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 FOR SUMMARY JUDGMENT
THAT CLAIM 1 OF THE '422 PATENT IS INVALID UNDER 35 U.S.C. § 112

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I. INTRODUCTION

Roche seeks to prove that Lin failed to describe the invention claimed in '422 claim 1 by ignoring the literal language of the claim and arguing instead that Lin was required to describe something else, something the claim does not recite. According to Roche, Dr. Lin's specification must state in *haec verba* that human erythropoietin has the 1-165 amino acid sequence depicted in Figure 6 to satisfy the requirements of § 112. But that is not what the claim recites, and it is not what the law requires. Rather, it is the *claimed* invention, "human erythropoietin," which must be described in the patent, not Roche's interpretation of the Court's claim construction.

Moreover, the law does not turn on the presence or absence of an "express recitation" or *in haec verba* description. Instead, the law requires a description, whether by words, experimental results, structures, figures, diagrams, formulas, etc., that is adequate to convey to those skilled in the art at the time of the invention that the inventor actually possessed the subject matter claimed as the invention.[1] The adequacy of Lin's disclosure is properly determined by asking whether a person of ordinary skill in the art would recognize from the disclosure that the inventor possessed what is claimed in the patent: human erythropoietin purified from mammalian cells grown in culture. The answer to that question is unequivocally "yes."

Here, Dr. Lin's specification is rich with corroborative words, data, and figures which more than reasonably convey to the artisan that Dr. Lin invented and had possession of "human erythropoietin." And while the law requires no more, Dr. Lin's patent also discloses that he invented and possessed a human erythropoietin "comprising a 165 amino acid sequence of human urinary EPO,"[2] just as Roche seeks.

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[1] *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, n.6 (Fed. Cir. 1991); *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956 (Fed. Cir. 2002).

[2] See Roche's June 11, 2007 Memorandum in Support of its Motion for Summary Judgment that

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 filling date of his application,[3] regardless of whether the specification expressly recites the claimed invention.[4]

There is no dispute that the "human erythropoietin" produced in Example 10 has the amino acid sequence of human urinary EPO and that Dr. Lin was in possession of such product when he filed the patent application giving rise to the '422 patent. None of Roche's experts contest these facts and, based presumably on these indisputable facts, this Court previously held, and the Federal Circuit affirmed, that '422 claim 1 meets all of the requirements of § 112 and is infringed by a product having the 1-165 amino acid sequence of human EPO. The fact that Dr. Lin did not know at the time that the amino acid residue at position 166 was cleaved prior to secretion from the CHO cells in which it was produced is immaterial. The fact that Dr. Lin described and taught the production of a human EPO product that has the 1-165 sequence – even if that fact was only learned later – is all that matters.

To further support its position, Roche asserts that Amgen admitted in the *TKT* litigation[5]

Claim 1 of the '422 Patent is Invalid Under 35 U.S.C. § 112 (Docket No. 483) (hereinafter "Roche's Br."), at 7, 9, and 13.

[3] *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 314 F.3d 1313, 1330 (Fed. Cir. 2003), *citing Vas-Cath Inc.*, 935 F.2d 1561. *See also, In re Kaslow*, 707 F.2d 1366, 1375 (Fed. Cir. 1983)("The test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language." (emphasis added)).

[4] *Regents of the Univ. of New Mexico v. Knight*, 321 F.3d 1111, 1122 (Fed. Cir. 2003); *Kennecott Corp. v. Kyocera*, 835 F.2d 1419, 1421-23 (Fed. Cir. 1987); *In re Nathan*, 328 F.2d 1005 (CCPA 1964). *See also ICN Photonics, Ltd. v. Cynosure, Inc.*, 73 Fed. Appx. 425 (Fed. Cir. 2003) (unpublished) (reversing D. Mass. grant of summary judgment of invalidity for lack written description where evidence showed that limitation was inherent in invention disclosed in the original application).

