UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, v. F. HOFFMANN-LA ROCHE LTD., a Swiss Company, ROCHE DIAGNOSTICS GmbH, a German Company and HOFFMANN-LA ROCHE 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 EXAMPLES IN THE LIN SPECIFICATION INHERENTLY PRODUCE HUMAN EPO WITH 165 AMINO ACID RESIDUES

Roche asks this Court to exclude Amgen's evidence showing that the human erythropoietin actually made and characterized by Dr. Lin was and is 165 amino acid human erythropoietin. Roche's arguments, however, suffer from two fatal flaws. First, Dr. Lin actually made, described and enabled human erythropoietin in his Patents that is 165 amino acid human erythropoietin, and second, the asserted claims of the patents-in-suit cover human erythropoietin independent of the amino acid sequence.

Dr. Lin's patent contains column after column of written description set forth at least in Examples 7-10 in which the recombinant production of human erythropoietin is described, made and enabled. Roche of course wants the Jury to believe that Dr. Lin did not make anything in Examples 7-10, but that wish and desire cannot be the basis for precluding Amgen from presenting this relevant evidence from Dr. Lin's preferred embodiment.

As the Federal Circuit and its predecessor, the Court of Customs and Patent Appeals, have both stated "the thing patented is not the formula but the compound identified by it."[1] Dr. Lin made, described, enabled and claimed human erythropoietin in his Patents. 165 amino acid EPO is the human erythropoietin made, described, enabled and claimed in Dr. Lin's Patents, *i.e.*, the thing patented is human erythropoietin, including 165 EPO.[2]

In the decisions in the *Chugai case,* both this Court and the Federal Circuit stated that EPO has 165 amino acids.[3] The PTO, in its DNA interference decision, clearly stated its understanding of the term "human erythropoietin" to be a 165 amino acid product.[4] In all these decisions, the courts and PTO held that Dr. Lin was entitled to claims that included the term "human erythropoietin."

Against this clear record, Roche reads into the claims a limitation regarding one specific amino acid sequence of Figure 6. But as held by this Court in *Hoechst I*, it is improper as a matter of law to read into the claim term "human erythropoietin" the 166 amino acid sequence of Figure 6.[5] Such a construction asks the claim language to do too much, and this Court correctly

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[1] *Regents of the Univ. of New Mexico v. Knight*, 321 F.3d 1111, 1122 (Fed. Cir. 2003); *In re Papersch*, 315 F.2d 381, 391 (C.C.P.A. 1963).

[2] *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F.Supp.2d 69, 94- 95, 158 (D.Mass. 2001) ("*Hoechst I*"); *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 13 U.S.P.Q.2d 1737, 1771-72 (D.Mass. 1989) ("*Chugai I*"); *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332, 1348 (Fed. Cir. 2003) ("*Hoechst II*"); *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 287 F.Supp.2d 126, 148 (D.Mass. 2001) ("*Hoechst III*"); *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1308 (Fed. Cir. 2006) ("*Hoechst IV*").

[3] *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).

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

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

ruled as a matter of law that "human erythropoietin" is not so limited.[6] This Court's construction in *Hoechst I* was echoed in *Hoechst IV* when the Federal Circuit stated that "human EPO" was not limited to the specific amino acid sequence of Figure 6, and instead embraced human erythropoietin independent of the amino acid sequence.[7] Human erythropoietin is made, described and enabled by Dr. Lin's specification and the human erythropoietin made in mammalian cells was identified as human erythropoietin using a variety of physical and biological assays.

I. THE EXAMPLES IN THE SPECIFICATION TO THE LIN PATENTS ARE RELEVANT TO DISPUTE ROCHE'S § 112 ALLEGATION BECAUSE THEY SHOW LIN PRODUCED HUMAN ERYTHROPOIETIN WITH A 165 AMINO ACID SEQUENCE

As Roche begrudgingly acknowledges in its motion, the law is clear that inherency is relevant to whether the written description requirement of § 112 is met.[8] This is because – as the Federal Circuit has consistently held – a product is adequately described under § 112 when the specification sufficiently describes the product, and a process needed to make the product.[9] In other words, Dr. Lin did not need to specifically identify a 165 amino acid sequence for human

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[6] *Id.*

[7] *Hoechst IV*, 457 F.3d at 1315; *see also, Hoechst III*, 287 F.Supp.2d at 149.

