UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, vs. F. HOFFMANN-LA ROCHE LTD; ROCHE DIAGNOSTICS GmbH; and HOFFMANN-LA ROCHE INC. Defendants.	CIVIL ACTION No.: 05-CV-12237WGY

MEMORANDUM OF LAW IN SUPPORT OF DEFENDANTS' MOTION FOR SUMMARY JUDGMENT THAT THE ASSERTED CLAIMS OF THE '933 PATENT ARE INVALID FOR INDEFINITENESS AND LACK OF WRITTEN DESCRIPTION

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Defendants F. Hoffmann-La Roche Ltd., Roche Diagnostics GmbH and Hoffmann-La Roche, Inc. (collectively "Roche") submit this memorandum in support of their motion for summary judgment that claims 3, 7, 8, 9, 11, 12 and 14 of U.S. Patent No. 5,547,933 (the '933 patent) are invalid under 35 U.S.C. § 112 because they are indefinite or violate the written description requirement.

I. INTRODUCTION

Amgen's product claims of the '933 patent cannot be valid if they cover products having structures that are identical to products that existed prior to Dr. Lin's invention date because, like all claims to products, they must be limited to new products. Recognizing this fundamental principle of patent law, during prosecution of the '933 patent Plaintiff Amgen attempted to distinguish the claimed erythropoietin ("EPO") glycoproteins over the prior art EPO by adding the term "non-naturally occurring" to the claims. In *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F.Supp. 2d 69, 91 (D. Mass. 2001) ("*Amgen I*"), this Court construed the claim term "non-naturally occurring" to refer to glycoproteins "not occurring in nature." The implication was that the products of the claims are glycoproteins which are structurally distinct, regardless of source or process of making, from structures that occur in nature.

Amgen now seems to allege that it is not the "non-naturally-occurring" limitation that saves the claims from covering the structures that are not novel, but rather the requirement that claims be the product of the expression in a mammalian host cell of an exogenous DNA sequence comprising a DNA sequence encoding erythropoietin (Suh Decl., Ex. C at ¶¶ 80-86; Suh Decl., Ex. D at 27 -30) ("it is very unlikely that scientists can ever develop an EPO production system using cells grown in culture that accurately duplicates the structure of urinary EPO").

Regardless of Amgen's approach, the fact is that distinguishing the EPO products claimed in the '933 patent from prior art EPO based on the source or process but not the structure of the claimed EPO products would not have been sufficient to make the claimed EPO patentable. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 n.20 (Fed. Cir. 2003) ("*Amgen II*"). Indeed, Amgen expert Ajit Varki asserts that the "process and source of limitations" of the claims "confer specific structures to the claimed products and that those specific structures are different from the structure of the EPO that was purified from human urine before [Amgen's inventor] Dr. Lin made his inventions." (Suh Decl., Ex. C at ¶ 58).

As demonstrated below, however, the asserted claims of the '933 patent are invalid under 35 U.S.C. § 112 because the undisputed fact is that the one and only alleged physical distinction between the claimed EPO products and EPO known in the prior art is their glycosylation.[1] Dr. Varki admits that "it is not possible to test all of the hypothetically possible recombinant EPOs" and show they have glycosylation that differs from all naturally occurring EPO. (Suh Decl., Ex. D at ¶27). Nevertheless, Amgen claims all recombinant EPO without providing a definite limitation that excludes the EPO products that competitors are free to make recombinantly, or otherwise.

Moreover, in *Amgen I*, this Court held that claims which expressly distinguished the claimed EPO from prior art human urinary EPO based on unspecified glycosylation differences were invalid for indefiniteness and lack of written description owing to the "enormous heterogeneity" of the glycosylation found in human urinary erythropoietin. *Amgen I* at 155. As this Court explained, "because neither the patent nor the prior art provides clear guidance as to which human urinary EPO standard ought to be used, one of ordinary skill in the

[1] "Glycosylation is the addition of carbohydrate side chains to amino acid residues in protein sequences to form glycoproteins." *Amgen II* at 1340.

art would be unable to determine whether a particular erythropoietin has glycosylation which differs from that of human urinary glycosylation." *Id.* at 156. This Court deemed glycosylation a "moving target" and hence a "standardless standard for use in defining the claimed EPO product." *Id.* at 129, 155.

