ORAL ARGUMENT NOT YET SCHEDULED

Nos. 15-5021, 15-5022

United States Court of Appeals
for the District of Columbia Circuit

TAKEDA PHARMACEUTICALS U.S.A., INC., *et al.*

Plaintiffs-Appellants,

v.

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

Defendants-Appellees,

and

HIKMA PHARMACEUTICALS PLC, *et al.*,

Intervenors-Defendants

On Appeal from the United States District Court for the District of Columbia, Docket No. 1:14-cv-1850 (K. Jackson, J.)

BRIEF OF *AMICUS CURIAE* GENERIC PHARMACEUTICAL ASSOCIATION IN SUPPORT OF APPELLEES AND INTERVENOR-APPELLEES

Carlos T. Angulo
Andrew N. Goldfarb
Zuckerman Spaeder LLP
1800 M Street, NW, Suite 1000
Washington, DC 20036
Telephone: (202) 778-1800
cangulo@zuckerman.com

October 23, 2015

Attorneys for Amicus Curiae Generic Pharmaceutical Association

TABLE OF CONTENTS

Page

TABLE OF CONTENTS i
CORPORATE AND FINANCIAL DISCLOSURE STATEMENT ii
TABLE OF AUTHORITIES iii
GLOSSARY v
CERTIFICATE OF PARTIES, RULINGS UNDER REVIEW, AND RELATED CASES v
STATUTES AND REGULATIONS v
STATEMENT OF IDENTITY AND INTEREST OF *AMICUS CURIAE* 1
SUMMARY OF ARGUMENT 2
ARGUMENT 7
I. Takeda's "most similar" test for listed drugs conflicts with the statutory text and FDA's consistent interpretation of section 505(b)(2). 7
A. Section 505(b)(2) gives the applicant the responsibility to select the listed drug. 7
B. The Court should preserve the intentional distinctions, in Hatch-Waxman and in FDA's administration of that law, between listed drugs for 505(b)(2) applications and RLDs for ANDAs. 11
II. Elliott's argument requiring a 505(b)(2) applicant to certify to all use patents covering the same use of the proposed drug would fundamentally distort the Hatch-Waxman framework for 505(b)(2) products. 14
III. Hatch-Waxman's "grand bargain" does not support Appellants' statutory interpretations. 17
CONCLUSION 18
CERTIFICATE OF COMPLIANCE 20

CORPORATE AND FINANCIAL DISCLOSURE STATEMENT PURSUANT TO FEDERAL RULES OF APPELLATE PROCEDURE 26.1 AND 29(c) AND D.C. CIRCUIT LOCAL RULE 26.1

Amicus curiae Generic Pharmaceutical Association ("GPhA") is a trade association with no parent corporation. No publicly held corporation has a 10% or greater ownership interest in GPhA.

/s/ Carlos T. Angulo
Carlos T. Angulo
Andrew N. Goldfarb
Zuckerman Spaeder LLP
1800 M Street, NW, Suite 1000
Washington, DC 20036
Telephone: (202) 778-1800
cangulo@zuckerman.com

Attorneys for Amicus Curiae
Generic Pharmaceutical Association

October 23, 2015

TABLE OF AUTHORITIES

Page(s)

CASES

Balt. Gas & Elec. Co. v. Nat. Res. Def. Council, Inc.,
462 U.S. 87 (1983) 11

Chevron U.S.A., Inc. v. Nat. Res. Def. Council, Inc.,
467 U.S. 837 (1984) 15

Hi-Tech Pharmacal Co. v. FDA,
587 F. Supp. 2d 1 (D.D.C. 2008) 14

Serono Labs., Inc. v. Shalala,
158 F.3d 1313 (D.C. Cir. 1998) 11

Takeda Pharms. U.S.A., Inc. v. West-Ward Pharm. Corp.,
785 F.3d 625 (Fed. Cir. 2015) 18

Teva Pharms. USA, Inc. v. Sebelius,
595 F.3d 1303 (D.C. Cir. 2010) 14

STATUTES

*21 U.S.C. § 355(b)(2).....2, 7

21 U.S.C. § 355(c)(3)(C) 4

21 U.S.C. § 355(c)(3)(E)(iii)..... 14, 18

21 U.S.C. § 355(j) 11

21 U.S.C. § 355(j)(2)(A).....12

21 U.S.C. § 355(j)(2)(A)(iv) 12

21 U.S.C. § 355(j)(2)(C) 12

21 U.S.C. § 355(j)(2)(C)(i) 12

*Authorities upon which we chiefly rely are marked with an asterisk.

