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 MEMORANDUM OF LAW IN OPPOSITION TO 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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Plaintiff Amgen, Inc. ("Amgen") submits this memorandum in opposition to Defendants F. Hoffmann-La Roche Ltd., Roche Diagnostics GmbH, and Hoffman-La Roche, Inc. (collectively "Roche")'s motion for summary judgment that the asserted claims of U.S. Patent 5,547,933 ("the '933 Patent") are invalid for indefiniteness and lack of written description.

I. INTRODUCTION

The plain meaning of the claim language, the intrinsic evidence, and the prior rulings of this Court and the Federal Circuit all demonstrate that the limitation "non-naturally occurring" is sufficiently definite to delineate the metes and bounds of the asserted '933 Patent claims and meet the requirements of 35 U.S.C. § 112.

To determine whether an accused product is "non-naturally occurring," one simply has to ask: "how was this product obtained?" In the Federal Circuit's words, the term "non-naturally occurring" "mean[s] just what [it] says . . . [it] limits only the source from which the EPO is obtained."[1] Thus, if an accused human erythropoietin ("EPO") product is isolated from a source that naturally contains or produces EPO without human intervention, such as human urine or blood, it does not infringe. If the accused human EPO product, like Roche's pegylated EPO preparation MIRCERA, is obtained from a source that does not naturally contain or produce EPO, such as genetically engineered mammalian host cells, it infringes.

Ignoring Amgen's clear intent in introducing the limitation, as evidenced by the intrinsic record and the Court's considered decision regarding the limitation, Roche contends that "non-naturally occurring" must reflect a physical distinction over the prior art. Roche then reasons that because the only other structural limitation previously considered (as set forth in '933 claim 1) — "glycosylation which differs from that of human urinary erythropoietin" — was held to be

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[1] *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1330 n.5 (Fed. Cir. 2003) [hereinafter *Amgen II*].

indefinite by this Court and the Federal Circuit, Amgen's other '933 claims must also be indefinite.[2] Like so much of Roche's defense, this contention is built on several false premises.

First, Roche's argument confuses the definiteness requirement of 35 U.S.C. §112 ¶ 2 with the novelty requirement of §102. Under §112 ¶ 2, definiteness requires the limitations of a patent claim to be "sufficiently precise to permit a potential competitor to determine whether or not he is infringing."[3] Here, the limitation "non-naturally occurring" is sufficiently definite because an accused infringer could readily determine whether or not its accused product was obtained from a source that naturally contains or produces EPO without human intervention. Whether the claimed inventions are distinct over the prior art is a determination made under 35 U.S.C. §102, not § 112, and that determination is based on the limitations of the claimed invention taken as a whole, not on a single limitation such as "non-naturally occurring."

Second, Roche's attempt to analogize the "non-naturally occurring" limitation of Claim 3 to the "glycosylation which differs from that of human urinary erythropoietin" limitation of Claim 1[4] is simply wrong. The latter limitation was held indefinite because the specification failed to identify which among many possible urinary EPO preparations provided *the* standard for comparison. Here, however, no such comparative standard is required. The accused EPO

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[2] 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 (Docket No. 506) [hereinafter Roche's Brief] at 15-16.

[3] *Amgen II, 314. F.3d at 1342* (citation omitted)*;* Roche's Brief at 14-15.

[4] In addition to the limitation "glycosylation which differs from that of human urinary erythropoietin," Claim 1 of the '933 Patent also contains the limitation "non-naturally occurring."

product either is or is not obtained from a source that contains or produces the recited product in the natural course. Roche's attempt to bolster its position by resort to collateral estoppel adds nothing to its argument. Not only is Claim 3 different from the previously adjudicated Claim 1, but the basis on which Claim 1 was held to be indefinite has no applicability to the "non-naturally occurring" limitation of Claim 3.

