UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

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

ROCHE'S REPLY TO AMGEN'S OPPOSITION TO ROCHE'S MOTION FOR SUMMARY JUDGMENT THAT CLAIM 7 OF THE '349 PATENT IS INVALID UNDER 35 U.S.C. § 112 AND IS NOT INFRINGED

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I. PRELIMINARY STATEMENT

Defendants F. Hoffmann-La Roche, Ltd, Roche Diagnostics GmbH, and Hoffmann-La Roche Inc., (collectively "Roche") submit this reply memorandum to respond to arguments raised by Amgen, Inc. ("Amgen") in its Opposition to Roche's Motion for Summary Judgment That Claim 7 of the '349 Patent Is Invalid Under 35 U.S.C. § 112 And Is Not Infringed.[1]

For the most part, Amgen's Opposition fails to even respond to Roche's Motion. Rather than confront the factual bases put forth by Roche, Amgen's response does nothing but obfuscate those issues of material fact that are beyond reasonable dispute. Indeed, Amgen's Opposition leaves undisputed critical facts that establish Roche's position, including:

- An RIA will not only detect erythropoietin but also EPO fragments or products that are not "erythropoietin;"
- "Units" are a measure of the *in vivo* biological activity of erythropoietin ("EPO");
- Rather than "Units" or "International Units," Amgen reported its own results in an undisclosed measurement of "Amgen (arbitrary) Units";
- Vertebrate cells according to claims 1-6 can, at the same time, be "capable" and not "capable" of producing "U of erythropoietin . . . as determined by radioimmunoassay" and are therefore indefinite.

Taken as a whole, in the context of the patent specification and claims, these facts provide clear and convincing evidence supporting Roche's contention that Claim 7 of the '349 patent is invalid for lack of definiteness, adequate written description and enablement. In addition, and largely for the same reasons, Amgen has failed to meet its burden of proving that Roche practiced the process of Claim 7. In the face of such compelling evidence, the Court should grant Roche's Motion for Summary Judgment.

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[1] This memorandum makes reference to the Memorandum of Law In Support of Roche's Mot. for Summ. J. that Claim 7 of the '349 Patent Is Invalid Under 35 U.S.C. § 112 And Is Not Infringed, dated Jun. 22, 2007, Docket Number 539 ("Roche's Motion") and Amgen's Opposition to Roche's Mot. for Summ. J. That Claim 7 of the '349 Patent Is Invalid Under 35 U.S.C. § 112 And Is Not Infringed, dated Jul. 5, 2007, Docket Number 628 ("Amgen's Opposition").

II. ARGUMENT

A. An Analysis of Indefiniteness Is Inextricably Intertwined With Claim Construction, Therefore Roche's Motion For Summary Judgment Regarding Indefiniteness Is Timely

Amgen's view that Roche waived its right to raise an indefiniteness challenge because the Court has already heard claim construction arguments is both illogical and contrary to settled law. The Court's claim construction, in fact, frames the issues for an indefiniteness finding because indefiniteness "is inextricably intertwined with claim construction."[2] Countless court decisions have found a claim to be indefinite after, and in many cases, as a direct consequence of claim construction.[3]

The Court should ignore Amgen's spurious allegation that Roche's Motion is a disguised "claim construction argument" concerning critical elements of the '349 patent claims. Roche does not dispute the meaning of "U of erythropoietin . . . as determined by radioimmunoassay" and "capable." Rather, Roche simply points out that the Court's construction for the term "human erythropoietin" – ***adopting Amgen's own definition*** – renders the claim taken as a

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[2] *Atmel Corp. v. Info. Storage Devices, Inc.*, 198 F.3d 1374, 1379 (Fed. Cir. 1999); s*ee Eli Lilly & Co. v. Aradigm Corp.*, 376 F.3d 1352, 1360 (Fed. Cir. 2004) ("An inventorship analysis, like an infringement or invalidity analysis, ***begins as a first step with a construction of each asserted claim*** to determine the subject matter encompassed thereby." (quoting *Trovan, Ltd. v. Sokymat SA*, 299 F.3d 1292, 1302 (Fed. Cir. 2002) (emphasis added)); *see also ASM Am. Inc. v. Genus, Inc.*, No. C-01-2190-EDL, 2002 WL 1892200, at *15 (N.D. Cal. Aug. 15, 2002) ("The Court concludes that the Federal Circuit's statements that indefiniteness is intertwined with claim construction mean only that ***the Court must attempt to determine what a claim means before it can determine whether the claim is invalid for indefiniteness***, and not that the Court must determine indefiniteness during the claim construction proceedings.") (emphasis added).

