No. 2009-1362

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

ORTHO-McNEIL PHARMACEUTICAL, INC., and ORTHO-McNEIL, INC.,

Plaintiffs-Appellees,

and

DAIICHI SANKYO CO., LTD.,

Plaintiff-Appellee,

v.

LUPIN PHARMACEUTICALS, INC., and LUPIN LTD.,

Defendants-Appellants.

APPEAL FROM THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF NEW JERSEY
IN CASE NO. 06-4999
CHIEF JUDGE GARRETT E. BROWN, JR.

BRIEF OF PLAINTIFFS-APPELLEES ORTHO-McNEIL PHARMACEUTICAL, INC., ORTHO-McNEIL, INC., AND DAIICHI SANKYO CO., LTD.

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CERTIFICATE OF INTEREST

Counsel for Plaintiffs-Appellees Ortho-McNeil Pharmaceutical, Inc. and Ortho-McNeil, Inc. certifies the following:

1. The full name of every party represented by me is:

   Ortho-McNeil Pharmaceutical, Inc. and Ortho-McNeil, Inc.

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:

   N/A

3. All parent corporations and any publicly held companies that own 10 percent of more of the stock of the parties represented by me are:

   Ortho-McNeil Pharmaceutical, Inc. and Ortho-McNeil, Inc. are wholly-owned subsidiaries of Johnson & Johnson

4. The names of all law firms and the partners or associates that appeared for the parties now represented by me in the trial court or are expected to appear in this court are:

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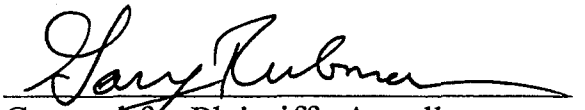

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1. The full name of every party represented by me is:

   Daiichi Sankyo Co. Ltd.

2. The name of the real party in interest (if the party named in the caption is not the real party in interest) represented by me is:

   N/A

3. All parent corporations and any publicly held companies that own 10 percent of more of the stock of the parties represented by me are:

   None.

4. The names of all law firms and the partners or associates that appeared for the parties now represented by me in the trial court or are expected to appear in this court are:

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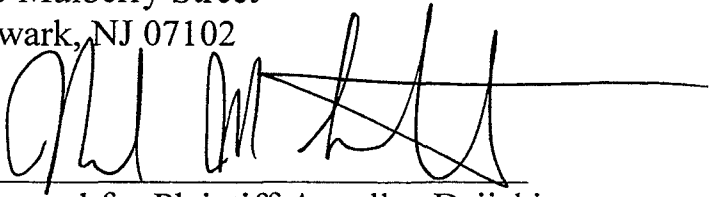

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STATEMENT OF RELATED CASES

In a prior appeal, this Court affirmed the District Court's construction of the claims of U.S. Patent No. 5,053,407 (the "'407 patent") and upheld the validity of the '407 patent. *See Ortho-McNeil Pharm. Inc. v. Mylan Labs., Inc.*, 161 Fed. Appx. 944 (Fed. Cir. 2005).

PRELIMINARY STATEMENT

Lupin seeks to overturn the District Court's considered judgment upholding the longstanding and well-established practice of two expert agencies, acting in concert in an area where they possess unique and specialized expertise, to treat racemates as single "active ingredients," distinct from their enantiomers, for purposes of patent term extensions. Due to the scientific and technical nature of the determinations of the PTO and FDA, "great deference" is owed to these agency decisions. As the District Court correctly found, Lupin cannot meet its burden of demonstrating by clear and convincing evidence that the decision of the PTO, informed by FDA expertise, to extend the term of the '407 patent was in any way incorrect.

The '407 patent claims levofloxacin, the active ingredient in the blockbuster anti-infective medication Levaquin®. The validity of the '407 patent, which has withstood several prior challenges, is not at issue in this case, nor is the issue of whether Lupin's proposed generic product will infringe the '407 patent. Instead, Lupin argues only that the District Court erred by failing to overturn the PTO's and FDA's policy of granting patent term extensions to enantiomer products notwithstanding the prior approval of the corresponding racemate – a policy that is entirely consistent with well-established agency practice and longstanding industry custom, including Lupin's own practice prior to the new theory that it advances in

this litigation. Lupin also asserts for the first time that the District Court's injunction is too broad.

Lupin's arguments should be rejected for the following reasons:

First, the determinations of the PTO and FDA, which are consistent with their longstanding practice, are entitled to "great deference." Lupin has failed to offer any reason why this Court should substitute its judgment for the sound judgment of the PTO and FDA, the two agencies that possess the expertise necessary to make the scientific determinations regarding eligibility for patent term extensions and that were delegated by Congress to do so. *See* Sections I, II.

Second, this Court should affirm on the alternative ground (raised by Plaintiffs below, but not addressed in the District Court's opinion) that, under the uncontested claim construction of the '407 patent, Floxin® (the racemate) does not contain what is *claimed* in the '407 patent. That is, without regard to deference or burdens, the FDA and PTO were correct to conclude that the approval of Levaquin® was the first permitted commercial marketing of the product claimed in the '407 patent. This conclusion is confirmed by the undisputed science.

Repeating the mistake of each of the prior unsuccessful generic challengers to the '407 patent, Lupin conflates racemic ofloxacin, the active ingredient in Floxin®, with optically active and substantially pure levofloxacin, the active ingredient in Levaquin® – this time to argue that the commercial marketing of the

former precludes a term extension for the latter. But this attack, like those before, must fail because of the undisputed factual record that levofloxacin and racemic ofloxacin are, in fact, very different compounds, with different chemical properties (*e.g.*, solubility) that result in vastly different biological properties and pharmacological effects in patients. Lupin does not contend, nor could it prove, that the FDA's approval of Floxin® permitted the commercial marketing or use of substantially optically pure levofloxacin, which is precisely the showing that Lupin must make to prevail in this case. *See* Section III.

Finally, Lupin has waived its right to challenge the scope of the injunction by failing to assert any objections below, but, in any event, the District Court's injunction is entirely consistent with Section 156. *See* Section IV.

COUNTERSTATEMENT OF THE ISSUES

Although Lupin presents four issues for the Court to review, this case involves only two issues that are properly before the Court and one newly-asserted issue that was not raised in the District Court and, therefore, was waived:

1. Did the District Court correctly conclude that no reasonable factfinder could find that Lupin would be able to demonstrate by clear and convincing evidence that the PTO and FDA – acting in a manner consistent with longstanding agency and industry practice and in an area where they possess expertise and are entitled to great deference – improperly granted a term extension to the '407 patent?
2. Alternatively, would Lupin have been able to demonstrate to a reasonable factfinder that, under the uncontested claim construction of the '407 patent and the undisputed science, the approval of Levaquin® did not constitute the first permitted commercial marketing of the product *claimed* in the '407 patent, *i.e.*, substantially optically pure levofloxacin, which is the showing that Lupin would have to make to invalidate the patent term extension?
3. Did Lupin waive any objection to the scope of the injunction by failing to raise this issue in the District Court and, if not, did the District Court err by enjoining Lupin from engaging in conduct that infringes the '407 patent?

COUNTERSTATEMENT OF THE CASE

Plaintiffs-Appellees Ortho-McNeil Pharmaceutical, Inc., Ortho-McNeil, Inc., and Daiichi Sankyo Co., Ltd. are, respectively, the exclusive U.S. licensees and owner of the '407 patent, which claims substantially optically pure levofloxacin, the active ingredient in the anti-infective Levaquin®. Floxin®, an anti-infective that has racemic ofloxacin as its active ingredient, was previously approved by the FDA. Ofloxacin is a racemate, consisting of equal amounts of its two enantiomers. The PTO, informed by FDA expertise and with full knowledge of the prior approval of Floxin®, granted a patent term extension to the '407 patent. Lupin filed an abbreviated new drug application ("ANDA") seeking to market a generic version of Levaquin® prior to the expiration of the '407 patent's term extension. Lupin's ANDA contained a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(VI) ("Paragraph IV certification") alleging that the '407 patent's term extension was invalidly granted. Plaintiffs-Appellees brought suit for patent infringement under 35 U.S.C. § 271(e)(2) in response to Lupin's notice letter notifying them of the Paragraph IV certification.

Lupin stipulated to the validity and infringement of the '407 patent. The parties filed cross-motions for summary judgment in the District Court on the sole issue before the Court: whether the patent term extension for the '407 patent was validly granted. The District Court upheld the validity of the term extension,

denying Lupin's motion and granting Plaintiffs-Appellees' cross-motion, concluding that Lupin "is not able to present clear and convincing evidence that the PTO's decision to extend the term of the '407 patent is invalid." The Court found that, given the consistent action of the PTO and FDA in granting term extensions to "patents covering enantiomeric products subsequent to approval of their corresponding racemates . . . the undisputed facts clearly establish the PTO has determined that enantiomers are 'products' eligible for patent term extension pursuant to 35 U.S.C. § 156 . . . [and] this Court must give great deference to this determination by the PTO." The District Court enjoined Lupin from "making, using, offering to sell, selling or importing ... the levofloxacin tablets described in ANDA No. 78-424 or bulk levofloxacin for use in manufacturing such tablets" prior to the expiration of the '407 patent, including all term extensions. Lupin appeals the District Court's decision.