[8] *See* Roche's Motion in Limine to Preclude Amgen from Arguing that Examples in the Lin Specification Inherently Produce Human EPO with 165 Amino Acid Residues, p. 2 (recognizing the proposition that "one may rely on inherency to support the written description requirement …").

[9] *Regents of the Univ. of New Mexico v. Knight*, 321 F.3d 1111, 1122 (Fed. Cir. 2003) (stating that "as the metes and bounds of a deed identify a plot of land, the thing that is patented is not the formula but the compound identified by it"); *Kennecott Corp. v. Kyocera*, 835 F.2d 1419, 1423 (Fed. Cir. 1987) (holding that "the disclosure in a subsequent patent application of an inherent property of a product does not deprive that product of the benefit of an earlier filing date"); *Petisi v. Rennhard*, 363 F.2d 903, 907 (CCPA 1966) (holding that the specifications examples describing the synthesis and analysis of the reaction met the requirements of § 112 because they made it possible for an ordinary skilled artist to conclude that the alleged compound had been prepared).

EPO, because that sequence is inherent in a product exemplified in his patent specification.[1011] For example, in *Kennecott v. Kyocera Int'l, Inc.*, the Federal Circuit reversed a lower court, holding that although the patentee did not describe his product as having a certain structure, the patent's written description covered such a product because the examples in the patent produced the product with that structure.[12] In regard to the very same patents in this suit, the Federal Circuit has already held it is "[t]he product [a DNA sequence encoding human erythropoietin], not the formula or name, [that] is the invention."[13]

"The purpose of the written description requirement is to prevent an applicant from later asserting that he invented that which he did not . . ."[14] Dr. Lin is not claiming a composition that he did not invent. 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.[15] Example 10 of the patents-in-suit describes the preferred commercial embodiment, the recombinant production of human erythropoietin in CHO cells. The human erythropoietin from CHO cells

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[10] Roche is trying to have it both ways: On the one hand, Roche contends that Dr. Goldwasser was in possession of uEPO and that the 1977 Miyake article describing its purification is prior art to Lin's patents, yet the record is uncontradicted that Dr. Goldwasser was not in possession of the amino acid sequence of uEPO. Thus, using other characterization methods, Roche contends that uEPO was in the possession of the prior art, but that Dr. Lin, when he used and described similar characterizations, was not in possession of recombinant human erythropoietin.

[11] *See Id.*

[12] 835 F.2d at 1420-21 (holding that patent covered a product with a "equiaxed microstructure" even though patent did not specifically identify this characteristic because "examples 1-30 [of the patent specification] produced, without undue experimentation, a product having an equiaxed microstructure").

[13] *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1330 (Fed. Cir. 2003) *citing Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1561 (Fed. Cir. 1991).

[14] *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1330 (Fed. Cir. 2003) ("*Hoechst II*").

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

was confirmed to be human erythropoietin by radioimmunoassay, an *in vitro* assay for erythropoietin activity, and physical characteristics of the recombinant erythropoietin.[16] All these confirmatory studies showed that Dr. Lin had in fact made human erythropoietin.