21 U.S.C. § 355(j)(5)(B)(IV) 14

OTHER AUTHORITIES

Consolidated Citizen Petition Response from Janet Woodcock to Katherine M. Sanzo, *et al.*, at 6, Docket Nos. 2001P-0323/CP1 & C5, 2002P-0447/CP1, and 2203P-0408/CP1 (Oct. 14, 2003) 8, 9

FDA, Orange Book, http://tinyurl.com/65wqgnt.....12

REGULATIONS

21 C.F.R. § 314.101(d)(9) (2014).....12

21 C.F.R. § 314.94(a)(3) (2014) 12

21 C.F.R. § 320.1(c) (2014).....13

GLOSSARY

ANDA	Abbreviated New Drug Application
FDA	U.S. Food and Drug Administration
FDCA	Federal Food, Drug and Cosmetic Act
JA	Joint Appendix
RLD	Reference Listed Drug

CERTIFICATE OF PARTIES, RULINGS UNDER REVIEW, AND RELATED CASES

The parties in this case and the ruling under review are set forth in the opening briefs for the Appellants.

STATUTES AND REGULATIONS

All applicable statutes and regulations are contained in the opening briefs for the Appellants.

STATEMENT OF IDENTITY AND INTEREST OF *AMICUS CURIAE*[1]

The Generic Pharmaceutical Association ("GPhA") is a nonprofit, voluntary association representing nearly 100 manufacturers and distributors of finished generic pharmaceutical products, manufacturers and distributors of bulk active pharmaceutical ingredients, and suppliers of other goods and services to the generic pharmaceutical industry. GPhA's core mission is to improve the lives of consumers by providing timely access to affordable pharmaceuticals. GPhA's members provide American consumers with generic drugs that are just as safe and effective as their brand-name counterparts, but substantially less expensive. Generic medicines account for roughly 86% of all prescriptions dispensed in the United States, but only 27% of the money spent on prescriptions. In this way, the products sold by GPhA members save consumers more than $200 billion each year. GPhA regularly participates in litigation as *amicus curiae*, taking legal positions that are adopted by GPhA's Board of Directors and that reflect the position of GPhA as an organization.

GPhA has a strong interest in the proper interpretation of the drug approval framework established by Congress in the "Hatch-Waxman" amendments to the

[1] No party's counsel authored this brief in whole or in part. No party or a party's counsel made a monetary contribution intended to fund the preparation or submission of this brief, and no person other than *amicus curiae*, its members, or its counsel made such a monetary contribution. All parties have consented to the filing of this *amicus* brief.

Federal Food, Drug, and Cosmetic Act ("FDCA"). In particular, GPhA has an overriding interest in ensuring that Hatch-Waxman is not interpreted to impose barriers to competition in pharmaceutical markets, or to reduce patients' access to safe, effective, and affordable medicines, in ways that Congress did not intend.

This case involves the Hatch-Waxman "505(b)(2)" drug approval pathway (21 U.S.C. § 355(b)(2)). The district court correctly upheld FDA's interpretation of section 505(b)(2) to allow the marketing of Intervenor-Appellees' (hereafter "Hikma") anti-gout product Mitigare. The contrary readings of the statute urged by Appellants unsuccessfully below and now on appeal are inconsistent with the clear statutory language and with FDA's longstanding interpretation of section 505(b)(2). If sustained by this Court, Appellants' groundless interpretation of those provisions would undermine the basic pro-competition and pro-access goals of Hatch-Waxman.