Given that the only physical distinction between the claimed EPO products and EPO in the prior art that is taught by the patents is their glycosylation and given that the glycosylation of naturally occurring EPO has already been held to be a "standardless standard," it follows that the asserted claims, which distinguish the claimed products as being "non-naturally occurring," or the product "in a mammalian host cell …" are invalid for indefiniteness and lack of written description. The claims do not enable potential infringers to determine whether particular EPO products are covered by the claims and the specification does not demonstrate that the patent applicant invented what was claimed.

As shown below, Amgen is now attempting to relitigate this Court's decision which was affirmed by the Federal Circuit. Amgen's experts have submitted lengthy reports which purport to distinguish non-naturally occurring EPO products from naturally occurring EPO, but only on the basis of glycosylation. Plainly, Amgen is collaterally estopped from disputing that glycosylation is an indefinite basis for distinguishing between the non-naturally occurring EPO products of the claims and naturally occurring EPO.

Accordingly, the *Amgen I* and *Amgen II* decisions mandate that independent claim 3 of the '933 patent, which recites a "non-naturally occurring glycoprotein product," and asserted claims 7, 8, 9, 11, 12 and 14, which depend therefrom directly or indirectly, are invalid on indefiniteness and written description grounds.

II. STATEMENT OF FACTS

A. The '933 Patent Claims At Issue

Amgen asserts claims 3, 7, 8, 9, 11, 12 and 14 of the '933 patent in this action.

Claim 3 is an independent claim directed to a non-naturally occurring glycoprotein product:

> "A non-naturally occurring glycoprotein product of the expression in a mammalian host cell of an exogenous DNA sequence comprising a DNA sequence encoding human erythropoietin said product possessing the in vivo biological property of causing bone marrow cells to increase production of reticulocyte and red blood cells."

Claims 7 and 8 also are directed to non-naturally occurring glycoprotein products. Both are dependent on claim 3 (among other claims), and they further limit the mammalian host cell of that claim. They provide:

> "The glycoprotein product according to Claim 3, 4, 5 or 6 wherein the host cell is a non-human mammalian cell."

> "The glycoprotein product of claim 7 wherein the non-human mammalian cell is a CHO cell."

Claims 9 and 12 of the '933 patent are directed to pharmaceutical compositions that include as an active ingredient the glycoprotein product of claims 3 and 7:

> "A pharmaceutical composition comprising an effective amount of a glycoprotein product for erythropoietin therapy according to claim 1, 2, 3, 4, 5 or 6 and a pharmaceutically acceptable diluent, adjuvant or carrier."

> "A pharmaceutical composition comprising an effective amount of a glycoprotein product effective for erythropoietin therapy according to claim 7 and a pharmaceutically acceptable diluent, adjuvant or carrier."

Claims 11 and 14 are method of treatment claims which depend on claims 9 and 12, respectively:

> "A method for treating a kidney dialysis patient which comprises administering a pharmaceutical composition of claim 9 in an amount effective to increase the hematocrit level of said product."
>
> "A method for treating a kidney dialysis patient which comprises administering a pharmaceutical composition of claim 12 in an amount effective to increase the hematocrit level of said product."

B. The Impact Of The TKT Litigation On The '933 Patent Claims

Amgen previously sued Hoechst Marion Roussel, Inc. and Transkaryotic Therapies, Inc. (the *TKT* litigation) in this Court, alleging infringement of claims 1, 2 and 9 of the '933 patent.