Roche makes the alternative argument that the asserted claims of the '933 Patent are invalid because Dr. Lin's written description fails to apprise those of ordinary skill in the art he actually invented EPO that was "non-naturally occurring." Again, Roche's argument fundamentally misconstrues the term "non-naturally occurring." Roche's written description argument begins with the erroneous assumption Lin's specification would have to describe a test for "glycosylation which differs from that of human urinary erythropoietin" in order to describe adequately "a non-naturally occurring glycoprotein." But, as described above, the "non-naturally occurring" limitation defines the source from which the product is obtained, not differences between the claimed glycoprotein and urinary EPO. As this Court found in the earlier litigation between Amgen and Hoechst Marion Roussel and Transkaryotic Therapies ("*HMR/TKT litigation*"), Dr. Lin disclosed the source of his non-naturally occurring human erythropoietin glycoproteins in complete detail:

> Dr. Lin disclosed a complete and detailed explanation of the production of non-naturally occurring human erythropoietin glycoproteins.[5]

Given Dr. Lin's extensive disclosure of the expression in a mammalian host cell of an exogenous DNA sequence comprising a DNA sequence encoding human erythropoietin, Roche cannot seriously criticize Dr. Lin's disclosure of non-naturally occurring EPO glycoproteins.

Roche has not shown — and indeed, it cannot show — by clear and convincing evidence

that the asserted claims of the '933 Patent are either indefinite or lack adequate support by the patent's written description. Under these circumstances, Roche's motion should be denied. [6]

II. LEGAL STANDARDS

A. DEFINITENESS

35 U.S.C. § 112 ¶ 2 requires that claims "particularly point[] out and distinctly claim[] the subject matter which the applicant regards as his invention" in order to be valid.[7] This requirement is satisfied when one of ordinary skill in the art would "understand the scope of the subject matter that is patented when the claim is read in conjunction with the rest of the specification."[8] The purpose of the definiteness requirement is to "ensure that the claims delineate the scope of the invention using language that adequately notifies the public of the patentee's right to exclude."[9]

A claim is presumed valid and therefore definite.[10] This presumption is based "in part on

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[5] *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 69, 154 (D. Mass. 2001) [hereinafter *Amgen I*] (citing '933 Patent at 23:1-24:38, 25:29-29:7 (Docket No. 534, Ex. 3)).

[6] *See Intel Corp. v. VIA Techs.*, 319 F.3d 1357, 1366 (Fed. Cir. 2003) ("Any fact critical to a holding on indefiniteness . . . must be proven by the challenger by clear and convincing evidence."); *Invitrogen Corp. v. Clontech Labs, Inc.*, 429 F.3d 1052, 1072 (Fed. Cir. 2005) ("[I]nvalidating a claim requires a showing by clear and convincing evidence that the written description requirement has not been satisfied.").

[7] 35 U.S.C. § 112.

[8] *S3 Inc. v. nVIDIA Corp.*, 259 F.3d 1364, 1367 (Fed. Cir. 2001).

[9] *Datamize, LLC v. Plumtree Software, Inc.*, 417 F.3d 1342, 1347 (Fed. Cir. 2005).

[10] 35 U.S.C. § 282.

the expertise of patent examiners presumed to have done their job."[11] Claims are considered indefinite only when they are "not amenable to construction or [are] insolubly ambiguous."[12] Claims need not be "plain on their face in order to avoid condemnation for indefiniteness."[13] Rather, a claim is definite so long as it is "amenable to construction, however difficult that task may be."[14] To this end, the amount of detail required of claim language depends on the particular invention[15] and the detail provided by the written description.[16]

In other words, "[i]f the meaning of a claim is discernable, even though the conclusion may be one over which reasonable persons will disagree," a claim will be held not indefinite.[17]

B. WRITTEN DESCRIPTION

The written description requirement embodied in the first paragraph of 35 U.S.C. § 112 requires "sufficient information in the specification to show that the inventor possessed the invention at the time of that original disclosure."[18] § 112 ¶ 1 does not require the applicant to

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[11] *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1574 (Fed. Cir. 1992) (citations omitted).

[12] *Datamize*, 417 F.3d at 1347 (citation omitted).

[13] *Exxon Research & Eng'g Co. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001).

[14] *Id.; Aero Prods. Int'l v. Intex Rec. Corp.*, 466 F.3d 1000, 1016 (Fed. Cir. 2006) (holding that claim was not indefinite because it was capable of being construed).

[15] *See, e.g., Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1575-1576 (Fed. Cir. 1986) (holding that the claim language describing a part of a wheelchair to be "so dimensioned" so as to fit through the door of an automobile was definite because the claims were intended to cover the use of the invention in a variety of automobiles and one of ordinary skill would know how to determine the appropriate dimensions).

