UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, v. F. HOFFMANN-LAROCHE LTD., a Swiss Company, ROCHE DIAGNOSTICS GmbH, a German Company and HOFFMANN LAROCHE INC., a New Jersey Corporation, Defendants.	)	Civil Action No.: 05-12237 WGY

AMGEN INC.'S OPPOSITION TO ROCHE'S MOTION *IN LIMINE* TO PRECLUDE AMGEN FROM ARGUING THAT LIN DESCRIBED HUMAN EPO WITH THE 1-165 AMINO ACID RESIDUES OF FIG.6

Roche's motion *in limine* to preclude Amgen from arguing and offering testimony that the Lin specification describes human EPO with the amino acid sequence of 1-165 is based on the inaccurate assertion that prior opinions have already decided this issue as to the claims at issue in this lawsuit. Contrary to Roche's conclusory and unfounded contention in its two-page motion, prior courts — including this Court and the Federal Circuit — have rejected the very claim Roche makes by this motion time-after-time. But Roche, by its motion, misleadingly references prior findings related to Dr. Lin's '080 patent, which Amgen does not assert as part of this lawsuit and which included express reference to an erythropoietin glycoprotein that "comprises the mature erythropoietin amino acid sequence of FIG. 6." None of the claims asserted in this litigation contain this same limitation. As to the claims actually at issue, this Court and the Federal Circuit have recognized that the Lin Patents provide ample and adequate written description support for human erythropoietin, including 165 amino acid EPO.

I. Roche's Reference To Findings Regarding Claims Not At Issue In This Litigation Is Immaterial; Instead *Stare Decisis* Requires A Finding That The Patents at Issue Are Adequately Described.

The findings from prior litigation that Roche references as part of this Motion are immaterial to the claims at issue in this case. Those prior findings related to Dr. Lin's '080 patent — which Amgen does not assert in this litigation — and were tied to the specific limitation within the claims of the '080 patent that the erythropoietin glycoprotein "comprises the mature erythropoietin amino acid sequence of FIG. 6…" Thus, the Federal Circuit held that the '080 claims were limited because the word "comprises" in the claim language ties the mature erythropoietin amino acid sequence to the specific sequence set forth in FIG. 6.[1] In reaching this decision, the Court recognized the distinction between the '080 claims, which specifically referenced the amino acid sequence of Figure 6, and those that did not, quoting this Court's opinion in *Hoechst I* that:

> [h]ad Amgen claimed only the mature erythropoietin amino acid sequence without associating or linking that amino acid sequence to Figure 6 its argument that its claims cover whatever sequence (whether it contained 165 or 166 amino acids) is ultimately secreted by the cell might have more momentum.[2]

As to the claims at issue in this case, this Court and the Federal Circuit have rejected the very assertion that Roche makes by this motion. Thus, in the 2001 *Hoechst I* decision, this Court recognized the difference in breadth between the '080 claims and the claims of the '422 and 933 patents when it held that "human erythropoietin" was not limited to 166 EPO.

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[1] *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1345 (Fed. Cir. 2003) ("*Hoechst II*") (stating "read properly in light of the term "comprising" this means that the claimed glycoprotein must have – at minimum – all 166 amino acids shown in Figure 6.")

[2] *Hoechst II*, 314 F.3d at 1344, *citing Amgen v. Hoechst Marion Roussel, Inc.*, 126 F.Supp. 2d. 69, 100 (D. Mass. 2001) ("*Hoechst I*").

> TKT thus seeks to read a 166 amino acid limitation into the claim term "human erythropoietin." ***This the Court cannot do***. As with the previous tack, this argument drifted far astray from the language of the claim and was therefore unpersuasive.[3]

Both this Court and the Federal Circuit recognized that the claim term "human erythropoietin" without the limiting language of the '080 patent covers human erythropoietin independent of its amino acid sequence. Thus, the Federal Circuit stated as to claim 1 of the '933 patent, it "encompassed EPO with any amino acid sequence.[4]" And this Court stated in 2003 regarding the '422 patent:

> Indeed, Amgen admits that it "could have sought broader claims that literally encompassed human EPO with a 165 amino acid sequence, and did in fact do so in the '422 Patent."[5]

Based on this construction, this Court and the Federal Circuit found that Epoetin delta which has the 1-165 amino acid residues of Figure 6 infringed claim 1 of the '422 Patent, and so, 1-165 Epoetin delta was "human erythropoietin" purified from mammalian cells grown in culture.[6] Thus, as to the patents at issue in this suit "human erythropoietin" encompasses EPO 165 in its literal terms.

In the decisions in the *Chugai case*, both this Court and the Federal Circuit stated that EPO has 165 amino acids.[7] The PTO, in its DNA interference decision, clearly stated its understanding of the term "human erythropoietin" to be a 165 amino acid product.[8] In all these decisions, the courts and PTO held that Dr. Lin was entitled to claims that included the term "human erythropoietin."

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[3] *Hoechst I*, 126 F.Supp.2d at 95.

[4] *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d at 1315 ("*Hoechst IV")*

[5] *Hoechst I*, 287 F.Supp.2d at 149.