Even Roche agrees that Amgen's process as described in Example 10 yields "human erythropoietin" with a 165 amino acid sequence. As Roche told the jury during it's opening, the commercial manifestation of the product produced according to Example 10 is a 165 amino acid product.[17] Moreover, Amgen will present evidence that attests to this fact. As such, Example 10 – and other similar Examples in the specification – are not only directly relevant to the written description requirement of § 112, they are dispositive to Roche's claim that Dr. Lin's patents did not meet this requirement.[18]

Roche's assertion that the well-established doctrine of inherency does not apply in this case is baseless. First, there is no support for Roche's claim that the inherency doctrine does not apply when the procedure disclosed in the specification produces the structure specifically disclosed as well as a structure inherently disclosed.[19] *Chen v. Bouchard*, the case Roche cites for this proposition, does not support Roche's claim.[20] In *Chen*, the court specifically recognized that the doctrine of inherency could apply, stating "our predecessor court observed that "the *product*, not the formula or name, is the invention."[21] The court found, however, that the inherency doctrine did not apply to Chen because he "did not simply misname or incorrectly illustrate the structural formula of the products that he later asserted were inherently produced;

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

[17] 9/5/07 Trial Transcript, pp. 126-127.

[18] *Hoechst I*, 126 F.Supp.2d at 94- 95; *Hoechst II*, 314 F.3d at 1332; *Hoechst III*, 287 F.Supp.2d at 148; *Chugai I*, 13 U.S.P.Q.2d at 1771-72.

[19] *See* Roche's Motion in Limine, pp. 2-3.

[20] 347 F.3d 1299 (Fed. Cir. 2003).

[21] 347 F.3d at 1306 (Also stating, "[l]ikewise, in *Regents of the University of New Mexico v. Knight* . . . there was sufficient evidence to show that the added structure was an inherent and more accurate description of the disclosed subject matter . . .").

he also failed to disclose any characteristics of those products that would evidence possession of the invention."[22]

Fiers is also inapplicable for it held that one cannot conceive of a DNA encoding a protein of unknown sequence until the DNA has been reduced to practice.[23] In *Fiers*, the Federal Circuit repeated the refrain that conception of a DNA is not satisfied by a research plan and a wish to know the structure of the claimed DNA.[24] *Rochester* is another case in which an inventor's application disclosed only a research plan and a wish to know a claimed chemical compound to be used in a method of treatment.[25] In *New Railhead*, the Court found an earlier priority application did not disclose the invention because the priority application did not disclose the structure of the claimed invention.[26]

All of Roche's cited cases are distinguishable from this case because in all them the putative inventor had not yet reduced to practice or disclosed the claimed invention. In this case, Dr. Lin's patent discloses the claimed invention through an actual reduction to practice of the claimed human erythropoietin along with the characterization of physical and biological properties of that human erythropoietin.[27]

Roche's second claim to avoid the inherency doctrine, that Amgen is reversing prior positions, is based on misleading characterizations of a prior Amgen brief. Amgen has never said that the patents-in-suit lack written descriptive support for the composition recited by Dr. Lin's claims. Roche's alleged support for this argument takes out of context statements Amgen made as part of a Rule 52(c) motion in the *TKT* case. There, Amgen argued that the *Festo*

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[22] 347 F.3d at 1307.

[23] *Fiers v. Revel*, 984 F.2d 1164, 1168-69 (Fed. Cir. 1993).

[24] *Id*.

[25] *Univ. Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 926 (Fed. Cir. 2004).

[26] *New Railhead Mfg, LLC v. Vermeer Mfg Co.*, 298 F.3d 1290, 1296-97 (Fed. Cir. 2002).

[27] The '933 Patent at Examples 7-10.

presumption against the application of the doctrine of equivalents did not apply to the '080 patent claims. Amgen argued that the written description requirement prevented Amgen from amending its '080 claims to recite a hypothetical claim limitation. Amgen's arguments were limited to whether there was support for that hypothetical limitation in a hypothetical claim. But Amgen's claims in this litigation do not involve the claims of Dr. Lin's '080 patent. Roche, however, ignored the relevant part of Amgen's Rule 52(c) motion that dealt with claims at issue in this lawsuit. Thus, in the same brief Amgen stated as to claim 1 of the '422 patent that there was ample written descriptive support that Dr. Lin's specifications encompassed the 165 amino-acid EPO product.[28]