COUNTERSTATEMENT OF THE FACTS

Invention of Ofloxacin and Levofloxacin

After years of research, Daiichi Pharmaceutical Company, Ltd. (predecessor to Daiichi) synthesized ofloxacin, a new quinolone anti-infective, for which it obtained U.S. Patent No. 4,382,892 ("the '892 patent") in 1983. In December 1990, the FDA approved Ortho's New Drug Application for Floxin®, which, as its FDA-approved labeling and its Orange Book entry confirm, contains a single active ingredient: ofloxacin. A17, A1170 (¶1), A1210 (Declaration of David T. Lin ("Lin") ¶25), A1461 (Lin Exhibit F).

Ofloxacin is a racemate, which is a compound[1] consisting of equal amounts of two "optical isomers" or "enantiomers," molecules that are identical except for the orientation of their atoms in space.[2] A1170 (¶2), A2492-93 (Wentland ¶15). Chemists distinguish enantiomers by their "optical activity" – *i.e.*, by the direction in which they rotate a plane of polarized light, with "(+)" indicating clockwise rotation ("dextrorotatory") and "(–)" indicating counter-clockwise rotation ("levorotatory"). A17, A1171 (¶¶3-4), A2495-96 (Wentland ¶21). Chemists also distinguish optical isomers more directly based on the spatial orientation of their

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[1] Contrary to Lupin's assertion, *see* Lupin Br. at 5, racemic ofloxacin is not a "mixture" of its two enantiomers. Rather, the undisputed scientific evidence is that ofloxacin is a distinct racemic compound. A2499-2500 (Declaration of Mark P. Wentland ("Wentland") ¶27), A1553-54 (Declaration of Allan S. Myerson ("Myerson") at n.3).

[2] Plaintiffs-Appellees use the terms "optical isomers" and "enantiomers" synonymously.

atoms, using nomenclature designations such as "S" and "R." A1171 (¶5), A2496-97 (Wentland ¶22). Racemates are, by definition, optically *in*active – *i.e.* they do not rotate a plane of polarized light – and are indicated by a "(±)" or "(RS)" symbol or the absence of any symbol. A1171 (¶6); *Ortho-McNeil Pharmaceutical Inc. v. Mylan Labs., Inc.*, 348 F. Supp. 2d 713, 721 (N.D. W. Va. 2004), *aff'd*, 161 Fed. Appx. 944 (Fed. Cir. 2005).

Ofloxacin was not an optimal anti-infective, and Daiichi spent years searching for a better quinolone. A1171 (¶7), A2331 (Declaration of George G. Zhanel ("Zhanel") ¶32). Among the many research paths they pursued, Daiichi scientists attempted to separate ofloxacin into its constituent enantiomers (a process known as resolution), although they doubted that the enantiomers would be more effective than ofloxacin itself. A1172 (¶9), A2502 (Wentland ¶31); *Mylan*, 348 F. Supp. 2d at 754. All such resolution attempts were unsuccessful. However, after four years of failure, Daiichi eventually succeeded in synthesizing the S(–) enantiomer, levofloxacin, using novel synthesis routes, rather than obtaining it from racemic ofloxacin. A18, A1172 (¶¶10-11), A2502 (Wentland ¶¶31-32). The substantially optically pure levorotatory enantiomer, or *levo*floxacin, was more active, more water-soluble and less toxic than ofloxacin (A18, A1172 (¶¶12-13), A1555 (Myerson ¶22), A2339 (Zhanel ¶55)), and was "pharmaceutically superior

to ofloxacin in virtually every relevant aspect." *Mylan*, 348 F. Supp. 2d at 751, 754. Levofloxacin turned out to be a totally different and dramatically better drug.

Patenting and Approval of Levofloxacin

On June 20, 1986, Daiichi filed the U.S. patent application that ultimately issued as the '407 patent. A18, A1173 (¶14), A1032 (Declaration of Karen A. Confoy ("Confoy") Exhibit F). The PTO initially rejected the claims as obvious in view of – though not anticipated by – ofloxacin. A18, A1173 (¶15), A2537-42 (Declaration of Noah M. Leibowitz ("Leibowitz") Exhibit A (file history excerpts)). However, after considering the unexpected benefits of levofloxacin over ofloxacin, the PTO allowed the claims, and the '407 patent issued on October 1, 1991. A18, A1173 (¶¶16-17), A2544-51, 2561 (Leibowitz Exhibit A (file history excerpts)); *Mylan*, 348 F. Supp. 2d at 743.

Claim 2 of the '407 patent is directed to an "S(–)" compound whose common name is levofloxacin. A19, A1174 (¶18), A1044 (Confoy Exhibit F). Claim 5 is directed to a process for treating a patient with "an antimicrobially effective amount" of the same compound. A19, A1174 (¶19), A1044 (Confoy Exhibit F). These claims were construed by Chief Judge Irene Keeley of the Northern District of West Virginia to refer to *optically active and substantially optically pure* levofloxacin (A19, A1174 (¶20); *Mylan*, 348 F. Supp. 2d at 728-30), a construction also adopted by the District of New Jersey in granting Plaintiffs-

Appellees summary judgment against several other ANDA challengers in *Ortho-McNeil Pharm. Inc. v. Teva Pharms. USA* (Civil Action No. 02-2794) (Brown, C.J.). A1174 (¶21). Lupin does not challenge the patentability of levofloxacin, nor the construction of claims 2 and 5 of the '407 patent as describing optically active and substantially optically pure levofloxacin. A1174 (¶22), A889-92 (Confoy Exhibit A). As construed, claims 2 and 5 necessarily exclude racemic ofloxacin because racemic ofloxacin, which contains an equal number of S(–) and R(+) molecules, is optically *in*active and optically *im*pure. A1174-75 (¶23); *Mylan*, 348 F. Supp. 2d at 726-29.

In 1996, the FDA approved Levaquin®, which is marketed by Ortho. Its FDA-approved labeling, as well as the Orange Book, identifies Levaquin® as containing a single active ingredient: levofloxacin. A19, A1175 (¶24), A1210 (Lin ¶25), A1496 (Lin Exhibit G).

Grant of Patent Term Extension

As part of the Hatch-Waxman Act, Congress amended the Patent Act to afford certain patents a term extension to compensate the patentee for time spent obtaining regulatory approval for the sale of products covered by the patent. *See, e.g.*, 35 U.S.C. §§ 155-156. Congress believed that, where a patentee must obtain regulatory approval before marketing a product covered by the patent (as with pharmaceuticals, which must be approved by the FDA), the patent term should be

extended to ensure that there is a sufficient patent term remaining after the product comes to market to protect the patentee's investment in innovation. *See* 130 Cong. Rec. S10504 (daily ed. Aug. 10, 1984) (statement of Sen. Hatch) ("[Congress sought to] restore to our domestic drug companies some of the incentive for innovation which has weakened as Federal pre-market approval requirements have become more expensive and time consuming.").

A decision on whether a U.S. patent should be extended under the Hatch-Waxman provisions, and for how long, involves both the PTO and FDA acting in concert to evaluate the merits of an extension request. A19, A1175 (¶25), A1778-80 (Declaration of Gerald J. Mossinghoff ("Mossinghoff") ¶10). The PTO and the FDA do so pursuant to a Memorandum of Understanding ("MOU") that sets forth the formal procedures to be followed to ensure that a patent meets all the qualifications for extension. A19-20, A1175 (¶26), A1778-80 (Mossinghoff ¶10), A1210 (Lin ¶24); *see* 52 Fed. Reg. 17,830 (May 12, 1987).

On February 18, 1997, Daiichi submitted to the PTO an application for term extension of the '407 patent. A19, A1175 (¶27), A1780 (Mossinghoff ¶11). Daiichi specifically informed the PTO that Floxin® had been previously approved by the FDA and that the term of the '892 patent covering racemic ofloxacin had previously been extended. A20, A1175 (¶28), A1780 (Mossinghoff ¶11). Pursuant to the MOU, the PTO sent the term extension application to the FDA,

indicating that the patent "would be eligible for extension of the patent term under 35 U.S.C. § 156 if the approval of Levaquin® is the first permitted marketing or use of the active ingredient thereof," and requesting confirmation of the same. A20, A1176 (¶29), A1780-81 (Mossinghoff ¶12), A1210 (Lin ¶27). The letter from the PTO further informed the FDA that "[a]pplicant has stated that the 'corresponding racemate Floxin' has been previously approved." A20, A1176 (¶30), A1780-81 (Mossinghoff ¶12).

On July 18, 1997, the FDA sent a letter to the PTO, stating that

> A review of the Food and Drug Administration's official records indicates that this product [Levaquin®] was subject to a regulatory review period before its commercial marketing or use, as required under 35 U.S.C. § 156(a)(4). *Our records also indicate that it represents the first permitted commercial marketing or use of the product*, as defined under 35 U.S.C. § 156(f)(1), and interpreted by the courts in *Glaxo Operations UK Ltd. v. Quigg,* 706 F. Supp[.] 1224 (E.D. Va. 1989), *aff'd* 894 F.2d 392 (Fed. Cir. 1990).

A20-21, A1176 (¶31), A1781 (Mossinghoff ¶13), A1548 (Lin Exhibit H) (emphasis added).

Additional correspondence between the PTO and the FDA established the length of the regulatory review period and the corresponding length of the patent term extension, and, on August 4, 1999, the PTO granted the requested patent term extension. A21, A1176 (¶32), A1781-85 (Mossinghoff ¶¶14-18).