This Court defined the claim term "non-naturally occurring," to mean "not occurring in nature." *Amgen I* at 91. The Court found that "[b]y including this limitation," Dr. Lin, the inventor, "meant to stand clear of the unpatentable, naturally occurring products. He intended nothing more." *Id.* The Court held all three claims not infringed or, alternatively, invalid for indefiniteness and lack of written description. Each invalidity holding was based on a glycosylation limitation recited in claim 1: that the claimed non-naturally occurring erythropoietin glycoprotein must have "glycosylation which differs from that of human urinary erythropoietin."[2] In light of the fact that the glycosylation of human urinary erythropoietin varies, the Court concluded that the glycosylation of human urinary erythropoietin is a "moving target" and, therefore, a "standardless standard" by which to measure the claimed invention. *Id.*, at 129, 155.[3]

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[2] As this Court noted in *Amgen I*, "the prosecution history makes clear that the Patent Office understood that 'naturally occurring EPO' included human urinary EPO." *Amgen I* at 140.

[3] The Court found that (1) the glycosylation of urinary erythropoietin has "enormous heterogeneity"; (2) different techniques of purifying urinary erythropoietin result in differing glycosylated erythropoietin populations; (3) the '933 patent does not identify which human urinary erythropoietin should be the standard; and (4) different urinary

The Court concluded that because "different urinary EPO samples can themselves have glycosylation differences," Amgen's showing that TKT's accused non-naturally occurring erythropoietin product had glycosylation that differed from but "one of the many heterogeneous urinary EPOs" was "insufficient as a matter of fact to prove literal infringement" of claims 1, 2 and 9. *Amgen I,* at 127. The Court further held, in the alternative, that if its non-infringement finding was deemed error by the Federal Circuit, then claims 1, 2 and 9 of the '933 patent would be invalid on three grounds: (1) lack of written description ("the patent fails to convey to one of ordinary skill in the art as of 1984 that Dr. Lin invented an erythropoietin product having glycosylation which differs from human urinary erythropoietin" (*Id.* at 155)); (2) indefiniteness ("because different urinary erythropoietin preparations differ in their glycosylation, and because neither the patent nor the prior art provides clear guidance as to which human urinary EPO standard ought to be used, one of ordinary skill in the art would be unable to determine whether a particular erythropoietin has a glycosylation which differs from that of human urinary erythropoietin" (*Id.* at 156)); and (3) nonenablement ("an ordinary skilled worker would be unable to perform the experimental analysis necessary to confirm whether the manufactured glycoprotein product has glycosylation which differs from that of human urinary erythropoietin" (*Id.* at 165.).

The Federal Circuit affirmed this Court's holding that claims 1, 2 and 9 of the '933 patent are invalid for indefiniteness. *Amgen II* at 1342.[4]

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erythropoietin samples have different glycosylation. *Amgen I* at 155. "As a result, making comparisons between the glycosylation of recombinant EPO and that of human urinary EPO is virtually impossible." *Id.*

[4] Amgen is also asserting claim 9 of the '933 patent in this case.

III. ARGUMENT

A. Summary Judgment Is Appropriate Here

As this Court has stated, "if there are no genuine issues of material fact, summary judgment is appropriate in a patent infringement case as in any other." *Amgen I* at 93. The Court's holding in *Amgen I* that claim 1 of the '933 patent is indefinite and lacks written description, together with the Court's subsidiary findings, mandate that the Court grant summary judgment here in Roche's favor on the grounds that the '933 and '080 patent claims asserted in this action are indefinite and lack written description.

B. The Asserted Claims Of The '933 Patent Are Invalid For Indefiniteness

1. The "Non-Naturally Occurring" Glycoprotein Products of the Claims Must Be Structurally Distinct

During prosecution of the '933 patent, the applicant introduced the "non-naturally occurring" limitation in what became claim 3 in order to "distinguish the subject matter claimed from all prior art reference relating to erythropoietin isolates." (Suh Decl., Ex. E, p. 7.) The applicant stated that in a Patent Office interview with the examiner "it was agreed that the negative limitation 'non-naturally occurring' would, when combined with the notation of glycosylation differences in [what became claims 1 and 5], meet Section 112 specificity requirements." (*Id.* at p. 6).

