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

MEMORANDUM IN SUPPORT OF DEFENDANTS' MOTION FOR RECONSIDERATION OF THE COURT'S GRANT OF SUMMARY JUDGMENT OF INFRINGEMENT OF '422 CLAIM 1

I. INTRODUCTION

Roche moves for reconsideration of this Court's grant of summary judgment of infringement of claim 1 of Amgen's '422 patent in light of new evidence -- explicit statements that Amgen made to this Court, in a co-pending case, after the motions for summary judgment in this case were briefed and argued.

Only days ago, in the *HMR/TKT* case, in attempting to narrow the meaning of claim 1 of the '422 patent in order to avoid prior art, Amgen filed a brief asserting that the claim 1 source limitation "purified from mammalian cells grown in culture" defines "structural and functional differences between recombinant urinary EPO and recombinant EPO." (Amgen's Brief on Remand Concerning Whether Goldwasser Anticipates '422 Claim 1, Document 863, *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, Civil Action No. 97-10814-WG4). Amgen argued that even though Dr. Eugene Goldwasser's urinary EPO, which was in the prior art, has the same amino

acid sequence as the EPO of Dr. Lin's claimed invention, there are various "structural and functional differences" that distinguish Dr. Goldwasser's EPO preparation from the EPO of the claim and make Dr. Goldwasser's EPO not an invalidating anticipation under 35 U.S.C. § 102. In other words, Amgen acknowledged that not all proteins having the amino acid sequence of human erythropoietin are included within the scope of the '422 patent claim 1.

In moving for summary judgment of infringement in the instant case, though, Amgen asserted that "the only difference between Lin's recombinant human EPO" and the EPO in CERA "is the attachment of a peg moiety to the EPO protein via a single bond." (Amgen Br. at 4). Amgen cited Roche's representation to the FDA that pegylation does not change the amino acid sequence of EPO, but made no showing that CERA is identical to the EPO of claim 1 in terms of the "structural and functional" features which Amgen now claims -- in the *HMR/TKT* case -- are required by the phrase "purified from mammalian cells grown in culture."

In short, Amgen cannot have it both ways. If, as Amgen now urges in the *HMR/TKT* case, the term "purified from mammalian cells grown in culture" defines the claimed erythropoietin product in terms of an array of very specific structural and functional features -- beyond the amino acid sequence -- then in moving for summary judgment here, Amgen did not make even a *prima facie* showing of infringement because Amgen did not cite a shred of evidence demonstrating that CERA has the various "structural and functional" characteristics of erythropoietin "purified from mammalian cells grown in culture." In fact, one cannot undertake a proper infringement analysis because Amgen has yet to explain what the structural features of its claimed human EPO actually are so that a potential competitor would be able to compare its product. Although specifically asked to do so at the July 17, 2007 summary judgment hearing,

no answer was forthcoming from Amgen. (7/17/07 Hearing Tr. 81:12-13, 82:18-83:12; *see also* 22:21-24:18).[1]

Roche respectfully requests that the Court reconsider Amgen's motion for summary judgment of infringement of the '422 patent claim 1 on grounds that -- in light of the position Amgen just adopted in the *HMR/TKT* case -- there is a genuine issue of material fact as to whether CERA satisfies all of the structural and functional limitations alleged by Amgen to be imparted by the phrase "purified from mammalian cells grown in culture."[2] Under the circumstances, allowing the Court's award of summary judgment in Amgen's favor to stand would be manifestly unjust.

II. STANDARD FOR RECONSIDERATION

A motion for reconsideration should be granted "only when the movant demonstrates (1) an intervening change in the law; (2) the discovery of new evidence not previously available; or (3) a clear error of law in the first order." *Davis v. Lehane*, 89 F.Supp.2d 142, 147 (D. Mass. 2000). *See also Arthrocare Corp. v. Smith & Nephew, Inc.*, 315 F.Supp. 2d 615, 618 (D. Del. 2004) ("The purpose of granting a motion for reconsideration is to 'correct manifest errors of law

[1] Indeed, there is no "structure" disclosed in the patent specification other than the 166 amino acid sequence of human EPO. When the PTO examined the '422 patent, the examiner found that Lin "fails to impose any definitive physical limitation of the claimed compositions" (Trial Ex. 2009 at 2009.507) and Lin subsequently added the "purified from mammalian cells grown in culture" language to claim 1 to "limit the source of EPO." (Trial Ex. 2009 at 2009.555). Moreover, the specification discloses no other structural feature known to Lin in 1983-84 upon which Amgen can now rely as defining a new, patentable product. The carbohydrate analysis data set forth in the specification (Trial Ex. 1, col. 28:51-67) cannot define a structure because the data is admittedly wrong. *Amgen Inc. v. Hoechst Marion Roussel, Inc*., 126 F.Supp.2d 69, 145 (D. Mass. 2001). Likewise, the Federal Circuit held that one cannot evaluate any structural differences in glycosylation between recombinant human EPO as and prior art human EPO. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1341 (Fed. Cir. 2003) ("One must know what the glycosylation of uEPO is with certainty before one can determine whether the claimed glycoprotein has a glycosylation different from that of uEPO. In its discussion characterizing recombinant glycoprotein products, the [Lin] specification . . . does not direct those of ordinary skill in the art to a standard by which the appropriate comparison can be made.").

[2] Roche limits this motion for reconsideration to the claim element "purified from mammalian cells grown in culture" without waiving any rights to appeal the Court's decision that the accused product satisfies other limitations of the claim, including "human erythropoietin" and "[a] pharmaceutical composition comprising . . . a diluent, adjuvant, or carrier."

or fact or to present newly discovered evidence"). "Reconsideration may be appropriate to avoid manifest injustice." *Ellis v. United States*, 313 F.3d 636, 648 (1st Cir. 2002) Here, Roche's motion is predicated on new facts -- statements by Amgen in a co-pending litigation – that did not yet exist when Amgen's motion was briefed and argued. Allowing the Court's order to stand without regard to Amgen's recent filing would be manifestly unjust.