The Present Action

On June 14, 2006, Lupin submitted ANDA No. 78-424 to the FDA seeking to market levofloxacin prior to the expiration of the '407 patent. A21-22, A883 (¶26). In response to Lupin's notice letter, Plaintiffs-Appellees filed a complaint seeking a declaration that the patent term extension granted for the '407 patent is valid. A22, A61-89 at A71 (Complaint ¶41). In a Joint Stipulation and Order entered on June 11, 2007, Lupin stipulated to the validity and enforceability of the '407 patent and agreed that it would contest only the validity of the term extension. A22, A108-111.

The parties filed cross-motions for summary judgment on this issue, and the District Court issued its decision on April 30, 2009 denying Lupin's motion and granting Plaintiffs-Appellees' motion. A16-29, A849-A2931. Lupin filed a notice of appeal on May 5, 2009. A15.

SUMMARY OF THE ARGUMENT

This Court should affirm the District Court's grant of summary judgment. The District Court correctly afforded "great deference" to the scientific and technical determinations of the PTO – based on the expertise of the FDA – that the '407 patent is entitled to a term extension. The determination of both agencies is consistent with their established procedures and longstanding practices to treat the "active ingredient" in racemic drugs as the racemate, distinct from either or both of its enantiomers, and, accordingly, to grant term extensions to patents covering enantiomeric products, notwithstanding the prior approval of the corresponding racemic product. The decisions of the PTO and FDA also were consistent with longstanding industry practice.

This Court already has rejected Lupin's principal argument that the term "active ingredient" must have an identical meaning for purposes of the Hatch-Waxman Act's patent term extension provisions and the non-patent regulatory exclusivity provisions. As this Court held in *Glaxo Operations UK Ltd. v. Quigg*, 894 F.2d 392, 399 (Fed. Cir. 1990), Congress used "well-established scientific terms" in Section 156 and "specifically selected terms with narrow meanings that it chose from among many alternatives." Congress did not intend the definition of "product" in Section 156 to mean "new chemical entity" or "active moiety," as used in the non-patent regulatory exclusivity provisions. *See id.* at 397-98. And,

contrary to Lupin's contention, even if "active ingredient" and "active moiety" were synonymous, levofloxacin and racemic ofloxacin would be distinct active moieties too.

Apart from the deference the District Court properly gave to the expertise of the PTO and FDA, the judgment can be affirmed on the alternative ground that the term extension decision was simply correct, as demonstrated by an extensive and undisputed factual showing below, which the District Court did not need to reach. Under the uncontested claim construction of the '407 patent, Levaquin® represents the first permitted commercial marketing of the product *claimed* in the '407 patent – optically active and substantially optically pure levofloxacin. As there is no dispute that Floxin® (the racemate) does not contain what is *claimed* in the '407 patent, Lupin cannot make the showing necessary to invalidate the patent term extension under Section 156(a). Also, the undisputed scientific evidence proves that racemic ofloxacin – not either of its individual enantiomers – was intended to and did furnish the pharmacological activity of Floxin® and therefore is properly regarded as Floxin®'s single "active ingredient." That is, the factual record below demonstrates beyond dispute that Levaquin® and Floxin® are distinct, with each having its own unique "active ingredient."

Finally, Lupin did not object to the scope of the District Court's injunction below and, therefore, cannot raise such objections for the first time in this appeal.

Even if preserved, however, Lupin's objections should be rejected because a patent holder's rights during a term extension period are indistinguishable from those held prior to the extension. Therefore, the District Court did not abuse its discretion by enjoining Lupin from making, using, offering to sell, selling and importing levofloxacin for its FDA approved use.

STANDARD OF REVIEW

This Court reviews a District Court's grant of summary judgment *de novo*. *See Revolution Eyewear, Inc. v. Aspex Eyewear, Inc.*, 563 F.3d 1358, 1365 (Fed. Cir. 2009). With respect to a District Court's denial of summary judgment, however, this Court gives "considerable deference to the trial court and will not disturb [the denial] unless [this Court] finds that the [district] court has indeed abused its discretion." *Id.* (quoting *Little Six, Inc. v. United States*, 280 F.3d 1371, 1373 (Fed. Cir. 2002)) (internal quotes omitted); *Suntiger, Inc. v. Scientific Research Funding Group*, 189 F.3d 1327, 1333 (Fed. Cir. 1999) ("When a district court *grants* summary judgment, we review without deference to the trial court. . . . By contrast, when a district court *denies* summary judgment, we review that decision with considerable deference to the court.") (internal citations omitted).

When conducting a *de novo* review, this Court applies the standard of proof that was applicable in the District Court, *see Carnegie Mellon Univ. v. Hoffman-La Roche, Inc.*, 541 F.3d 1115, 1121 (Fed. Cir. 2008), and must view "the evidence presented through the prism of the substantive evidentiary burden." *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 254 (1986); *see Quad Envtl. Techs. Corp. v. Union Sanitary Dist.*, 946 F.2d 870, 872 (Fed. Cir. 1991). Here, because the "presumption of validity applies to the PTO's determination to grant a patent term extension," *Pfizer, Inc. v. Ranbaxy Labs. Ltd.*, 405 F. Supp. 2d 495, 511 (D. Del.

2005), *aff'd in part, rev'd in part on other grounds*, 457 F.3d 1284 (Fed. Cir. 2006), this Court can reverse the District Court's grant of summary judgment only if it concludes that at trial Lupin affirmatively could have advanced clear and convincing evidence that the term extension of the '407 patent was invalid. *See Pfizer*, 457 F.3d at 1291 ("Ranbaxy failed to establish by clear and convincing evidence that the term extension was invalid."). Clear and convincing evidence exists when the movant "place[s] in [the mind of] the ultimate factfinder an abiding conviction that the truth of its factual contentions are 'highly probable.'" *Colorado v. New Mexico*, 467 U.S. 310, 316 (1984) (internal citations omitted). Lupin's burden is particularly high in this case because it must overturn the determinations of not one, but two agencies that possess expertise in this area and are entitled to "great deference." *See infra* at Section I.

This Court reviews the District Court's decision to grant an injunction and the scope of that injunction for abuse of discretion. *Joy Techs., Inc. v. Flakt, Inc.*, 6 F.3d 770, 772 (Fed. Cir. 1993). Lupin can show abuse of discretion only if the District Court made a clear error of judgment or exercised its discretion based upon an error of law or clearly erroneous factual findings. *Id.*

ARGUMENT

The patent term extension provisions of the Hatch-Waxman Act are codified at 35 U.S.C. § 156. Section 156(a) provides in relevant part as follows:

> The term of a patent which claims a product, a method of using a product, or a method of manufacturing a product shall be extended ... if--
>
> **(1)** the term of the patent has not expired before an application is submitted under subsection (d)(1) for its extension;
>
> **(2)** the term of the patent has never been extended under subsection (e)(1) of this section;
>
> **(3)** an application for extension is submitted by the owner of record of the patent or its agent and in accordance with the requirements of paragraphs (1) through (4) of subsection (d);
>
> **(4)** the product has been subject to a regulatory review period before its commercial marketing or use;
>
> **(5)(A)** except as provided in subparagraph (B) or (C), the permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred...

There is no dispute in this case that the provisions of Section 156(a)(1)-(4) are satisfied in the case of the '407 patent. Lupin's sole argument is that the FDA's approval of Levaquin® was not the "first permitted commercial marketing or use of the product" claimed in the '407 patent because the FDA had previously approved Floxin®. *See* Lupin Br. at 5.

Section 156(f) provides the relevant definition of "product" for purposes of Section 156(a) as meaning "drug product," and goes on to define "drug product" as follows:

> **(2)** The term "drug product" means the active ingredient of--
>
> **(A)** a new drug, antibiotic drug, or human biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act), ...
>
> including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient.

Finally, the parties here agree that the FDA defines "active ingredient" for purposes of Section 156 as follows:

> Active ingredient means any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or of animals. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect.

21 C.F.R. § 60.3(b)(2); *see* Lupin Br. at 14 (adopting this definition).

Thus, the central question here is whether Lupin can prove by clear and convincing evidence that the "component that is intended to furnish pharmacological activity or other direct effect" in Levaquin® was previously

approved in Floxin®, and therefore the FDA's approval of Levaquin® was not the "first permitted commercial marketing or use of the product."

As discussed more fully below, Lupin cannot possibly meet its burden here based on (1) the contrary decision of the FDA and PTO in this case, which observes the agencies' longstanding policy of granting patent term extensions in like circumstances, is entirely consistent with longstanding industry practice and is entitled to "great deference;" and (2) the uncontested claim construction and undisputed scientific evidence proving that substantially optically pure levofloxacin – the "component that is intended to furnish pharmacological activity or other direct effect" in Levaquin® – is categorically different from racemic ofloxacin – the "component that is intended to furnish pharmacological activity or other direct effect" in Floxin®. This Court should therefore affirm the District Court's grant of summary judgment to Plaintiffs-Appellees.

I. THE DISTRICT COURT CORRECTLY AFFORDED "GREAT DEFERENCE" TO THE DETERMINATION BY THE PTO AND FDA THAT LEVAQUIN® CONSTITUTES THE FIRST PERMITTED COMMERCIAL MARKETING OR USE OF LEVOFLOXACIN

The decision to grant a term extension to the '407 patent, which involved the application of the long-standing and accepted definition of "active ingredient" to a set of highly complex scientific facts, is entitled to "great deference" under this Court's precedent as well as fundamental principles of federal judicial review. Lupin attempts to avoid the "great deference" standard by suggesting that this case

involves issues of statutory construction, *see* Lupin Br. at 18-19, but Lupin has not identified any statutory provision that requires construction.