SUMMARY OF ARGUMENT

FDA's approval of Hikma's colchicine anti-gout product Mitigare under section 505(b)(2) of the FDCA followed FDA's longstanding approach to that pathway to market. Instead of undertaking costly, duplicative studies to establish the safety and effectiveness of colchicine—an inexpensive drug that has been used to treat gout for centuries—Hikma relied on FDA's previous approval of a related, approved colchicine-probenecid combination drug product, Col-Probenecid.

Hikma supplemented that preexisting approval with its own studies of certain drug-drug interactions relating to colchicine. Based on this combined information, FDA determined that Mitigare was safe and effective and in 2014 approved Hikma's application, increasing price competition in the market for colchicine products. This is exactly how section 505(b)(2) is supposed to work: as an accelerated path to market for drug products that differ from previously approved products, giving patients new therapies and increasing price competition.

In 2009, Appellant Takeda had, like Hikma, used the 505(b)(2) pathway to obtain approval for its colchicine product, Colcrys®; and like Mitigare, Takeda relied on a colchicine-probenecid combination product as its listed drug. Granted exclusive marketing rights for single-ingredient colchicine for three years, Takeda increased the price of the drug 50-fold. Appellants now contend that FDA's approval of Mitigare was illegal and seek to have it rescinded. Their goal is clear: to reinstate Takeda's monopoly in the colchicine product market and avoid genuine price competition in that market for as long as possible. Appellants' various arguments largely boil down to the view that Hikma should have had to identify Colcrys as its listed drug and therefore certify to Takeda's patents for Colcrys. Appellants complain that Hikma avoided patent certification obligations by relying on Col-Probenecid, which is not patent-protected, as its listed drug. Under Hatch-Waxman, if Hikma had been required to certify to the Colcrys patents, Takeda

could have initiated patent litigation that would have delayed FDA's approval of Mitigare by up to 30 months and thereby delayed price competition in the market for colchicine products. 21 U.S.C. § 355(c)(3)(C).

This brief addresses two distinct statutory arguments that Appellants, in their attempt to force Mitigare off the market unless and until Hikma certifies to the Colcrys patents, made unsuccessfully in the District Court and press again on appeal.[2]

First, Appellant Takeda argues that FDA must require, and historically has required, that a 505(b)(2) applicant identify as its listed drug, and therefore certify to patents claiming, the approved drug "most similar" to its test product. Takeda claims that, in the case of Mitigare, the "most similar" drug was Colcrys. Takeda Br. 19-21. But as the district court correctly concluded (JA47-72), FDA has never adopted Takeda's "most similar" test. The inflexible standard Takeda seeks conflicts with the text of section 505(b)(2) and FDA's consistent interpretation that it is the responsibility of the 505(b)(2) applicant to determine which listed drug to

[2] GPhA does not address certain of Appellants' other arguments, other than to agree with Appellees and Intervenor-Appellees that these arguments, which were also uniformly rejected by the district court, are baseless. For example, GPhA does not address Appellants' argument that FDA's reliance on data as part of the 505(b)(2) approval process, not just the applicant's reliance in its application, triggers certification requirements. This argument was correctly rejected by the district court (JA55-63), and in any event the district court also correctly concluded that FDA *in fact* did not rely on Colcrys data to approve Mitigare (JA63-66). Nor does GPhA address Appellants' argument, also rejected below (JA85-93), that FDA improperly approved the label for Mitigare.

reference and how best to combine FDA's prior approval of the listed drug with new studies to secure a determination of safety and effectiveness from the agency. By congressional design, the 505(b)(2) approach for listed drugs differs from the more defined and narrow "reference listed drug" ("RLD") requirements for abbreviated new drug applications ("ANDAs") for generic copies of branded drug products under FDCA section 505(j). Takeda and its *amicus* the Pharmaceutical Research and Manufacturers of America ("PhRMA") seek to impose a parallel RLD requirement for 505(b)(2) products that ignores these differences.

