IN THE UNITED STATES DISTRICT COURT
FOR THE 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

U.S. District Judge Young

ORAL ARGUMENT REQUESTED

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

Defendants F. Hoffman-La Roche LTD, Roche Diagnostics GmbH and Hoffmann-La Roche, Inc. ("Roche") respectfully move for summary judgment that claim 1 of U.S. Patent 5,955,422 ("the '422 patent"), owned by Plaintiff Amgen Inc. ("Amgen"), is invalid under 35 U.S.C. §112, ¶1 for lack of adequate written description and as indefinite under 35 U.S.C. §112, ¶2.

I. INTRODUCTION

When Dr. Lin rushed to file his series of patent applications with the United States Patent and Trademark Office relating to human erythropoietin ("EPO"), he told the Patent Office — and the world — that he was the first to disclose the amino acid sequence of human EPO. Claiming to have made and possessed human EPO, he described it as the 166 amino acid sequence set forth in Figure 6 of the specification. Now, nearly 24 years later, Amgen impermissibly relies on knowledge it gained from its competitors and which is not set forth in the Lin disclosure to assert that claim 1 of the '422 patent claims "a protein having the amino acid sequence of human EPO, such as the amino acid sequence of EPO isolated from human urine"— *i.e*, a protein with a 165 amino acid sequence. This Amgen should not be allowed to do because, indisputably, the '422 specification does not describe a 165 amino acid sequence for human EPO and, in fact, does not describe a correct or complete sequence for human EPO isolated from urine.

In prior litigation before this Court, Amgen unequivocally admitted that Lin's specification as drafted and submitted, did not expressly recite an EPO having the 1-165 sequence now known for human urinary EPO. Amgen also admitted that, although example 10 of the '422 application may inherently produce human EPO with 165 amino acids, neither Figure 6 nor any other portion of the specification meets the statutory written description requirement to support claiming that amino acid sequence. Amgen further admitted that a 165

amino acid sequence would constitute new matter and the Court acknowledged that Dr. Lin would have been required to file a continuation-in-part application to claim the sequence.

Clearly the amino acid sequence that Amgen now claims is new matter given that nearly a year after Lin's disclosure was submitted to the Patent Office, Amgen also told the U. S. Food and Drug Administration that human erythropoietin was 166 amino acids. Not until 1987, when scientists at Genetics Institute — one of Amgen's rivals — published the 165 amino acid sequence of human EPO was the public informed of the amino acid sequence that Amgen now claims.

Accordingly, because the scope of claim 1 of the '422 patent captures subject matter that plainly is not described by Lin's disclosure, the claim is invalid for lack of written description pursuant to 35 U.S.C. §112, ¶1.

Furthermore, the construction of human erythropoietin also renders claim 1 of the '422 patent indefinite pursuant to 35 U.S.C. §112, ¶2. One of skill in the art, reading the Lin disclosure, would not be able to correctly ascertain the amino acid sequence of human erythropoietin but only the sequence of Figure 6. Amgen has argued both in the prosecution history of the Lin patents and during litigation that several working examples in the specification also describe human erythropoietin to one of skill in the art; however, (1) each of these examples has an amino acid sequence that differs from that of EPO isolated from human urine, and (2) several of the disclosed amino acid sequences are simply ambiguous or wrong. Therefore, one of skill in the art reading Lin's disclosure cannot determine the amino acid sequence Amgen claims as human erythropoietin and is unable to establish the bounds of the claim. Moreover, the use of "such as" in defining human EPO indicates that the 165 amino acid sequence of human urinary EPO is merely one example of "human erythropoietin" — not the only possible amino acid sequence claimed — and, thus, does not unambiguously identify the scope of the claim.

Based upon this memorandum, its supporting exhibits, and the accompanying Declaration of Krista M. Rycroft, Roche requests summary judgment that claim 1 of the '422 patent is invalid because "human erythropoietin" is not adequately described and is indefinite.

II. STATEMENT OF UNDISPUTED FACTS

The following facts are beyond genuine dispute and, as a matter of law, compel summary judgment that claim 1 of the '422 patent is invalid for lack of written description and as indefinite.

Each patent-in-suit, including the '422 patent, shares a common disclosure and specification. *See Amgen v. Hoechst Marion Roussel, Inc.*, 126 F. Supp 2d 69, 79 (D. Mass. 2001). In this case Amgen has asserted, *inter alia*, claim 1 of the '422 patent:

> 1. 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.

(Ex. 1, '422 patent, claim 1).[1]

At Amgen's request, the Court has construed the claim limitation "human erythropoietin" as "a protein having the amino acid sequence of human EPO, such as the amino acid sequence of EPO isolated from human urine." (Ex. 2, Amgen Inc.'s Response to Defendants' Claim Construction Brief filed 3/19/07 ("Amgen's Response Br."; Docket No. 323) at 5; Ex. 3, 4/17/07 Markman Tr. 39:7-10). The Federal Circuit determined additional research conducted *after* the Lin patent disclosure was filed revealed that the full sequence of human EPO is actually 165 amino acids. *Amgen v. Hoechst Marion Roussel, Inc.*, 314 F.3d. at 1343.