In fact, both sides agree that the term "active ingredient" had a "well-defined, ordinary, common meaning when Congress enacted the [Hatch-Waxman] Act [in 1984]." *See* Lupin Br. at 25 (quoting *Glaxo*, 894 F.2d at 395). This definition has remained unchanged since the FDA first adopted it in the 1970s, years before the enactment of Hatch-Waxman. *See id.* Accordingly, there is no dispute that the well-understood meaning of the term "active ingredient" is the definition set forth in the FDA's regulations: "any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or of animals." *Id.*; 21 CFR § 210.3(b)(7). At no point has Lupin identified any particular statutory "construction" or "interpretation" that in any way departs from the FDA's long-standing definition. Thus, as Lupin readily admitted in its summary judgment briefing below, this case involves agency *application* of this accepted definition to a particular set of circumstances, not the *interpretation* of a statute. *See* A2572 (Lupin's Opposition and Reply Brief on Summary Judgment at 5 & n.1) (agreeing with the statement that "[t]he issue presented by these dueling motions is not one of statutory

interpretation, but rather the application of the long-standing definition of 'active ingredient' by the FDA when it approved the racemic product Floxin®").

Under controlling Federal Circuit precedent, the determination of the PTO – made after consulting the FDA, which provided the controlling definition of "active ingredient" – of whether the "active ingredient" contained in Levaquin® was previously approved as an "active ingredient" in Floxin® is entitled to "great deference."[3] In *Glaxo*, this Court concluded that Congress used "well-established scientific terms" (including "active ingredient") in the definition of "product" in the patent term extension provisions of Section 156, and that those terms had unambiguous meanings. *Glaxo*, 894 F.2d at 398, 399. Accordingly, the Court gave little deference to the PTO's own interpretation of the statutory term "product," but afforded "great deference" to the PTO's "determinations as to which patented chemical compounds fall within Congress' definition of 'products.'" *Id.* at 399 ("[A]ll Congress left to the Commissioner's technical expertise was determining *whether* any patented chemical compound named in a patent term extension application fell within the statutory definition of 'product,' but *not what* 'product' was to mean.") (emphasis in original). This is precisely the determination that the PTO, on advice of the FDA, made here and as this Court has

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[3] Contrary to Lupin's suggestion (*see* Lupin Br. at 16-17), the lesser "power to persuade" deference set forth in *Skidmore v. Swift & Co.*, 323 U.S. 134 (1944), applies only in cases involving statutory construction and, as *Glaxo* makes clear, is not relevant to this case.

explained, "[s]ignificant deference is due to an agency's technical expertise when Congress has explicitly or implicitly delegated to the agency the making of scientific determinations." *Id.*

Moreover, deference to the scientific and technical determinations of agencies is a bedrock principle of federal judicial review. For example, the Supreme Court has instructed that "a reviewing court must generally be at its most deferential" when examining a "scientific determination" within the agency's "area of special expertise." *Baltimore Gas & Elec. Co. v. NRDC*, 462 U.S. 87, 103 (1983). Accordingly, courts routinely have afforded deference in cases similar to this one in which they were asked to review scientific or technical determinations by agencies that possess unique expertise. *See, e.g., American Ocean Campaign v. Daley*, 183 F. Supp. 2d 1, 11 (D. D.C. 2000) ("Where the agency decision turns on issues requiring the exercise of technical or scientific judgment, it is essential for judges to 'look at the decision not as a chemist, biologist, or statistician that we are qualified neither by training nor experience to be, but as a reviewing court exercising our narrowly defined duty of holding agencies to certain minimal standards of rationality.'") (citations omitted); *American Legion v. Derwinski*, 54 F.3d 789, 795 (D.C. Cir. 1995) ("Given the nature of the scientific expertise brought to bear on the issue ... the court's review is at its most deferential."); *Bd. of Regents of the Univ. of Washington v. EPA*, 86 F.3d 1214, 1218 (D.C. Cir. 1996)

("[P]articularly as the decision is a technical one within the EPA's expertise, we naturally defer to the decision."); *National Ass'n of Manufs. v. United States Dep't of Interior*, 134 F.3d 1095, 1115 (D.C. Cir. 1998) ("[A] deferential standard ... applies when an agency's scientific and technical judgment is at issue."); *United States v. Alpine Land and Reservoir Co.*, 887 F.2d 207, 213 (9th Cir. 1989) ("Deference to an agency's technical expertise and experience is particularly warranted with respect to questions involving engineering and scientific matters.").

There is no dispute that the FDA possesses special expertise necessary to make the scientific determinations as to whether a chemical compound is "intended to furnish pharmacological activity or other direct effect." Indeed, this expertise is specifically recognized in the MOU entered between the FDA and PTO, and published in the Federal Register, that sets forth a formalized process for both agencies to follow when considering eligibility for term extensions. *See* 52 Fed. Reg. 17,830 (May 12, 1987). In the MOU, the agencies acknowledged that the FDA "possesses expertise and records" regarding four of the six conditions for patent term extension eligibility, including the requirement that the approval be the "first permitted commercial marketing or use of the product." *Id.* Accordingly, the MOU requires the FDA to consult its "records and experts" when making eligibility determinations. *See id.* In light of this undisputed expertise, this Court, like the District Court below, must afford "great deference" to the decision of the

PTO – which, pursuant to the MOU, was based upon the FDA's expertise – that Levaquin® represents the first permitted commercial marketing of "the product" claimed in the '407 patent (*i.e.,* levofloxacin).

II. THE DISTRICT COURT CORRECTLY FOUND THAT LUPIN CANNOT SATISFY ITS BURDEN OF PROVING THAT THE '407 PATENT TERM EXTENSION IS INVALID

A. The Decisions Of The PTO And FDA Were Consistent With Their Longstanding Practice

The decision of the PTO, informed by FDA expertise, to grant a term extension to the '407 patent is entirely consistent with the practice of the two agencies dating back decades, including prior to the enactment of the Hatch-Waxman Act. Both agencies have treated the active ingredient in racemic drugs as the racemate (*i.e.,* ofloxacin), distinct from either of its enantiomers, which is precisely the same conclusion they reached here.

1. FDA-Approved Labeling And The FDA's Orange Book Always List The Active Ingredient In A Racemic Drug As The Racemate

The FDA has approved dozens of racemic drugs and, in each instance, has characterized the active ingredient as the racemate rather than one or both of its enantiomers. This long-standing practice is evident from the FDA-approved labeling and Orange Book descriptions for racemic drug products, which uniformly identify a single "active ingredient" – the racemate itself – not one or both of its

enantiomers. *See* A1208 (Lin ¶20).[4] Consistent with this practice, the FDA-approved labeling and Orange Book descriptions for Floxin® identify its "active ingredient" as ofloxacin (the racemate) and the FDA-approved labeling and Orange Book descriptions for Levaquin® identify its "active ingredient" as levofloxacin (the enantiomer). *See* A1461, A1496 (Lin Exhibits F (Floxin®) & G (Levaquin®)).

In fact, prior to this lawsuit, Lupin itself recognized the FDA's longstanding practice regarding the identification of the "active ingredient" in racemic products. For example, Lupin submitted a citizen's petition to the FDA requesting permission to submit an application to market a generic version of fexofenadine, which is a racemate. *See* A1209 (Lin ¶22). Lupin's proposed labeling, submitted along with the application, identified the "active ingredient" in the drug as *racemic* fexofenadine. *See id.* Under the theory Lupin urges on this Court, however, that

[4] In support of their motion for summary judgment, Plaintiffs-Appellees submitted a declaration of David T. Lin, a former acting Division Director in the FDA's Division of New Drug Chemistry III, Office of New Drug Chemistry. *See* A1202-A1548). Dr. Lin is an expert in the fields of FDA practice and procedure as applicable to the chemical characterization of drugs and the review of Investigational New Drug Applications and New Drug Applications. *See id.* at A1203 (Lin ¶4). Dr. Lin declared that "in each and every instance in which it has considered the question, the FDA has described a racemate as a single active ingredient, distinct from its enantiomers, and each enantiomer as a single active ingredient distinct from the other and from the racemate." *Id.* at A1208 (Lin ¶20). Dr. Lin attached to his declaration a list of drugs containing racemic active ingredients along with examples of product labeling and Orange Book descriptions. *See* A1278-A1439 (Lin Exhibit C). Lupin has not challenged Dr. Lin's credentials or disputed the accuracy of his declaration and did not submit a competing declaration from anyone with FDA expertise.

identification is incorrect; it should have identified the "active ingredient" as one or both of its enantiomers.

Lupin's theory also is inconsistent with the testimony of its own corporate representative during this litigation. Lupin's Rule 30(b)(6) witness, Sophia Mumtaz, testified that she agreed with the FDA's characterization of racemic ofloxacin as *the* active ingredient in Floxin®:

> Q: Do you disagree with the FDA's characterization [of] ofloxacin being *the* active ingredient in Floxin?
>
> A: No.

A2863 (Mumtaz Tr. at 70:8-11 (Exhibit 1 to the Declaration of Gary M. Rubman ("Rubman")) (emphasis added). In contrast to the theory Lupin advances for purposes of this litigation, Ms. Mumtaz's testimony is consistent with the FDA's longstanding practice.

2. In Every Other Instance, The PTO And FDA Have Granted Term Extensions To Enantiomer Patents Notwithstanding The Prior Approval Of The Corresponding Racemate

The PTO's and FDA's decision also was consistent with each of the prior instances in which the agencies considered similar issues in the context of patent term extensions. Indeed, over the past decade, the PTO, informed by the expertise of the FDA pursuant to the formal procedures set forth in the MOU, has considered at least five other applications for patent term extensions for patents covering enantiomeric products subsequent to approval of their corresponding racemates.