[3] In *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 91 (D. Mass. 2001) [hereinafter *Amgen I*], this Court construed the term "glycosylation which differs from that of human urinary erythropoietin" during *Markman* in late March and early April 2000. *See id.* at 92 (citing Tr. of Markman Hr'g, Vol. III at 102:18:23). Subsequently, during trial, this Court properly held the term "glycosylation which differs from that of human urinary erythropoietin" to be invalid for indefiniteness. *Id.* at 123-29. Also, in *Atmel*, in response to the defendants motion for summary judgment that a claim was indefinite, the court ruled "that it would be more efficient to construe the claims before ruling on validity." 198 F.3d at 1376.

whole invalid.[4] Amgen's insistence on such a broad reading of this term renders the claims of the '349 patent indefinite and uninterpretable for conducting a proper infringement analysis.

Elsewhere, Amgen argues that the "erythropoietin" of the '349 patent would be comprehensible as "polypeptides of the invention," or, in other words, any one of the nearly 300 polypeptides[5] disclosed in the patent specification.[6] This reading of the term impermissibly broadens the term "human erythropoietin" to include claimed matter, such as erythropoietin analogs, to which this Court and the Federal Circuit has already held Amgen is not entitled.[7]

Recognizing its weakness on the merits, Amgen seems to suggest that Roche's willingness to consider a stipulation to avoid possible damaging disclosure of its cell lie to competitors is evidence. On the contrary, Amgen's argument contravenes the spirit behind the rules of civil litigation and forgets that Roche specifically indicated it was considering alternatives solely because Amgen wanted Roche's cell line - its "manufacturing plant." Roche's willingness to consider stipulating to something it did not know to avoid dissemination of its critical trade secret information to its adversaries and competitors is not evidence of anything other than a concern that discovery and disclosure in this case is being used for anticompetitive purposes. Certainly Amgen must be aware that any correspondence regarding

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[4] *See* DI # 613, 7/3/07 Mem. & Order, at 15. Adopting Amgen's construction, this Court has decided that "human erythropoietin," in the context of the claims of the patents-in-suit, means "a protein ***having the amino acid sequence*** of human EPO, such as ***the amino acid sequence*** of EPO isolated from human urine." (emphasis added).

[5] See DI# 485, 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, dated Jun. 11, 2007, Ex. 1 at col. 29 l. 46; Id. col. 31 l. 10; Id. col. 34 l. 56 (table); Id. col. 35 l. 28; Id. col. 35 l. 49; Id. col. 35 l. 57; Id. col. 35 l. 59; col.35 l. 63; Id. col. 36 l. 7.

[6] *See* DI # 532, Amgen Inc.'s Memorandum in Support of its Motion for Summary Judgment that Dr. Lin's Asserted Claims are Definite, Adequately Described and Enabled, dated Jun. 20, 2007, at 14-18.

[7] See *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1214 (Fed. Cir. 1991) (In invalidating Amgen's claims to EPO analogs under Section 112, the Court states that "[c]onsidering the structural complexity of the EPO gene, the manifold possibilities for change in its structure, with attendant uncertainty as to what utility will be possessed by these analogs, we consider that more is needed concerning identifying the various analogs that are within the scope of the claim, methods for making them, and structural requirements for producing compounds with EPO-like activity.") (emphasis added).

settlement negotiations of any claim in a litigation is inadmissible as evidence at trial.[8] Amgen's attempt to raise these negotiations during summary judgment is a dangerous subversion of the strong public policy favoring settlement among parties to a dispute.[9] Moreover, all such correspondence took place prior to ***any*** fact or expert discovery in this litigation, and prior to any meaningful understanding of the scope of the term "erythropoietin."[10] In fact, Amgen's futile attempt to collect any documentary or experimental evidence that would have supported the merits of the proposed stipulation illustrates the insoluble ambiguity of the claim limitations at issue.