Lin, however, told the world that his claimed human EPO had a 166 amino acid sequence. The patent disclosure specifically explains to one of skill in the art that the sequence

[1] "Ex. __" refers to the exhibits attached to the accompanying Declaration of Krista M. Rycroft In Support of Roche's Motion for Summary Judgment That Claim 1 of the '422 Patent Is Invalid Under 35 U.S.C. §112.

of "FIG. 6 thus serves to identify the primary structural conformation (amino acid sequence) of mature human EPO as including 166 specified amino acid residues (estimated M.W. = 18,399)." (Ex. 1, '422 patent, col. 20:66-21:2; *see also* Fig. 9 & col. 19:28-36, 21:2-5, 35:4-11). Amgen subsequently has relied upon example 1, example 11 and example 12 as also describing the amino acid sequence of human EPO — but none of these examples describes the 165 amino acid sequence of EPO isolated from urine.

In fact, Amgen admitted to this Court in prior litigation that "when the written description of Amgen's specification was drafted and submitted [in 1984], the specification did not expressly recite an EPO having the 1-165 sequence." (Ex. 4, Amgen's Post-Hearing Memo. at 5 (AM-ITC 00852563)). Amgen also admitted that, although example 10 of the '422 application may inherently produce human EPO with 165 amino acids, neither Figure 6 nor any other portion of the specification meets the statutory written description requirement to support claiming the 165 amino acid sequence. (Ex. 4, Amgen's Post-Hearing Memo. at 6, 7-8 (AM-ITC 00852568, AM-ITC 00852569-70). Likewise, Amgen also admitted that the 165 amino acid sequence of EPO isolated from human urine would constitute "new matter" and this Court acknowledged that Lin would have been required to file a continuation-in-part application to claim the amino acid sequence. *Amgen v. Hoechst Marion Roussel, Inc.*, 287 F. Supp. 2d 126, 144 & fn.22 (D. Mass. 2003), *aff'd in relevant part*, 457 F.3d 1293 (Fed. Cir. 2006).

Indeed, it was scientists from Genetics Institute, in 1987, who first publicly described, the 165 amino acid sequence now claimed by Amgen. (Ex. 5, Recny *et al.*, "Structural Characterization of Natural Human Urinary and Recombinant DNA-derived Erythropoietin," *J. Biol. Chem.*, 262(35); 17156-17163 (1987)).

Additional undisputed material facts relied upon by Roche are set forth in its Rule 56.1 Statement of Undisputed Material Facts, filed herewith, and are incorporated within Section III, *infra*.

III. ARGUMENT

Summary judgment is appropriate if "there is no genuine issue as to any material fact ... and the moving party is entitled to judgment as a matter of law." Fed.R.Civ.P. 56(c). "The evidence submitted by the nonmovant, in opposition to a motion for summary judgment, is to be believed, and all justifiable inferences are to be drawn in [its] favor." *Tone Bros., Inc. v. Sysco Corp.*, 28 F.3d 1192, 1196 (Fed. Cir. 1994) (citations omitted). However, the nonmoving party "must do more than merely raise doubt as to the existence of a fact" to defeat a summary judgment motion. *Avia Group Int'l. v. L.A. Gear California, Inc.*, 853 F.2d 1557, 1560 (Fed. Cir. 1988). Evidence that is merely colorable or not significantly probative will not avoid summary judgment. *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 249-50 (1986).

A. The Specification Must Adequately Describe All Claim Terms

The patent law requires that "the specification shall contain a written description of the invention ...." 35 U.S.C. §112, ¶1; *New Railhead Mfg. LLC v. Vermeer Mfg.*, 298 F.3d 1290, 1295 (Fed. Cir. 2002)("The adequacy of the written description (i.e., the disclosure) is measured from the face of the application."). Compliance with the written description requirement is determined as of the filing date of the application upon which the patentees relies. *TurboCare Div. of Demag Delavel Turbomachinery Corp. v. GE*, 264 F.3d 1111, 1118 (Fed. Cir. 2001). However, when determining whether there is adequate written description the "invention is, for purposes of the 'written description' inquiry, ***whatever is now claimed***." *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991)(emphasis in original).