[5] *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, Civil Action No. 97-10814-WGY (D. Mass. April 15, 1997) ("*TKT*").

that Dr. Lin did not describe the very 165-amino acid EPO product that it accused of infringing Dr. Lin's patents. That is simply not true. Amgen did ***not*** admit that the '422 patent lacks written descriptive support for the pharmaceutical composition recited in '422 claim 1. Rather, Amgen argued that the *Festo* presumption did not apply to the ***'080*** patent claims because Amgen would have been precluded from amending ***those*** claims to recite "the mature erythropoietin amino acid sequence 1-165 of Fig. 6." Roche conspicuously ignores that in its Rule 52(c) motion in the *TKT* case, Amgen expressly argued that '422 claim 1 encompassed a 165-amino-acid EPO product, and the '422 patent provides written descriptive support for that product. Amgen's statements in its *TKT* motion did not constitute an admission or a basis for judicial estoppel that '422 claim 1 is not adequately described.

Roche's assertion that the term "human erythropoietin," as construed by this Court, is indefinite is equally flawed. Definiteness requires that a patent specification conclude with one or more claims "particularly pointing out and distinctly claiming subject matter which the applicant regards as his invention."[6] The standard for assessing whether a patent claim is sufficiently definite to satisfy this statutory requirement is whether "one skilled in the art would understand the bounds of the claim when read in light of the specification."[7] As held by the Federal Circuit, § 112, second paragraph does not require that a claim be absolutely precise, only that its meaning be discernable.[8]

At *Markman,* Roche advocated a claim construction for "human erythropoietin" that referred to the same amino acid sequence as set forth in the Court's construction,[9] as well as

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[6] 35 U.S.C. § 112, ¶ 2.

[7] *Exxon Res. & Eng'g Co. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001), *quoting Miles Labs., Inc. v. Shandon, Inc.*, 997 F.2d 870, 875 (Fed. Cir. 1993).

[8] *Exxon*, 265 F.3d at 1375.

[9] Defs.' Opening Mem. in Supp. of Their Proposed Claim Construction (Docket No. 311), at p 1 ("a glycoprotein having the ***amino acid sequence of erythropoietin isolated from human urine***

additional limitations that would aid it in its attempt to avoid liability. It never asserted that the limitation, or indeed a construction that referred to an amino acid sequence for human erythropoietin, was too indefinite to have meaning. It was only after its position was not adopted that Roche changed its tune. But this change in tune comes too late.

Moreover, Roche's motion for indefiniteness relies on its assertion that because Dr. Lin's specification describes various amino acid sequences for "human erythropoietin" and because some of these sequences are in error, '422 claim 1 is indefinite. This argument fails because it is based on two incorrect premises. First, it assumes that Dr. Lin did not disclose a 1-165 amino acid polypeptide having the same amino acid sequence as the human urinary EPO purified by Dr. Goldwasser. But it is indisputable that the product of Example 10 does comprise such an EPO polypeptide. Second, it assumes that Dr. Lin's claims to "human erythropoietin" are limited to a single species of human EPO. But as the intrinsic record makes plain, the human erythropoietin contemplated by Amgen's claims include the natural allelic variants of human erythropoietin. Thus, like Roche's argument that "human erythropoietin" is not adequately described, Roche's argument that the same term is indefinite must also fail.

II. ARGUMENT

The written description and definiteness requirements are set forth at 35 U.S.C. § 112, which provides in relevant part:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it . . .
>
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.[10]

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having the structure that would be produced in mammalian cells as of the invention date").

[10] 35 U.S.C. § 112, ¶¶ 1-2.

Whether a claim satisfies the written description requirement is a question of fact.[11] In contrast, definiteness is a question of law.[12]

A. Because Dr. Lin's specification demonstrates that he was in possession of "human erythropoietin," he adequately describes it.

On April 17, 2007, the Court construed "human erythropoietin" to mean "a protein having the amino acid sequence of human EPO, ***such as*** the amino acid sequence of EPO isolated from human urine."[13] Realizing that this construction does not support its non-infringement arguments, Roche seeks to circumvent the construction by asserting that the term, as construed, is not adequately described. To do this, Roche first reconstrues the term, by asserting that "human erythropoietin" means a protein consisting of the 1-165 amino acid sequence of Dr. Goldwasser's human urinary EPO preparation.[14] Roche then argues that, because such sequence is not expressly set forth in the '422 patent specification, '422 claim 1 must not satisfy § 112's written description requirement. Because Roche has impermissibly modified the Court's construction, and because Roche's arguments are legally incorrect, Roche's motion should be denied.

1. Dr. Lin's specification makes plain that he possessed "human erythropoietin."

Throughout his specification, Dr. Lin affirmatively states that the products of his invention include "human erythropoietin."[15] To demonstrate this fact, Dr. Lin teaches that he

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[11] *Tronzo v. Biomet, Inc.*, 156 F.3d 1154, 1158 (Fed. Cir. 1998).

