No. 2009-1362

In the
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-CV-4999, Chief Judge Garrett E. Brown, Jr.

REPLY BRIEF OF DEFENDANTS-APPELLANTS LUPIN PHARMACEUTICALS, INC. AND LUPIN LTD.

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CERTIFICATE OF INTEREST

Counsel for Defendants-Appellants Lupin Pharmaceuticals, Inc. and Lupin Ltd. certifies the following:

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

Lupin Pharmaceuticals, Inc. and Lupin Ltd.

2. The name of the real parties in interest represented by me is:

Lupin Pharmaceuticals, Inc. and Lupin Ltd.

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

Lupin Pharmaceuticals, Inc. is a wholly-owned subsidiary of Lupin Ltd. Lupin Ltd. has no parent corporation, and no publicly held company owns 10 percent or more of Lupin Ltd.

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

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Dated: July 13, 2009

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SUMMARY OF THE ARGUMENT

Lupin respectfully requests this Court to apply the patent term extension provisions of 35 U.S.C. § 156 in a manner consistent with this Court's prior decisions. This Court has held that Section 156 "requires this Court to examine a drug product patent eligibility for extension on a component-by-component, or an ingredient-by-ingredient basis." *See Arnold Partn. v. Dudas,* 362 F.3d 1338, 1341 (Fed. Cir. 2004). Lupin asks for nothing more in the present appeal.

The patent term extension of U.S. Patent No. 5,503,407 ("the '407 patent") is based upon the U.S. Food and Drug Administration's ("FDA") approval of Levaquin® which contains levofloxacin as the active ingredient. Prior to the FDA's approval of Levaquin®, the FDA approved the drug product FLOXIN® which contains ofloxacin as an active ingredient. Ofloxacin is a racemate that contains equal parts of two molecules referred to as enantiomers. One of the enantiomers in ofloxacin is levofloxacin. The purpose of administering ofloxacin (and thus its two component enantiomers) was to furnish pharmacological activity, namely to treat various bacteria-related diseases. Accordingly, the FDA's approval of Levaquin® did not represent the first approval by the FDA of levofloxacin as an active ingredient, and the patent term extension of the '407 patent is invalid.

I. THE LEVOFLOXACIN ENANTIOMER WAS A COMPONENT IN FLOXIN®

Plaintiffs appear to argue that although ofloxacin was present in FLOXIN®, and although ofloxacin is comprised of levofloxacin and its corresponding enantiomer, levofloxacin was not a "component" of Floxin®. This argument, however, is contrary to the position espoused by Plaintiffs' own experts.

A. Plaintiffs' Expert Dr. Wentland Specifically Opined That a Medicinal Chemist Would Understand That Ofloxacin is Comprised of Two Components, One Being "the (S) enantiomer (levofloxacin)"

Plaintiffs' technical expert, Dr. Wentland, characterizes levofloxacin (*i.e.*, the (S) enantiomer of ofloxacin) as a component of FLOXIN® (ofloxacin) in his declaration, and confirmed this characterization during his deposition. In the former, he states:

> Upon examining this structure of ofloxacin, a medicinal chemist would understand that ofloxacin is "racemic," meaning that **it is comprised of two components in equal amounts, namely, the (S) enantiomer (levofloxacin)** and the (R) enantiomer.

A2489; A2492-A2493 ; A2497-A2498 (Fig. 8). Dr. Wentland repeated this characterization in other portions of his declaration, *e.g.*, in describing the process for preparing ofloxacin in Plaintiffs' prior patent on ofloxacin (U.S. Patent 4,382,892, *A45-A53*), wherein he again confirmed that levofloxacin is a component of ofloxacin: the "result [of the process of preparing ofloxacin] is a single

compound **made up of its two component enantiomers**." *A2489; A2498-A2499* (emphasis added). Dr. Wentland later stated that "a racemic compound [*e.g.*, ofloxacin] can be resolved into its **component** enantiomers," yet again confirming that levofloxacin is a component of ofloxacin. *A2489; A2501* (emphasis added). Additionally, during his deposition, Dr. Wentland confirmed multiple times that ofloxacin has two components: the (S) enantiomer and the (R) enantiomer. *A2648; A2649-A2650; A2653-A2657.*