The underlying purpose of the written description requirement is to protect the public from an inventor "'pretending that his invention is more than what it really is, or different from its ostensible objects.'" *Vas-Cath*, 935 F.2d at 1561 (quoting *Evans v. Eaton*, 20 U.S. (7 Wheat.) (1822)). In other words, "[t]he function of the description requirement is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him." *In re Wertheim*, 541 F.2d 257, 262 (C.C.P.A. 1976). However, "[a]pplication of the written description requirement ... is not subsumed by the 'possession' inquiry. A showing of 'possession' is ancillary to the ***statutory*** mandate that '[t]he specification shall contain a written description of the invention,' and that requirement is not met if, despite a showing of possession, the specification does not adequately describe the claimed invention." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 969 (Fed. Cir. 2002) (emphasis in original). In addition, although a patent specification may render the claimed invention obvious, that disclosure "is not sufficient to satisfy the written description requirement of that invention." *Regents of Univ. of Cal. v. Eli Lilly & Co*, 119 F.3d 1559, 1567 Fed. Cir. 1997; *Lockwood v. American Airlines*, 107 F.3d 1565, 1572 (Fed. Cir. 1997) ("The question is not whether a claimed invention is an obvious variant of that which is disclosed in the specification.").

Although compliance with the written description requirement is a question of fact, the issue is amenable to summary judgment. *See, e.g.*, *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916 (Fed. Cir. 2004); *New Railhead*, 298 F.3d 1290 (Fed. Cir. 2002); *LizardTech, Inc. v. Earth Res. Mapping Inc.*, 424 F.3d 1336 (Fed. Cir. 2005).

B. Claim 1 of the '422 Patent Fails To Adequately Describe The 165 Amino Acid Sequence of Human Erythropoietin, Such As EPO Isolated From Human Urine

Claim 1 of the '422 patent (Ex. 1) is:

> 1. 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.

The Court has construed the claim limitation "human erythropoietin" as "a protein having the amino acid sequence of human EPO, such as the amino acid sequence of EPO isolated from human urine." (Ex. 2, Amgen's Response Br. at 5; Ex. 3, 4/17/07 Markman Tr. 39:7-10). It is now understood that EPO isolated from human urine is a 165 amino acid sequence starting with an alanine at the 1 position and ending with aspartic acid at the 165 position, glycosylated at four specific residues. (Ex. 5, Recny *et al.*, "Structural Characterization of Natural Human Urinary and Recombinant DNA-derived Erythropoietin," *J. Biol. Chem.*, 262(35); 17156-17163 (1987)).

Accordingly, the invention "now claimed" by Amgen is an EPO protein with the 165 amino acid sequence of EPO isolated from human urine.[2] However, as discussed below, Lin's disclosure admittedly does not adequately describe to one of ordinary skill in the art the claimed 165 amino acid sequence and the sequence would have constituted new matter. Lin should have corrected his specification to specifically describe the invention Amgen now wants to claim and he did not. *Amgen v. Hoescht Marion Roussel, Inc.*, 287 F. Supp. 2d 126, 144 & n.22 (D. Mass. 2003). Amgen can not use this Court to correct what it now characterizes as a mere "mistake" in Lin's specification.

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[2] Interestingly, for purposes of infringement Amgen claims that human erythropoietin is defined without regard to glycosylation and other changes to side chains of the molecule. In stark contrast, to protect the validity of its claims, Amgen limits the claim to particular structure and glycosylation and relies on purported differences in structure to distinguish over prior art such as Dr. Goldwasser's human urinary EPO preparation. Amgen cannot have it both ways.

1. The Lin Disclosure Does Not Describe The 165 Amino Acid Sequence of EPO Isolated From Human Urine

As Amgen previously has acknowledged, in the early 1980's, the company was in a race with Genetics Institute and other companies to be the first to develop a commercial human erythropoietin product — a product that promised to be a profitable venture if Amgen were to be the exclusive source in the United States. Amgen knew that to gain future market exclusivity it needed to first secure patent protection and, thus, recognized that it was advantageous to be the first to file an application with the Patent Office. As a result, Dr. Lin filed his applications directed to Amgen's work with human EPO.

When the Lin disclosure was submitted to the Patent Office, in exchange for prospective patent protection, he told the Patent Office that he was the first to describe the amino acid sequence of human EPO, claiming to have made and possessed a protein with at least a 166 amino acid sequence. The Lin disclosure specifically explains to one of skill in the art that the sequence of "FIG. 6 thus serves to identify the primary structural conformation (amino acid sequence) of mature human EPO as including 166 specified amino acid residues (estimated M.W. = 18,399)." (Ex. 1, '422 patent, col. 20:66-21:2).[3] Similarly, Figure 9 of the '422 patent also shows human EPO as a 166 amino acid sequence with the additional 27 amino acid leader sequence "which is excised prior to entry of mature EPO into circulation". (Ex. 1, '422 patent, Figure 9 & col. 19:28-36, 21:2-5, 35:4-11).[4] Thus, upon reading the Lin disclosure, one of skill in the art would understand that human erythropoietin has a 166 amino acid sequence.

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[3] This Court has held that Dr. Lin "essentially defined the term 'mature' to mean the 'fully processed form of the protein ...." *Amgen v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 86 (D. Mass. 2001), *aff'd in relevant part*, 314 F.3d. 1313, 1344-45 (Fed. Cir. 2003).