Roche's motion for invalidity and noninfringement rests squarely on the Court's existing construction. It is both proper and timely to raise these contentions in a summary judgment motion at this point in the litigation.

B. An Extensive Corpus of Evidence Supports Roche's Motion That Claim 7 Of The '349 Patent Is Invalid And Not Infringed

In its motion, Roche has argued that claim 7 of the '349 patent is indefinite because, *inter alia*, the antibodies used in RIA cannot discriminate between "erythropoietin" and other products containing immunogenic epitopes that the antibodies will recognize, including EPO fragments. Amgen counters by asserting that Roche provided no evidence to support this

[8] *See* Fed. R. Evid. 408. ("Evidence of the following is not admissible on behalf of any party, when offered to prove liability for, invalidity of, or amount of a claim that was disputed as to validity or amount, or to impeach through a prior inconsistent statement or contradiction: (1) ...and (2) conduct or statements made in compromise negotiations regarding the claim, except when offered in a criminal case and the negotiations related to a claim by a public office or agency in the exercise of regulatory, investigative, or enforcement authority.").

[9] *See* Fed. R. Evid. 408, Advisory Committee's Notes, Jan. 2, 1975, P.L. 93-595, § 1, 88 Stat. 1933 ("As a matter of general agreement, evidence of an offer-to compromise a claim is not receivable in evidence as an admission of, as the case may be, the validity or invalidity of the claim... [A] more consistently impressive ground is promotion of the public policy favoring the compromise and settlement of disputes.").

[10] Roche first learned of Amgen's proposed claim construction on March 5, 2007 in Amgen Inc.'s Claims Construction Brief. Claim construction hearing held on April 17, 2007, and Markman order issued July 3, 2007. Hence, discovery took place months after correspondence in Amgen Ex. 29, dated February 7, 2007.

position. This is not true. Roche pointed to specific statements and testimony of Amgen's own fact and expert witnesses,[11] as well as the patent specification itself, which confirms that an RIA is not necessarily specific for "erythropoietin."[12] As this Court has stated, "[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.'"[13] Amgen cannot argue that the admissions of its own experts, who are obviously skilled in the art, do not create a factual predicate for concluding that the claim phrase "U of erythropoietin...as determined by radioimmunoassay" could not have a clear and definite meaning to one of ordinary skill in the art. This imprecision cannot be appropriate for a patent claim. While assumptions surrounding RIA measurement may be defensible for purified samples with known biological activity or samples from human serum, such rarefied conditions are not enumerated in either the patent specification or the claims of the '349 patent. In the face of such ambiguity and guesswork, this limitation must be indefinite and lack enablement, and because of these infirmities, it is impossible to determine whether Roche or anyone else practices the process of claim 7.

Amgen's experts agree that RIA does not measure only "erythropoietin" as construed by the Court in this litigation.[14] Amgen's experts therefore confirm Roche's position that an RIA does not exclusively measure "a protein having the amino acid sequence of human EPO, such as the amino acid sequence of EPO isolated from human urine" but also recognizes relevant portions of the partial protein, such as those present in EPO fragments.[15] Dr. Goldwasser confirmed this fact and also that the presence of EPO fragments leads to an overestimation of

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[11] Roche's Motion at 8-9.
[12] Roche's Motion at 9-10.
[13] *Amgen I* at 156 (quoting *Personalized Media Communications, LLC v. Int'l Trade Comm'n,* 161 F.3d 696, 705 (Fed. Cir. 1998)) (emphasis added).
[14] *See* DI # 613, 7/3/07 Mem. & Order, at 15 "Human erythropoietin: A protein having the amino acid sequence of human EPO, such as the amino acid sequence of EPO isolated from human urine."
[15] Roche Ex. J. at 220:4-20; 151:18-152-8.