[12] *Atmel Corp. v. Info. Storage Devices, Inc.*, 198 F.3d 1374, 1378 (Fed. Cir. 1999).

[13] Docket No. 514, Exh. 40 (4/17/07 *Markman* Hearing Tr.), at pp. 23:17-39:10 (emphasis added). The Court took under advisement whether the term should include reference to glycosylation as well as human erythropoietin's amino acid sequence.

[14] *See* Roche Br., at p.7.

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

obtains his product using the DNA sequence encoding human erythropoietin,[16] that the N-terminal amino acid sequence of his product corresponds to the N-terminal sequence of human urinary EPO,[17] that his product possesses the expected biological activity of human erythropoietin, as measured using a variety of *in vivo* and *in vitro* assays,[18] and that his product is appropriately glycosylated.[19] Indeed, this is why this Court previously found, and the Federal Circuit affirmed, that '422 claim 1 satisfies § 112's written description requirement.[20] Because Roche's motion does not address or even attempt to refute these indisputable facts, Roche's motion should be denied.

2. Even assuming that the Court's construction limits '422 claim 1 to a composition comprising a 1-165 amino acid human EPO,[21] because the product described in Example 10 of Dr. Lin's specification is such a product, Roche cannot show by clear and convincing evidence that claim 1 is invalid.

"The purpose of the written description requirement is to prevent an applicant from later asserting that he invented that which he did not; the applicant is therefore required 'to recount his invention in such detail that his future claims can be determined to be encompassed within his original creation.'"[22] When considering whether a product claim is adequately described, it is "[t]he product, not the formula or name, [that] is the invention" that must be considered.[23]

As the Federal Circuit has consistently held, a product is adequately described if a

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

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

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

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

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

[21] As more fully set forth below in response to Roche's indefiniteness attack, the term "human erythropoietin" is not so limited and includes the naturally occurring allelic variants of human erythropoietin that are also described in Dr. Lin's specification.

[22] *Amgen*, 314 F.3d at 1330, *citing Vas-Cath*, 935 F.2d at 1561.

specification sufficiently describes the process and products needed to make the product.[24] In other words, assuming that Dr. Lin is required to specifically disclose a 1-165 amino acid sequence for human urinary EPO, if that sequence is inherent in a product exemplified in Dr. Lin's specification, the written description requirement is satisfied.[25] For example, in *Regents of the Univ. of New Mexico v. Knight*, the Federal Circuit affirmed the district court's grant of summary judgment,[26] holding that no new matter was added in an amendment correcting the compounds' structural formulas and other description of their physical characteristics because the structure was inherent in the originally described compounds.[27]

More analogous to the instant case is *Petisi v. Rennhard*.[28] There, the Federal Circuit's predecessor court, considering a Board of Patent Appeals and Interferences decision, held that the appellants were entitled to the prior filing date under the law of inherency. In their original application, the appellants had described the structures of the claimed product as "not as yet . . . proven unequivocally" but "believed" to be isomers to which an aromatic ring was attached at different positions.[29] Despite the appellants' failure to unequivocally identify any embodiment within the interference count, the court determined that such positive identification was not necessarily required for a constructive reduction to practice.[30]

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[23] *Petisi v. Rennhard*, 363 F.2d 903, 907 (CCPA 1966).

[24] *Regents of the Univ. of New Mexico v. Knight*, 321 F.3d at 1122; *Kennecott Corp. v. Kyocera*, 835 F.2d at 1421-23.

[25] *Id.*; *see also Pall Corp. v. Micron Separations, Inc.*, 792 F. Supp. 1298 (D. Mass. 1992) (express language enumerating inherent properties does not introduce new matter).

[26] 321 F.3d at 1112.

[27] *Id.* at 1122 ("The amendments did not describe different inventions; they only clarified and corrected the erroneous characterization of the already disclosed inventions. Such amendments do not add or change the nature of the disclosed inventions.").

[28] 363 F.2d 903 (CCPA 1966).

[29] *Id.* at 906.

[30] *Id.* at 907.