See A1785-93 (Mossinghoff ¶20). In each case, the PTO, relying on the expert advice of the FDA, determined that the patent covering the enantiomeric product was entitled to extension. In doing so, the agencies concluded that approval of the racemate did not constitute prior approval of the active ingredient in the enantiomeric product. *See id.* Plaintiffs are not aware of any instance in which the PTO and the FDA reached the contrary conclusion.[5]

One example that highlights the careful review of applications for patent terms extensions conducted by the PTO and the FDA involves Nexium® and Nexium® IV. Nexium® (esomeprazole magnesium) is an enantiomer. *See* A1792-93 (Mossinghoff ¶20). Its corresponding racemate (omeprazole) previously had been approved as Prilosec®. *See id.* Nonetheless, the PTO and the FDA determined that the patent covering Nexium® was entitled to a term extension,

[5] In support of their motion for summary judgment, Plaintiffs-Appellees submitted a declaration of former PTO Commissioner, Gerald Mossinghoff. Lupin has not challenged Mr. Mossinghoff's credentials or disputed the accuracy of his declaration and did not submit a competing declaration from anyone with PTO expertise. To the extent Lupin attempts to rely on PTO decisions regarding Symbicort® and Metvixia®, its reliance is misplaced and, in fact, was rejected by the district court below. *See* A26 (observing that, in each case where the FDA and PTO have considered analogous applications for extensions of patents covering enantiomers of previously approved racemates, they have granted the extension). As discussed at length in Plaintiffs-Appellees' briefs below (*see* A1153-55 (Plaintiffs-Appellees' Brief on Summary Judgment at 26-28), A2826-27 (Plaintiffs-Appellees' Reply Brief on Summary Judgment)), the Symbicort® application involved a traditional "combination product" comprised of two active ingredients, each of which had previously been approved. The Metvixia® application, which also did not involve racemates and enantiomers, was rejected by the PTO under the "including any salt or ester" language in Section 156. In fact, Judge O'Grady of the Eastern District of Virginia recently overturned the PTO's determination denying a patent term extension for Metvixia®. *See Photocure ASA v. Dudas*, Civ. Action No. 1:08-cv-718 (E.D. Va. Mar. 31, 2009), *appeal pending*, No. 2009-1393. A2932-52.

concluding that the prior approval of Prilosec® was not approval of the same "active ingredient" as in the enantiomeric Nexium® for purposes of 35 U.S.C. § 156. *See id.* The PTO and the FDA, however, *denied* an application for a term extension for a separate patent that covered the intravenous version of Nexium®, Nexium® IV. *See* A1796-98 (Mossinghoff ¶27). Nexium® IV (esomeprazole sodium) is also enantiomeric, but a different salt form of Nexium® (esomeprazole magnesium). The PTO and the FDA denied the term extension for Nexium® IV based on the prior approval of Nexium® and the "any salt or ester" language in 35 U.S.C. § 156. *See id.* In doing so, however, the PTO pointed out that "Nexium® IV [the enantiomer] *does not* have the same active ingredient as Prilosec® [the racemate]." *Id.* (emphasis added).

3. The FDA Has Never Considered Racemates "Combination Drugs" Or Regulated Them As Such

Lupin's argument that Floxin® is essentially a combination of multiple active ingredients (*i.e.*, the S(-) and R(+) enantiomers), *see* Lupin Br. at 26-27, also is inconsistent with the FDA's longstanding policy *not* to treat racemates as "combination" products under the FDA's rules. Under the "combination" rules, which govern the approval of drugs that contain a combination of active ingredients, a drug product sponsor must conduct testing on each active ingredient *individually and in combination* to show the contribution of each active ingredient to the efficacy and safety of the combination product. *See* A1209-10 (Lin ¶23).

The FDA, however, has *never* subjected racemates to these "combination rules" and does not require the sponsor of racemic products to test each enantiomer individually. *See id.* To the contrary, the FDA will not approve a racemic product based solely on tests conducted on one or both of its individual enantiomers and will not approve an enantiomeric product based solely on tests conducted on the corresponding racemate. *See* A1208-09 (Lin ¶21). The FDA did not subject Floxin® to these rules and, indeed, required an entirely new NDA – based on entirely new testing – when Plaintiffs sought approval for Levaquin®. *See* A1211 (Lin ¶26). Under Lupin's theory, the special "combination rules" should apply in each instance when approval is sought for racemic products, which would be a dramatic departure from the FDA's long-standing new drug approval process.

B. Patent Term Extensions Are Not Limited To New Chemical Entities

Lupin argues that "the term 'active ingredient' must have the identical meaning in both the Section 156 patent term extension provisions [Title II of Hatch-Waxman] and the new product exclusivity provisions [Title I of Hatch-Waxman]." Lupin Br. at 28-31. Lupin is mistaken.

In the first place, although it may sometimes be appropriate for identical words appearing in different parts of the same statute to have the same meaning, there is not, as Lupin contends, a rigid rule that this "must" be so or that it is "required." Rather, as the Supreme Court held nearly eighty years ago, "[i]t is not

unusual for the same word to be used with different meanings in the same act, and there is no rule of statutory construction which precludes the courts from giving to the word the meaning which the legislature intended it should have in each instance." *Atlantic Cleaners & Dyers, Inc. v. United States*, 286 U.S. 427, 433-34 (1932) (according different meanings to term "trade or commerce" in different sections of Sherman Act and noting that "the meaning of the word 'Legislature,' used several times in the Federal Constitution, differs according to the connection in which it is employed"). This Court is in accord. *See Nike Inc. v. Wal-Mart Stores, Inc.*, 138 F.3d 1437, 1445-46 (Fed. Cir. 1998) (the term "damages" has different meanings in different sections of the Patent Act); *Libbey Glass v. United States*, 921 F.2d 1263, 1265 (Fed. Cir. 1990) (the term "toughened (specially tempered)" has different meanings in different sections of Tariff Schedules).

Accordingly, this Court in *Glaxo* rejected precisely the same argument that Lupin raises here – the attempt to equate the meaning of "active ingredient" for purposes of the patent term extension provisions with "active moiety" for purposes of *non-patent* regulatory exclusivity. After extensive review of the statute and legislative history, the district court in *Glaxo* held that "neither this Court, nor the Commissioner is at liberty to ignore ... the fact that the statute uses 'ingredient,' not 'moiety.' Equating 'active moiety' with 'active ingredient' ... results in reading out of the statute the plain meaning of the phrase Congress chose." *Glaxo,*

706 F.Supp. at 1228. This Court affirmed, explaining that "Congress chose particular terms – 'active ingredient, ... including any salt or ester of an active ingredient. . . .' Accordingly, we can infer that in so choosing, Congress may have deliberately rejected the very terms the Commissioner asserts were the intended meaning of section 156," *e.g.*, "active moiety." *Glaxo*, 894 F.2d at 397; *see also id.* at 399 (Congress "specifically selected terms with narrow meanings that it chose from among many alternatives").

Further, in *Glaxo*, this Court held that Congress used "well-established scientific terms" in Section 156. Because the terms used in Section 156 had "well-defined, ordinary, common meanings" when Congress enacted the statute, the *Glaxo* court rejected the argument – the same one Lupin advances here – that Congress intended the definition of "product" in Section 156 to mean "new chemical entity" or "active moiety." *Id.* at 397.

Likewise, the parties in this case agree that the term "active ingredient" in Section 156 has a "well-defined, ordinary, common meaning" – *i.e.,* "any component that is intended to furnish pharmacological activity or other direct effect...." 21 CFR § 60.3(b)(2); *see also* Lupin Br. at 25 (quoting *Glaxo*, 894 F.2d at 395).[6] As Lupin concedes, this definition was "specifically incorporated into the

[6] Applying that definition to the undisputed facts of this case, the compound "intended to furnish pharmacological activity or other direct effect" in Floxin® is racemic ofloxacin and in Levquin® it is levofloxacin, establishing that these are two distinct "active ingredients" within the statutory definition.

FDA regulations concerning patent term extensions when those regulations were first issued in 1988" and has remained unchanged to date. *See* Lupin Br. at 26. Given this unambiguous definition of "active ingredient" for purposes of Section 156, there is no need to import the definitions of "new chemical entity" or "active moiety" from the *non-patent* regulatory exclusivity provisions of Title I and no inconsistency results from not doing so.

Without acknowledging the holding of *Glaxo*, Lupin relies on *Pfizer, Inc. v. Dr. Reddy's Labs., Ltd.*, 359 F.3d 1361 (Fed. Cir. 2004). Any reliance on *Pfizer*, however, is misplaced. As *Pfizer* was a panel decision, it could not have overruled the earlier panel decision in *Glaxo*. *See Barclay v. U.S.*, 443 F.3d 1368, 1373 (Fed. Cir. 2006) ("Panels of this court are bound by previous precedential decisions [unless and] until overturned by the Supreme Court or by this court *en banc*."); FED. CIR. R. 35(a)(1) ("only the court *en banc* may overrule a binding precedent").[7] Thus, Lupin's theory – *i.e.*, that "active ingredient" in Section 156 is equivalent to "new chemical entity" or "active moiety" as used in the regulatory exclusivity provisions – should be rejected under *Glaxo*, which is controlling precedent.