[4] Figure 9 of the '422 patent also purports to show the similarities and differences between the amino acid sequences of monkey EPO and human EPO as disclosed by Dr. Lin. (Ex. 1, '422 patent, Fig. 9 & col. 21:16-24). The Lin disclosure describes only monkey erythropoietin as having 165 amino acids. (*Id.* at Figure 5 & col: 19:37-40 ("the M.W. of the 165 residues of the polypeptide constituting mature monkey EPO").

The Federal Circuit has already held that *after* the Lin patent was drafted additional research showed that the amino acid sequence of human EPO is actually 165 amino residues. *Amgen v. Hoechst Marion Roussel, Inc.*, 314 F.3d. at 1343. Now, nearly 24 years after Lin filed his disclosure, Amgen relies on this subsequent knowledge that is not part of Lin's disclosure to assert that claim 1 of the '422 patent claims "a protein having the amino acid sequence of human EPO, such as the amino acid sequence of EPO isolated from human urine" — *i.e*, a protein with a 165 amino acid sequence.[5] However, a patent specification must adequately describe what is claimed for the asserted claim to be valid.[6] Indeed, "[t]he 'written description' requirement serves a teaching function, as a 'quid pro quo' in which the public is given 'meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time.'" *Univ. of Rochester*, 358 F.3d at 922.

Indisputably, Lin never gave disclosure of the 165 amino acid sequence that is now claimed by Amgen and, therefore, the claim is invalid. This result is consistent with Federal Circuit precedent which states that a claim term must cover only what the specification described *at the time of the application* if it is to be held valid. *See Schering Corp. v. Amgen Inc.*, 222 F.3d 1347, 1355 (Fed. Cir. 2000) (Schering's claims could not be construed to cover the mature polypeptide which required post-translational processes to remove extra DNA sequences because the inventor "had not identified the extraneous sequences nor the need to remove them" and thus "the district court correctly construed the claims as covering only immature polypeptides."); *In*

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[5] Amgen's expert, Dr. Lodish, who has testified for many years on behalf of Amgen has admitted to this Court that: "Although it was not known at the time of the applications for Amgen's Patents were filed, it is now well-understood scientifically that mature human EPO has a 165-amino-acid sequence." (Ex.6, 12/20/99 Expert Statement of Lodish at ¶124). *See also* Section III.B.2, below, regarding other Amgen admissions.

[6] *See, e.g*., *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1327 (Fed. Cir. 2000) (Claims invalid where patentees "pick a characteristic possessed by two of their formulations, a characteristic that is not discussed even in passing in the disclosure, and then make it the basis of claims....").

re Fox, 128 U.S.P.Q. 157, 158-59 (Bd. Pat. App. & Interf. 1957) (disclosure was inadequate to claim product by new name and formula designated after filing).

2. Amgen Admitted That There Is No Adequate Written Description of Human EPO As A Protein With The 165 Amino Acid Sequence of EPO Isolated From Human Urine

There is no question that Lin's specification does not adequately describe human erythropoietin as Amgen now claims. In prior litigation, Amgen unequivocally admitted: (1) that there is no adequate written description of human EPO with the 165 amino acid sequence of EPO isolated from urine, and (2) that Lin would have had to file a continuation-in-part application to describe that amino acid sequence. Amgen's admissions are dispositive. *See U.S. v. Raphelson*, 802 F.2d 588, 592 (1st Cir. 1986); *see also Boston Sci. Corp. v. Schneider (Eur.) AG*, 983 F. Supp. 245, 255-56 (D. Mass. 1997) (issue preclusion bars "relitigation of any factual or legal issue that was already decided in previous litigation whether on same or different claim"); *Patriot Cinemas, Inc. v. Gen. Cinemas, Corp.*, 834 F.2d 208 (1st Cir. 1987) ("Judicial estoppel should be employed when a litigant is 'playing fast and loose with the courts,' and when 'intentional self-contradiction is being used as a means of obtaining unfair advantage in a forum provided for suitors seeking justice.'").

Specifically, in *Amgen v. Hoechst Marion Roussel, Inc.*, Amgen admitted to this Court that "when the written description of Amgen's specification was drafted and submitted [in 1984], the specification did not expressly recite an EPO having the 1-165 sequence." (Ex. 4, Amgen's Post-Hearing Memo. at 5 (AM-ITC 00852563)). Amgen also admitted that "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." (Ex. 4, Amgen's Post-Hearing Memo. at 9

(AM-ITC 00852571)).[7] Amgen admitted that it could not rely on Figure 6 or any other portion of the specification to meet the statutory written description requirement vis-à-vis human erythropoietin such as the 165 amino acid residues of EPO isolated from human urine:

> Although then amino acid sequence of 165 human EPO is depicted within the 166 amino acid sequence shown in Figure 6, that fact alone is not sufficient to support a claim that recites the 165 human EPO sequence. Where 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 species within that genus (e.g., 1-165) is not supported unless the specification expressly recites that species as the applicant's invention.
>
> * * *
>
> Defendants [HMR/TKT] pointed to certain language in Amgen's specification as purportedly providing written support for a claim to 165 human EPO. But the specification only speaks of generic "fragments" of EPO or "DNA sequences encoding part or all of" the EPO sequence. Such reference to a genus of fragments or to DNA sequences of different lengths cannot constitute "blazemarks" pointing to the particular 165 amino acid EPO equivalent in question here, and therefore could not support a claim specifically to such a species.

(Ex. 4, Amgen's Post-Hearing Memo. at 6, 7-8 (AM-ITC 00852568, AM-ITC 00852569-70) (footnotes omitted)).

Amgen also admitted that the 165 amino acid residue sequence would constitute new matter and that to adequately describe the sequence Dr. Lin would have been required to file a continuation-in-part application. As Amgen explained: "To subsequently add a description of the later-discovered equivalent — in this case, the fact that the product of example 10 has only 165 amino acids — would violate the statutory prohibition against adding new matter to the application." (Ex. 4, Amgen's Post-Hearing Memo. at 5 (AM-ITC 00852567)). Indeed, by definition one cannot have described "new matter", and its axiomatic that claiming new matter violates the written description requirement. *TurboCare*, 264 F.3d at 1118 ("The written

[7] The actual quote cites the '080 patent specification, however, each patent-in-suit, including the '422 patent shares a common disclosure and specification. *See Amgen v. Hoescht Marion Roussel, Inc.*, 126 F. Supp. 2d at 79.

description requirement and its corollary, the new matter prohibition of 35 U.S.C. §132, both serve to ensure that the patent applicant was in full possession of the claimed subject matter on the application filing date."); *Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1255 (Fed. Cir. 2004)("Chiron cannot satisfy the written description requirement for the new matter appearing in the '561 patent, namely chimeric antibodies.").

Given Amgen's clear admissions, this Court agreed that to support an 165 amino acid sequence, such as EPO isolated from urine, Amgen would have had to file another continuation-in-part application disclosing that amino acid sequence. The Court acknowledged that: (1) "if, as Amgen suggests, there is new matter to add that is necessary to complete or correct the patent description and protect the invention, the patentee can and should re-file the application" and (2) "Amgen's argument that this [165 amino acid sequence] is new matter suggests that an amendment was not the correct vehicle to make its desired changes but instead that the more appropriate action would have been for Amgen to have filed a continuation-in-part application." *Amgen v. Hoescht Marion Roussel, Inc.*, 287 F. Supp. 2d 126, 144 & n.22 (D. Mass. 2003), *aff'd in relevant part*, 457 F.3d 1293 (Fed. Cir. 2006), *cert. denied*, -- S.Ct. --, 2007 WL 904205 (U.S. May 14, 2007).

In an effort to protect claim 1 and preserve its monopoly until at least the expiration of the '422 patent in 2013, Amgen will most likely argue — as it did at the April 17, 2007 *Markman* hearing — that Lin "possessed" the 165 amino acid sequence of human EPO because example 10 teaches how to make an erythropoietin that may in fact share the 165 amino acid sequence of EPO isolated from human urine rather than the 166 amino acid sequence EPO that Lin described. While at first glance this may be an appealing argument, it has no basis in fact and no foundation in the law. First, this argument flatly contradicts Amgen's binding admissions

that there is no adequate written description. Second, "possession" or "proof of a reduction to practice, absent an adequate written description in the specification of what is reduced to practice, does not serve to describe or identify the invention for purposes of §112, ¶1." *Enzo*, 323 F.3d at 969. ("A showing of 'possession' is ancillary to the *statutory* mandate that '[t]he specification shall contain a written description of the invention,' and that requirement is not met if, despite a showing of possession, the specification does not adequately describe the claimed invention.").[8] Indeed, the written description requirement is not met "if one of ordinary skill in the art must first make the patented invention before he can ascertain the claimed features of that invention." *New Railhead*, 298 F.3d at 1295. Furthermore, the question of whether Lin's disclosure teaches one of skill in the art how to make an erythropoietin with the 165 amino acid sequence of EPO isolated from urine is irrelevant to the written description inquiry. That question relates to enablement of the claimed invention which is a statutory requirement separate and distinct from the written description requirement. *Univ. of Rochester*, 358 F.3d at 921 ("an invention may be enabled even though it has not been described").

The bottom line is that Amgen has impermissibly altered the scope of claim 1 by urging that "human erythropoietin" is a protein with the 165 amino acid sequence of EPO isolated from human urine: an amino acid sequence that (1) admittedly Lin did not adequately describe in his patent disclosure and (2) admittedly would have been new matter. This is the exact type of *post hoc* claiming that the written description requirement is meant to prevent. *Vas-Cath*, 935 F.2d at 1561 (written description requirement "guards against the inventor's overreaching").