Second, Appellant Elliott argues that whether or not Colcrys was required to be the listed drug for Mitigare, Hikma was required to certify to the Colcrys use patents because a 505(b)(2) applicant is required to certify to any patents that claim the same use as the test product, including use patents for drug products other than the listed drug. Elliott Br. 16-21. PhRMA's *amicus* brief varies this argument slightly to claim that a 505(b)(2) applicant must certify to any patent for a product that is "essential" to the test product's approval, whether or not the patent was for the listed drug. PhRMA Br. 23-25. Both these interpretations conflict with the clear language of Hatch-Waxman (and FDA's consistent interpretation of that language), which requires a 505(b)(2) applicant to certify *only* to patents claimed for a listed drug and none other. Elliott's and PhRMA's interpretations fundamentally distort the basic Hatch-Waxman *quid pro quo*. The statute requires

an applicant to certify to patents *for a listed drug product* as a price for being able to rely on FDA's prior approval *of that same product.* Elliott's and PhRMA's readings would grant brand companies windfall opportunities to delay competition through litigation on patents claimed for products that were not actually relied on by the 505(b)(2) applicant.

Both of Appellants' statutory arguments, if accepted, would have far-reaching implications for 505(b)(2) products by expanding an applicant's certification obligations—and, therefore, the ability of brand companies to delay competition from 505(b)(2) products through patent litigation—well beyond the parameters established by Congress and applied by FDA. The district court rejected Appellants' construction of the FDCA and FDA regulations, and so too should this Court.

While Appellants and PhRMA claim that their readings of Hatch-Waxman are necessary to effectuate the "grand bargain" struck by Congress between increasing competition and incentivizing innovation, these readings would in fact *skew* that balance, by expanding patent certification obligations well beyond what Congress expressly included and intended in Hatch-Waxman. Appellants' bid to impose these requirements in this case—where Takeda (1) itself used the very same 505(b)(2) approval process that it now seeks to deny Hikma; and (2) has

already pursued litigation against Hikma over Colcrys patents *and lost*—is particularly misplaced.

ARGUMENT

I. Takeda's "most similar" test for listed drugs conflicts with the statutory text and FDA's consistent interpretation of section 505(b)(2).

Takeda contends that FDA has historically required a 505(b)(2) applicant to use as its listed drug the product "most similar" to the test product, and that therefore Hikma should have been required to choose Colcrys as the listed drug for its 505(b)(2) application for Mitigare. The district court correctly concluded that Takeda's argument "hinges on the existence of an FDA drug reference policy that does not exist" (JA67), rejecting Takeda's efforts to cobble together a supportive agency position out of unrelated FDA statements that Takeda mischaracterizes or takes out of context. JA67-72.

A. Section 505(b)(2) gives the applicant the responsibility to select the listed drug.

Section 505(b)(2) authorizes a manufacturer to submit for FDA approval an application "for a drug for which *the investigations . . . relied upon by the applicant* for approval . . . 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." 21 U.S.C. § 355(b)(2) (emphasis added). Under this section, the relevant investigations are those "relied upon [that is, *chosen*] by the applicant." This language in no way limits which product the

applicant can rely upon to supply these investigations, much less requires that the listed drug be the product "most similar" to the test product.

Consistent with the statutory text, FDA's longstanding position has been that it is *the 505(b)(2) applicant* that "should determine which listed drug[s] is most appropriate for its development program." JA658; JA68. *See also* Consolidated Citizen Petition Response from Janet Woodcock to Katherine M. Sanzo, *et al.*, at 6, Docket Nos. 2001P-0323/CP1 & C5, 2002P-0447/CP1, and 2203P-0408/CP1 (Oct. 14, 2003) ("*505(b)(2) Petition Response*") (stating that the 505(b)(2) applicant may rely on FDA's finding of safety and effectiveness for "the listed drug it references").

