UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, v. F. HOFFMANN-LA ROCHE LTD ROCHE DIAGNOSTICS GmbH and HOFFMANN-LA ROCHE INC. Defendants.	CIVIL ACTION No.: 05-CV-12237WGY

ROCHE'S OPPOSITION TO AMGEN'S MOTION *IN LIMINE* NO. 6 TO EXCLUDE REFERENCE TO AMGEN'S REQUEST FOR INJUNCTIVE RELIEF

Amgen would have this Court believe that it is seeking to exclude statements about its request for injunctive relief when, in fact, Amgen is actually seeking to prevent Roche from arguing that it does not infringe Amgen's patents. In its motion, Amgen seeks to prevent Roche from referring to how Mircera® has different clinical attributes than Amgen's products – evidence that goes to the heart of Roche's non-infringement defense. Thus, the evidence Amgen seeks to exclude relates directly to Roche's non-infringement defenses and are thus relevant, probative, non-prejudicial, and admissible. Accordingly, this Court should deny Amgen's motion.

BACKGROUND FACTS

To defend itself against Amgen's infringement allegations, Roche contends Mircera differs both structurally and functionally from the claimed pharmaceutical compositions and processes for making them. For example, Mircera is an entirely different molecule than Amgen's claimed inventions. In addition, Mircera has a significantly longer "half-life," meaning

that it stays intact in the body longer, and can be administered much less frequently than Amgen's anti-anemia drugs. Indeed, Mircera can be administered once per month, while Amgen's Epogen drug—the product supposedly covered by Amgen's patents--must be administered two or three times per week. *See* Roche's Rule 56.1 Statement of Material Facts in Support of Defendants' Opposition to Amgen's Motion for Summary Judgment of Infringement of '422 Claim 1, '933 Claim 3, and '698 Claim 6 and Response to Amgen's Statement of Undisputed Material Facts Pursuant to Local Rule 56.1 (Docket No. 607) at ¶¶ 82-83, 98-105. Mircera also provides greater hematocrit levels (*i.e*., the concentration of red blood cells per unit of whole blood) and otherwise exhibits greater potency than the EPO compositions claimed in Amgen's patents. *Id*. at ¶¶ 87-88, 98-105. Thus, Mircera's clinical benefits for anemia patients, and consequent choice if offers patients, is directly relevant to Roche's defense against Amgen's infringement allegations.

Amgen cites to Roche statements in the pretrial memorandum as evidence of a plan to argue to the jury the public interest prong of the injunction inquiry. *See* Brief in Support of Amgen's Motion *In Limine* No. 6 [Docket No. 840] at fn. 1. Tellingly, Amgen does not actually quote the statements but rather identifies them by document and paragraph number. Had Amgen actually quoted the statements, it would be immediately obvious that they were not made in the context of the injunction inquiry. Rather, the facts and law relate to Roche's infringement defenses. The Roche statements cited by Amgen are:

- Whether MIRCERA® is a unique compound, different from epoetin and Aranesp®, that achieves clinical advantages because it works in a substantially different way to get a substantially different and better result. Exhibit B, Roche's Statement of Contested Issues of Fact (Docket No. 807-3) at ¶ 104.

- A finding that subsequent processes confer superior properties relating to the basic utility of the product of the patented process, e.g., increased potency, supports a finding of material change. *See Eli Lilly & Co. v. American Cyanamid*

Co., 66 F. Supp. 2d 924, 932 (S.D. Ind. 1999). Exhibit D, Roche's Statement of Legal Standards and Burdens of Proof (Docket No. 807-5) at ¶ 147.

- A new product or process that uses a new technology that makes a real difference in how the process works or what is produced would not infringe under the reverse doctrine of equivalents. *See Amgen, Inc. v. Hoechst Marion Roussel Inc*., 339 F. Supp. 2d 202, 301 (D. Mass. 2004). *Id*. at ¶ 170.

- Changes to a drug's biologic or therapeutic effects can be considered a real difference for purposes of the reverse doctrine of equivalents. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc*., 339 F. Supp. 2d 202, 295 (D. Mass. 2004). *Id*. at ¶ 171.