[16] *See, e.g., Howmedica Osetonics Corp. v. Tranquil Prospects, Ltd.*, 401 F.3d 1367, 1371-72 (Fed. Cir. 2005) (concluding that an ordinary skilled artisan "would readily ascertain from the written description of the patents" the meaning of the disputed term and reversing the district court's finding of indefiniteness).

[17] *Bancorp Services, L.L.C. v. Hartford Life Insurance Co.*, 359 F.3d 1367, 1372 (Fed. Cir. 2004) (citing *Exxon*, 265 F.3d at 1375).

[18] *Pandrol USA, LP v. Airboss Ry. Prods.*, 424 F.3d 1161, 1165 (Fed. Cir. 2005) (citation omitted).

describe exactly the subject matter claimed. "Rather, the Patent Act and this court's case law require only sufficient description to show one of skill in the refining art that the inventor possessed the claimed invention at the time of filing."[19]

III. ARGUMENT

A. BECAUSE ONE OF ORDINARY SKILL IN THE ART COULD READILY DETERMINE WHETHER AN ACCUSED RECOMBINANT HUMAN ERYTHROPOIETIN IS MAN-MADE OR NATURALLY OCCURRING, DR. LIN'S ASSERTED '933 PATENT CLAIMS ARE NOT INDEFINITE

1. "Non-naturally occurring" is a negative source limitation that requires only that the claimed product not be obtained from a natural source.

As the Federal Circuit has held, and Roche has acknowledged, the term "non-naturally occurring" is a negative source limitation that "merely prevents Amgen from claiming the human EPO produced in the natural course."[20] The limitation "mean[s] just what [it] says . . . [it] limits only the source from which the EPO is obtained."[21]

Use of the limitation "non-naturally occurring" has long precedent. In 1980, the United States Supreme Court, in differentiating a patentable genetically engineered bacterium from an unpatentable bacterium that could be found in nature, described the claimed invention as "not a hitherto unknown natural phenomenon, but…a ***nonnaturally occurring*** manufacture or composition of matter — ***a product of human ingenuity having a distinctive name, character***

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[19] *Union Oil Co. of Cal. v. Atl. Richfield Co.*, 208 F.3d 989, 997 (Fed. Cir. 2000).

[20] *Amgen II*, 314 F.3d at 1329; *see* Roche's Brief at 5.

[21] *Amgen II*, 314 F.3d at 1330 n.5.

and use."[22] Applying this distinction, the Federal Circuit has held that applicants for patents claiming biological products can use the limiting term "non-natural" to specify the source of a product as man-made and thereby avoid rejection for unpatentability under § 101.[23] More than 460 patents containing a "non-naturally occurring" or "nonnaturally occurring" claim limitation have been issued to patentees,[24] including Roche's own U.S. Patent No. 5,362,646.[25]

As evidenced by the intrinsic record, "non-naturally occurring" has the same meaning here.[26] The prosecution history of the '933 Patent confirms that the "non-naturally occurring" limitation was inserted by agreement of the patentee and examiner for the very purpose of overcoming a prior rejection on the ground of indefiniteness:

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[22] *Diamond v. Chakrabarty*, 447 U.S. 303, 309-10 (1980) (citation omitted) (emphasis added).

[23] *Amgen II*, 314 F.3d at 1329, *citing Animal Legal Def. Fund v. Quigg*, 932 F.2d 920, 923 (Fed. Cir. 1991).

[24] http://www/USPTO.gov/patft/index.html (last visited June 22, 2007).

[25] Decl. of Adam Arthur Bier in Support of Amgen, Inc.'s Opposition to Roche's Motion for Summary Judgment That the Asserted Claims of the '933 Patent Are Invalid For Indefiniteness and Lack of Written Description [hereinafter Bier Decl.], Ex. 1, US Pat 5,362,646, Cl. 9 (emphasis added), which provides:

> 9. A ***non-naturally occurring*** E. coli bacterium which contains a 1) an expression control sequence comprising a T-coliphage promoter sequence having a low signal strength in the induced state and a high in vivo promoter strength combined with a lac-operator sequence from a lac-operator/repressor system wherein said system has a high association rate prior to said combination with said promoter; and 2) a sequence which codes for the lac-repressor polypeptide of the lac-operator/repressor system

All citations to exhibits herein refer to exhibits to the Bier Decl.