Contrary to Lupin's assertion, *Pfizer* did not hold that "active ingredient" means "active moiety" for purposes of determining the propriety of a patent term

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[7] The recent decision of Judge O'Grady in *Photocure* discussed above (at note 5), discussed the conflict between *Glaxo* and *Pfizer* and concluded that *Glaxo* remains binding precedent. *See* A2946-47 (*Photocure*, Civ. Action No. 1:08-cv-718, at 13-14).

extension. Rather, *Pfizer* concerned whether a patent during its term extension period was *infringed* by a different salt of the approved "product" under 35 U.S.C. § 156(b) and did not address the question of eligibility for such an extension under Section 156(a), which is the issue in this case. *Pfizer*, 359 F.3d at 1362 ("Pfizer Inc. appeals the judgment ... ruling that defendants ... do not infringe the extended term of Pfizer's [patent]."). The *Pfizer* court held that by explicitly defining "product" in Section 156(f) to "includ[e] any salt or ester of the active ingredient" Congress "foresaw variation in the salt or ester of an active ingredient, and guarded against the very loophole now urged," *id.* at 1366 – thereby supporting a finding of infringement.

The *Pfizer* court did mention the FDA's definition of "active moiety" for purposes of new product exclusivity as secondary support for its interpretation, but only after finding that the plain meaning of the statute controls. *Id.* at 1366 ("[T]he text of the statute shows that it was not intended to be defeated by simply changing the salt."). *Pfizer* simply addressed the impact of the "any salt or ester" language of Section 156(f) on the scope of an admittedly proper term extension – the issue of whether and when to grant a term extension in the case of an enantiomer and its corresponding racemate was *not* before the Court.

Moreover, the *Pfizer* court explained that nothing argued in "the district court or on this appeal suggests a statutory intent to provide the generic producer

with access to the pioneer's approved uses and data while barring extension of patent coverage of the drug product whose approvals and data are provided." *Id.* at 1366. This is precisely the irrational outcome urged by Lupin here – Lupin has made use of Plaintiffs-Appellees' approvals and data for Levaquin® for purposes of its ANDA, but seeks to invalidate the term extension granted to the patent protecting Levaquin®. The *Pfizer* court rejected this inequitable result, and this Court should do likewise.

Lupin's attempt to equate "active ingredient" and "active moiety" also is inconsistent with the views of the FDA, the expert agency that promulgated the definition of "active ingredient" that all parties agree applies in this case. For example, in the "Frequently Asked Questions on the Patent Term Restoration Program" section of the FDA website, the FDA makes clear the distinction between the use of the term "active ingredient" in the patent term extension provisions on the one hand and the new product exclusivity provisions on the other:

> **7. How is active ingredient defined with regard to the first permitted commercial marketing or use of the product?** Permission for commercial marketing or use must be the first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred. A product is the active ingredients contained therein for patent term extension purposes. *Active ingredient does not equal active moiety* (generally the molecule or ion responsible for the physiological or pharmacological action).

See http://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusiness Assistance/ucm069959.htm (last visited July 2, 2009) (emphasis added).

Lupin incongruously relies upon legislation enacted by Congress in 2007 relating to the non-patent regulatory exclusivity provisions to support its equation of "active ingredient" with "active moiety." *See* Lupin Br. at 31-33. But Lupin fails to explain how 2007 legislation relating to regulatory exclusivity provisions sheds any light on Congressional intent in 1984, when the patent term extension provisions were enacted.

Indeed, Lupin's reliance on the 2007 legislation turns logic on its head. Congress in 2007 was fully aware *both* of the longstanding policy of the PTO and FDA to grant term extensions to patents covering enantiomeric products notwithstanding the prior approval of the corresponding racemate, and of the equally longstanding policy of the FDA to deny new chemical entity exclusivity to enantiomers under like circumstances. In the 2007 legislation, Congress modified the FDA policy with respect to new chemical entity exclusivity for enantiomers, explicitly providing for the first time that under certain circumstances enantiomers *are* entitled to such exclusivity even where the corresponding racemate was previously approved. At the same time, Congress chose not to disturb the equally clear and consistent practice of the PTO and FDA to grant patent term extensions in precisely these same circumstances. If anything, this record shows that

Congress has no quarrel with the PTO's and FDA's application of Section 156 to grant extensions to enantiomer patents notwithstanding the approval of the corresponding racemates, and apparently is not troubled by any inconsistency in the definition of "active ingredient" for purposes of the regulatory exclusivity provisions on the one hand and the patent term extension provisions on the other. *See Young v. Cmty. Nutrition Inst.*, 476 U.S. 974, 983 (1986) ("This failure to change the scheme under which the FDA operated is significant, for a congressional failure to revise or repeal the agency's interpretation is persuasive evidence that the interpretation is the one intended by Congress.") (internal citations omitted); *Ad Hoc Comm. v. United States*, 13 F.3d 398, 402 n.9 (Fed. Cir. 1994) ("That Congress knew of the agency's prior interpretation of the Act and, despite twice amending other Act provisions, did nothing to change the interpretation or the statutory language on which it was based is persuasive evidence that the agency's prior interpretation was the one intended by Congress.").

Finally, should this Court conclude that "active ingredient" equals "active moiety" for purposes of Section 156, the '407 patent's term extension was nonetheless validly granted because levofloxacin, as claimed in the '407 patent, is a distinct "active moiety" from racemic ofloxacin.[8] The FDA has defined "active

[8] Lupin incorrectly asserts that the FDA denied the five-year new product exclusivity for Levaquin®. *See* Lupin Br. at 15. Ortho did not request such exclusivity and Lupin has cited to nothing in the record to the contrary.

moiety" as "the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance." 21 C.F.R. § 314.108(a). As the undisputed science proved in this case, racemic ofloxacin – not substantially optically pure levofloxacin – is "responsible for the physiological or pharmacological action" in Floxin® and therefore Levaquin® constitutes the first permitted commercial marketing of substantially optically pure levofloxacin. *See* Section III.B.[9]

C. The Decisions Of The PTO And FDA Were Consistent With Longstanding Industry Practice

The PTO's and FDA's longstanding treatment of racemates and their component enantiomers as different products for purposes of patent term extensions is not surprising given the undisputed industry understanding that racemates themselves – not their component enantiomers – constitute active ingredients. Lupin has not disputed that pharmaceutical manufacturing is divided into two phases, the first of which (the "primary manufacturing phase") results in the substance known in the industry as the "active pharmaceutical ingredient"

[9] Although Lupin has proffered no competing evidence, should this Court find any material issue of disputed fact on this issue the proper course would be to remand for trial.

("API") or simply as the active ingredient:[10] *i.e.*, the substance *intended* to furnish the desired pharmacological effect. *See* A1551 (Myerson ¶12).[11] The second phase (the "secondary manufacturing phase") then consists of adding inactive ingredients or excipients to arrive at the final drug product. *See* A1552-53 (Myerson ¶16).

The manufacture of Floxin® and Levaquin® involve a two phase process. For Floxin®, the primary phase results in the purified active ingredient, ofloxacin, which is then blended with excipients in the secondary phase to produce Floxin®. *See* A1553-54 (Myerson ¶18). In contrast, for Levaquin®, the primary phase results in the purified active ingredient, levofloxacin, which is then blended with excipients during the secondary phase to produce Levaquin®. *See id.* Thus, from the pharmaceutical manufacturing perspective, the "active ingredient" – the end product of the primary phase – in Floxin® is ofloxacin, whereas the "active ingredient" in Levaquin® is levofloxacin. *See id.* These facts are not in dispute.[12]

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[10] Lupin's Rule 30(b)(6) witness admitted that "API" and "active ingredient" are synonymous. *See* A2865 (Mumtaz Tr. at 118:14-19 (Rubman Exhibit 1)).

[11] Plaintiffs submitted a declaration of Dr. Allan Myerson, who explained the differences between the primary and secondary phases that are used in the manufacture of small molecule pharmaceuticals. *See* A1549-A1773. According to Dr. Myerson, the distinction between the primary and secondary phases "is widespread in the industry." A1553 (Myerson ¶17). Lupin has not disputed Dr. Myerson's testimony regarding this issue and did not offer a competing declaration of anyone with industry knowledge or expertise.

[12] Likewise, according to its ANDA, Lupin intends to use a two phase manufacturing process for its proposed generic product. *See* A1553 (Myerson

III. THE UNCONTESTED CLAIM CONSTRUCTION AND UNDISPUTED SCIENCE DEMONSTRATE LEVOFLOXACIN IS NOT AN ACTIVE INGREDIENT IN FLOXIN® AND WAS NOT APPROVED FOR COMMERCIAL MARKETING OR USE IN FLOXIN®

The District Court did not find it necessary to consider the uncontested claim construction and undisputed scientific evidence in this case, instead concluding as a matter of law that Lupin cannot meet its burden of proving the '407 patent's term extension invalid by clear and convincing evidence given the "great deference" accorded the PTO decision, informed by FDA expertise, to the contrary. Should this Court disagree with the District Court's analysis – which for the reasons discussed above it should not – the claim construction and scientific evidence here prove levofloxacin is *not* an active ingredient in Floxin® and was not approved for commercial marketing or use in Floxin®. Therefore, the decision of the PTO and FDA to extend the '407 patent's term was entirely consistent with the requirements of Section 156. These points – fully briefed below – provide alternative grounds for affirmance.[13] *Bailey v. Dart Container Corp. of Michigan*, 292 F.3d 1360 (Fed.