II. DR. LIN'S POSSESSION OF HUMAN EPO DIRECTLY REBUTS ROCHE'S CLAIM THAT HE DID NOT ADEQUATELY DESCRIBE HUMAN EPO

Roche's claim that possession is irrelevant to the § 112 requirements is also fundamentally incorrect. It is black letter law that the written description requirement of § 112 is satisfied if a specification demonstrates that an inventor is in possession of his claimed invention as of the filing date of his application, regardless of whether the specification expressly recites the claimed invention.[29] Thus, the Federal Circuit has stated that written description must convey that the inventor actually possessed the subject matter claimed as the invention.[30] This showing can be by words, experimental results, structures, figures, diagrams or formulas.[31] Roche's claim that looking at possession "invites legal error by conflating the written description

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[28] Amgen's Rule 52(c) motion stated ("[a]s Amgen has explained, the dispositive issue is not whether Amgen could have drafted any claim that would cover 165 human EPO. If that were the dispositive issue, the Federal Circuit would not have remanded the issue of rebuttal for decision by this Court. As this Court previously found and the Federal Circuit affirmed, Amgen drafted another claim that encompasses Defendants' 165 amino acid product (claim 1 of the '422 patent) . . .").

[29] *Chen*, 347 F.3d at 1306; *Regents of the Univ. of New Mexico*, 321 F.3d at 1122; *Kennecott Corp.*, 835 F.2d at 1421-1423.

[30] *Vas-Cath Inc.*, 935 F.2d at 1563, n.6.

[31] *Id.*

requirement with enablement" ignores the well-established relationship between written description and enablement. As the Federal Circuit has stated, "[t]he purpose of the [§ 112] requirement … is to state what is needed to fulfil the enablement criteria. These requirements may be viewed separately, but they are intertwined."[32]

Dr. Lin's patents make clear that he was in possession of, and his inventions included, "human erythropoietin," independent of whether that human erythropoietin is an 166 or 165 amino-acid sequence. Thus, throughout his specification, Dr. Lin affirmatively states that the products of his invention include "human erythropoietin."[33] To demonstrate this fact, Dr. Lin teaches that he obtains is product using the DNA sequence encoding human erythropoietin,[34] the N-terminal amino acid sequence of his product corresponds to the N-terminal sequence of human urinary EPO,[35] that his product possesses the expected biological activity of human erythropoietin, as measured using a variety of *in vivo* and *in vitro* assays,[36] and that his product is appropriately glycosylated.[37] In Example 10, Dr. Lin reduces to practice a "human erythropoietin" that was "purified from mammalian cells grown in culture." That Dr. Lin disclosed the deduced 1-166 amino acid sequence does not change that fact that the process he exemplified in Example 10 reduced to practice a human erythropoietin that was and is a 165 amino acid EPO. Indeed, this is why this Court and the Federal Circuit have previously held that the patents-in-suit satisfied § 112's written description requirement.[38]

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[32] *Kennecott Corp*, 835 F.2d at 1421.

[33] *See e.g.*, '933 Patent, at col. 27:47-51.

[34] *Id.* at Examples 7, 10, and 11.

[35] *Id.* at col. 28:11-12.

[36] *Id.* at col. 28: 1-28.

[37] *See, generally, id.* at col. 28: 33-29:67.

[38] *Amgen v. Hoechst Marion Roussel, Inc.*, 126 F.Supp. 2d 69, 151 (D. Mass 2001), *aff'd* 314 F.3d 1313 (Fed. Cir. 2003).

Roche cannot legitimately dispute the relevancy to a § 112 inquiry of Examples in a patent specification that show an inventor possessed a product, including when a property of the product, though not described, is inherent from the description. Example 10 goes directly to this issue and thus Roche's motion *in limine* to preclude Amgen from arguing that examples in the Lin specification inherently produce human EPO with 165 amino acid residues must be denied.

DATED: September 23, 2007

Respectfully Submitted,

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