The examiner's rejections which gave rise to the amendment (Suh Decl., Ex. F, pp. 4-6) had cited *In re Brown*, 459 F.2d 531, 535 (C.C.P.A. 1972), where the court stated that "the lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, *it is the patentability of the product claimed and not of the recited process steps which must be established*." (Emphasis added). In *Amgen II* the Federal Circuit similarly

stated that "a claimed product shown to be present in the prior art cannot be rendered patentable solely by the addition of source or process limitations." 314 F.3d at 1354. *See also General Elec. Co. v. Wabash Appliance Corp.*, 304 U.S. 364, 373 (1938) ("a patentee who does not distinguish his product from what is old except by reference, express or constructive, to the process by which he produced it, cannot secure a monopoly on the product by whatever means produced").

More recently, based on the same principle, the Federal Circuit held invalid two product-by-process claims in a pharmaceutical composition patent. The patentee there argued that the recitation of a novel process in the claims was sufficient to overcome a prior art patent that described all the structural elements of the claimed products. The court rejected the argument, holding that "a prior art disclosure of a product precludes a future claim to that same product, even if it is made by an allegedly novel process." *SmithKline Beecham Corp. v. Apotex Corp.*, 439 F.3d 1312, 1319 n.7 (Fed. Cir. 2006).

Significantly, in prosecuting the application for Amgen's U.S. Patent No. 5,955,422, also asserted in this case, the examiner rejected a claim to a composition containing "recombinant EPO" notwithstanding the supporting expert declaration of Dr. Richard Cummings. The declaration was "not deemed persuasive in regard to distinguishing the subject matter of claim 63 drawn to EPO from that found in urine, which the declaration indicates that some forms of recombinant EPO may be alternatively glycosylated, the use of the generic term 'recombinant' fails to impose any definitive physical limitation on the claimed compositions." (Suh Decl., Ex. G).

Simply put, claims to EPO products read on the prior art if they encompass products that are identical to prior art EPO regardless of the source of the products. Product

claims cannot preclude the use of a prior art compound merely because the product is made a new way. Thus, the addition of the term "non-naturally occurring" to the claims of the '933 patent, to overcome prior art, had to reflect a physical difference -- not merely a difference in source -- between the claimed EPO products and the naturally occurring EPO of the prior art. Indeed, in construing the claim term "non-naturally occurring" to mean "not occurring in nature" this Court read the claims as covering EPO glycoproteins which are distinguishable from any EPO which exists in nature.

2. The '933 Patent Distinguishes Non-Naturally Occurring EPO Products from Naturally Occurring EPO Based Only on Glycosylation

The only physical distinction between naturally occurring EPO glycoproteins and the non-naturally occurring EPO glycoproteins of the claims that is recited in the specification of the '933 patent is their glycosylation:

> "[P]olypeptides of the invention may be glycosylated with mammalian or other encaryotic carbohydrates or may be non-glycosylated. . . . Novel glycoprotein products of the invention include those having a primary structural conformation sufficiently duplicative of that of a naturally-occurring (*e.g.*, human) erythropoietin to allow possession of one or more of the biological properties thereof and having an average carbohydrate composition which differs from that of naturally-occurring (*e.g.*, human) erythropoietin.

(Suh Decl., Ex. A, col. 10: 29-40).

Example 10 of the '933 patent experimentally distinguished the claimed glycoprotein from a naturally occurring EPO based on their average carbohydrate compositions, i.e., their glycosylation. The Example states that, after removal of all of the attached carbohydrates, recombinant EPO and urinary EPO were "substantially homogenous products having essentially identical molecular weight characteristics." (Suh Decl., Ex. A, col. 28:48-50). The specification summarizes the results of the Example 10 experiment as follows:

> "Glycoprotein products provided by the present invention are thus comprehensive of products having a primary structural conformation [amino acid sequence] sufficiently duplicative of that of a naturally-occurring erythropoietin to allow possession of one or more of the biological properties thereof and *having an average carbohydrate composition [glycosylation] which differs from that of naturally-occurring erythropoietin*."