¶17). A separate company, Matrix, which specializes in the manufacture of APIs, will perform the first step: production of the API, bulk levofloxacin. *See id.* Matrix will then deliver the levofloxacin to Lupin, which will perform the second manufacturing phrase, *i.e.,* combining the API (levofloxacin) with inactive ingredients to create the final drug product. *See id.*

[13] If the Court finds any disputed issue of material fact as to the science, this case must be remanded to the District Court for fact finding on the question of whether, as a matter of scientific fact, levofloxacin was intended to furnish pharmacological activity or other direct effect in Floxin®. In denying Plaintiffs-Appellees' motion for additional discovery, the District Court intimated that

Cir. 2002) (appellee may assert alternative grounds for affirming the judgment that are supported by the record, "even if those particular arguments were rejected or ignored by the trial court").

A. It Is Undisputed That Levofloxacin As Claimed In The '407 Patent Is Not Present In Racemic Ofloxacin

The patent term extension provision, 35 U.S.C. § 156(a), states in relevant part as follows (emphasis added):

> The term of a patent which claims *a product* ... shall be extended ... if ...
>
> (5)(A) the permission for the commercial marketing or use of *the product* after such regulatory review period is the first permitted commercial marketing or use of *the product* ...

Thus, "the product" of Section 156(a)(5)(A), is precisely the same "product" referred to at the beginning of Section 156(a) – the product "claim[ed]" in the relevant patent, here the '407 patent.

Claims 2 and 5 of the '407 patent were construed in prior litigation to be directed to levofloxacin that is optically active and substantially optically pure, and to exclude both racemic ofloxacin *and the S(–) molecules contained in racemic ofloxacin*. *Mylan*, 348 F. Supp. 2d at 723, 728-30. This construction formed the basis of the District Court's holding in that case – after an eight week bench trial –

Plaintiffs-Appellees might be entitled to further discovery if Lupin's motion for summary judgment is denied. A2962 (Mem. Opinion dated August 28, 2008 at 8). This discovery period would be followed by trial.

that racemic ofloxacin neither anticipates nor renders obvious the claims of the '407 patent, which this Court affirmed on appeal. *See Ortho-McNeil Pharmaceutical Inc. v. Mylan Labs., Inc.*, 161 Fed. Appx. 944 (Fed. Cir. 2005).

Lupin does not challenge this claim construction here. In fact, Lupin adopted this construction below, explaining that the '407 patent claims "'a collection of levofloxacin molecules' that, *inter alia*, rotate polarized light (*since the levofloxacin is substantially free of the (R) enantiomer*)." A2581 (Lupin's Opposition and Reply Brief on Summary Judgment at 14) (emphasis added). Accordingly, Lupin cannot – and does not – contend that Floxin® contains what is *claimed* in the '407 patent, and therefore cannot prove that the approval of Levaquin® was not "the first permitted commercial marketing or use of the product" *claimed* in the '407 patent – precisely the showing that Lupin must make to prove the patent term extension invalid. *See* 35 U.S.C. § 156(a).[14] Unlike the levofloxacin claimed in the '407 patent, the S(–) molecules in racemic ofloxacin are neither optically active nor substantially pure because they are, by definition, present together with an equal number of R(+) molecules. *See Mylan*, 348 F.

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[14] Although Lupin does not address this point in its principal brief on appeal, below Lupin misread Section 156(a) as simply defining the "type" of patent that qualifies for term extension. *See* A2580-82 (Lupin's Opposition and Reply Brief on Summary Judgment at 13-15). As is evident from the language of the statute, however, "the product" of Section 156(a)(5)(A) relies on the antecedent basis of "a product" at the beginning of Section 156(a), and therefore properly refers to the product "claim[ed]" by the relevant patent.

Supp. 2d at 726-30. Thus, the product *claimed* in the '407 patent – levofloxacin that is optically active and substantially optically pure – was first approved for commercial marketing or use in Levaquin® and the '407 patent meets all the requirements necessary for a patent term extension.[15]

For this reason, the contention peppered throughout Lupin's principal brief that levofloxacin "was present" in Floxin® is misleading. And Lupin's assertion that "there is no dispute that levofloxacin was a component of a product (Floxin®)" is simply false. *Levofloxacin as claimed in the '407 patent* is *not* a component of, nor is it present in, Floxin®. This is equally true as a matter of claim construction and as a matter of scientific fact.

B. The Undisputed Science Proves That Levofloxacin Is Not An "Active Ingredient" In Floxin®

Below, Plaintiffs-Appellees offered the unrebutted declarations of Drs. Wentland, Zhanel and Myerson, three preeminent scientists, that Floxin® and Levaquin® have vastly different biological properties due to the different physical and chemical characteristics of their distinct active ingredients: racemic ofloxacin in Floxin® and levofloxacin in Levaquin®. *See, e.g.,* A2502-08 (Wentland ¶¶33-39); A2341-47 (Zhanel ¶¶60-72). This scientific evidence, which Lupin did not dispute or attempt to refute with a contrary proffer below, proves that it is racemic

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[15] This applies equally to the term "active ingredient" if substituted for "product" as Lupin does at Br. 24 ("[t]he term of a patent which *claims an active ingredient* ...") (emphasis added).

ofloxacin – not either of its individual enantiomers – that is intended to (and does) furnish the pharmacological activity of Floxin® and therefore is properly regarded as Floxin®'s single "active ingredient." *See, e.g.,* A1160-64 (Plaintiffs-Appellees' Brief on Summary Judgment at 33-37).

1. The Levofloxacin In Levaquin® And Ofloxacin In Floxin® Are Different As A Matter Of Medicinal Chemistry

From a medicinal chemistry perspective, the levofloxacin in Levaquin® and the racemic ofloxacin in Floxin® are different compounds. Medicinal chemists view a racemate like ofloxacin – which consists of two enantiomers that cannot be physically separated because they are tightly bound together – to be a single compound that is distinct from the pure forms of its individual enantiomers. *See* A1187 (¶86), A2498-2502 (Wentland ¶¶24-32).

Indeed, the undisputed evidence below showed that in racemic ofloxacin the S(–) and R(+) enantiomers interact with each other to form a stable complex in solid crystalline form, in solution and at the bacterial binding site. *See* A1187 (¶88), A2507-08 (Wentland ¶39), A2342-47 (Zhanel ¶¶66-72).[16] Consequently,

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[16] Lupin argued below that Plaintiffs-Appellees failed to prove that the two ofloxacin enantiomers "associate" with each other in solution and in the body. *See* A2587-95 (Lupin's Opposition and Reply Brief on Summary Judgment at 20-28). Whether the enantiomers formally "associate" is irrelevant. Plaintiffs-Appellees' experts relied on sound science that is widely accepted in their fields and concluded that the enantiomers of ofloxacin interact with and impact each other. *See* A2342-45 (Zhanel ¶¶66-70) ("several authors hypothesized that enantiomer-enantiomer interactions between the S(-) and R(+) enantiomers were likely

the racemic ofloxacin in Floxin® and the levofloxacin in Levaquin® have vastly different physical, chemical and ultimately biological properties, and, when administered, differ in their interactions with the receptor site. *See* A2507-08 (Wentland ¶39).

2. Levaquin® And Floxin® Are Different From The Clinical, Pharmacological, And Microbiological Perspectives

The undisputed evidence also demonstrates that Levaquin® and Floxin are different from the clinical, pharmacological and microbiological perspectives. For example, Levaquin® is effective at and indicated by the FDA for treating community acquired respiratory infections, including those caused by penicillin-resistant *Streptococcus pneumoniae*, whereas Floxin® is not indicated for such use and is inferior at treating these and many other infections. *See* A1185 (¶79), A2330-36 (Zhanel ¶¶29-31 & 37-45). The pharmacodynamics of the levofloxacin in Levaquin® are different from, and superior to those of the racemic ofloxacin in Floxin®. *See* A1186 (¶80), A2331-33 (Zhanel ¶¶32-36). Levaquin® differs from Floxin® in its effects on resistant microorganisms and in its likelihood of

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occurring..."); A2345-47 (Zhanel ¶¶71-72) (discussing *in vitro* studies); A2504-07 (Wentland ¶¶37-38) (the "Shen Model" is "the most commonly accepted model for quinolone action and how these drugs bind to the target"). Lupin failed to proffer any evidence on this point to rebut Plaintiffs-Appellees' experts. Nonetheless, if the Court finds any genuine dispute of material fact on this question, this case should be remanded to the District Court for trial.

developing resistance in microorganisms – and, again, it is superior to Floxin® in both respects. *See* A1186 (¶81), A2336-38 (Zhanel ¶¶46-54).

Levaquin® is also a safer drug than Floxin®, having the highest therapeutic index (the ratio between effective dose and toxic dose) of any quinolone and lower central nervous system toxicity than Floxin®. *See* A1186 (¶82), A2339-41 (Zhanel ¶¶55-59). This allows for higher dosing of Levaquin® than Floxin®, which conveys important clinical benefits. *See* A1186 (¶83), A2339-41 (Zhanel ¶¶56-59).

The far greater solubility of levofloxacin than racemic ofloxacin also makes Levaquin® a different drug than Floxin®. *See* A1186 (¶84), A2341-42 (Zhanel ¶¶60-63). Solubility is important to a drug's dissolution, absorption, and bioavailability, all of which influence a drug's effectiveness and toxicity. *See id.* Notably, the solubility of both levofloxacin and the substantially optically pure R(+) enantiomer of ofloxacin are each ten times greater than that of racemic ofloxacin (*see* A36 ('407 patent Table 4)) – proof that the clinical properties of Floxin® are a function of its single, distinct active ingredient – racemic ofloxacin – and not that of levofloxacin, nor the sum of levofloxacin and the R(+) enantiomer.