[26] 4/17/07 *Markman* Hearing Tr. at 40:20-41:1 (Docket No. 514, Ex. 40). A claim as construed cannot have different meanings in different contexts. *See*, *e.g.*, *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1375 (Fed. Cir. 2001) (claims cannot be construed one way for invalidity purposes and another for infringement purposes); *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1351 (Fed. Cir. 2001) (same holding). While, for this reason, prior constructions of the claim language at issue govern equally whether one is assessing the language for definiteness, subject-matter patentability, or novelty, Roche's discussion of cases holding that the addition of a source limitation cannot overcome prior art is irrelevant here.

> (h) at the interview it was agreed that the negative limitation, "non-naturally occurring" would, when combined with the notation of glycosylation differences in prior claims 87 and 99 (corresponding to new claims 100 and 105) meet Section 112 specificity requirements. All of independent claims 100-105 are similarly limited.[27]

These remarks demonstrate that the examiner, whose expertise supports a "weighty presumption of correctness,"[28] had actually determined that the "non-naturally occurring" limitation ***cured, not caused*** an indefiniteness issue.

Dr. Lin's claims and specification also establish that "non-naturally occurring" is a source, and not a structural, limitation. For example, the specification uses "naturally derived" to distinguish products based on source,[29] and during prosecution, Dr. Lin consistently used the term "non-naturally occurring" to contrast his invention with erythropoietin products that were produced in the natural course.[30] Finally, in the context of the much-vaunted invalidation of Claim 1 of the '933 Patent, this Court and the Federal Circuit focused on whether "human

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[27] '933 Prosecution History, 12/20/95 Secondary Preliminary Amendment and Remarks at 6 (Docket No. 534, Ex. 25).

[28] *Brooktree Corp.*, 977 F.2d at 1574-75 (citation omitted).

[29] '933 Patent at 33:39-44 (Docket No. 534, Ex. 3) ("***Products of the invention, by virtue of their production by recombinant methods***, are expected to be free of pyrogens, natural inhibitory substances, and the like, and are thus likely to provide enhanced overall effectiveness in therapeutic processes ***vis-à-vis naturally derived products***.") (emphasis added).

[30] *See* '933 Prosecution History, 6/5/89 Amendment Under Rule 116 at 4 (Docket No. 534, Ex. 25) ("All of the references cited by the Examiner in this rejection [Miyake, Chiba, Takezawa, and Sugimoto] relate to naturally occurring erythropoietin. *The claims of the subject invention related to erythropoietin which is produced through recombinant DNA techniques*.") (emphasis in original); *id*. at 6; '933 Prosecution History 11/30/88, Strickland Declaration at ¶ 5 (Docket No. 534, Ex. 25). *See also*, '933 Prosecution History, 6/2/88 Office Action at 4, 9 (Docket No. 534, Ex. 25) (wherein the Examiner similarly used the term "native" EPO to refer to EPO obtained from natural sources).

urinary erythropoietin" was a "standardless standard," ***not*** whether the term "non-naturally occurring," as it also appears in the claim, was indefinite.[31] Indeed, as set forth above, the Court construed "non-naturally occurring" to have a definite meaning.

In short, the plain meaning of the term "non-naturally occurring," its longstanding usage by the courts, and the language used by the inventor in the drafting and prosecution of his claim makes clear that the limitation negatively defines the ***source*** of the material claimed as the invention. This, and "nothing more," was the inventor's intent,[32] and is reflected in the construction the Federal Circuit has previously applied.[33]

2. One of ordinary skill in the art can readily determine whether an accused glycoprotein product was obtained from a natural or non-natural source.

Roche, quoting this Court's opinion in *Amgen I*, states the correct standard of law for determining whether a claim term is definite:

> Determining 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.[34]

In order for ordinarily skilled artisans to assess whether their EPO preparation falls inside the bounds of this claim language (and whether their product might thereby infringe), they need only ask themselves, "where did this product come from?" If the material was obtained from a source that naturally contains EPO without human intervention, it is outside the bounds of the claim. If not, it will be within the scope of the claim if all other limitations are met.

In either case, no further inquiry as to the "non-naturally occurring" limitation need be made. It is difficult to imagine how this task, which requires only an alleged infringer's

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[31] *Amgen I*, 126 F. Supp. 2d at 91.