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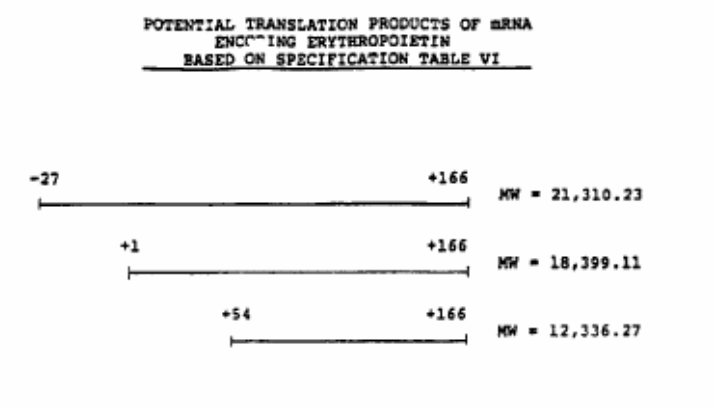
[8] To even secure a valid patent claim, "a party must show possession of every feature recited in the count, and that every limitation of the count must have been known to the inventor at the time of the alleged conception." *Coleman v. Dines*, 754 F.2d 353, 359 (Fed. Cir. 1985). Lin, however, never conceived or possessed the sequence of 165 amino acid residues now being claimed by Amgen.

3. Lin Could Not Have Described or Possessed What He Did Not Conceive

It is not surprising that Lin did not adequately describe the 165 amino acid sequence of human EPO as now claimed. That is because Lin, in fact, did not know the amino acid sequence for human EPO when he rushed to file his patent disclosure, and he was not the first to conceive the 165 amino acid sequence for human EPO now being claimed.

In addition to the explicit disclosure in the Lin specification of human EPO having at least the 166 amino acid sequence set forth in Figure 6, further evidence demonstrates that Lin did not possess or conceive of human EPO with a 165 amino acid sequence. In 1985 — nearly 1 year after Lin's disclosure was submitted to the Patent Office — Amgen also told the U.S. Food and Drug Administration that it had confirmed, using a gas-phase sequencer, that human erythropoietin had a 166 amino acid sequence corresponding to the amino acid sequence deduced from the genomic EPO clone. (Ex. 7, 9/27/85 Notice of Claimed Investigational Exemption for Recombinant-Human Erythropoietin (r-HuEPO) at AM-ITC 00595293 ("the amino acid sequence of natural (urine derived) human erythropoietin and r-HuEPO are identical, and that both conform to the amino acid sequence deduced from DNA sequence analysis of the gHuEPO [genomic human EPO] clone"); *see also* Ex. 7 at AM-ITC 00596039-042). Likewise, in 1985, a published article co-authored by Lin reported that human EPO was a "166-amino acid mature protein". (Ex. 8, Lin *et al.*, "Cloning and expression of the human erythropoietin gene," *PNAS*, 82; 7580-7584 (1985) at 7580 and Figure 3).

In 1986, during prosecution of a parent application to the '422 patent, Lin argued that there were three potential amino acid sequences for EPO based on Figure 6 — none of which is the 165 amino acid sequence of human EPO now claimed:



(Ex. 9, '298 File History, Paper 12, Ex. 8 of 10/2/86 Amendment and Reply; *see also* Ex. 10, '298 File History, Paper 12, 10/2/86 Amendment and Reply at 35-37).[9] Thus, it is clear, that Lin did not possess and had not conceived the 165 amino acid sequence of human EPO now claimed when he filed his patent disclosure.

Not until 1987, when scientists at Genetics Institute published their discovery that human EPO had a 165 amino acid sequence, did anyone publicly describe the amino acid sequence of human erythropoietin that Amgen now claims. (Ex. 5, Recny *et al*. ("Our discovery that the natural hormone purified from urine and recombinant hormone purified from CHO cell-conditioned media are both des-Arg^{166} EPO ....)). In short, Amgen now wants to claim someone else's discovery as its own. This it should not be allowed to do.

Because Dr. Lin did not conceive of a 165 amino acid sequence as required by the claim limitation "human erythropoietin" he could not have possessed the sequence and could not have adequately described it to one of skill in the art claim 1 of the '422 patent. *Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993) ("one cannot describe what one has not conceived").

[9] "Table VI" was redesignated as Figure 6 during prosecution. (*See, e.g.*, Ex. 11, '422 File History, Paper 2, 11/6/90 Preliminary Amendment at 2 (AM-ITC 00899076-87)).