FDA's policy of leaving the choice of the listed drug to the 505(b)(2) applicant is also the only policy that makes sense given the hybrid nature of this type of drug approval application. By its very nature, the 505(b)(2) pathway involves drugs that differ from previously approved drugs in some significant respect. *505(b)(2) Petition Response* at 3 ("a 505(b)(2) application often describes a drug with substantial differences from the listed drug it references," such as "a new dosage form"). As a result, the 505(b)(2) applicant (unlike a manufacturer seeking approval of an ANDA for a generic copy of a brand product under FDCA Section 505(j)) cannot rely entirely on the listed drug to supply all of the safety and effectiveness data it needs for approval. Rather, the applicant relies on some

combination of (1) preexisting information about the listed drug (such as FDA's finding of safety and effectiveness for that product) and (2) the applicant's own studies, to prove the test product's safety and effectiveness. JA654, 659; *505(b)(2) Petition Response* at 3. In these circumstances, it is entirely possible that different combinations of preexisting information and new data may yield the same ultimate conclusion: that the proposed drug is safe and effective for its intended use. Thus, it makes eminent sense for 505(b)(2) applicants to determine in the first instance the mix of old and new information that it thinks will sustain its burden.

The applicant's choice of the listed drug will of course inform the quantity and type of new data needed to fill in the gaps left by the data for the listed drug relied upon by the 505(b)(2) applicant. As FDA has logically stated: "An applicant choosing to rely on FDA's finding of safety and effectiveness for a listed drug very similar to the [test product] would generally need to submit less additional data to support the differences between the proposed product and the listed drug for approval of the 505(b)(2) application." JA658. *See also* JA68 ("[T]here is a direct correlation between the drug the applicant chooses to reference and the applicant's burden of proof."). But as long as the combination of old and new data supports FDA's finding of safety and effectiveness, it is, and should be, largely irrelevant to FDA which listed drug is chosen. *See* JA70-71 ("[I]n addition to the lack of any policy on the part of FDA regarding which drug must be referenced in a Section

505(b)(2) new drug application, there is also no record evidence that clearly demonstrates that the mere existence of 'similar' approved drug products matters to FDA in practice.").

Amicus PhRMA supports the "most similar" listed drug test for 505(b)(2) products by arguing that "there must be consequences that attach to the decision not to cite a closely-related drug—in particular, the loss of ability to rely on the findings of safety and efficacy for the omitted drug's NDA." PhRMA Br. 28-29. Putting aside the fact that neither Hikma nor FDA relied on Colcrys in connection with the Mitigare application and that Mitigare is "closely related" to Col-Probenecid, the "consequences" for a 505(b)(2) applicant who does not cite the "closest-related" listed drug are already built into section 505(b)(2): the applicant must conduct or sponsor more research to fill in the (larger) gaps left by the less-similar listed drug. This tradeoff is inherent in the 505(b)(2) pathway; there is no statutory basis or policy reason (other than Appellants' interest in creating new advantages for patent holders) to impose a new requirement that the applicant choose a particular, "most closely-related" listed drug.

Of course, the 505(b)(2) applicant must prove that the information from the listed drug is "scientifically appropriate and must submit data necessary to support any aspects of the proposed drug product that represent modifications to the listed drug(s)." JA659. If FDA reviews a 505(b)(2) application and concludes that the

sponsor's new studies do not sufficiently fill in any gaps left by a preexisting FDA approval (or other preexisting information relied on by the applicant), the sponsor may well have to reconsider the combination of data in its original application—including, for example, by choosing a different listed drug or conducting additional studies. In this case, FDA, exercising expert scientific judgment which is due the utmost deference from the courts,[3] concluded that no such reconsideration was necessary, and that Hikma's combination of old and new information supported approval of Mitigare as safe and effective. But in any event, FDA's administration of the FDCA has consistently reflected the flexibility that section 505(b)(2) affords the applicant, and the agency has not simply mandated the appropriate listed drug.

B. The Court should preserve the intentional distinctions, in Hatch-Waxman and in FDA's administration of that law, between listed drugs for 505(b)(2) applications and RLDs for ANDAs.