[32] *Id*.

[33] *Amgen II*, 314 F.3d at 1329.

knowledge of where he obtained his product, can reasonably be said to be anything other than trivial for a person of ordinary skill in the art.

3. Roche's arguments about distinguishing the prior art are both irrelevant and unsupported.

Because it cannot win at invalidating as indefinite the straightforward language of the asserted claims, Roche attempts to confuse by raising unrelated issues that are legally irrelevant and factually misleading. Chief among these is Roche's reliance on arguments related to the requirement of 35 U.S.C. § 102 that a patented invention be novel in light of the prior art.[35]

Roche contends that "'non-naturally occurring' must reflect a physical distinction over the prior art."[36] Elsewhere, it argues that "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 . . . ,"[37] citing a footnote from the Federal Circuit's *Amgen II* opinion noting 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.[38] Each of these statements is both irrelevant and misleading.

They are irrelevant because § 112 ¶ 2 imposes no such requirement; all that is required for a claim limitation to be definite is that it "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

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[34] *Amgen I*, 126 F. Supp. 2d at 156 (citation omitted).

[35] *See* Roche's Brief at 1-3, 7-8, 15-16.

[36] Roche's Brief at 16.

[37] Roche's Brief at 9.

the patent owner, can determine whether or not they infringe."[39] As discussed above, "non-naturally occurring," the only claim limitation Roche has accused as being indefinite, readily gives notice to the public that the '933 Patent's protection extends only to products containing erythropoietin obtained from a source that does not occur in nature.

Roche's statements are also misleading in that they imply that the "non-naturally occurring" limitation alone must physically distinguish the claimed invention from prior art EPO, and that such structural differentiation was the reason for the limitation's insertion. This implication is wrong on several counts. First, the novelty requirement of § 102 applies to claims as whole, not to individual limitations.[40] Taken as a whole, Claim 3 and its dependent claims are readily distinguishable over the prior art. Claim 3 recites:

> 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 reticulocytes and red blood cells.

Certainly, none of the prior art references raised by Roche to date teach such a product made by such a process.

Moreover, the record is replete with evidence that EPO glycoproteins produced according to '933 claim 3 and its dependent claims are structurally distinct from prior art EPOs, even if the process by which the EPOs are made is discounted.[41] As Dr. Goldwasser testified at length at

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[38] *Amgen II*, 314 F.3d at 1354 n.20.

[39] *Default Proof Credit Card System, Inc. v. Home Depo U.S.A., Inc.*, 412 F.3d 1291, 1302-03 (Fed. Cir. 2005).

[40] *See e.g.*, *Hakim v. Cannon Advent Group, PLC*, 479 F.3d 1313, 1319 (Fed. Cir. 2007) (a claim is anticipated when "all of the elements and limitations of the claim are described in a single prior art reference") (citation omitted).

[41] Amgen has provided extensive evidence of the differences between its claimed products and the prior art in, among others, the Expert Report of Dr. Ajit Varki. Because this evidence is

deposition in this matter, experiments reported in a paper published in 1997[42] demonstrate numerous other differences between recombinant and urinary erythropoietin. These differences, including specific activity,[43] accessibility to iodination,[44] inactivation by iodination,[45] trypsin inactivation,[46] and circular dichroism,[47] each indicates that recombinant and urinary erythropoietin differ conformationally, i.e., in the way the molecules of each are folded, a structural difference.[48] All of these differences, as well as differences in glycosylation, are the direct consequence of the process of production recited in 933 claim 1 and distinguish the claimed invention from prior art naturally-occurring urinary EPO.[49]

Roche's motion also fails because its assertion that the "non-naturally occurring"

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irrelevant to the proper legal analysis of Roche's motion, Amgen will not burden the Court by providing it in declaration form at this time.

[42] Ex. 2, 2/26/07 Goldwasser Tr. at 468:10-469:8; Ex. 3, C. Kung and E. Goldwasser, "A Probable Conformational Difference Between Recombinant and Urinary Erythropoietins," *Proteins: Structure, Function, and Genetics*, 28(1):94-98 (1997).

[43] Ex. 2, 2/26/07 Goldwasser Tr. at 461:8-464:6; *see also* Miyake et al., "Purification of Human Erythropoietin," *J. Biol. Chem.*, 252(15):5558-5564 (1977) (Docket No. 502, Ex. E-4) at 5563 (reporting specific activity for urinary EPO of 70,400 unites/mg of protein).