C. A Valid Claim Must Be Definite

Section 112 also requires that the specification "conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention". 35 U.S.C. §112, ¶2. Whether a claim is invalid for indefiniteness is a question of law, and the inquiry focuses on whether one of ordinary skill in the art would understand the scope of the claim when read in light of the specification. *Allen Eng'g Corp. v. Bartell Indus.*, 299 F.3d. 1336, 1348 (Fed. Cir. 2002). Indefiniteness often arises when the claim language is "not sufficiently precise to permit a potential competitor to determine whether or not he is infringing." *Morton Int'l. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470 (Fed. Cir. 1993); *Semmler v. American Honda Motor Co.*, 990 F. Supp. 967, 975 (S.D. Ohio 1997); *Halliburton Energy Servs., Inc. v. MI, LLC*, 456 F. Supp. 2d 811, 817 (E.D. Tex. 2006).

D. The Claim Term "Human Erythropoietin" Is Indefinite

The Court's construction of "human erythropoietin" also renders claim 1 of the '422 patent indefinite because one of ordinary skill of the art is unable to determine the scope of the claim with certainty. As used by Amgen, the term human EPO covers amino acid sequences such as the 165 amino acid sequence of EPO isolated from human urine — which Lin did not describe — but also may potentially cover other amino acid sequences as well.

Where the patent provides examples of the amino acid sequence of human erythropoietin, those examples are wrong, contradict one another, and create hopeless confusion as to the amino acid sequence being claimed. For example, during the prosecution of the '422 patent, Amgen told the Patent Office that:

> Human erythropoietin as recited in Claim 64 is disclosed in several examples of the application. Example 1 discloses the use of human erythropoietin isolated from the urine of patients afflicted with aplastic anemia ("urinary EPO") to produce tryptic fragments and the amino acid sequencing of those fragments. Examples 7 and 10 disclose the production of human erythropoietin in COS-1 and

> CHO cells, respectively. ***Thus, human 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***.

(Ex. 12, '197 File History, Paper 33, 4/28/99 Amendment at 4-5 (emphasis added)).

The amino acid sequence information disclosed in Example 1 of the Lin disclosure, however, does not accurately reflect the amino acid sequence of human urinary EPO, let alone disclose the complete amino acid sequence of human erythropoietin.[10] Example 1 discloses 17 discrete fragments of human urinary erythropoietin that was analyzed for the amino acid sequence. (Ex. 1, '422 patent, col. 15:21-53). Lin reports that two of the 17 fragments, T30 and T38, were "not unambiguously determined" (*Id.*, col. 15:28-53), thus, failing to define those portions of the amino acid sequence of human EPO isolated from urine to one of skill in the art.

Example 1 also discloses an amino acid sequence for another fragment, T28, as E-A-I-S-P-P-D-A-A-M-A-A-P-L-R. (*Id.*, col. 15:47). However, it was subsequently determined by scientists at Amgen that human EPO isolated from urine does not contain such a sequence. By 1985, Amgen was aware that the sequence of human urinary erythropoietin included a glycosylated serine ("S") instead of the expected methionine ("M") based on the T28 fragment disclosed by Lin. (Ex. 7, 9/27/85 Notice of Claimed Investigational Exemption for Recombinant-Human Erythropoietin Figure 4B-7 at AM-ITC 00596041-42; AM-ITC 00595293 ("The complete amino acid sequence for human urinary-derived EPO protein in [sic] shown in Figure 4B-7")).[11] Amgen, however, never corrected the Lin disclosure to set forth the correct

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[10] Although Roche maintains that the sequence of human urinary EPO could have been obtained by a person of ordinary skill in the art in 1983-1984 if Dr. Goldwasser's EPO had been accessible, Amgen alleges that the sequence of EPO isolated from urine could not be obtained even with state of the art sequencing technology.

[11] In addition, a scientific article published by Amgen scientists and Eugene Goldwasser in 1986 also demonstrates that the T28 sequence described in the patent is not a sequence found in human erythropoietin. This publication, like the sequence given to the FDA, indicates that T28 -- including the amino acid in position 126 of human erythropoietin -- has a serine and not a methionine as disclosed by the '422 patent. (Ex. 13, Lai *et al.* 1986;

sequence. Therefore, for this reason as well, Example 1 does not disclose to one of skill in the art the amino acid sequence of human EPO.

Likewise, Examples 7 and 10 do not accurately disclose the amino acid sequence of human EPO as defined. Both examples purport to produce human erythropoietin described by Figure 6 which, as discussed above, expressly discloses a 166 amino acid sequence, not the amino acid sequence of EPO isolated from urine. Thus, one of skill in the art would not have known the scope of claim 1 of the '422 as now claimed at all, let alone with the certainty required by §112, ¶2.