Noting that the application's uncertainty resulted not from "a shotgun announcement, or blind speculation, but direct to-the-point disclosure of what appellants believe[d]," the court determined that the specification's examples describing the synthesis and analysis of the reaction products met the requirements of § 112 because they made it possible for an ordinary skilled artist to conclude that the alleged compound had been prepared.[31] In reaching this conclusion, the court emphasized that "[t]he product, not the formula or name, is the invention, and it is as to this that priority has been shown."[32]

Here, like the appellant in *Petisi*, Dr. Lin's specification makes clear that the 166 amino acid sequence disclosed in Dr. Lin's specification is a "deduced" sequence – in other words, it was derived from the DNA sequence that Dr. Lin had isolated, not from actual sequencing of the entire product:

> FIG. 9, illustrates the extent of polypeptide sequence homology between human and monkey EPO. In the upper continuous line of the Figure, single letter designations are employed to represent the deduced translated polypeptide sequences of human EPO commencing with residue -27 and the lower continuous line shows the ***deduced*** polypeptide sequence of monkey EPO commencing at assigned residue number -27.[33]

That this deduced amino acid sequence was later found to be subject to further post-translation processing does not render '422 claim 1 invalid under § 112, paragraph 1.

Even assuming, as Roche does, that "human erythropoietin" means only the 1-165 amino acid sequence of Dr. Goldwasser's urinary human erythropoietin, there is no dispute that the product produced by following the process exemplified in Dr. Lin's preferred embodiment,

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[31] *Id.*

[32] *Id.* (emphasis removed).

[33] '933 Patent, at col. 21:20-27 (emphasis added). *See also*,'933 Patent, at col. 10:64-11:2; Exhibit A to the Declaration of Linda A. Sasaki-Baxley in Support of Amgen's Opposition to Roche's Motion for Summary Judgment That Claim 1 of the '422 Patent is Invalid Under 35 U.S.C. § 112 ("Sasaki-Baxley Decl., Exh. A") (3/28/07 Lin Depo. Tr.), at pp. 77-78.

Example 10 of Dr. Lin's specification, inherently yields a 1-165 amino acid product or that the product's inherent amino acid sequence corresponds to the amino acid sequence of a human urinary EPO preparation.[34] As such, Dr. Lin's specification plainly satisfies § 112's written description requirement.

3. Roche's summary dismissal of Dr. Lin's teachings is contrary to applicable case law and fact.

Ignoring *Regents of the Univ. of New Mexico v. Knight* and the long line of cases on which the Federal Circuit relied in reaching that decision, Roche argues that whether Dr. Lin was in "possession" of a 1-165 amino acid human erythropoietin is not the relevant inquiry and that "there is no foundation in the law" for Amgen's assertion at *Markman* that Dr. Lin described a 1-165 amino acid human erythropoietin because the product described in Example 10 is such a human erythropoietin.[35] It then argues that there is "no basis in fact" for Amgen's position either because Dr. Lin never "conceived" a 1-165 amino acid sequence.[36]

As set forth above, Roche's characterizations of the law are incorrect. The Federal Circuit's position regarding whether an inherent characteristic of a product that is described satisfies the written description requirement for that characteristic is clear — it does.[37] The cases that Roche cites, *Enzo Biochem, Inc. v. Gen-Probe Inc.*[38] and *New Railhead Mfg., LLC v. Vermeer Mfg.*[39] (both of which were decided before *Regents of Univ. of New Mexico*), do not trump this law. As the Federal Circuit acknowledged in *Enzo*, an actual recitation of the claimed product (which we assume *arguendo* to be the 1-165 amino acid species of human EPO) is not

[34] Sasaki-Baxley Decl., Exh. A (3/28/07 Lin Depo. Tr.), at 223:16-20; Roche's Br., Exh. 5 (Recny *et al. J. Biol. Chem.* 262(35): 17156-163 (1987)).

[35] *See* Roche's Br., at pp. 12-13.

[36] *See* Roche's Br., at pp. 12, 14-15.

[37] *See supra* at Section II(A)(2).

[38] 323 F.3d 956 (Fed. Cir. 2002).

required so long as the specification uses some reasonable means to describe that claimed product ("human erythropoietin"):

> Rather, we clarified that the written description requirement is satisfied by the patentee's disclosure of "such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention."[40]

Moreover, the *New Railhead* case is inapposite here, because as Roche acknowledges in its own description of the case, the product at issue in *New Railhead* had never been manufactured prior to the filing of the application. Rather, the structure needing description was implicit in the eyes of the inventor in a drawing included in the original application.[41] Here, there is no dispute that Dr. Lin had produced the claimed "human erythropoietin" at the time that he filed his application or that that product is has the same 1-165 amino acid sequence as human urinary erythropoietin.