[44] Ex. 2, 2/26/07 Goldwasser Tr. at 471:19-473:8.

[45] *Id*. at 474:1-475:13.

[46] *Id.* at 475:15-476:16.

[47] *Id.* at 476:21-478:18.

[48] *Id.* at 463:12-464:6.

[49] Because all of the other asserted '933 claims depend from '933 Claim 3, they are also distinct from the prior art for this reason. Additionally, each of the six asserted dependent claims also contains at least one ***further*** limitation that distinguishes what is claimed from the prior art. Thus, even if Claim 3 were to be found to have been anticipated, Claims 7, 8, 9, 11, 12, and 14 Roche would have to prove that each is invalid separately — without reference to the "non-

limitation was inserted solely "to 'distinguish the subject matter claimed from all prior art references relating to erythropoietin isolates'" is incorrect and misleading.[50] Roche's editorial replacement of "operates to"[51] with "in order to" and omission of the previous page's discussion of the limitation having been added to "meet Section 112 specificity requirements"[52] distorts the prosecution history.

Roche also misleads by suggesting that validating the claimed invention against the prior art requires the examination of "all the hypothetically possible recombinant EPOs."[53] Just as it did for the prosecution history, Roche's selective quotation distorts the Supplemental Expert Report of Amgen's expert Dr. Ajit Varki. As the full passage Roche cites makes clear, examining all possible recombinant EPOs is not required to show that glycosylation differs between naturally-occurring and man-made EPOs:

> 27. Dr. Imperiali's statement that it has not been shown that "all recombinant EPO has glycosylation which differs from all naturally occurring EPO" sets an unrealistically high and practically impossible standard. It is not possible to test all hypothetically possible recombinant EPOs. However, all of the comparison experiments that have been performed on real recombinant EPOs that have actually been produced support my opinion that such differences do exist. Neither Dr. Bertozzi nor Dr. Imperiali has identified any data on any rEPO that contradicts my conclusions.[54]

In the context of the definiteness inquiry now before the Court, even this straightforward comparison is unnecessary. As discussed above, § 112 ¶ 2, as applied to the asserted claims,

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naturally occurring limitation — by clear and convincing evidence. And that is something Roche, in its various motions for summary judgment, has not even attempted to do.

[50] Roche's Brief at 7 (quoting '933 Prosecution History, 12/20/95 Secondary Preliminary Amendment and Remarks at 7 (Docket No. 534, Ex. 25)).

[51] '933 Prosecution History, 12/20/95 Secondary Preliminary Amendment and Remarks at 7 (Docket No. 534, Ex. 25).

[52] *Id.* at 6.

[53] Roche's Brief at 2 (citing Supplemental Expert Report of Ajit Varki, MD (Docket No. 507-9, Exhibit D at ¶ 27)).

only requires an inquiry into the source of an EPO product. By definition, the definiteness of a source limitation like "non-naturally occurring" does not depend on any physical difference in structure.

4. Roche cannot read the limitation "having glycosylation which differs from that of human urinary erythropoietin" into the limitation "non-naturally occurring."

Having not identified any legitimate basis for asserting that Claim 3 and its dependent claims are indefinite, Roche attempts to leverage the decision as to Claim 1 of the '933 Patent in the TKT/HMR litigation onto each of the claims now at issue before this Court by arguing that the limitation "having a glycosylation which differs from that of human urinary erythropoietin" must be read into the limitation "non-naturally occurring."

As discussed above, no limitation in the asserted claims requires a potential infringer to compare the glycosylation of their product to that of human urinary erythropoietin — of any variety — in order to determine whether it might infringe. Ignoring this indisputable fact, Roche supports its motion by asserting that "non-naturally occurring" is indefinite because "glycosylation which differs from that of human urinary erythropoietin" is encompassed within "non-naturally occurring."[55] But the two different limitations, appearing in the same claim, cannot be construed to mean the same thing.[56]

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[54] Supplemental Expert Report of Ajit Varki, MD (Docket No. 507-9, Exhibit D at ¶ 27).

[55] *See e.g.*, Roche's Brief at 15.