Moreover, Amgen also contends that examples 11 and 12 of the '422 patent define human EPO to one of skill in the art. (Ex. 2, Amgen's Response Br. at 7, fns. 22 & 23; Ex. 3 4/17/07 Markman Tr. at 35:15-22). As Amgen's own expert admits, however, the products of examples 11 and 12 include "an additional methionine amino acid residue (at position -1)" which is not found in the 165 amino acid sequence of EPO isolated from human urine. (*See* Ex. 14, Lodish Decl. at ¶¶32-33; Ex. 15, 6/4/07 Supplemental Expert Report of Harvey F. Lodish, Ph.D. ¶¶ 26-27; Ex. 1, '422 patent, col. 29:42-45). Therefore, examples 11 and 12 disclose that human EPO has ***a 167 amino acid sequence***. Example 12 also describes yet another amino acid sequence purported by Amgen to be human EPO in which the terminal methionone and the initial alanine (at position +1) are not present. (Ex. 1, '422 patent, col. 32:10-17). Therefore, while Amgen asserts that product of example 12 describes human erythropoietin, the resulting product has a 165 amino acid sequence of +2 through +166, which is a ***different*** 165 amino acid sequence than that of EPO isolated from human urine. The '422 patent also explains that *in vivo* the product of example 12 "differed markedly from the human urinary EPO standard." (*Id*. at col. 32:22-24).

Figure 1 ("Analysis of the DNA sequence indicated that a serine is present at position 126 (10, 11). One possible explanation for these results is that position 126 is a glycosylated serine.")).

The uncertainty to one of skill in the art in trying to determine the meaning of human EPO as claimed by Amgen is exemplified by the prosecution history. If one of skill in the art were to consult the file history of the '422 patent, even more ambiguity is introduced into determining the actual amino acid sequence covered by claim 1. *See Datamize LLC v. Plumtree Software Inc.*, 417 F.3d 1342 (Fed. Cir. 2005). In addition to the three different amino acid sequences disclosed by Figure 6, example 11 and example 12 of the specification (and the incorrect partial sequence disclosed in example 1), to overcome a prior art rejection in 1986, Lin argued that there actually were two other amino acid sequences for human erythropoietin (1) ***a 193 amino acid sequence*** of -27 to +166 and (2) ***a 113 amino acid sequence*** of +54 to +166. (Ex. 10, '298 File History, Paper 12, 10/2/86 Amendment and Reply at 35-37; Ex. 9, '298 File History, Paper 12, Exhibit 8 to 10/2/86 Amendment and Reply).[12]

As a result, when taken as a whole, Amgen contends that there are at least five distinctly different amino acid sequences — none of which is the 165 amino acid sequence of EPO isolated from human urine (which, as discussed above, was not described) — that are disclosed and define the claim term "human erythropoietin". However, given the numerous alternatives for the amino acid sequence disclosed by Lin — none of which has ***the*** amino acid sequence of human erythropoietin — one of skill in the art would be unable to determine what Amgen actually claims as human EPO in claim 1 of the '422 patent.[13]

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[12] Because the '422 patent is a continuation application, its prosecution history includes the file histories of the parent applications from which the patent claims priority. *See Biovail Corp. v. Andrx Pharms., Inc.*, 239 F.3d 1297, 1301 (Fed. Cir. 2001) (claim language "must be read consistently with the totality of the patent's applicable prosecution history," including parent applications).

[13] Amgen argues that the 165 amino acid fragment of Figure 6 is also "human erythropoietin". Clearly there are numerous fragments encompassed by Figure 6. Given that Dr. Lodish's definition of human EPO also includes a 167 amino acid sequence, what amino acid sequence is human EPO? How many deletions and additions of amino acids can be made to still qualify as human EPO? The bottom line is that one of skill in the art is left guessing, which is impermissible as a matter of law.

This confusion in clearly defining human EPO is reflected by Amgen's construction of the claim term. The term "such as" apparently means that the 165 amino acid sequence of human urinary EPO is but one example of the claimed "human erythropoietin." *See Ex parte Wu*, 10 U.S.P.Q.2d 2031, 2033 (B.P.A.I. 1989); Ex. 16, MPEP §2173.05(d) (8th ed. Rev. 5, Aug. 2006) (The use of the term "such as" "may lead to confusion over the intended scope of a claim."); Ex. 17, MPEP §706.03(d) (8th ed. Rev. 5, Aug. 2006) (using the phrase "such as" is indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention). However, the construction also gives no guidance to one of skill in the art concerning what other amino acid sequences, other than the 165 amino acid sequence of EPO isolated from urine, also fall within the claim. *Geneva Pharms., Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1384 (Fed. Cir. 2003) ("A claim is indefinite if its legal scope is not clear enough that a person of ordinary skill in the art could determine whether a particular composition infringes or not.")

Accordingly, the claim 1 of the is invalid as indefinite.

IV. CONCLUSION

Based on the foregoing, Roche respectfully requests that this Court grant summary judgment that claim 1 of the '422 patent is invalid for lack of written description and as indefinite.

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Respectfully submitted,

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