Roche's citations of *Schering Corp. v. Amgen Inc.*[42] and *In re Fox*[43] to support its assertion that Dr. Lin's disclosure is insufficient to describe a 165 amino acid product also fail to undermine the Federal Circuit's holding in *Regents of the University of New Mexico* or *Kennecott* or their applicability here.[44] Tellingly, *Schering* is a claims construction case that does not directly address the written description issue. And, unlike *Regents of Univ. of New Mexico* or *Kennecott*, the Board's 1957 decision in *Fox* was never reviewed on appeal, never cited by the Federal Circuit or its predecessor court, and has been distinguished by every Board decision but one that has cited it.

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[39] 298 F.3d 1290 (Fed. Cir. 2002).

[40] *Enzo*, 323 F.3d at 969, *quoting Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997). In *Enzo*, the deposit of biological material and citation to the deposit by accession number in the specification was found sufficient to describe the claims. *Id.*

[41] *New Railhead*, 298 F.3d at 1295.

[42] 222 F.3d 1347, 1355 (Fed. Cir. 2000).

[43] 128 U.S.P.Q. 157 (BPAI. 1957).

[44] Roche's Br., at pp. 9-10.

Finally, Roche's assertion that Dr. Lin never conceived of a 165 amino acid human erythropoietin is a red herring. Dr. Lin conceived of and reduced to practice a "human erythropoietin" that was "purified from mammalian cells grown in culture" [45] and exemplified such a product at Example 10 of his specification. That Dr. Lin also disclosed the deduced 1-166 amino acid sequence for human erythropoietin based on the DNA sequence encoding it does not change this fact.

4. Amgen did not admit that the '422 patent lacks written descriptive support for a 165-amino-acid EPO product.

Roche's motion makes much ado about Amgen's so-called admissions, in the context of the '080 patent, that Amgen could not introduce a limitation that specifically referred to a 1-165 amino acid sequence product, and thus offered instead the term "mature amino acid sequence of Figure 6." As a careful reading of these so-called admissions shows, although Amgen's statements generally referred to Dr. Lin's failure to "expressly" recite a 1-165 amino acid product,[46] they also consistently made plain that such structure was inherent in the product described in Example 10.[47]

To support its argument, Roche says that Amgen's August 18, 2003, Rule 52(c) motion,

[45] '422 claim 1. At footnote 2 of Roche's Brief (at p. 7), Roche asserts that Amgen should not be allowed to construe "human erythropoietin" one way for purposes of infringement and a different way when considering validity. Amgen agrees and is not seeking two different constructions. Consistent with its *Markman* submissions, it is Amgen's position that the limitations "pharmaceutical composition" and "purified from mammalian cells grown in culture" are what distinguishes Dr. Lin's claimed products from the products in the prior art, not the limitation "human erythropoietin."

[46] *See* Roche's Br., Exh. 4, at p. 9 (as quoted at page 10 of Roche's Brief) ("even though 165 human EPO was inherently produced in Example 10, it was not ***expressly recited*** as being Amgen's invention in the '422 patent specification."); *id.* at 5 ("when the written description was drafted and submitted, the specification did not ***expressly recite*** an EPO having the 1-165 sequence."); *id.* at 6 ("[w]here a specification describes a genus of compounds, such as EPO having the sequence of Figure 6 and fragments thereof, a claim reciting a specific single speces within that genus (e.g., 1-165) is not supported unless the specification ***expressly recites*** that species as the applicant's invention.").

along with statements made during the prosecution history, show that Dr. Lin did not conceive the human EPO recited in '422 claim 1.[48] Roche's assertions misrepresent Amgen's positions and/or reflect Roche's misunderstanding of the documents cited in support of its motion.