B. Plaintiffs' Package Insert Indicates That the Purpose of Administering Ofloxacin Was to Furnish Pharmacological Activity and That Ofloxacin Was Racemic

Plaintiffs argue that "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." *See Plaintiffs' Brief ("PB") at 15.* Defendants agree that racemic ofloxacin was intended to furnish the pharmacological activity of FLOXIN®. But there is no evidence at all that the individuals enantiomers of ofloxacin (including levofloxacin) were *not* intended to furnish pharmacological activity. As for Plaintiffs' position that racemic ofloxacin and not either of its enantiomers, *did* furnish the pharmacological activity of FLOXIN®, that argument again is contradicted by their own package insert for

Levaquin® which states that "the antibacterial activity of ofloxacin resides primarily in the L-isomer [another term for levofloxacin]." *A1498-A1545 at A1506.* But, whether in fact the levofloxacin molecule in ofloxacin provided pharmacological activity is irrelevant to the issue in this appeal.

Plaintiffs also appear to contend that levofloxacin in FLOXIN® was not an active ingredient because it was not "a component intended to furnish pharmacological activity." However, FLOXIN® contained, according to Plaintiffs' own package insert, ofloxacin, which was described as a racemate ("ofloxacin... is the racemate") *A2812-A2820 at A2817.* This racemate is comprised of two components: the molecule levofloxacin (the (S) enantiomer of ofloxacin), and the (R) enantiomeric molecule of ofloxacin. *See PB* at 8. The package insert for FLOXIN® also clearly indicates that the purpose of administering ofloxacin was to furnish pharmacological activity. ("Ofloxacin has *in vitro* activity against a broad-spectrum of gram-positive and gram-negative aerobic and anaerobic bacteria.") *A2818.* Levofloxacin, as part of ofloxacin, thus necessarily furnished pharmacological activity when FLOXIN® was administered.

There is absolutely no doubt—and no fact issue—that levofloxacin in FLOXIN® was a component intended to furnish pharmacological activity. The FDA focused directly on this point in 1989, when it stated its long-standing position that an enantiomer of a previously-approved racemate does not qualify for

five years of non-patent exclusivity. The FDA did so using its technical expertise and clearly explained its rationale: "a single enantiomer of a previously approved racemate contains a previously approved active moiety." *See* 54 Fed. Reg. 28872 at 28897-98 (July 10, 1989). The latter term is defined as "the molecule . . . responsible for the physiological or pharmacological action of the drug." *Id.* at 28898. As a matter of science, as explained by the FDA, when one administers a racemate one is administering its component molecules—enantiomers—knowing that they are "responsible for the physiological or pharmacological action of the drug substance." *Id.* Whether when separated one enantiomer may perform better or worse than the other, or the combination of the two, is irrelevant to this question.

C. The Mechanism of Action of the Levofloxacin Molecule in Ofloxacin is Irrelevant

Plaintiffs spend considerable briefing urging a distinction between ofloxacin and levofloxacin based on function. *See, e.g., PB at 45-49.* The fact remains, however, that the means by which ofloxacin or levofloxacin function in the body to bring about a therapeutic treatment is not relevant to the issue before this Court. The undisputed facts establish that the levofloxacin in Plaintiffs' previously-approved and commercialized ofloxacin product (FLOXIN®) was a component

"intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease . . . ." 21 CFR § 60.3(b)(2).

In particular, Plaintiffs now urge this Court to investigate the mechanism by which levofloxacin achieved pharmacological effect in the prior FLOXIN® product. Plaintiffs argue that in FLOXIN® the levofloxacin molecules may have been "associated" with their mirror image molecules, the (R) enantiomers (in solution, at the active binding site, or both). *See PB at 45-46.*

Plaintiffs' association theory propounded by Plaintiffs' expert Dr. Wentland was not supported by one of Plaintiffs' other experts, Dr. Myerson, who testified that once in an aqueous environment, the enantiomers of ofloxacin would separate and be solubilized individually. *A2747; A2750-A2751.* Dr. Myerson also testified that no one knows whether Dr. Wentland's hypothetical association theory is correct, calling it "in question." *A2750-A2751.* Further, Dr. Wentland's association hypothesis was first postulated sometime two years or so after Plaintiffs' NDA for FLOXIN® was filed with the FDA. *A2502-A2504 and A2763.*

As for Dr. Wentland's hypothesis that when ofloxacin is administered, the result is an association of (S) and (R) enantiomers at the binding site, that too has no support in the scientific literature. *A2648; A2651-A2652.*

Nothing in the statutory scheme at issue here requires or even sanctions as relevant an investigation into "how" a molecule, component, or active ingredient actually furnishes pharmacological activity.