(Suh Decl., Ex. A, col. 29:1-7; emphasis added.)[5]

3. Amgen's Experts Distinguish the Claimed EPO Products On the Basis of Glycosylation

Recognizing that the EPO products of the claims cannot be patentably distinguished over the naturally occurring EPO of the prior art based on source alone, Amgen relies on the expert opinions of Drs. Ajit Varki and Don Catlin who assert that the non-naturally occurring EPO products of the claims and the naturally occurring EPO of the prior art are physically distinguishable. However, the only distinction identified by the experts is glycosylation.

In his May 11, 2007 expert report, Dr. Varki opines that the "process and source limitations confer specific structures to the claimed products and that those specific structures are different from the structure of the EPO that was purified from human urine before Dr. Lin made his inventions." (Suh Decl., Ex. C, at ¶ 58).[6] Dr. Varki explains that "the glycosylation

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[5] Amgen has admitted that the ratios of carbohydrates on naturally occurring EPO and recombinant EPO, as reported in the patent, are wrong. *See Fritsch v. Lin, Interference* No. 102,334,21 U.S.P.Q.2d 1739, 1741 (Bd. Pat. App. & Interf. 1992).

[6] Dr. Varki argues that the term "non-naturally occurring" must be definite because the Court interpreted the term to mean "not occurring in nature" and Roche "did not contest the Court's interpretation of this term nor argue that the meaning of the term was not discernable. (Suh Decl., Ex. C at ¶ 46). However, Roche does not maintain that the term "non-naturally occurring," as such, is necessarily indefinite. The claims are indefinite in that Amgen's expert reports make clear that the only possible basis for distinguishing the EPO products of the claims as being non-naturally occurring is their glycosylation. And this Court has already rejected glycosylation as a "standardless standard."

structures imparted by cells grown in culture are inherently different than those imparted by the cells in the kidney that naturally produce EPO." (*Id*. at ¶ 211). According to Dr. Varki:

> "[I]t it not surprising that no recombinant EPO can accurately reproduce the precise structure the mixture of glycoforms in naturally-occurring prior art EPO. When a gene for a secreted glycoprotein is removed from its normal cellular environment, and inserted into a different type of cell -- often from a different species -- which is grown under far different conditions than its *in situ* environment in the body, it is completely unsurprising that the glycoprotein that is produced has different glycan structures than the naturally-occurring glycoprotein. One would have understood that it would have been extremely unlikely and practically impossible to reproduce the glycosylation found on naturally occurring EPO because of both the difficulty in reproducing the cell type that normally makes EPO and the difficulty in reproducing the environment in which those cells normally grow.

(*Id*. at ¶ 84).

Dr. Catlin's May 11, 2007 expert report recites that he used an isoelectric focusing method, first described in 2000, to test several samples of recombinant EPO and urinary EPO. (Suh Decl., Ex. H at ¶¶ 58-59). Dr. Catlin concluded that "[a]ll recombinant EPOs tested could clearly be distinguished from both EPO in normal urine and the International standard for urinary EPO. The difference in each case is the presence of several isoforms in urinary EPO which are lacking for each recombinant EPO." (*Id*. at ¶ 69(ii)).[7] Dr. Catlin explained that IEF differentiates molecules on the basis of the "pI," which is "a reflection of all the charged groups attached to the protein molecule." (*Id*. at ¶ 26). According to Dr. Catlin, the charged groups can include "sugar groups like sialic acid."[8] Dr. Catlin does not suggest that his IEF results are attributable to anything other than glycosylation differences.[9]

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[7] Thus, Dr.Catlin admits that all the isoforms in the recombinant EPO are found in urinary EPO. He says that urinary EPO has additional molecules.

[8] Dr. Catlin, explained that "isoforms" are versions of proteins which differ in a measurable characteristic. (Suh Decl., Ex. H at ¶ 23 n.6). "Glycoforms" are isoforms

Amgen has previously cited IEF testing as demonstrating that non-naturally occurring EPO and naturally-occurring EPO differ in their glycosylation. During the *TKT* litigation, Amgen relied on the expert testimony of Richard D. Cummings who, for purposes of that litigation, ran SDS polyacrylamide gels and western blot testing of the accused recombinant EPO received from the defendants (Hoechst and Transkaroytic) which showed "that the recombinant material from the defendants has a higher apparent molecular weight on the SDS gels than the naturally occurring EPO, and that the difference is due to glycosylation." (6/5/00 Trial Tr. 629-30). Dr. Cummings also "did an isoelectric focusing experiment" comparing the urine derived EPO with the accused recombinant product, the results of which were consistent with his SDS gel and western blot experiments demonstrating "that the urine derived EPO is glycosylated differently and probably due to sialic acid in this case from the recombinant EPO." (*Id*. at 648-49).