First, Amgen has ***never*** admitted that Dr. Lin's patents lack written descriptive support for the composition recited in '422 claim 1.[49] In Amgen's Rule 52(c) motion in the *TKT* case, Amgen argued that the *Festo* presumption against the application of the doctrine of equivalents did not apply to the '080 patent claims. In that motion, Amgen argued that the written description requirement prevented Amgen from amending its '080 patent claims to recite a hypothetical claim limitation ("human EPO having the specific 1-165 amino acid sequence of Figure. 6.").[50] Amgen's arguments were limited to whether there was support for that hypothetical limitation in a ***hypothetical*** claim. In pressing its invalidity argument, Roche completely ignores the fact that Amgen's Rule 52(c) Motion explicitly stated that claim 1 of the '422 patent encompassed the 165-amino-acid EPO product, for which there was ample written descriptive support:

> Defendants argue that Amgen cannot rebut the presumption of estoppel unless it shows that it could not have drafted a claim that encompasses 165 human EPO. As 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). If the only question was whether Amgen could have drafted a claim that encompassed 165 human EPO, the Federal Circuit would have held that Amgen had already done so in the '422 claim 1 and therefore could not rebut

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[47] *See, e.g., id.* at 9.

[48] Roche's Br., at pp. 14-15.

[49] Roche Br., at 14-15.

[50] Roche's Br., Exh. 4, at p. 9 (Docket No. 485-7, at p. 3).

the presumption.[51]

No "admission" was made concerning any claim other than the hypothetical claim relevant to the *Festo* inquiry. Indeed, Amgen said exactly the opposite of what Roche has represented. Consequently, Amgen is not estopped from arguing that the '422 patent adequately describes '422 claim 1.

In its motion, Roche cites statements in the prosecution history concerning various EPO "translation products."[52] Roche misrepresents Amgen's statements in those prosecution history documents, perhaps because Roche does not understand the underlying documents that Amgen was discussing in those statements.

In an October 2, 1986, Amendment and Reply to a Patent Office action during prosecution of the '422 patent, Amgen argued that Dr. Lin's pending claims were not obvious over the cited prior art.[53] Amgen's arguments centered on the failed prior-art attempt by Dr. Sylvia Lee-Huang and her colleagues to clone the human EPO gene.[54] In the action, the Patent Office cited an article by Dr. Lee-Huang and her colleagues in which they suggested that they had cloned the human EPO gene based on the production of translation products (made by translating cDNAs produced from RNA isolated from human kidney tumor tissue) in an in vitro bacterial translation system.[55]

In response, Amgen argued that the DNA sequence described for the first time in Figure 6 of Dr. Lin's patent application, along with computer-assisted modeling, showed that Dr. Lee-

[51] Roche's Br., Exh. 4, at pp. 8-9 (Docket No. 485-7 at pp. 2-3).

[52] Roche's Br., at pp. 14-15.

[53] Roche's Br., Exh. 10, at pp. 24-37 (Docket No. 485-16, at p. 4 – 485-17, at p.7).

[54] *Id*. at pp. 29-37 (Docket No. 485-16, at p. 9 – 485-17, at p.7) (*discussing* Lee-Huang *et al*., *Proc. Nat'l Acad. Sci. U S A* (1984) 81: 2708-2712).

[55] *Id*. at pp. 13-14, 16-18 (Docket No. 485-15, at pp. 3-4, 6-8).

Huang and her colleagues could not possibly have cloned the human EPO gene.[56] Amgen showed that the DNA sequence encoding human EPO described by Dr. Lin in Figure 6 has a limited number of cleavage sites recognized by the restriction enzymes employed by Dr. Lee-Huang to cleave purported cDNA molecules created in her *in vitro* system, and that none of Dr. Lee-Huang's purported cDNA clones could have been an authentic cDNA encoding the EPO polypeptide. Amgen then showed that the translation products created in Dr. Lee-Huang's *in vitro* bacterial translation system did not match the human EPO protein information disclosed in Figure 6 of Dr. Lin's specification.

Amgen did not argue that "there actually were two other amino acid sequences for human erythropoietin,"[57] or that Dr. Lin failed to understand what human EPO products were produced by his genetically engineered cells. Rather, Amgen argued that Dr. Lee-Huang's "translation products" could not possibly have been authentic human EPO proteins because none of their purported lengths matched the length of a protein that could hypothetically have been produced if an authentic EPO mRNA had been translated in Dr. Lee-Huang's *in vitro* bacterial translation system.[58]

B. "Human erythropoietin" is definite.

1. One of ordinarily skill in the art would understand the metes and bounds of "human erythropoietin" as that term appears in '422 claim 1.

As more fully set forth in Amgen's June 20, 2007 Motion for Summary Judgment, the intrinsic record amply supports this Court's construction of "human erythropoietin."