[6] *Hoechst I*, 126 F.Supp.2d at 95, *affirmed*, *Hoechst II*, 314 F.3d at 1348.

[7] *Amgen, Inc. v. Chugai Pharm. Co., Ltd*., 927 F.2d 1200, 1203 (Fed. Cir. 1991); *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 13 U.S.P.Q.2d 1737, 1741 (D. Mass 1989).

[8] *Fritsch v. Lin*, 21 U.S.P.Q.2d 1731, 1733 (Bd. Pat. App. & Int. 1991).

Furthermore, these prior determinations that "human erythropoietin" is not limited to 166 amino acid EPO is bolstered by the doctrine that "a claim interpretation that reads out a preferred embodiment 'is rarely, if ever, correct and would require highly persuasive evidentiary support.'"[9] The preferred embodiment of Dr. Lin's Patent is Example 10, which indisputably makes 165 amino acid recombinant EPO. Roche's attempt to limit the claim term "human erythropoietin" to 166 EPO would exclude the preferred embodiment of the patent.

Finally, it is the law of this case that "human erythropoietin" encompasses 165 EPO because this Court held at summary judgment that claim 1 of the '422 Patent was infringed by the 1-165 Epoetin beta in MIRCERA.[10] Roche cannot re-litigate this issue now through this cursory, and misleading, Motion *in Limine.*

II. Dr. Lin's Patents Provide Ample and Adequate Written Description Support for Human Erythropoietin, Including 165 Amino Acid EPO.

At its core, Roche's assertions in this motion and the accompanying motion *in limine* on inherency (Docket No. 1066) stem from its argument that Dr. Lin's specification does not disclose that human erythropoietin is 165 amino acids. But this reading ignores the actual written description of Dr. Lin's patents and the fact that he was the first person in the world to produce 165 amino acid recombinant EPO – a fact that Roche does not dispute.

"The purpose of the written description requirement is to prevent an applicant from later asserting that he invented that which he did not . . ."[11] There is no question that Dr. Lin's specification describes the production of 165 amino acid EPO, and thus his possession of

[9] *Hoechst II*, 314 F.3d at 1349.

[10] August 28, 2007 Order ("Amgen's Motion for Summary Judgment is ALLOWED as to infringement of the '422 patent.")

[11] *Hoechst II*, 314 F.3d at 1330.

recombinant human erythropoietin. Indeed, this Court, the Federal Circuit, and the PTO have so held on numerous occasions.[12]

Dr. Lin is not claiming a composition that he did not invent. As claimed in the '422 patent, the thing patented by Dr. Lin is "human erythropoietin" purified from "mammalian cells grown in culture." In the '933 Patent, claim 3, he claimed a "glycoprotein product of the expression in a mammalian host cell of an exogenous DNA sequence comprising a DNA sequence encoding human erythropoietin." Neither the claims of the '422 Patent nor the claims of the '933 Patent identify Dr. Lin's recombinantly produced human erythropoietin by the amino acid sequence of Figure 6, and ample written description supports these claims. Indeed, Examples 7-9 of the patents-in-suit describe the recombinant production of human erythropoietin in COS cells. The protein made in these COS cells was confirmed to be human erythropoietin by a radioimmunoassay, an *in vitro* assay for erythropoietin activity, and an inhibition study showing that anti-EPO antibodies neutralized EPO bioactivity.[13] Example 10 of the patents-in-suit describes the preferred commercial embodiment, the recombinant production of human erythropoietin in CHO cells. The patent disclosure describes the product of Example 10 as "human erythropoietin." Its identity was confirmed by radioimmunoassay, an *in vitro* assay for erythropoietin activity, an *in vivo* assay measuring increases in hematocrit, and physical

[12] *Fritsch v. Lin*, Interference No. 102,096, Paper No. 152 (Board Decision) at 6-8 ; *Fritsch v. Lin*, Interference No. 102,096, Paper No. 152 (Board Decision) at 6-8 ("Accordingly, we hold that Fritsch has failed to establish an adequate conception of the invention at issue prior to Lin's reduction to practice"); *Amgen Inc., v. Chugai Pharm. Co.*, 13 USPQ2d 1737, 1739, 1763-64 (D. Mass. 1989); *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1207 (Fed. Cir. 1991).

[13] '933 Patent at col. 24:58 to 25:27.

characteristics of the recombinant erythropoietin.[14] All these confirmatory studies showed that Dr. Lin had in fact made human erythropoietin.[15]

The prior opinions which Roche relies on from the *HMR/TKT* matter support the fact that Dr. Lin's patents at issue in this lawsuit adequately describe the product of his invention — human erythropoietin. Roche's claims as to this motion are based on findings that do not apply to the claims at issue here. Accordingly, this Court should deny Roche's motion *in limine*.

Dated: September 23, 2007

Respectfully Submitted,

AMGEN INC.,
By its attorneys,

[14] *Id*. at col. 26:4-18, 27:45-53, 28:1 to 29:7.

[15] Moreover, this Court's construction of "human erythropoietin" likewise did not limit that claim term to Figure 6, but instead, referenced the protein by comparing the amino acid sequence to that found naturally.

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