Takeda's argument in essence seeks to graft onto section 505(b)(2) a "most similar" listed drug requirement analogous to the RLD requirement governing ANDAs under section 505(j) (21 U.S.C. § 355(j)). But the listed drugs under these two approval pathways are treated differently, with good reason, and Takeda's attempts to blur these differences are unavailing.

In the 505(j) context, unlike the 505(b)(2) context, the ANDA applicant must show that the proposed generic product is in all significant respects the "same

[3] *Balt. Gas & Elec. Co. v. Nat. Res. Def. Council, Inc.*, 462 U.S. 87, 103 (1983); *Serono Labs., Inc. v. Shalala*, 158 F.3d 1313, 1320-21 (D.C. Cir. 1998).

as" the RLD—i.e., that the two products share, among other things, the same active ingredient, route of administration, dosage form, strength, and labeling (21 U.S.C. § 355(j)(2)(A))—and that the two products are "bioequivalent." 21 U.S.C. § 355(j)(2)(A)(iv).[4] *FDA* generally chooses the RLD, picking the approved product to which the duplicate test product must be bioequivalent. *See*, *e.g.*, 21 C.F.R. § 314.94(a)(3) (2014) ("An [ANDA] must refer to a listed drug. Ordinarily, that listed drug will be the drug product selected by the agency as the reference standard for conducting bioequivalence testing.").

Where different products are supposed to be "the same," and therefore substitutable for one another, it makes sense for FDA to determine the appropriate RLD to ensure consistency between and among products. *See* FDA, Orange Book, http://tinyurl.com/65wqgnt ("By designating a single reference listed drug as the standard to which all generic versions must be shown to be bioequivalent, FDA hopes to avoid possible significant variations among generic drugs and their brand

[4] If an ANDA applicant seeks approval of a product that differs in certain respects from the RLD, it must first file a "suitability petition" with FDA. 21 U.S.C. § 355(j)(2)(C). If FDA finds that additional investigations would be required to establish the safety or effectiveness of the drug with the different feature, then it will deny the petition and require the applicant to file a 505(b)(2) petition instead. 21 U.S.C. § 355(j)(2)(C)(i). Conversely, if a drug is a duplicate of an approved drug, its sponsor must file an ANDA under 505(j) and may not proceed under section 505(b)(2). 21 C.F.R. § 314.101(d)(9) (2014); JA204-05, 207 ("[S]ection 505(b)(2) applications should not be submitted for duplicates of approved products that are eligible for approval under 505(j)").

name counterpart.").[5] But where, as in the 505(b)(2) context, safety and effectiveness can be established through different combinations of old and new data, not simply by reference to a single duplicate product, the decision of which combination to employ, and the related decision of which listed drug to choose, sensibly rests in the first instance with the applicant.

[5] For example, in this very case, FDA determined that all "duplicates" (*i.e.*, pharmaceutical equivalents) of Colcrys were required to follow the 505(j) pathway and use Colcrys as the RLD. JA483. Mitigare, which is a capsule, is indisputably not a "duplicate" of Colcrys, which is a tablet. *See* 21 C.F.R. § 320.1(c) (2014) (defining "pharmaceutical equivalents" as "drug products in *identical dosage forms* that contain identical amounts of the identical active drug ingredient. . . .") (emphasis added); JA212.

In sum, FDA has interpreted the section 505(b)(2) provisions with due regard for its differences from the 505(j) pathway, and this interpretation is correct.[6]

II. Elliott's argument requiring a 505(b)(2) applicant to certify to all patents covering the same use of the proposed drug would fundamentally distort the Hatch-Waxman framework for 505(b)(2) products.