For example, as used in the specification, "erythropoietin" refers to polypeptides having the same sequence of amino acid residues as naturally occurring erythropoietin:

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[56] *Id*. at pp. 29-37 (Docket No. 485-16, p. 9 – 485-17, p.7).

[57] Roche's Br., at p. 19.

> The present invention provides, for the first time, novel purified and isolated polypeptide products having part or ***all of the primary structural conformation (i.e., continuous sequence of amino acid residues)*** and one or more of the biological properties (e.g., immunological properties and in vivo and in vitro biological activity) of naturally-occurring erythropoietin, including allelic variants thereof.[59]
>
> According to the present invention, DNA sequences encoding part or ***all of the polypeptide sequence of human and monkey species erythropoietin (hereafter, at times, "EPO"***) have been isolated and characterized.[60]

The prosecution history of the '422 patent similarly makes plain that "human erythropoietin" includes any polypeptide that has the same sequence of amino acid residues as EPO isolated from human urine:

> [H]uman erythropoietin is understood to include any polypeptide having the amino acid sequence of EPO isolated from human urine and may be produced in human cells or in other mammalian cells.[61]

"Human erythropoietin" also includes any naturally occurring allelic variations in the amino acid sequence of human EPO.[62]

Roche offered a similar construction for "human erythropoietin" at *Markman* except that Roche sought to further limit the term by also requiring the presence of particular glycosylation (carbohydrate structures) attached to the amino acid sequence by mammalian cells as of Lin's invention date:[63]

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[58] Roche's Br., Exh. 10, at pp. 33-37 (Docket No. 485-17 at pp. 3-7 of 9).

[59] '933 Patent, at col. 10:9-15 (emphasis added).

[60] '933 Patent, at col. 13:50-53 (emphasis added).

[61] Roche's Br., Exh. 12, at p. 5.

[62] '933 Patent, at cols. 21:11-19, 35:10-20, 35:27-39.

[63] In taking this position, Roche sought to read the term "purified from mammalian cells grown in culture" out of the claim all together, asserting that it was a "source limitation which does not define the claimed product." Defs.' Opening Mem. in Supp. of Their Proposed Claim Construction (Docket No. 311), at p. 2.

> a glycoprotein having the amino acid sequence of erythropoietin isolated from human urine having the same structure that would be produced by mammalian cells as of the invention date.[64]

Roche argued that its proffered definition "was supported by the patentee's definition and use of this term in the specification and the prosecution histories,"[65] and was consistent with the understanding of an ordinarily skilled artisan.[66] Having failed to persuade the Court to adopt its attempt to read both a source and temporal limitation of unknown origin into the term "human erythropoietin," Roche now asserts that the term is indefinable and without meaning to one of ordinary skill in the art. It should not be allowed to do so.

Not only is this position inconsistent with Roche's arguments at *Markman*, but it also flies in the face of this Court's previous finding that the claims containing the term "human erythropoietin" were sufficiently definite to be found infringed.[67] The finding that Dr. Lin's "human erythropoietin" claims were infringed necessarily implies that the claims were also sufficiently definite in meaning and in scope to sustain a judgment of infringement — a legal determination that should also apply to an indefiniteness analysis under principles of *stare decisis*.[68]

Finally, Roche's position is inconsistent with the understanding of Roche's own expert witnesses. Roche's expert witnesses have acknowledged that human erythropoietin contains the same amino acid sequence as human urinary erythropoietin, which has the 1-165 amino acid sequence. For example, Roche's expert Dr. Bertozzi explained that human urinary erythropoietin is encoded by the erythropoietin gene:

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[64] *Id.* at 1.

[65] *Id.* at 6.

[66] *Id.* at 6-7.

[67] *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 52-62, 165 (D. Mass. 2001) ("*Amgen/HMR I*"); *Amgen/HMR II*, 314 F.3d at 1347-50, 1358.

[68] *Wang Labs., Inc. v. Oki Elec. Indus. Co.*, 15 F. Supp. 2d 166, 175-76 (D. Mass. 1998).

Q What do you understand the phrase "urinary erythropoietin protein" to mean?

A Again erythropoietin protein, and I don't know that there is such a thing in urine. Because when you say "erythropoietin protein" you include all the different glycosylated forms.

Q Right.