EPO levels using RIA.[16] Further, the claim at issue, and claims 1-6, recite "U," or "units" which several experts testified, is a measure of *in vivo* biological activity.[17] Neither the claims nor the specification disclose an amount of EPO sufficient to meet the claims.[18]

Amgen mischaracterizes the testimony and reports of its own experts. Amgen contends that Dr. Goldwasser's opinion is grounded only in theory. This contention is not true. Dr. Goldwasser ran RIA assays over the course of many years for himself and for others. Because the proper inquiry for indefiniteness hinges on the knowledge of one skilled in the art at the time of the invention, Goldwasser's contemporaneous statements that presence of fragments can result in overestimating EPO levels made in published papers in 1981 are prime evidence of the knowledge of those skilled in the art at the time of the invention.[19] Later retractions, made while one or more the Lin patents was under the cloud of litigation in this Court, are both non-credible and irrelevant. Importantly however, even in offering a retraction, Dr. Goldwasser never discounted the possibility that he had observed fragments in his original study in 1981.[20]

Further, Dr. McLawhon did not "explicitly refuse to speculate" about whether an EPO RIA will recognize fragments. In fact, Dr. McLawhon stated that in general one would want to develop an RIA assay that recognizes "relevant portions" of the molecule.[21] Antibodies to these "relevant portions" will not necessarily recognize the entire protein and will detect fragments.[22]

Dr. McLawhon's refined commercially-available kit, and his usage of such refined materials in the past, in no way sheds light on the state of knowledge of one of skill in the art in 1983 concerning EPO RIAs. Tests for cross-reactivity in this kit were performed with ***purified***

[16] Roche Ex. E at 49-50; Roche Ex. K at AM-ITC 01006801-05; Roche Ex. L.
[17] Roche's Motion at 4.
[18] Roche Ex. B.
[19] Roche Ex. E at 49-50; Roche Ex. K at AM-ITC 01006801-05; Roche Ex. L.
[20] Amgen Ex. 9.
[21] Roche Ex. J at 220:4-20.
[22] Roche Ex. J

proteins under sterile conditions, not proteins that would be produced by the vertebrate cells of the ’349 patent claims. Amgen can not properly use evidence of an experiment conducted in 2007 as a showing of knowledge of one skilled in the art in 1983.

Lest there be no doubt that an RIA will detect non-“erythropoietin” products, the Court need only look at the data within Amgen’s working examples within the patent. For example, Example 10 purports to describe a sample of ***monkey*** erythropoietin yielding 41.2 ± 1.4 U/mg as measured by RIA.[23] The patent goes on to describe that amino acid sequencing revealed that this product actually contained “3 residues of the ‘leader’ sequence adjacent the putative amino terminal alanine.”[24] Thus, the patent demonstrates that the same RIA used to detect human erythropoietin was being used to measure a different protein: monkey erythropoietin. The inherent indefiniteness of an RIA to determine “U of erythropoietin” is further confirmed by the fact that Example 10 in fact measured something that was not even monkey erythropoietin, but an ***analog*** that possessed additional amino acid residues.

The specification is replete with other examples of the inherent indefiniteness of the ’349 patent claims. For example, the patent describes production of 150,000 to 160,000 U/mg of an alleged erythropoietin product expressed in *E. coli* as determined by RIA.[25] Upon protein sequencing, however, up to one third of the measured sample did not contain “erythropoietin” at all, but a deletion fragment that was missing the initial alanine at the N terminal end of the protein, described as “[des Ala^{1}]hEPO.”[26] The RIA nevertheless reported that “U of erythropoietin” was present while in fact the sample contained significant amounts of EPO fragments.