III. STATEMENT OF FACTS

A. Claim 1 Of The '422 Patent

Claim 1 of the '422 patent provides:

> A pharmaceutical composition comprising a therapeutically effective amount of human erythropoietin and a pharmaceutically acceptable diluent, adjuvant or carrier, wherein said erythropoietin is *purified from mammalian cells grown in culture*.

(Emphasis added).

B. Amgen's Motion For Summary Judgment Of Infringement

In moving in this case for summary judgment of infringement of claim 1 of the '422 patent, Amgen relied on evidence that (1) the Epoetin beta that Roche uses in making CERA is purified from mammalian cells grown in culture; (2) CERA has the amino acid sequence of Epoetin beta; and (3) CERA has the glycosylation of Epoetin beta. (Amgen Br. at 4-5). That evidence apparently satisfied the Court that even though CERA is not itself a product of mammalian cells, it is indistinguishable from "erythropoietin purified from mammalian cells grown in culture" as is required of the pharmaceutical composition of claim 1.

Amgen's motion was argued on July 17, 2007, and the motion was granted on August 28, 2007.

C. The Facts That Have Changed Since Amgen's Summary Judgment Motion Was Briefed And Argued

On August 24, 2007, in *Amgen Inc. v. Hoechst Marion Roussel, Inc., et al.*, Civil Action No. 97-10814-2G7, in an effort to preserve the validity of the '422 patent, Amgen filed a brief taking a position regarding the scope of claim 1 of the '422 patent which is dramatically different from the position Amgen took in moving for and obtaining summary judgment of infringement here. Not surprisingly, Amgen casts claim 1 very narrowly for validity purposes, but very broadly for infringement purposes.

It is fundamental, though, that a patent claim is to have a single meaning for both infringement and validity. *Scripps Clinic & Res. Found. v. Genentech, Inc.*, 927 F.2d 1565, 1583 (Fed. Cir. 1991) ("Since claims must be construed the same way for validity and for infringement, the correct reading of product-by-process claims is that they are not limited to product prepared by the process set forth in the claims"). As the Federal Circuit stated in *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1351 (Fed. Cir. 2001): "Because the claims of a patent measure the invention at issue, the claims must be interpreted and given the same meaning for purposes of both validity and infringement analyses. 'A patent may not, like a "nose of wax," be twisted one way to avoid anticipation and another to find infringement.'" (Citations omitted).

In its newly filed *HMR/TKT* brief, Amgen has argued that it was able to define the product of claim 1 of the '422 patent "by means of the source limitation 'purified from mammalian cells grown in culture' precisely because Lin's recombinant EPO is a novel product." (Doc. 863 at 15). According to Amgen, "the source limitation 'purified from mammalian cells grown in culture' defines structural and functional differences between urinary EPO and recombinant EPO." (*Id.*). Amgen thus distinguished the prior art human erythropoietin

from the erythropoietin of '422 claim 1 in terms of: glycosylation; conformation (folding); susceptibility to degradation by trypsin; ease of iodination; inactivation by iodination; and second derivative and circular dichroic spectra. (*Id*. at 16). In addition, Amgen alleged that the human erythropoietin of the prior art "and the EPO of claim 1 differed significantly in terms of *in vivo* potency (specific activity), clearance rate, half-life and therapeutic effect. (*Id*. at 18).

In accordance with Amgen's position in the *HMR/TKT* case, proving infringement of claim 1 of the '422 patent requires a showing not only that the accused product has the amino acid sequence of Dr. Lin's EPO, but also that the accused product is indistinguishable from Dr. Lin's EPO in terms of the structural and functional criteria that Amgen now claims define an EPO that is "purified from mammalian cells grown in culture." However, in moving for and obtaining summary judgment of infringement in this case, Amgen submitted no evidence about CERA's conformation, susceptibility to degradation by trypsin, ease of iodination, inactivation by iodination, or second derivative and circular dichroic spectra. Nor did Amgen show that CERA matches EPO "purified from mammalian cells grown in culture" in terms of *in vivo* potency, clearance rate, half-life and therapeutic effect.

In fact, the evidence will show that CERA differs from Dr. Lin's EPO at least in terms of *in vivo* potency, clearance rate, half-life and therapeutic effect. In its *HMR/TKT* brief, Amgen argued that Dr. Goldwasser's EPO did not anticipate the '422 patent because the specific activity of his human erythropoietin was "70,400 U/mg, while recombinant EPO has a specific activity of 174,000 U/mg." (Doc. 863 at 20). By contrast, the specific activity of CERA is lower (8,000 - 12,5000 U/mg (ITC-R-BLA-00004343)) than that of the human erythropoietin of the prior art. Amgen also argued there that "recombinant human erythropoietin has been shown to have a half-life ranging from 4 to 13 hours when administered intravenously." (Doc. 863 at 18). Yet, the

half-life of CERA is nearly 10 times as long as recombinant human EPO. Owing to these pronounced functional differences, CERA is readily distinguishable from erythropoietin "purified from mammalian cells grown in culture" as that phrase is explained by Amgen in the *HMR/TKT* cases. At a minimum, there are fact issues regarding infringement that should preclude summary judgment.

IV. CONCLUSION

Based on the new evidence described above, Roche requests that Court reconsider its decision in granting summary judgment of infringement of claim 1 of the '422 patent and allow the jury to decide the issue.

Dated: September 12, 2007
Boston, Massachusetts

Respectfully submitted,

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