Appellant Elliott goes one step further even than Takeda, arguing that even if a 505(b)(2) applicant is not required to list a particular drug product as its listed

[6] An important related difference between 505(j) products and 505(b)(2) products is that the first 505(j) applicant referencing a particular RLD that includes a "Paragraph IV" certification challenging one of the RLD's patents may be eligible for 180 days of "generic exclusivity"—i.e., a six-month head start on all other generic versions of the RLD (21 U.S.C. § 355(j)(5)(B)(IV))—while 505(b)(2) applicants are ineligible for this exclusivity. Congress included this potentially lucrative incentive to Hatch-Waxman to encourage patent challenges by ANDA applicants. *Teva Pharms. USA, Inc. v. Sebelius*, 595 F.3d 1303, 1305 (D.C. Cir. 2010) ("Th[e] promise of initial marketing exclusivity is [] intended to increase competition by expediting the availability of generic equivalents.") (citations omitted); *Hi-Tech Pharmacal Co. v. FDA*, 587 F. Supp. 2d 1, 4 (D.D.C. 2008) ("As an incentive for generic pharmaceutical companies to undertake the risk of litigation and further the statutory purpose of accelerating public access to lower-cost drugs, the first ANDA-applicant that files a paragraph IV certification is entitled to a 180-day period of generic marketing exclusivity.") (citation omitted). *However, section 505(b)(2) products are ineligible for 180-day exclusivity*. Instead, Hatch-Waxman gives 505(b)(2) applicants an incentive that rewards innovation: three years of exclusivity if they conduct or sponsor new clinical studies "essential" to approval. 21 U.S.C. § 355(c)(3)(E)(iii). The unavailability of 180-day exclusivity for 505(b)(2) products means that 505(b)(2) applicants have less of an incentive to challenge brand company patents, and more of an incentive to choose, as Hikma did, a pathway that avoids any patent certification obligations but still provides an expedited path to FDA approval. In other words, Hikma's choice of development programs in this case is explained by, and appropriate given, the incentive structure built into Hatch-Waxman by Congress.

drug, it must certify to *any* patents that claim the method of using the drug *substance* for which 505(b)(2) approval is sought, *whether or not that patent was for the listed drug and whether or not the applicant relied on data relating to investigations of the drug product covered by the patent*. Elliott Br. 16-29.

The district court roundly rejected this interpretation of Hatch-Waxman, upholding under "*Chevron* Step One" FDA's contrary interpretation that a 505(b)(2) applicant need only certify to patents claimed by the drug product relied on by the applicant. JA74-75 (citing *Chevron U.S.A., Inc. v. Nat. Res. Def. Council, Inc.*, 467 U.S. 837, 842-43 (1984)). The district court's analysis was correct, as was its conclusion that even if Hatch-Waxman is ambiguous on this issue, FDA's interpretation is a reasonable interpretation entitled to deference under "*Chevron* Step Two." JA84-85.

GPhA need not restate the extensive textual and structural support for the district court's conclusion, except to emphasize that Elliott's unprecedented reading of Hatch-Waxman would fundamentally upset the careful balance Congress sought to achieve between encouraging innovation and expediting market competition. As the district court explained (JA82), the *quid pro quo* at the heart of Hatch-Waxman is that a 505(b)(2) or 505(j) applicant must certify to the listed drug's patents (and provide notice of certification to the patent-holder) as a price for being able to rely on the investigations relating to the listed drug. But if

an applicant must also certify to use patents for products on which it did not rely, it is paying a steep price—exposure to resource-draining patent litigation, a 30-month delay in marketing approval, and greater overall uncertainty regarding its business—without receiving anything in return. This reading of Hatch-Waxman simply cannot be squared with the statute's basic framework and purposes and would significantly disincentivize use of the 505(b)(2) pathway.

Far from "undermin[ing] the interlocking system of benefits and burdens Congress built into the Hatch-Waxman Act" (PhRMA Br. 22), the district court's decision maintains the Hatch-Waxman system against Elliott's efforts to distort it. *See* JA82 ("[F]rom the standpoint of what Congress intended, if Congress really meant to tip the carefully-balanced Hatch-Waxman scales so dramatically toward the protection if innovator's patent rights, there would be no reason at all for the statute to so clearly reflect Congress's interest in achieving that balance at all.").