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[23] Roche Ex. B at col. 27, ll. 42-55
[24] *Id.*
[25] Roche Ex. B at col. 31, ll. 34-54.
[26] *Id.*

In that same example, erythropoietin analogs were also tested with RIA. One analog of erythropoietin that ***deleted several amino acids from the protein*** and had an arginine substitution at position 2 was determined to be present at 11,000 U/mg in the RIA.[27] Another analog having a histidine substitution at position 7 recorded 41,000 U/ml.[28] Therefore, Amgen's own patent reveals numerous instances where an RIA will detect analogs and deletion fragments that are not "erythropoietin" as that term has been construed. This evidence is incontrovertible, since this was Dr. Lin's description of his invention.

In fact, Amgen's citation to publications in its opposition only support the undisputed fact that the inherent limitations of an RIA allow it to measure material that is not "erythropoietin." Amgen makes reference to a Cotes, et al., 1982 paper.[29] That paper specifically indicates that:

> [b]ioassays and immunoassays respectively reflect functional and structural characteristics of erythropoietin and estimates by these two different types of system are unlikely to be identical. ***For example, precursors and degradation products of erythropoietin as*** well as the native serum hormone (which is itself almost certainly heterogeneous) ***may react in a radioimmunoassay***.[30]

Cotes et al. therefore confirms what the Lin patent discloses: that an RIA will detect precursors, such as those with the unwanted leader sequence, and will measure degradation products, such as deletion fragments.

Amgen also cites the Sherwood and Goldwasser 1979 publication.[31] That paper states quite clearly that non-erythropoietin products that have been iodinated will react with an RIA despite their loss of biological activity.

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[27] Roche Ex. B at col. 31, ll. 55-65.
[28] Id. (Measuring [His7]hEPO expression product)
[29] *See* Amgen Ex. 25.
[30] Amgen Ex. 25 at 437 (emphasis added).
[31] *See* Amgen Ex. 10.

> Intact biologic activity of epo is not necessary for its immunologic activity. Substitution of iodine on the tyrosine residues of epo by means of the Iodogen method, or on the free amino groups by the Bolton-Hunter method, results in loss of biologic activity (unpublished data); the displacement curves found with these two differently labeled epo preparations, however, are parallel and show essentially identical 50% displacement points.
>
> Similarly, removal of sialic acid residues does not alter the immunoreactivity of epo. This was shown by Garcia and by our finding that the displacement curve for asialoepo is parallel to that found for the native hormone.[32]

Amgen also makes reference to a Garcia *et al*., 1979 paper.[33] However, that paper states unequivocally that non-intact erythropoietin that has been desialated reacts identically with an RIA than native erythropoietin.

> We have also noted that desialated erythropoietin reacts with anti-erythropoietin with the same avidity as does intact erythropoietin. This observation was also true in an earlier radioimmunoassay attempt. [2][34]

Later, the article concludes that certain high level RIA measurements were due to non-erythropoietin products and contaminants. It states:

> The high value seen in the serum from anephric patients were probably due to certain non-erythropoietin materials which exist in high concentration and to the presence of similarly labeled contaminants which had not been removed by the procedure employed.[35]

Thus, the evidence is overwhelming and categorical. As Roche pointed out in its moving papers, Amgen's own experts admitted that an RIA will detect non-erythropoietin materials, such as fragments. This is further demonstrated by data within the Lin patents themselves, as well as scientific publications that Amgen itself has cited. Viewing the evidence in a light

[32] Amgen Ex. 10 at 892 (Fig. 6).
[33] *See* Amgen Ex. 24.
[34] Amgen Ex. 24 at 411.
[35] Amgen Ex. 24 at 414.

favorable to Amgen still leads to the inevitable conclusion that an RIA cannot determine only "erythropoietin." As a result, claim 7 of the '349 patent should be held invalid for lack of definiteness and enablement.

C. Amgen Has Not Nor Cannot Dispute That Units Of Erythropoietin Are A Measure of In Vivo Biological Activity

Amgen believes that one of ordinary skill in 1983 would have understood that "U of erythropoietin" as determined by RIA refers to an "amount" of EPO. This position is entirely at odds with the record developed thus far. It was widely known in the art that "U" was a measure of *in vivo* biological activity that RIA could not measure.[36] Amgen's experts agree that "Units of erythropoietin" is a measure of *in vivo* biological activity.[37] Amgen's own documents further support this fact. [38] Further, Amgen and Roche experts agree that RIA cannot measure *in vivo* biological activity.[39] Hence, there is simply no dispute that RIA alone cannot determine "U of erythropoietin" as required by the claims of the '349 patent.

