Circuit using the appellate CM/ECF system. Service was accomplished on the following parties via the Court's CM/ECF system:

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