PhRMA offers a variant on Elliott's argument by claiming that an applicant's certification obligations under section 505(b)(2) must extend beyond patents for products that were the subject of the investigations actually "relied upon" by the applicant, to patents for products that were "essential" to the 505(b)(2) application's approval. PhRMA Br. 23-24. This reading of the statute untethers the term "investigations relied upon by the applicant" language from its plain meaning: to PhRMA, "investigations relied upon by the applicant" includes

investigations that were *not* relied on by the applicant. And like Elliott's statutory interpretation, PhRMA's interpretation would expand an applicant's patent certification obligations well beyond the scope of the "reliance benefit" received by the applicant.

III. Hatch-Waxman's "grand bargain" does not support Appellants' statutory interpretations.

Appellants and their *amicus* PhRMA repeatedly allude to the "grand bargain" effected by Hatch-Waxman in support of their statutory interpretations, which as the district court properly found, would dramatically tilt the Hatch-Waxman balance of interests in favor of patentholders. JA82.

The particular facts of this case further undercut Appellants' and PhRMA's reliance on the "grand bargain." First, PhRMA makes much of the billions of dollars spent by brand companies on the development of innovative new medicines, arguing that Appellants' reading of the statute (which would change how Hatch-Waxman has been interpreted in the 31 years since its enactment) is necessary to incentivize continued investment. PhRMA Br. 24. But the reality is that colchicine—singly or in combination with probenecid—has been used for centuries as a safe and effective treatment of gout; *both* Takeda and Hikma sold colchicine products in the past; and Takeda, like Hikma, relied on FDA's prior approval of a colchicine combination product under the 505(b)(2) pathway for *its* approval. Appellants, having taken advantage of FDA's prior approval of Col-

Probenecid through the expedited 505(b)(2) pathway, are now trying to unwind Hikma's successful use of that same pathway to regain their monopoly position and reap monopoly profits for another 30 months. That is not an outcome that Hatch-Waxman's "grand bargain" was designed to protect.[7]

In addition, while Hatch-Waxman's patent certification process provides a mechanism to expedite the resolution of patent disputes before FDA approves generic or 505(b)(2) alternatives, that process is no longer necessary here because Takeda has already litigated its patent infringement claims against Hikma over Colcrys patents, and lost. *Takeda Pharms. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625 (Fed. Cir. 2015). Requiring Hikma to follow the certification procedures at this point would simply give Appellants a windfall by allowing them to initiate a repeat round of patent litigation, triggering another mandatory 30-month stay. This relief has no justification in the text, structure, or policies of Hatch-Waxman.

CONCLUSION

For the foregoing reasons, this Court should affirm the decision below.

[7] To the extent that Takeda undertook new drug-drug interaction studies to support its approval for Colcrys, it has already received a significant Hatch-Waxman benefit from that investment, in the form of three-year statutory data exclusivity that expired in 2013. 21 U.S.C. § 355(c)(3)(E)(iii).

October 23, 2015

Respectfully submitted,

/s/ Carlos T. Angulo

Carlos T. Angulo
Andrew N. Goldfarb
Zuckerman Spaeder LLP
1800 M Street, NW, Suite 1000
Washington, DC 20036
Telephone: (202) 778-1800
cangulo@zuckerman.com

Attorneys for Amicus Curiae
Generic Pharmaceutical Association

CERTIFICATE OF COMPLIANCE WITH FEDERAL RULE OF APPELLATE PROCEDURE 32(a)

This brief complies with the type-volume limitation of Federal Rule of Appellate Procedure 32(a)(7)(B) because this brief contains 4,442 words, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(a)(7)(B)(iii).

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 in 14-point Times New Roman font.

/s/ Carlos T. Angulo
Carlos T. Angulo

CERTIFICATE OF SERVICE

Pursuant to D.C. Circuit Local Rule 25(c), I hereby certify that on this 23rd day of October, 2015, I electronically filed the foregoing **BRIEF OF *AMICUS CURIAE* GENERIC PHARMACEUTICAL ASSOCIATION** with the Court by using the CM/ECF system. All parties to the case have been served through the CM/ECF system.

/s/ Carlos T. Angulo
Carlos T. Angulo