Amgen is unable to point to any structural differences between recombinant EPO and urine derived EPO. In fact, Amgen's own expert witness, Dr. Eugene Goldwasser testified that, "we don't know anything about the secondary structure . . . of urinary EPO." (Suh Decl., Ex. J at 104:21 - 105:8). Testifying further on the unknown conformation of urinary EPO, Goldwasser noted that "nobody has determined a three-dimensional structure of urinary EPO."

"which differ specifically in the structure of their attached sugar structures." (*Id.*). (See also Suh Decl., Ex. I at ¶ 32).

[9] To the extent Dr. Catlin relies on testing methodology which was unknown at the time of the patent application, his opinion cannot cure the indefiniteness problem of the patents-in-suit. According to the Federal Circuit, "[t]he perspective of a person of ordinary skill in the art at the time of the patent application governs the definiteness analysis." *Howmedica Osteonics Corp. v. Tranquil Prospects, Ltd.*, 401 F.3d 1367, 1371 (Fed. Cir. 2005); *W.G. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1556 (Fed. Cir. 1983; ("§ 112 speaks as of the application filing date"); *Bancorp Servs., LLC v. Hartford Life Ins. Co.*, 2002 U.S. Dist. LEXIS 27200 *12 (E.D. Mo. 2002) ("Indefiniteness is determined as of the *filing date* of the patent application").

(*Id.* at 90:10 - 91:5). Goldwasser attempted to determine the crystallization of urinary EPO "on and off for . . . about three years" with no success. (*Id.* at 93: 1-18). Simply put, by the admission of Amgen's own expert witness, not enough information about the structure of urinary EPO is known to make any sort of comparison, let alone a meaningful structural distinction between urinary EPO and recombinant EPO.

4. The Definiteness Requirement of 35 U.S.C.§ 112

Paragraph 2 of 35 U.S.C. § 112 provides that "[t]he specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." According to the Federal Circuit, "[t]he "requirement of claim definiteness set out in § 112 ¶ 2 assures that claims in a patent are 'sufficiently precise to permit a potential competitor to determine whether or not he is infringing.'" *Amgen II* at 1342. *See also Oakley, Inc. v. Sunglass Hut, Int'l*, 316 F.3d 1331, 1340 (Fed. Cir. 2003) ("The primary purpose of the definiteness requirement is to ensure that the claims are written in such a way that they give notice to the public of the extent of the legal protection afforded by the patent, so that interested members of the public, *e.g.*, competitors of the patent owner, can determine whether or not they infringe").

As this Court stated in *Amgen I*, "[d]etermining whether a claim is definite requires an analysis of 'whether one skilled in the art would understand the bounds of the claim when read in light of the specification.'" *Amgen I* at 156 (quoting *Personalized Media Communications, LLC v. ITC*, 161 F.3d 696, 705 (Fed. Cir. 1998)). "The focus of the inquiry . . . is on the clarity of the claim terms and the extent to which such terms, viewed from the perspective of one of ordinary skill in the art, sufficiently identify the actual invention." *Amgen I* at 156. Compliance with the definiteness requirement is a question of law. *Personalized Media Communications, LLC v. ITC*, 161 F.3d 696, 705 (Fed. Cir. 1998).

5. The Claims of the '933 Patent which Distinguish the Claimed EPO as Being Non-Naturally Occurring Are Indefinite

The asserted claims of the '933 patent are invalid because they fail to identify a definite physical basis for distinguishing the claimed non-naturally occurring EPO products from naturally occurring EPO which is outside the claims.