Importantly, each of these differences between Levaquin® and Floxin® are not due to differences in excipients or a change in formulation (*e.g.*, from immediate to controlled release), but rather to their distinct "active ingredients" –

levofloxacin in Levaquin® and racemic ofloxacin in Floxin® – which act differently on a molecular level. *See* A1186 (¶85), A2342-47 (Zhanel ¶¶64-72). Based on preclinical (animal), laboratory, and clinical studies, the evidence is that when Floxin® is administered, the two enantiomers in racemic ofloxacin do not act separately, but instead interact with each other and *together* interact with the binding site. *See id.* This is consistent with the observed clinical properties of levofloxacin and ofloxacin, and reinforces the fact that racemic ofloxacin is itself a single active ingredient, distinct from levofloxacin. *See* A2346-47 (Zhanel ¶72).

If Floxin®'s properties were simply the result of the actions of levofloxacin, there would be no difference between Floxin® and Levaquin® once one adjusted for the potency difference of the R(+) enantiomer. But the clinical, pharmacological, and microbiological differences are huge, due to the different properties of their distinct active ingredients – racemic ofloxacin and levofloxacin, respectively.[17] A2342 (Zhanel ¶¶64-65); *see also* A2869-70 (Zhanel Tr. at 26:16-

[17] Lupin relies on a statement in the '407 patent's prosecution history and a snippet taken out of context from the District Court's decision to incorrectly assert that the pharmacological activity of Floxin® is provided in whole or in part by levofloxacin. *See* Lupin Br. at 9 and 26-27. While it is true that optically pure levofloxacin has more activity than the pure R(+) enantiomer, Lupin entirely misses the salient point of the prosecution history passage, which is to *contrast* the properties of levofloxacin with that of racemic ofloxacin. These differences (which cannot be explained simply by subtracting the R(+) enantiomer) confirm the undisputed evidence, discussed above, that the activity of racemic ofloxacin involves substantial interaction between its two enantiomers, which are always present together when Floxin® is administered. *See, e.g,* A2868-73 (Zhanel Tr. at 19:7-19, 26:16-27:4, 41:13-43:19 (Rubman Exhibit 2)).

27:4 (Rubman Exhibit 2)). As the FDA and PTO – the two agencies with scientific expertise charged with making determinations under Section 156(a) – have concluded, it is scientifically incorrect to characterize an enantiomer like levofloxacin as an "active ingredient" in a product containing the corresponding racemate, here Floxin®. For this additional reason, the judgment of the District Court must be affirmed.

IV. THE DISTRICT COURT DID NOT ABUSE ITS DISCRETION IN DECIDING THE SCOPE OF THE INJUNCTION

Lupin argues that the injunction granted by the District Court is "overly broad" and exceeds the scope authorized by 35 U.S.C. § 156. *See* Lupin Br. at 33-34.[18] As explained below, however, Lupin's challenge is both improperly raised for the first time on appeal and without merit.

A. Lupin Never Contested The Scope Of The Injunction Below

As this Court has repeatedly explained, "appellate courts do not consider a party's new theories, lodged first on appeal. . . . In short, this court does not 'review' that which was not presented to the district court." *Sage Prods. v. Devon Indus.*, 126 F.3d 1420, 1426 (Fed. Cir. 1997); *see also Rentrop v. Spectranetrics Corp.*, 550 F.3d 1112, 1116-1117 (Fed. Cir. 2008) ("Where possible, every legal argument should be presented first to the trial court."); *Fuji Photo Film Co. v. Jazz*

[18] Lupin does not contend that the injunction lacks specificity under Fed. R. Civ. P. 65(d), nor could it support any such contention.

Photo Corp., 394 F.3d 1368, 1381 (Fed. Cir. 2005); *Forshey v. Principi*, 284 F.3d 1335, 1355-57 (Fed. Cir. 2002).

Here, Lupin never contested the scope of the injunction in the District Court, despite numerous opportunities to do so. As required by Local Rule 7.1(e) of the District of New Jersey,[19] together with its cross-motion for summary judgment Plaintiffs-Appellees filed a "proposed order" including an injunction of precisely the same scope – indeed having identical language – as that which the District Court entered and Lupin now challenges. *Compare* A2965 (Proposed Order at 2) *with* A29 (Order at 2). In its response to Plaintiffs-Appellees' motion, Lupin did not object to or even address the proposed order or the scope of the proposed injunction. *See generally* A2565-96 (Lupin's Opposition and Reply Brief on Summary Judgment). Likewise, after the District Court enjoined Lupin, Lupin did not move to modify or set aside the injunction, or otherwise contest its scope below. Having failed to take exception to the injunction before the District Court, Lupin cannot now raise this issue for the first time on appeal.

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[19] **(e) Preparation of Order.** All filed motions shall have annexed thereto a proposed order. If the proposed order does not adequately reflect the Court's ruling, the prevailing party, if directed by the Court, shall submit an order within five calendar days of the ruling on the motion on notice to all other parties. Unless the Court otherwise directs, if no specific objection to that order with reasons therefor is received within seven calendar days of its receipt by the Court, the order may be signed. If such an objection is made, the matter may be listed for hearing at the discretion of the Court.

B. The Scope Of The Injunction Is Proper

Even if Lupin's challenge to the scope of the injunction were properly before this Court, which it is not, it is still without merit. As the legislative history of Section 156 makes clear, a patent holder's rights during the term extension period are generally indistinguishable from those held prior to the extension. *See e.g.*, HR. Rep. 98-857(I), 1984 U.S.C.C.A.N. 2647 at 2672 (1984) ("[A]ll provisions of the patent law apply to the patent during the period of extension.").

For example, the defendant in *Genetics Institute v. Novartis Vaccines & Diagnostics, Inc.*, asserted (as Lupin asserts here) that a patent during the term extension period cannot be the subject of an interference proceeding because the rights it confers are limited to the "use approved for the product." Civ. No. 08-289-SLR, Slip Op. at *9-10 (D. Del. May 7, 2009). After reviewing the case law and the legislative history of Section 156, the court in *Genetics Institute* rejected that argument, holding that "there is no indication that § 156 confers anything less than the full scope of a patentee's rights during the extension period." *Id.* at *10. The *Genetics Institute* court explicitly declined to "distinguish the period between the patent's original expiration date and [the extended expiration date]." *Id.*

Lupin misreads the "use approved for the product" language of Section 156(b) as a limitation on the *type of infringing conduct* proscribed during the term extension period. It is not. Instead, the House Report to the 1982 bill that initially

proposed this language explains that it simply requires that the infringing conduct of whatever type (*e.g.*, making, selling or importing) be related to an approved use of the product – as opposed to some other "commercial use." *See* H.R. Rep. No. 97-696, at 10 (1982) ("[I]f a chemical is subjected to regulatory review for new drug uses, but is also marketed for other commercial uses, the patent term extension would apply only to the new drug uses for which regulatory review was required."). It is well-settled that "[t]he FDA ... grants approval to *make, use, and sell* a drug for a specific purpose for which that drug has been demonstrated to be safe and efficacious." *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1356 (Fed. Cir. 2003) (emphasis added). Thus, any infringing conduct related to an approved use for the product properly may be enjoined. *See* 35 U.S.C. §§ 271(a), 271(e)(4)(B) and 283.

As the above legislative history makes clear, Lupin's reliance on the "use approved for the product" language of Section 156(b) is entirely inapposite here. This language is intended to function where a chemical is marketed both for approved "drug uses" and for "other commercial uses." That is not the situation in this case. Levaquin® is not marketed for any use other than its FDA approved use – and it is precisely this approved use for which Lupin intends to market its generic levofloxacin product. Furthermore, the District Court's injunction is narrowly tailored to Lupin's ANDA – "the levofloxacin tablets described in ANDA No. 78-

424 or bulk levofloxacin for use in manufacturing such tablets" (A29)[20] – which, by definition, can seek marketing approval *only* for those uses already approved by the FDA. *See* 21 U.S.C. § 355(j)(2)(A)(i); *Warner-Lambert*, 316 F.3d at 1356 ("[A]n ANDA may not seek approval for an unapproved or off-label use of a drug."). Thus, the District Court did not abuse its discretion by enjoining Lupin from making, using, offering to sell, selling and importing levofloxacin for its FDA approved use.

[20] To the extent Lupin argues that the restriction on "bulk levofloxacin" improperly broadens the scope of the injunction, Lupin is mistaken. As is the case with Section 156(a), the "product" of Section 156(b) is defined as the "active ingredient of ... a new drug." *See* 35 U.S.C. § 156(f). Lupin's ANDA seeks approval for a generic equivalent to Levaquin®, which has levofloxacin as its active ingredient. Thus, levofloxacin (in bulk form – not only when formulated as Levaquin® tablets) is the Section 156(b) "product," and its approved use is as the active ingredient in Levaquin®. Accordingly, the injunction – explicitly limited to bulk levofloxacin "for use in manufacturing [the] tablets" described in Lupin's ANDA – is entirely proper.

CONCLUSION

For the foregoing reasons, this Court should affirm the District Court's judgment.

Respectfully submitted,

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CERTIFICATE OF SERVICE

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CERTIFICATE OF COMPLIANCE

1. This brief complies with the type-volume limitation of Federal Rule of Appellate Procedure 32(a)(7)(B).

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