D. None Of The References Cited By Amgen Contradict The Indisputable Facts That Warrant A Judgment That Claim 7 Is Invalid

Amgen's citations to scientific publications do not raise credible issues of material fact that contradict the assertions set forth in Roche's Motion. In fact, as discussed above, these same references actually support Roche's position. Moreover, whether the claims are valid depends on the perception of one skilled in the art at the time of the invention such as several of

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[36] *See* Roche Ex. P at 99 ("The International Unit for Erythropoietin, Human, Urinary, for Bioassay was defined as the activity contained in 0.50 mg of the second International Reference Preparation.").

[37] Roche Ex. G ¶ 49. In addition, according to Dr. McLawhon, the RIA "says nothing about the biological activity directly." Roche Ex. J at 133:24-25. The claim requires measurement of "U," which both at the time of the invention and today is universally understood to be a measure of biological activity. Roche Ex. E at 50:20-51:21, 52:7-16, 52:20-54:1, 56:1-6; Roche Ex. F at ¶ 75,

[38] Roche Ex. M, AM ITC 00156691 ("RIA is a quantitative measure of native protein structure but not a direct measure of its in vivo potency.")

[39] Roche Motion at 10-11 (citing Roche Ex. E at 50:20-51:21, 52:7-16, 52:20-54:1, 56:1-6; Roche Ex. F at ¶ 75, Roche Ex. J at 133:24-25).

Amgen's fact and expert witnesses.[40] As summarized below, and as set forth in Roche's Memorandum, evidence from these witnesses and Amgen's own documents buttress Roche's conclusion that claim 7 is invalid.

Amgen's documents firmly establish that different standards can give different results in the same assay, even for a ***known*** sample.[41] Amgen's documents further confirm that Amgen didn't believe the standards in place at the time of the invention to be adequate.[42] Amgen fact witness, Dr. Egrie, confirmed that at the time of the invention the international community had not yet assigned a standard specifically for RIAs.[43] Dr. Goldwasser confirmed that there was never a single standard used in RIA testing.[44] Moreover, though there were a variety of EPO standards that could be used in RIA testing, each would produce a different result.[45]

Underscoring the indefiniteness of the state of art at the time, years after the patent's filing date, Amgen confirmed that, unlike those of skill in the art, it had not been reporting its results in International Units because no correlation with its internal "arbitrary (Amgen) units" existed.[46] It should be noted that even here Amgen calls it Units, those of <u>specific activity</u>,

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[40] In order to satisfy the written description 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." The test for enablement is whether one reasonably skilled in the art could make or use the invention based on the written disclosures of the patent coupled with information known in the art, without undue experimentation. *Enzo Biochem Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1371 (Fed. Cir. 1999). 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. Int'l Trade Comm'n*, 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.

[41] Roche Ex. CC at AM-ITC 00550986.

[42] Roche Ex. O at AM-ITC 00558662; Roche Ex. Q at UCH000005950-51, Roche Ex. I at 54-57.

[43] Roche Ex. I at 182-83.

[44] Roche Ex. E at 53.

[45] Roche Motion at 12.

[46] Ex. T. at AM-ITC 00558618 ("[Amgen] should be absolutely fastidious in reporting specific activity in arbitrary (Amgen) units until we can establish an excellent correlation with international units. I do not believe such correlation exists today . . . I think we have also been careless with respect to what is

contrary to its current argument. Amgen's witness, Dr. Egrie, further establish the uncertainty of standards to be used as Amgen relied upon different EPO standards for its assays.[47]

Amgen attempts to deflect these unassailable facts by citing certain cases for the unremarkable proposition that "patent documents need not include subject matter that is known in the field of the invention and is in the prior art."[48] However, Amgen's reasoning is misplaced because, as demonstrated in Roche's moving brief, the prior art at the time contained numerous standards, each yielding different RIA results. Moreover, Amgen's reliance on the prior art is based on a misreading of the case law. Regarding the proposition that the specification need not disclose what is already known in the art,. the Federal Circuit has explained:

> However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.[49]

Here, Amgen's lack of disclosing any erythropoietin standard for its RIA invention cannot be considered an "omission of minor details," since claim 7 of the '349 would be meaningless and indefinite without this information. Accordingly, Amgen's claim should be held invalid for indefiniteness and lack of enablement.