In *Amgen I*, this Court held that the limitation in claim 1 of the '933 patent "having glycosylation which differs from that of human urinary erythropoietin" is indefinite. *Amgen I* at 156. Plainly, human urinary EPO is naturally occurring. The Court found that "the glycosylation of human urinary erythropoietin was in 1984, and continues to be a moving target." *Id.* at 129. The Court stated:

> "Although the [claim] language contemplates that a competitor concerned with infringing the'933 patent can empirically determine whether it's product's glycosylation of human urinary erythropoietin, a definitive comparison is rendered impossible by the fact that human urinary erythropoietin itself varies significantly. This is not the kind of particular pointing out and distinct claiming that is required by the statute."

Id. at 156. As the Court pointed out: "[H]ow can one prove that a recombinant EPO has glycosylation which differs from that of urinary EPO when the glycosylation of urinary EPO itself varies?" *Amgen I* at 129.[10]

In *Amgen II*, the Federal Circuit agreed, stating: "By definition, one must know what the glycosylation of uEPO [EPO isolated from human urine] is with certainty before one can determine whether the claimed glycoprotein has a glycosylation different from that of uEPO. In its discussion characterizing recombinant glycoprotein products, the specification of the '933

[10] This Court's invalidity holding was stated in the alternative: "Because the claim term [glycosylation which differs from that of naturally occurring erythropoietin] fails to apprise those skilled in the art of the scope of the invention, TKT has proved by clear and convincing evidence that the claim is indefinite, and if upon review, the finding of non-infringement is in error, the Court so rules." *Amgen I* at 157.

patent does not direct those of ordinary skill in the art to a standard by which the appropriate comparison can be made." 314 F.3d at 1341. The Federal Circuit thus observed: "One cannot logically determine whether an accused product comes within the bounds of a claim of unascertainable scope." *Id.* at 1342.

Because the '933 patent differentiates a non-naturally occurring EPO product from naturally occurring EPO based only on glycosylation and because that standard has already been held by this Court to be indefinite, claim 3 of the '933 patent -- which distinguishes the claimed EPO products as being "non-naturally occurring" -- is necessarily indefinite. Moreover, because claims 7-9, 11, 12 and 14 of the '933 patent incorporate claim 3 directly or indirectly, each of those claims is also invalid as indefinite. A potential infringer of any of the asserted claims would be unable to determine whether its product, method, or composition is, contains or uses erythropoietin which is non-naturally occurring.

Amgen expert, Dr. Varki, argues that the claims of the '933 patent are definite because one of ordinary skill in the art "would have no difficulty determining" whether an EPO sample is non-naturally occurring: "if the product was isolated from a natural source, such as urine or blood, it is not 'non-naturally' occurring. If the product is derived from any other unnatural source, it is non-naturally occurring." (Suh Decl., Ex. C at ¶ 49). However, in construing the term "non-naturally occurring" to mean "not occurring in nature," this Court has distinguished the claimed products themselves -- not merely their source -- as being distinct from any EPO "occurring in nature."

Moreover, as explained above, if the products of the claims are distinguishable only by source, then they are invalid in view of the prior art. The Patent Office specifically rejected a claim to "recombinant EPO" as being indistinguishable from urinary EPO. In the case

of the asserted claims of the '933 patent, all of which are product claims or depend therefrom, the issue is the novelty of the product, not how it was made. Consequently, the source of the EPO product -- without regard to structure -- is not sufficient to distinguish a claimed non-naturally occurring EPO product from naturally occurring EPO which is outside of the claims.

In sum, the term "non-naturally occurring" must reflect a physical distinction over the prior art, but the only distinction recited in the patents-in-suit or otherwise cited by Amgen has already been held indefinite by this Court and the Federal Circuit.

6. Amgen Is Collaterally Estopped from Disputing that Glycosylation Is an Indefinite Standard for Distinguishing Non-Naturally Occurring EPO

Amgen submits the Varki and Catlin expert reports in a thinly veiled attempt to relitigate this Court's holding that glycosylation is an indefinite grounds for distinguishing non-naturally occurring EPO products from naturally occurring EPO. Under the doctrine of issue preclusion, however, Amgen is foreclosed from reopening the issue which this Court has already decided against Amgen. Hence, Amgen's expert reports do not even raise a triable issue of fact.