Moreover, nothing in the record indicates that either the FDA or the U.S. Patent and Trademark Office ("USPTO"), when determining qualification for a patent term extension, cared how the levofloxacin enantiomer functioned in either ofloxacin or levofloxacin. And the reason is clear. First, such an inquiry is not required or sanctioned by the applicable statute and regulations. Second, it is often the case that the exact mechanism of action is not known. The only question is whether the levofloxacin enantiomer in ofloxacin was "intended to furnish pharmacological activity...."

To the extent that Plaintiffs' position is that the USPTO and FDA decided that the '407 patent was entitled to a patent term extension because levofloxacin in Levaquin® had a different mechanism of action than it did in FLOXIN®, the record is devoid of any such support. Certainly Plaintiffs have not cited to any instance wherein the USPTO or FDA considered such an issue.

II. LITTLE OR NO DEFERENCE SHOULD BE ACCORDED THE USPTO/FDA DETERMINATION TO GRANT THE PATENT TERM EXTENSION

Plaintiffs oppose Lupin's position on deference, arguing that the decision by the USPTO to grant the patent term extension is entitled to "great deference." *See PB at 23; Lupin's Brief ("LB") at 16-17.*

As an initial matter, as both parties agree that there are no genuine issues of material fact, this Court need only decide the same question of law decided by the district court on summary judgment. Because that question is one of statutory interpretation, this Court may make an independent determination without deference to the trial court's interpretation. This standard of review is not affected by any deference to USPTO or FDA agency interpretation of the meaning of Section 156. *See, e.g, Glaxo Oper. UK Ltd. v. Quigg,* 894 F.2d 392, 395, n.5 (Fed. Cir. 1990).

The issue of statutory interpretation of the term "active ingredient" arises because the definition of this term does not specifically recite terms relevant here, *e.g.*, "racemate" and "enantiomers." *See* 35 U.S.C. § 156. In order to reach a decision, an understanding of the meaning of this term in the context of Section 156 must be reached, and this is done via the process of statutory interpretation. It is only after the statute has been properly interpreted that it may be applied to the undisputed facts, and a correct decision reached. Interpretation is often carried out

by courts, *e.g.*, when assessing whether the Constitutional restriction on unreasonable searches and seizures applies to a given fact pattern. An interpretation is required because the applicable rule of law (*i.e.*, the Fourth Amendment) does not itself include a reference to every fact scenario that is contemplated thereby.

Turning to the issue of deference, Plaintiffs argue that because the USPTO applied its "technical expertise" in determining "whether the 'active ingredient' contained in Levaquin® was previously approved as an 'active ingredient' in Floxin®," the USPTO determination in the affirmative is entitled to "great deference," citing *Glaxo*. *See PB at 23*. While the USPTO did issue a decision granting the term extension, the USPTO did not use any of its own "technical expertise" in rendering that decision. On the contrary, and as Plaintiffs admit in their brief, it was the FDA, and not the USPTO, who reached a conclusion concerning the previous approval issue, which conclusion was then adopted by the USPTO and used as the sole basis for its alleged "decision." However, there is not a single fact in the record indicating that the FDA, let alone the USPTO, used any "technical expertise" at all in reaching this conclusion. The sole basis in the record for the FDA's conclusion is set forth in a single sentence in the FDA's letter to the USPTO:

> 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. 1998), *aff'd,* 894 F.2d 392 (Fed. Cir. 1990).