A So human urinary erythropoietin protein in your vernacular would be the collection of molecules in the human urine that have a common linkage of amino acids that being encoded by the DNA.

Q Encoded by the erythropoietin gene?

A The erythropoietin gene. In other words, the linkage of amino acids that's specified by the sequence of the gene which in the case of the human urinary erythropoietin would not be a recombinant gene. It would be the gene as it exists in the human chromosomes.[69]

2. The fact that Dr. Lin's specification identifies different variants of "human erythropoietin" does not render '422 claim 1 indefinite.

Ignoring the import of the intrinsic record and the affirmed findings of this Court, Roche attempts to revive the same "166-amino-acids-encoded" versus "165-amino-acids-secreted" argument that was thoroughly vetted in the *TKT* case. Roche argues that based on Dr. Lin's Figure 6, which depicts the DNA sequence for the human EPO gene and the amino acid sequence deduced from that genomic DNA sequence, "human erythropoietin" should be construed to require 166 amino acids. In the alternative, Roche argues that any 165-amino acid sequence set forth in the specification is erroneous. But neither argument renders the claim term "human erythropoietin" indefinite. Rather, Dr. Lin's specification makes plain that "human erythropoietin" refers to a protein having the same amino acid sequence as human urinary EPO (and allelic variants thereof) as well as proteins produced in a variety of recombinant cells using DNA encoding human EPO.[70]

[69] Sasaki-Baxley Decl., Exh. B (6/6/07 Bertozzi Depo. Tr.), at pp. 96:17-97:17.

[70] *See* '933 Patent, at col. 15:13-26. *See, generally, S3 Inc. v. nVIDIA Corp.*, 259 F.3d 1364,

The fact that Dr. Lin's description allows for some variation in the amino acid sequence of "human erythropoietin" does not render the term "human erythropoietin" indefinite. As the specification specifically contemplates, "human erythropoietin" may include proteins with an amino acid sequence that corresponds to allelic variants.[71]

Example 10 of the specification, describing a method for producing "human erythropoietin," discloses products that have a 1-165 amino acid sequence.[72] The fact that different embodiments of "human erythropoietin" are described in Dr. Lin's specification, and that "human erythropoietin" includes these different embodiments, is no basis for finding '422 claim 1 indefinite.[73]

Roche points to the so-called "errors" in the fragments described in Example 1 of Dr. Lin's specification as supporting its argument. They do not. As expressly set forth in the specification, and as one of ordinary skill in 1983 would have understood, microsequencing of peptides was not exact. Thus, as Dr. Lin noted in his specification in discussing the discrepancies in the urinary EPO peptide sequences disclosed in Example 1 and the deduced EPO sequence shown at Figure 6, his claims were not limited to human erythropoietins having the deduced Figure 6 sequence. Rather they would include embodiments having slightly different amino acid sequences from that set forth in Figure 6, such as allelic variants:

> It is worthy of note that the specific amino acid sequence of FIG. 6 likely constitutes that of a naturally occurring allelic form of human erythropoietin. Support for this position is found in the results of continued efforts at sequencing of urinary isolates of human

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1367 (Fed. Cir. 2001) (the definiteness requirement of 35 U.S.C. § 112 is satisfied when an ordinarily skilled artisan would "understand the scope of the subject matter that is patented when the claim is read in conjunction with the rest of the specification.")

[71] '933 Patent, at col. 35:17-31, 10:8-14.

[72] Sasaki-Baxley Decl., Exh. C (9/28/99 Decl. of Jeffrey K. Browne, Ph.D.).

[73] *Exxon*, 265 F.3d at 1375 (stating that a claim is not indefinite "if the meaning of the claim is discernible, even though the task may be formidable and the conclusion may be one over which reasonable persons will disagree.").

> erythropoietin which provided the finding that a significant number of erythropoietin molecules therin [sic] have a methionine at residue 126 as opposed to a serine as shown in the Figure.[74]

Roche's assertions to the contrary are not supported by the intrinsic record and the extrinsic evidence cited in its brief does not contradict this definition.

III. CONCLUSION

Because the Court's construction of "human erythropoietin" is clear, and Roche's § 112 attacks are based on impermissibly reading additional limitations into the term, Roche's motion for summary judgment should be denied.

[74] '933 Patent, at col. 21:11-19; *see also, id.* at col. 35:17-39.

Respectfully Submitted,

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June 29, 2007

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