In patent cases, the Federal Circuit applies the issue preclusion law of the regional circuit. *Vardon Golf Co. v. Karsten Mfg. Corp.*, 294 F.3d 1330, 1333 (Fed. Cir. 2002). In the First Circuit, courts look for five essential elements in applying collateral estoppel: "(1) the issue sought to be precluded must be the same as that involved in the prior action; (2) the issues must have been actually litigated; (3) the issue must have been determined by a valid and binding final judgment; and, (4) the determination of the issue must have been essential to the judgment; and (5) the party to the second action must be the same as or in privity with the parties in the first action." *Boston Sci. Corp. v. SciMed Life Sys., Inc.*, 983 F. Supp. 245, 255 (D. Mass. 1997) (relying on *NLRB v. Donna-Lee Sportswear Co.*, 836 F.2d 31, 34 (1st Cir. 1987)).

Here, all of the requirements of issue preclusion are met: Whether glycosylation would allow a potential infringer to distinguish between naturally occurring and non-naturally occurring EPO was actually at issue in the *TKT* litigation. That question was fully litigated by Amgen in the district court and the district court's indefiniteness holding was essential to the final judgment of the district court holding claims 1, 2 and 9 of the '933 patent invalid. The judgment was affirmed on appeal. Consequently, Amgen is foreclosed from reopening the issue.

C. The Asserted Claims Of The '933 Patent Are Invalid On Written Description Grounds

35 U.S.C. § 112 ¶ 1 requires that each claim be supported by a "written description of the invention." In order to satisfy the requirements of § 112 ¶ 1, "the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989). "[I]t is in the patent specification where the written description requirement must be met." *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927 (Fed. Cir. 2004) (affirming summary judgment on written description grounds).

Section 112 thus "requires this Court to determine whether Amgen's specification, considered as a whole, conveys to one of ordinary skill in the art, either explicitly or inherently, that [the inventor] Dr. Lin invented the subject matter claimed in the patents-in-suit." *Amgen I* at 147-48. As explained above, however, in *Amgen I* this Court held that the '933 patent makes "comparisons between the glycosylation of recombinant EPO [of the claims] and that of human urinary EPO . . . virtually impossible." *Id.* at 155. The Court found that "one of ordinary skill in the art" would not have known "which of the varying urinary EPO preparations ought to be utilized" as a standard of comparison and that "[a]s a result, the patent fails to convey to one of ordinary skill in the art as of 1984 that Dr. Lin invented an

erythropoietin glycoprotein product having glycosylation which differs from that of human urinary erythropoietin." *Id*. Accordingly, this Court stated that "if [its] finding of non-infringement were to be ruled error, this Court would, in the alternative, rule that all three asserted claims of the '933 patent invalid for lack of written description." *Id*. at 155-56.

The asserted claims of the '933 patent similarly lack the requisite written description to the extent that they would distinguish the claimed non-naturally occurring EPO products from naturally occurring EPO on the basis of glycosylation alone. The specification does not teach that the patent applicant invented EPO, whatever its source, that was physically distinct from naturally occurring EPO. Moreover, as shown above, Amgen is collaterally estopped from arguing the contrary. Stated otherwise, in view of *Amgen I* and *Amgen II*, where naturally occurring EPO was characterized as a moving target, the patent specification does not support claims to EPO products which are defined, by negative limitation, as being something other than naturally occurring EPO.

Claim 3 of the '933 patent, which claims a "non-naturally occurring erythropoietin glycoprotein," is thus invalid on written description grounds. The claims which depend from those claims are also invalid for lack of written description because they have no further limitation which would show that the inventor had invented EPO which is physically distinct from the structure of naturally occurring EPO.

IV. CONCLUSION

For all of the foregoing reasons, this Court should grant summary judgment in Roche's favor holding invalid, for indefiniteness and lack of written description, all of the claims of the '933 patent that Amgen has asserted in this action.

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Respectfully submitted,

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