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the precision or uncertainty (accuracy) of our data . . . I think we should understand how any standard can deviate from 'parallelism' trying to relate to international units."). Apparently, Amgen did not rely on the International Units that it now asserts were the norm at the time.

[47] Roche Ex. I at 45:18-25, 134:9-11; 170:17-171:20; 183:20-184:3; 184:14-185:2.

[48] Amgen Opposition at 15, quoting *S3 Inc. v. nVIDIA Corp.*, 259 F.3d 1364, 1371 (Fed. Cir. 2001).

[49] *Genentech v. Novo Nordisk, A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997).

E. Claim 7 of the '349 Patent Is Rendered Invalid by the Term "Capable"

Roche has argued in its moving papers that claim 7 is invalid because the clause "capable of" (or "capable upon") in the context of the claim is indefinite.[50] As stated in Roche's moving brief, those of skill in the art would not know whether they were infringing this claim because it does not specific an actual product level, but only requires that the cells be "capable" of making a certain amount.[51] This is further exacerbated by the fact that the claim does not specify what nutrient conditions be used to grow the cells. Thus, a skilled worker could produce 75 units of erythropoietin under one set of conditions, but still would not know whether this infringed claim 7 of the '349 patent because under a completely different set of conditions, these same cells could be "capable" of producing 100 units, and thus potentially fall within the production ranges set forth in claim 7.

Amgen sidesteps this obvious flaw within its claim by suggesting to the Court that it should simply read out the "capable of" language. Amgen argues that "[t]here is simply no basis for concluding that a potential infringer would be incapable of using a radioimmunoassay to determine whether, under the conditions used in his process for making EPO, the cells used in that process were producing the amounts of EPO recited in the '349 patent."[52] However, Amgen specifically chose to claim its invention with the "capable of" limitation in order to expand its claim scope. It cannot now simply pretend that this language be ignored when the breadth of the claims is not being challenged under Section 112.[53]

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[50] Roche's Motion at 14-17.
[51] Roche Ex. U. at ¶¶ 46-50.
[52] Amgen Opposition at 12-13.
[53] *See Freedman Seating Co. v. American Seating Co.*, 420 F.3d 1350, 1358 (Fed. Cir. 2005) (each element contained in a patent claim is deemed material in defining its claim).

Moreover, Amgen further responds by asserting that the limitation "capable" in the vertebrate cell inventions of claims 1-6 is interpretable in light of the process of claim 7.[54] However, this does not relieve the inherent indefiniteness of claims 1-6 because claim 7 merely recites the process of using those vertebrate cells. Furthermore, by relying upon claim 7 to make the former claims more definite, Amgen therefore admits that one skilled in the art cannot interpret ***independent*** claims 1-6 without guidance from the recitation in ***dependent*** claim 7 of the limitation "growing, under suitable nutrient conditions."[55] According to Amgen's views, claim 7 does not further limit any one of the independent claims from which it depends. This is a clear violation of proper claim dependency as required by 35 U.S.C. 112 ¶ 4 .[56] Therefore, either claims 1-6 are invalid for indefiniteness under paragraph 2 as alleged by Roche, or claim 7 is invalid for improper dependent form under paragraph 4. Roche's motion should therefore be granted.

F. Amgen Ignores Critical Details Concerning Its Proffered "Evidence" Concerning Infringement, And As A Result, Has Failed To Meet Its Burden Of Proof

Amgen incorrectly states that it is Roche's burden of proving non-infringement. "Summary judgment of noninfringement is appropriate where the patent owner's proof is deficient in meeting an essential part of the legal standard for infringement since such failure will render all other facts immaterial."[57] The legal standard for infringement mandates that a

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[54] Amgen Opposition at 2-3.