A1888. As there is no evidence of the use of any "technical expertise" by the USPTO (or the FDA) in reaching the previous approval issue, the decision granting the term extension is not entitled to "great deference." *See LB at 18-20.*

Moreover, the FDA's stated reliance on *Glaxo* was misplaced, as the facts in *Glaxo* are distinct from those presented in this appeal. In *Glaxo,* the products in issue were an ester and a salt of cefuroxime, respectively. *See Glaxo,* 894 F.2d at 393-94. Here, the products are a racemate (ofloxacin) and an enantiomer thereof (levofloxacin). The *Glaxo* case thus fails to support Plaintiffs' argument that the USPTO decision is entitled to "great deference." *See LB at 18-20.*

III. PLAINTIFFS RAISE IRRELEVANT ARGUMENTS TO OBSCURE THE REAL ISSUE

A. "Longstanding Practice" of the FDA Does Not Equate to Legal Correctness

Irrelevant to the present issue is how long or how many times the FDA has (improperly) granted patent term extensions for enantiomers when the racemic mixture was previously approved for marketing by the FDA. Prior decisions by the USPTO and FDA should not provide any support for Plaintiffs' position because those decisions were inconsistent with the plain words of the applicable

regulation. *See In re McDaniel*, 293 F.3d 1379, 1385 (Fed. Cir. 2002) ("deference is not appropriate where the agency's interpretation is 'plainly erroneous or inconsistent with the regulation.'"); *see also Demahy v. Wyeth Inc.*, 2008 WL 4758615, at *1, *11 (E.D. La. Oct. 27, 2008) (FDA's inconsistent interpretation of its own unambiguous regulation is only entitled to deference to the extent that it has the "power to persuade"). Plaintiffs' arguments in this regard (*see PB at 26-30*) are irrelevant.

Cases are legion wherein a court overturns the decision of a governmental agency based on an improper construction of a statute by the agency, or wherein the agency misapplies the law to a set of facts. *See, e.g., Am. Bioscience, Inc. v. Thompson*, 269 F.3d 1077, 1084-86 (D.C. Cir. 2001) (vacating FDA's approval of Abbreviated New Drug Application ("ANDA") where FDA acted unreasonably and in direct contravention of its own regulations); *Purepac Pharm. Co. v. Thompson*, 238 F. Supp. 2d 191, 210-12 (D.C. Cir. 2002) (refusing to grant deference to FDA's action when it is "irreconcilable with the language and intent of the FDCA"); *McDaniel*, 293 F.3d at 1385 (vacating a decision of the Board of Patent Appeals and Interferences where the Board's interpretation of a regulation ignored a requirement in the text of the regulation).

Further, there is no language in the applicable regulation which sanctions the result sought by Plaintiffs. In this situation, where the regulatory language is clear,

no deference is due to an agency's interpretation of the regulation. *See Christensen v. Harris County*, 529 U.S. 576, 588 (2000) ("deference is warranted only when the regulation's language is ambiguous"). All the regulation requires is a determination of whether the levofloxacin in the previously-commercialized ofloxacin product (FLOXIN®) was a component "intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease . . . ." 21 CFR §§ 60.3(6)(2) and 201.3(b)(7); *A1100-A1105 and A905-A1025,* respectively. If it was, then the term extension granted to the '407 patent is invalid.

B. Plaintiffs' Argument That Patent Term Extensions are Not Limited to New Chemical Entities Misses the Point

Plaintiffs spend substantial space arguing that patent term extensions are not limited to new chemical entities. As explained in Lupin's opening brief, that is not the issue in the present appeal, nor does the issue raised in the present appeal concern the issue raised in *Glaxo* relating to the phrase "active ingredient... including any salt or ester," as found in Section 156(f)(2). *See, e.g., LB at 18-20.* Plaintiffs argue that "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." *See PB at 32.* But that is not the issue raised in this appeal.

Lupin is not arguing that this Court must interpret the "active ingredient" language in § 156 to mean "active moiety." Indeed, Lupin's position is straight forward, namely that the term "active ingredient" must mean the same in both the patent term extension provisions of § 156 and in the non-patent exclusivity provisions because that same term "active ingredient" is employed in both provisions. But this Court need not agree with Lupin even on that point for Lupin to prevail in this appeal.

To be clear, Lupin respectfully submits that all this Court need do is, as stated before, apply this Court's recognized requirement of examining the eligibility of the '407 patent to be entitled to a patent term extension "on a component-by-component basis."

