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 TO PRECLUDE ROCHE FROM INTRODUCING EVIDENCE REGARDING DOSING AND EFFICACY OF MIRCERA

Amgen's motion (D.I. 1265), cynically attempts to prevent Roche from presenting evidence regarding the clinical attributes of Mircera® that go to the heart of Roche's non-infringement defense by deliberately confusing two separate issues -- the dosing and other clinical attributes of Mircera as will be approved by appropriate regulatory authorities, and baseless suggestions that Amgen's experts have made that Roche's product may raise safety issues, which Amgen knows are untrue. In a classic case of obfuscation, Amgen argues that because Roche has said that the baseless safety issues are not at all relevant to the issues at trial, Roche has also contended that important clinical attributes of its product -- including the dosing -- are irrelevant. That is pure nonsense, and Roche has said no such thing.

Differences in product attributes support Roche's position that Mircera is not the same as Amgen's claimed products or products of their claimed process. Product

attribute evidence is also centrally relevant to Roche's position that Mircera is materially changed pursuant to section 271(g), that Mircera does not infringe pursuant to the doctrine of equivalents, and that Mircera does not infringe pursuant to the reverse doctrine of equivalents. In contrast, speculation about the safety of Mircera by Amgen's experts has no bearing on the issue of whether Roche's product is the same as Amgen's or whether Mircera infringes literally or pursuant to the doctrine of equivalents. In short, spurious safety allegations about Mircera are not relevant to infringement, but clinical attributes showing differences such as dosing are relevant.

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 -- which Amgen contends, but has not proven, is covered by the asserted claims of its patents -- must be administered three times per week to kidney disease patients. Ultimately, the issue of the dosing and clinical efficacy of Mircera will be determined by the FDA, just as the European authorities have already determined in approving Mircera and its label.

A. Clinical Efficacy Data Is Unquestionably Relevant to Roche's Non-Infringement Defenses

The clinical attributes of Mircera are unquestionably relevant to material change and reverse doctrine of equivalents defenses, and counter Amgen's argument that Mircera infringes pursuant to the doctrine of equivalents. One of Roche's non-infringement

defenses to Amgen's process patents is the "material change" defense of 35 U.S.C. § 271(g)(1) (providing 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 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 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.

Evidence concerning the clinical benefits of Mircera is also directly relevant to a reverse doctrine of equivalents defense. 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.

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. The clinical attributes of Mircera that Amgen seeks to exclude are directly relevant to this defense.

Evidence relating to the clinical benefits of Mircera is also relevant to rebut Amgen's contention that Mircera infringes pursuant to the doctrine of equivalents. To establish Mircera infringes under the doctrine of equivalents, Amgen would have to prove, among other things, that Mircera "performs substantially the same function in substantially the same way to obtain the same result" as the product claimed in the asserted claims. *Hughes Aircraft Co. v. United States*, 717 F.2d 1351 (Fed. Cir. 1983), *quoting Graver Tank & Mfg. Co. v. Linde Air Products Co.*, 339 U.S. 605, 608 (1950). Evidence concerning the clinical benefits of Mircera is relevant to rebut the contention that Mircera performs the same function, does it in the same way, and achieves the same result as the claimed product.

B. Relevant Clinical Attribute Evidence Is Not The Same As Amgen's Baseless Speculation About Mircera Safety

The product attributes of Mircera that are relevant to the material change and reverse doctrine of equivalents defenses are a far cry from the baseless safety allegations that this Court has ruled Amgen cannot raise during Roche's infringement case.[1] Nor can Amgen back-door these spurious safety issues by claiming that Roche will introduce evidence of "supposed product improvements." Mircera's dosing advantage and other clinical attributes are not "supposed"; the European authorities have approved a label containing those attributes (including dosing), and the FDA -- which has all the clinical testing data on Mircera -- will determine itself whether to do likewise. Amgen's true motivation is to slander Roche's product before the jury as evident by the fact that any supposed safety allegations regarding Mircera that Amgen's experts seek to make do not support Amgen's infringement position. Alleged safety differences between Mircera and the product Amgen claims is a commercial embodiment of the claimed invention, Epogen, are not evidence of infringement - they are irrelevant. Amgen is not seeking to introduce this evidence to the jury for any legitimate purpose in proving infringement, but rather so the jury will get the mistaken impression that Mircera is not safe - an issue not relevant to infringement.

In essence, Amgen claims that any mention by Roche of what Mircera does -- how it works, what effect it has on patients, how often patients should take it -- opens the door to Amgen's introduction of unsupported speculation by its experts that there is some issue of safety regarding Mircera. The Court should reject Amgen's gambit because

[1] Order dated 9/24/07 allowing motion *in limine* (D.I. 970).

evidence of what Mircera does is a key part of Roche's non-infringement defense here, while speculation related to the alleged safety of Mircera is not relevant to infringement..

CONCLUSION

For the foregoing reasons, Amgen's Motion (D.I. 1265) to Preclude Roche should be denied in all respects.

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Boston, Massachusetts

Respectfully submitted,

F. HOFFMANN-LA ROCHE LTD,
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