The first statement cited above, from Roche's Contested Issues of Fact, appears in a section directed to Roche's "material change" argument. The second statement (¶ 147 from Roche's Statement of Legal Standards) appears in a section entitled "Material Change under 35 U.S.C. § 271(g)." Material change is a defense to Amgen's assertion that Roche infringes the asserted process claims, including for example, Claim 6 of the '698 patent. This evidence can also be relevant to the doctrine of equivalents defense. The next two statements are, obviously, directed to Roche's arguments under the reverse doctrine of equivalents, a doctrine that is a legitimate defense to infringement.

Functional differences of Roche's accused Mircera product (such as its longer half-life and increased *in vivo* potency) show that Mircera is structurally different from the claimed products and that it has been materially changed. Indeed, as Roche has previously argued, Amgen's own experts have acknowledged that "EPO function is inextricably tied to structure." Defendants' Opposition to Amgen's Motion for Summary Judgment of Infringement of '422 Claim 1, '933 Claim 3, and '698 Claim 6 [Docket No. 588] at 16. Such structural and functional differences support the material change and reverse doctrine of equivalents arguments. As such, and as argued below, Roche must be allowed to cite the important functional differences of Mircera.

ARGUMENT

Amgen's motion has nothing to do with Amgen's request for an injunction. Framing the motion as such was merely Amgen's ruse for attempting to block Roche from raising its infringement defenses. The statements and associated evidence relate at least to Roche's "material change" and reverse doctrine of equivalents defenses and thus should be admitted. *See* Fed. R. Evid. Rule 401-402; *see also, e.g., E.I. Du Pont de Nemours & Co. v. Phillips Petroleum Co.*, 849 F.2d 1430, 1436 (Fed. Cir. 1988) (trial court improperly excluded evidence relevant to a invalidity defense); *Blue Cross and Blue Shield of New Jersey, Inc. v. Philip Morris, Inc.*, 138 F. Supp. 2d 357, 365 (E.D.N.Y. 2001) (evidence is relevant and thus admissible if it is logically related, either directly or indirectly, to at least one element of a claim or defense in the case).

A. The Evidence Relates to Roche's "Material Change" Defense

Amgen accuses Roche of infringing certain process claims, including for example, Claim 6 of the '698 Patent. Claim 6 is directed to a "process for the production of a glycosylated erythropoietin polypeptide" having certain biological properties. Roche produces Mircera in Europe and imports it into the United States. In defense to Amgen's infringement claims, Roche relies, *inter alia*, on the material change defense of Section 271(g), which provides in relevant part as follows:

> (g) Whoever without authority imports into the United States or offers to sell, sells, or uses within the United States a product which is made by a process patented in the United States shall be liable as an infringer if the important, offer to sell, sale, or use of the product occurs during the term of such process patent. . . . A product which is made by a patented process will, for purposes of this title, not be considered to be so made after--
>
> (1) it is materially changed by subsequent processes; or . . .

35 U.S.C. § 271(g) (emphasis added).

Section 271(g)(1) thus provides that an importer does not infringe a process claim when the imported product has been "materially changed" by subsequent processes. A "change in the physical or chemical properties of a product, even though minor, may be 'material' if the change relates to a physical or chemical property which is an important feature of the product produced by the patented process." *Eli Lilly and Co. v. American Cyanamid Co.*, 82 F.3d 1568, 1577 (Fed. Cir. 1996) (citing a Senate committee report).

Courts have found a material change when a subsequent process confers an additional, distinct, and valuable property to the imported product. Indeed, in a case similar to this one, a court found that that a pharmaceutical compound was materially changed, and thus did not infringe under § 271(g), because it could be administered orally (the patented compound could not), had increased antibiotic effect over the patented compound, and was "far superior" to the patented compound. *See Eli Lilly & Co. v. American Cyanamid Co.*, 66 F. Supp. 2d 924, 931-32 (S.D. Ind. 1999). In other words, the increased efficacy of the new compound helped to show that it was materially changed.

Amgen seeks to exclude evidence that Mircera "achieves clinical advantages because it works in a substantially different way to get a substantially different and better result." Roche's Statement of Contested Issues of Fact (Docket No. 807-3) at ¶ 104. Likewise, Amgen seeks to exclude evidence showing that "subsequent processes confer superior properties [on Mircera] relating to the basic utility of the product of the patented process, e.g., increased potency." Roche's Statement of Legal Standards and Burdens of Proof (Docket No. 807-5) at ¶ 147. Such evidence includes, for example, the greater half-life and potency of Mircera, among other structural and functional differences that bestow on Mircera clinical advantages and greater utility over Amgen's products.