C. Longstanding Industry Practice is Irrelevant

While on the one hand agreeing that the term "active ingredient" is in issue, and that 21 CFR provides a definition for this term, Plaintiffs introduce confusion by introducing a new term, Active Pharmaceutical Ingredient ("API"), in their memorandum, and proceed to use API interchangeably with the term "active ingredient." *See PB at 39-40.* There is no basis for equating these terms. While the term API is used by the FDA, Plaintiffs have failed to show that the definition

relevant here—as set forth in 21 CFR §§ 60.3(6)(2) & 210.3(b)(7)—also applies to API. Further, the term API is not defined in either Parts 60 or 201 of 21 CFR. As API and "active ingredient" are not themselves literally identical, and because Plaintiffs have not shown that API also is defined in the relevant FDA regulations, Plaintiffs' references to API in their memorandum are irrelevant, and should be ignored.

IV. THE USPTO/FDA PRACTICE OF GRANTING PATENT TERM EXTENSIONS FOR ENANTIOMERS OF PREVIOUSLY APPROVED RACEMATES IS INCONSISTENT WITH ITS OWN POSITION IN NOT AWARDING FIVE-YEAR EXCLUSIVITY

Plaintiffs argue that it is improper for this Court to look to FDA regulations concerning new product exclusivities to construe the term "active ingredient" as used in the patent term extension provisions of Section 156(f)(2). *See PB at 31-32.* The rationale underlying Plaintiffs' argument, however, fails upon close inspection.

Plaintiffs open by acknowledging the merit of Lupin's position: "it may sometimes be appropriate for identical words appearing in different parts of the same statute to have the same meaning . . . ," before launching into what may be considered to be exceptions to the general rule. *See PB at 31, 32.* This Court has recently and clearly stated that Lupin's position is the "normal rule of statutory

construction," *i.e.*, identical words used in different parts of the same act are intended to have the same meaning. *See Voracek v. Nicholson*, 421 F.3d 1299, 1304 (Fed. Cir. 2005). Indeed, this Court noted in *Voracek* that the plaintiff failed to offer any persuasive reason to overcome what this Court has referred to as a "presumption." *Id.*

While Plaintiffs cite three cases where the foregoing presumption was not applied, it fails to provide any analysis of these cases which supports its call for discarding the presumption in this appeal.

In one of these cases, *Atlantic Cleaners & Dyers, Inc. v. U.S.*, 286 U.S. 427, 435 (1932), the Supreme Court recognized the presumption, but wanted to provide a meaning to the disputed term which would "best manifest the legislative purpose." In doing so, the court looked to factors such as whether the subject matter where the terms appear is the same. *Id.* at 434. While the Supreme Court determined that the factors favored the assignment of different meanings for a term appearing in different sections of the Sherman Act, the record in the present case provides no basis for deviating from the presumption. Here, for example, a purpose of the legislation to which the term relates and the subject matter are aligned and favor application of the presumption: both provisions of the legislation encourage new drug research by providing a benefit to an innovator in the form of an exclusionary right. The benefit provided by one portion of the legislation was

in the form of a patent term extension, while the second benefit provided by the legislation was in the form of an exclusivity period. The *Atlantic* case thus provides no basis for deviating from the presumption.

Similarly, in *Nike, Inc. v. Wal-Mart Stores, Inc.*, 138 F.3d 1437 (Fed. Cir. 1998), this Court acknowledged the "natural presumption" set forth above, but deviated therefrom only because to do otherwise would be to ignore the history of marking as applied to recovery of profits in equity, and negate the purpose of the marking statute. *Id.* at 1446. Indeed, as interpreting the term "active ingredient" as Lupin proposes would not negate the purpose of the statute (and Plaintiffs have not alleged same), the rationale set forth in the *Nike* case provides no basis for discarding the presumption.

Plaintiffs' reliance on *Libbey Glass v. U.S.* also is misplaced. After acknowledging the presumption, this Court found the term in issue to be in such "dissimilar connections" that applying the same meaning would be improper—the term was used on a tariff schedule in connection with glass products having different uses and properties. *See Libbey Glass v. U.S.*, 921 F.2d 1263, 1265 (Fed. Cir. 1990). Moreover, this Court found that the legislative history supported different meanings. *Id.* at 1265-66. As Plaintiffs have failed to allege, let alone identify any support for, the existence of such factors, *Libbey Glass* fails to support Plaintiffs' call for overturning the presumption.