[56] *CAE Screenplates Inc. v. Heinrich Fiedler GmbH & Co. KG*, 224 F.3d 1308, 1317 (Fed. Cir. 2000) ("In the absence of any evidence to the contrary, we must presume that the use of these different terms in the claims connotes different meanings."); *Applied Med. Res. Corp. v. U.S.*

5. Amgen cannot be collaterally estopped by a prior ruling on an unrelated structural limitation of a different claim.

In order for a party to be precluded from relitigating an issue by collateral estoppel: (1) the issue sought to be precluded must be the same as that involved in the prior action; (2) the issue must have been actually litigated; (3) the issue must have been determined by a valid and binding final judgment; (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.[57]

The definiteness of the "non-naturally occurring" negative source limitation found in '933 claim 3 was not at issue in the prior HMR/TKT litigation. Rather, this Court[58] and the Federal Circuit[59] each concluded that independent Claims 1 and 2 and Claim 9, as it depended on Claims 1 and 2, were rendered indefinite because of the structural limitation "having a glycosylation which differs from that of human urinary erythropoietin." ***But this limitation is not found in any of the claims asserted in the present action***. As explained above, the issue posed by Roche is wholly irrelevant to whether '933 claim 3 and its dependent claims are invalid due to the indefiniteness. The first requirement of collateral estoppel is therefore unsatisfied.

Amgen's position here is entirely consistent with the Court's prior rulings. Indeed, it is *Roche* who now seeks to take a position inconsistent with past proceedings, having acceded during the recent *Markman* proceedings to the construction of "non-naturally occurring" given

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Surgical Corp., 448 F.3d 1324, 1333 n.3 (Fed. Cir. 2006) ("[T]he use of two terms in a claim requires that they connote different meanings. . . .").

[57] *Boston Scientific. Corp. v. Schneider (Europe) AG*, 983 F. Supp. 245, 255 (D. Mass. 1997).

[58] *Amgen I*, 126 F. Supp. 2d at 156-67.

[59] *Amgen II*, 314 F.3d at 1342.

by this Court in *Amgen I*.[60] Like the faulty substantive indefiniteness arguments upon which it is premised, Roche's collateral estoppel argument must fail.

B. BECAUSE ONE OF ORDINARY SKILL IN THE ART CAN DETERMINE FROM DR. LIN'S SPECIFICATION THAT HE ACTUALLY INVENTED A "NON-NATURALLY OCCURING" PRODUCT, THE ASSERTED '933 CLAIMS ARE ADEQUATELY DESCRIBED.

35 U.S.C. § 112 ¶ 1 requires that a patent's written description "clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."[61] Here, in order for a claim containing the limitation "non-naturally occurring" to be valid, the claim must be supported by a specification that demonstrates to the ordinarily skilled artisan that Dr. Lin actually invented the claimed erythropoietin glycoprotein obtained from a source that does not occur in nature.

In basing its written description position on the Court's § 112 ¶ 1 analysis of '933 claims 1 and 2 in the prior litigation, Roche simply repackages its indefiniteness arguments. Conspicuously, Roche makes no attempt to explain substantively why it contends the § 112 ¶ 1 written description requirement is not met for the "non-naturally occurring" source limitation by a specification that explains in great detail the methods used by the inventor to obtain, for the first time, erythropoietin from sources not occurring in nature.[62] Nor does Roche cite to any language in either *Amgen* opinion to support such a contention. Perhaps this is because, in contrast to the Court's finding in the *HMR/TKT* litigation that claims relying on a "having a

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[60] Defendant's [sic] Memorandum in Opposition to Amgen, Inc.'s Claims Construction Brief (Docket No. 322, App. B at 10).

[61] *Amgen I*, 126 F. Supp. 2d at 147 (quoting *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989)).

glycosylation which differs from that of human urinary erythropoietin" limitation were inadequately supported in the written description (a finding which is irrelevant here, where no such limitation is present), this Court has expressly upheld as valid a claim—supported by the same specification as that of the '933 Patent—which includes "non-naturally occurring."