This evidence is relevant to the material change defense. At trial, Roche will show that the additional processes that lead to Mircera result in increased efficacy and superior properties. As in the *Eli Lilly* case cited above, such evidence of superior quality and increased efficacy help to show that a pharmaceutical compound is different from the claimed compound and thus has been materially changed. As such, this Court should allow the evidence and ignore Amgen's attempt to equate this evidence with the injunction inquiry.[1]

B. The Evidence Also Relates to Roche's Reverse Doctrine of Equivalents Defense

Evidence concerning the functional differences and benefits of Mircera is directly relevant to Roche's defense based on the reverse doctrine of equivalents. Under this doctrine, a product does not infringe if, despite its literal infringement, "the product is so far changed in principle that it performs the same or similar function in a substantially different way." *SRI Int'l. v. Matsushita Electric Corp. of Am.*, 775 F.2d 1107, 1124 (Fed. Cir. 1985); *Amgen, Inc. v. Hoechst Marion Roussel, Inc*., 339 F. Supp. 2d 202, 287 (D. Mass. 2004) (recognizing that the reverse doctrine of equivalents "supports innovation--especially in the area of biotechnology where blocking patents are common--because it offers some chance of protection to those that make substantial changes or radical improvements to inventions"). Whether an accused product escapes infringement under the reverse doctrine of equivalents is a question of fact for the jury. *SRI Int'l.*, 775 F.2d at 1124.

[1] This same evidence supporting material change can also be relevant to the doctrine of equivalents analysis, particularly because it tends to show that Mircera functions differently and produces a different result. *See Genentech, Inc. v. The Wellcome Foundation Ltd*., 29 F.3d 1555, 1569 (Fed. Cir. 1994) (accused protein, formed through recombinant DNA technology, did not infringe under doctrine of equivalents because, *inter alia*, it had a far longer "half-life" and had other clinical advantages, thus showing that it achieved a different result)

Accordingly, evidence showing whether the accused product is so far changed in principle is relevant to the jury's determination of non-infringement under the reverse doctrine of equivalents. Evidence tending to support this finding would include, for example, that the compound "worked in some substantially different way . . . and enabled it to produce significantly more EPO or EPO that somehow differed in its biologic or therapeutic effects . . . ." *Amgen*, 339 F. Supp. 2d at 295. Evidence that the accused product or process uses "a new technology that makes a real difference in how the process works or what is produced" would also support a finding of non-infringement under the reverse doctrine of equivalents. *Id*. at 301.

Amgen, however, would have this Court exclude evidence directed to just these points. Roche will show that Mircera differs both structurally and functionally from the claimed pharmaceutical compositions and processes for making them and is based on a new technology that increases efficacy. For example, Mircera has a significantly longer "half-life," meaning that it stays intact in the body longer. Indeed, Mircera is so far advanced that it can be injected just one per month, as opposed to two to three times a week, like Amgen's anti-anemia drugs. CERA also provides greater hematocrit levels and otherwise exhibits greater potency than the claimed EPO products. This evidence shows that Mircera is "so far changed in principle" that it is, in fact, a different and non-infringing product.

CONCLUSION

For the foregoing reasons, Amgen's Motion in Limine No. 6 should be denied in all respects.

Dated: September 1, 2007
Boston, Massachusetts

Respectfully submitted,

F. HOFFMANN-LA ROCHE LTD,
ROCHE DIAGNOSTICS GMBH, and
HOFFMANN-LA ROCHE INC.

By their Attorneys,

/s/ Thomas F. Fleming
Leora Ben-Ami (*pro hac vice*)
Patricia A. Carson (*pro hac vice*)
Thomas F. Fleming (*pro hac vice*)
Howard S. Suh (*pro hac vice*)
Peter Fratangelo (BBO# 639775)
Vladimir Drozdoff (*pro hac vice*)
KAYE SCHOLER LLP
425 Park Avenue
New York, New York 10022
Tel. (212) 836-8000

Lee Carl Bromberg (BBO# 058480)
Robert L. Kann (BBO# 258025)
Julia Huston (BBO# 562160)
Keith E. Toms (BBO# 663369)
Nicole A. Rizzo (BBO# 663853)
Kregg T. Brooks (BBO# 667348)
BROMBERG & SUNSTEIN LLP
125 Summer Street
Boston, MA 02110
Tel. (617) 443-9292

CERTIFICATE OF SERVICE

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/s/ Thomas F. Fleming
Thomas F. Fleming