V. PLAINTIFFS' USE OF PATENT CLAIMS TO DETERMINE ELIGIBILITY FOR A PATENT TERM EXTENSION IS UNSUPPORTABLE

Plaintiffs' alternative ground for affirming the district court's judgment (not addressed by the district court) truly turns the provisions of Section 156 upside down. Plaintiffs' argument is that "under the uncontested claim construction of the '407 patent, FLOXIN® (the racemate) does not contain what is claimed in the '407 patent" and therefore "the approval of Levaquin® did not constitute the first permitted commercial marketing of the product claimed in '407 patent." *See PB at 43.* Consequently, Plaintiffs' position is that so long as the patent term extension is for a patent that contains claims that define an active ingredient in some fashion such that those claims would not read on the prior approved product, Plaintiffs are entitled to a patent term extension.

Of course, Plaintiffs cite to no case to support their position: Indeed, the very history of the patent term extension for the '407 patent shows that such an analysis was not requested nor performed.

The relevant portion of Section 156(a)(5)(A), with the statutory definition of "product" substituted therein, defines what *type* of patent qualifies for a patent term extension under this section. Such a patent must be one that "claims [an active ingredient . . . as a single entity or in combination with another active ingredient]." *See* 35 U.S.C. § 156(a)(5)(A). The '407 patent does so by claiming a "collection

of levofloxacin molecules" that, *inter alia*, rotate polarized light (since the levofloxacin is substantially free of the (R) enantiomer). *See Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 348 F. Supp. 2d 713, 729 (N.D.W.V. 2004).

There was no discussion regarding the scope of the claims in this exchange between the USPTO and the FDA and indeed nothing to indicate that the FDA was even given a copy of the '407 patent—and for good reason. Such an inquiry would have been irrelevant.

Plaintiffs have quoted from some of the communications between the USPTO and the FDA, such as that from the February 27, 1997, USPTO letter that contains the statement that the '407 patent "would be eligible for extension of a 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." *See LB at 11-12.* But that excerpt alone is misleading. First, the USPTO requested confirmation from the FDA that the product identified in the application, Levaquin®, "has been subject to a regulatory review period within the meaning of 35 U.S.C. § 156(g) before its first commercial marketing or use and that the application for patent term extension was filed within the sixty-day period after the product was approved." *A1886.*

Then, in the same letter, the USPTO specifically stated that it had *not* made a determination "whether the patent in question claims a product which has been

subject to the Federal Food, Drug and Cosmetic Act." *A1886.* There certainly was no instruction to the FDA about the scope of the claims of the '407 patent.

In response, the FDA, in a letter dated July 18, 1997, states "that this product 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)." *A1888.* The FDA response contained no technical analysis.

In the July 18, 1997 letter, the FDA also specifically requested the following of the USPTO: "[s]hould you conclude that the subject patent is eligible for patent term extension, please advise us accordingly. As required by 35 U.S.C. § 156(d)(2)(A) we will then determine the applicable regulatory review period, publish the determination in the *Federal Register*, and notify you of our determination." *A1888.* In response, the USPTO informed the FDA on July 30, 1997, that the "patent claims a product that was subject to regulatory review under the Federal Food, Drug and Cosmetic Act." *A1890.*

The scope of the patent claims played no part in the foregoing procedure other than in determining whether the claims covered the Levaquin® product, an

analysis performed ***after*** the determination was made by the FDA that Levaquin® represented the first FDA approval of that product.

Adopting Plaintiffs' approach would open the floodgates for patent term extensions, a clearly undesired result. For example, under Plaintiffs' approach, a patent covering a new polymorph of an old active ingredient would be designated as a "new" active ingredient and, if used in an FDA approved drug, could then have its patent term extended. Even a patent covering a more pure form of an active ingredient could be extended. Again, by example, a first drug product uses an active ingredient that is 95 percent pure. A second later-approved drug product uses the same active ingredient, but of higher purity, *e.g.*, 98 percent pure. If a patent exists that covers the active ingredient with 98 percent purity, under Plaintiffs' approach that patent would be eligible for a patent term extension. The examples are endless (as would be the number of patent term extensions) if this Court adopts Plaintiffs' interpretation of Section 156.