[55] Amgen Opposition at 12.

[56] *See Pfizer, Inc. v. Ranbaxy Labs. Ltd.*, 457 F.3d 1284, 1292 (Fed. Cir. 2006) (A dependent claim must incorporate by reference all the limitations of the claim to which it refers and then also specify a further limitation of the subject matter claimed); *See also, AK Steel Corp., vs. Sollac, et al.,* 344 F.3d 1234, 1242 (Fed Cir. 2003) (A dependent claim is presumed to be narrower in scope than the independent claim from which it depends under the doctrine of claim differentiation.)

[57] See *Telemac Cellular Corp. v. Topp Telecom, Inc.*, 247 F.3d 1316 , 1323 (Fed. Cir. 2001); *Novartis Corp. v. Ben Venue Labs., Inc.*, 271 F.3d 1043, 1046 (Fed. Cir. 2001) ("..the ultimate burden of proving infringement rests with the patentee, an accused infringer seeking summary judgment of non-infringement may meet its initial responsibility either by providing evidence that would preclude a

patent owner prove "...that every limitation of the patent claims asserted to be infringed is found in the accused [product], either literally or by an equivalent."[58]

Amgen additionally alleges that Roche failed to offer any evidence in support of its argument that Amgen did not test the nutrient conditions used by Roche. This is entirely untrue. Roche specifically cited to Dr. Kolodner's expert report where he admits that he "***attempted to recreate*** [Roche's] Medium," but ultimately failed.[59] Dr. Kolodner confirmed this in his deposition testifying that he used "media that was as close as possible to the media that was described in the Roche technical documents," but not the same.[60] For example, Dr. Kolodner testified as to the following differences between the media he used and Roche's media:

- Differences "in the concentration of sodium chloride, pyridoxal -- vitamin B -- thymidine and hypoxanthine."[61]
- "…There are several differences. So, for example, our medium has thymidine in it, and the Roche medium does not. Our medium has slightly more phenol red, as an example. Our medium has hypoxanthine in it. And I'm trying to find the sodium chloride. . . . So our media has slightly more sodium chloride in it, for example."[62]

As the evidence in Roche's memorandum demonstrates, Amgen can not meet its burden of showing that every limitation is found in Roche's product. Because Amgen's proof has been

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finding of infringement, or by showing that the evidence on file fails to establish a material issue of fact essential to the patentee's case.").

[58] *Smithkline Diagnostics, Inc. v. Helena Laboratories Corp.*, 859 F.2d 878, 889 (Fed. Cir. 1988)

[59] Roche's Motion at 19, citing Ex. BB at ¶¶ 12-13 (emphasis added).

[60] *See* Ex. EE to the accompanying Declaration of Howard S. Suh, in support of Roche's Reply To Amgen's Opposition To Roche's Motion For Summary Judgment That Claim 7 Of The '349 Patent Is Invalid Under 35 U.S.C. § 112 And Is Not Infringed, at 31:4-15.

[61] Ex. EE at 35:14-36:3.

[62] Ex. EE at 70:19-71:20.

"deficient in meeting an essential part of the legal standard for infringement," summary judgment of non-infringement of claim 7 is appropriate.

III. CONCLUSION

For the all reasons set forth above and in Roche's Motion, no genuine issue of material fact exists, and therefore the Court should grant Roche's Motion (D.I. No. 539) that claim 7 of the '349 patent is invalid and is not infringed.[63]

[63] Roche respectfully requests that the Court also deny that portion of Amgen's Motion For Summary Judgment That The Lin Patents Are Definite, Adequately Described and Enabled, dated July 5, 2007 (DI #630) that reiterate the issues raised herein.

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Boston, Massachusetts

Respectfully submitted,

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I hereby certify that a redacted version of this document was filed through the ECF system and was sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF) and paper copies were sent to those indicated as non registered participants on the above date.

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