Claim 3 of U.S. Patent No. 5,621,080 ("the '080 Patent") reads:

> 3. A non-naturally occurring erythropoietin glycoprotein having the in vivo biological activity of causing bone marrow cells to increase production of reticulocytes and red blood cells, wherein said erythropoietin glycoprotein comprises the mature erythropoietin amino acid sequence of FIG. 6.[63]

Rejecting the HMR/TKT defendants' § 112 ¶ 1 challenge to this claim, this Court found:

> Various passages of the specification describe ***all of the elements of these claims***. The very first sentence of the "Brief Summary" section explains that "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." The isolation and purification of expressed polypeptides is also referenced in the "Brief Summary" section as well as in the context of subsequent examples. In addition, Figure 6 is described extensively in the specification and Figure 6 itself provides critical information regarding the sequence of erythropoietin amino acid residues necessary for the production of claimed EPO glycoproteins. Furthermore, ***the specification contains complete and detailed descriptions of the production of isolated and non-naturally occurring human EPO glycoproteins.*** . . .[64]

The inventor, the Court held, was "required to show to those skilled in the art in 1984 that Dr. Lin, in fact, had obtained [the claimed EPO products]. His specification meets this requirement."[65] As confirmed many times by this and other Courts, before Dr. Lin's inventions, no one had obtained EPO from a non-naturally occurring source as claimed and described in the

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[62] '933 Patent at 23:1-24:38, 25:29-29:7 (Docket No. 534, Ex. 3).

[63] U.S. Patent No. 5,621,080, Cl. 3 (Docket No. 313, Ex. D).

[64] *Amgen I*, 126 F. Supp. 2d at 151 (citing '080 Patent at 10:9-15, 10:34-40, 10:50-60, 32:3-19,23:1-24:38, 25:29-29:7, 33:22-30).

'933 Patent and its relatives; all EPO up to that time had been obtained from natural sources such as urine.[66] Dr. Lin opened the floodgates for the production of large quantities of therapeutically useful non-naturally occurring human erythropoietin.

By contrast, as Roche points out, the Court held that the then-asserted Claims 1, 2, and 9 (as it depends on Claims 1 and 2) of the '933 Patent were invalid under § 112 ¶ 1.[67] What Roche fails to mention, however, is that the Court's holding was not based on the "non-naturally occurring" source limitation, which the Court, again pointing to Examples 7 and 10 of the specification, found ***was*** properly supported by the written description ("Dr. Lin disclosed a complete and detailed explanation of the production of non-naturally occurring human erythropoietin glycoproteins").[68] Rather, the Court held,

> ***Despite these findings*** [that 'non-naturally occurring' and other claim limitations were supported by the specification] favorable to Amgen, TKT persuades the Court by clear and convincing evidence that Dr. Lin's disclosure fails adequately to describe an EPO glycoprotein whose glycosylation differs from that of human urinary erythropoietin, and that this failure is fatal to all three of its asserted '933 Claims.[69]

In other words, the sole § 112 ¶ 1 defect in Claims 1, 2, and 9 of the '933 Patent was the phrase "having a glycosylation which differs from that of human urinary erythropoietin," a limitation

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[65] *Amgen I*, 126 F. Supp. 2d at 152.

[66] *See Amgen, Inc. v. Chugai Pharm.Co., Ltd.*, 927 F.2d 1200, 1203 (Fed. Cir. 1991); *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, No. 87-2617-Y, 1989 U.S. Dist. LEXIS 16110, at *96 (D. Mass. Dec. 11, 1989); *Amgen I*, 126 F. Supp. 2d at 116.

[67] *Amgen I*, 126 F. Supp. 2d at 154-56.

[68] *Amgen I*, 126 F. Supp. 2d at 154 (citing '933 Patent at 23:1-24:38, 25:29-29:7 (Docket No. 534, Ex. 3)).

[69] *Amgen I*, 126 F. Supp. 2d at 155 (emphasis added).

which is absent from the claims asserted in this action. The Court's reasoning in *Amgen I* was clear and refutes Roche's untenable position.

IV. CONCLUSION

For the reasons set forth above, Amgen respectfully requests that the Court deny Roche's Motion for Summary Judgment That the Asserted Claims of the '933 Patent Are Invalid for Indefiniteness and Lack of Written Description its entirety. Indeed, as more fully set forth in Amgen's Motion for Summary Judgment of Validity, each of the asserted claims of the '933 Patent should be found definite and adequately described.

Respectfully Submitted,

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June 29, 2007

CERTIFICATE OF SERVICE

I hereby certify that this document, filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing and paper copies will be sent to those indicated as on-registered participants.

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