VI. THE DISTRICT COURT INJUNCTION WAS OVERLY BROAD AND LUPIN DID NOT WAIVE ITS RIGHT TO RAISE THE ISSUE

A. The Injunction was Overly Broad

Plaintiffs argue that Lupin improperly applies 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. Plaintiffs base their

argument on an ambiguous at best statement from the legislative history ("[A]ll provisions of the patent law apply to the patent during the extension period"), a district court case dealing with the right to an interference, and another statement in the legislative history that actually supports Lupin's position ("[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."). *See PB at 51-53.*

Indeed, Section 156(b) states that "the rights derived from any patent the term of which is extended under this section shall during the period during which the term of the patent is extended... in the case of a patent which claims a product *be limited to any use approved for the product.*" *See 35 U.S.C. § 156(b).*

B. Lupin Did Not Waive Its Right to Raise the Issue

Plaintiffs argue that Lupin cannot properly challenge the scope of the district court's injunction in this appeal because Lupin never contested the scope of the injunction in the district court. *See PB at 49-50.* This argument fails for several reasons.

From a timing perspective, Lupin has attempted to expedite the resolution of this case. The '407 patent has expired, and Lupin has received FDA approval to market its levofloxacin drug product. The sole remaining barrier to Lupin's market entry is the patent term extension which is the subject of this appeal. Within two

business days after receipt of the district court's order, Lupin filed this appeal. Lupin followed this filing with a motion (which was opposed by Plaintiffs) to expedite the briefing schedule, and for an early oral argument.

In one of cases cited by Plaintiffs, *Forshey*, this Court notes that the Supreme Court has emphasized that the question of whether to consider an issue on appeal "is one left primarily to the discretion of the courts of appeals . . . ." *See Forshey v. Principi*, 284 F.3d 1335,1355 (Fed. Cir. 2002) (*citing Singleton v. Wulff,* 428 U.S. 106 (1976)). Thus, this Court under any circumstances may exercise its discretion and consider the scope of the injunction issue.

Setting aside the foregoing, Plaintiffs argue that Lupin should have filed a motion in the district court to modify the injunction. *See PB at 50.* Assuming Lupin did so, this process would have added weeks, and perhaps months, to the schedule. Further, assuming *arguendo* Lupin's motion was successful and the scope of the injunction was modified, the filing of this appeal would remain necessary as Lupin would remain unable to market its approved product.

As part of this argument, Plaintiffs argue the relevancy of Local Rule 7.1(e), and suggests that Lupin violated its provisions. *See PB at 50.* However, this rule applies only when a prevailing party is directed by the Court to submit a revised order after a ruling. *Id.* The district court did not direct Plaintiffs to submit any such order after its ruling. Thus, this local rule, and particularly the portion of this

rule relating to raising a "specific objection" to an order submitted by the prevailing party after a court ruling, is simply not applicable. There was no violation of this rule.

The case law cited by Plaintiffs also fails to support its argument. None of the cases involve the appeal of the scope of an injunction (the facts presented here), but are instead directed to situations where new infringement arguments are presented on appeal (*Sage Products)*, where jury instructions were incorrect because defendant, having received an adverse jury verdict but prior to entry of judgment, failed to bring a relevant Supreme Court decision to the attention of the district court despite knowing of that decision for almost four months prior to entry of judgment (*Rentrop*); and where plaintiff had failed to argue it was entitled to enhanced damages under a bad faith theory (*Fuji Film*). *See PB at 49-50.*

CONCLUSION

Lupin respectfully requests that this Court reverse the judgment of the district court that the patent term extension granted to U.S. Patent No. 5,053,407 is valid, and reverse the district court's order granting injunctive relief.

Respectfully submitted,

Dated: July 13, 2009

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that true copies of the foregoing REPLY BRIEF OF DEFENDANTS-APPELLANTS LUPIN PHARMACEUTICALS, INC. AND LUPIN LTD. were served July 13, 2009, *via* overnight courier, on the following:

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CERTIFICATE OF COMPLIANCE WITH FED. R. APP. P. 32(a)(7)

I, Christopher T. Griffith, certify that this brief complies with the type-volume limitation of FED. R. APP. P. 32(a)(7)(B) because it contains 6,327 words (including footnotes and figures), excluding those portions of the brief exempted by FED. R. APP. P. 32(a)(7)(B)(iii) and FED. CIR. R. 32(b).

I, Christopher T. Griffith, further certify that this brief complies with the typeface requirements of FED. R. APP. P. 32(a)(5) and the type style requirements of FED. R. APP. P. 32(a)(6) because it has been prepared in a proportionally-spaced typeface using Microsoft WORD Version 2007 in 14 point Times New Roman font.

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