IN THE UNITED STATES DISTRICT COURT
FOR THE 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 12237 WGY

U.S. District Judge William G. Young

ORAL ARGUMENT REQUESTED

MEMORANDUM IN SUPPORT OF DEFENDANTS' MOTION FOR SUMMARY JUDGMENT THAT AMGEN IS ESTOPPED FROM ASSERTING INFRINGEMENT UNDER THE DOCTRINE OF EQUIVALENTS OF THE ASSERTED CLAIMS OF THE '933 AND '422 PATENTS

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Dated: July 3, 2007

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STATUTES

35 U.S.C. § 112 6

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 Amgen is estopped from asserting infringement of claims 3, 7-9, 11-12 and 14 of U.S. Patent No. 5,547,933 (the '933 patent) and claim 1 of U.S. Patent No. 5,955,422 (the '422 patent) under the doctrine of equivalents.

I. INTRODUCTION

As shown below, the '933 patent, which claims non-naturally occurring glycoproteins made using "a DNA sequence encoding human erythropoietin" issued after narrowing amendments made in response to rejections of claims which encompassed erythropoietin fragments, analogs and synthetic polypeptides. Having narrowed the claims specifically to overcome those rejections, Amgen should be estopped from arguing that the term "DNA sequence encoding human erythropoietin" is entitled to encompass such molecules under the doctrine of equivalents. Thus, Amgen is limited to claiming human EPO and is estopped from arguing that the product of the asserted claims can be anything other than human EPO.

Furthermore, in order to overcome cited prior art, the applicant rewrote the '933 claims in a product by a process format, requiring that the claimed glycoprotein product be "of the expression in a mammalian host cell of an exogenous DNA sequence," and emphasized that the claimed product was defined by the process for production. In that Amgen narrowed its claims by introducing the phrase "product of the expression", Amgen should be estopped, under *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722 (2002), from any molecules that do not have the structure and function of the direct product of the expression of an exogenous DNA sequence, under the doctrine of equivalents.

As shown below, the applicant for the '422 patent added the claim element "wherein said erythropoietin is purified from mammalian cells grown in culture" for the specific purpose of narrowing the scope of the claim to a particular source.[1] In amending the claim which issued as claim 1, Amgen expressly stated that the phrase limited the source of the EPO and was intended to "include any EPO produced by mammalian cells (human, CHO, COS etc.) that are grown in culture, which means in vitro." Having narrowed the claims to limit the source of the claimed EPO, Amgen should be foreclosed under *Festo*, from asserting that the term "wherein said erythropoietin is purified from mammalian cells grown in culture" is satisfied under the doctrine of equivalents.[2]

II. STATEMENT OF FACTS

A. The Asserted Claims Of The '933 Patent

Amgen alleges that Roche infringes claims 3, 7-9, 11-12 and 14 of the '933 patent.

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

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[1] Roche does not agree that the source language in the '422 patent claim 1, "wherein said erythropoietin is purified from mammalian cells grown in culture," imparts structural or functional limits on the human erythropoietin element recited earlier in the claim. There is nothing in the intrinsic evidence to suggest to a person of skill in the art that such language would put limits on the structures, or what the limited class of structures might be. This, however, is all old ground that the Court has already addressed, and Amgen should be precluded from re-arguing to the contrary. This Court, applying the guidance it received from the Federal Circuit, has already rejected Amgen's argument that claim 1 of the '422 patent is structurally limited by the source. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 339 F. Supp. 2d 202, 317 (D. Mass 2004).

[2] Roche makes this motion based on its current understanding of the Court's claim construction and Amgen's contentions as to the meaning of the asserted claims. In addition, Amgen has failed to articulate its position regarding doctrine of equivalents in any meaningful way. Roche therefore reserves the right to ask that Amgen be foreclosed from relying on the doctrine of equivalents as to other terms if Amgen clarifies its positions or in response to changes in claim construction.

> 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.

(Ex. 18, '933 patent col. 38, ll. 26-31).[3]

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 purport to 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.

Id. at col. 38, ll. 64-67.

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.

Id. at col. 39, ll. 1-4, 12-13.

Claim 14 is a method of treatment claim which depends from claim 12:

[3] All Exhibits cited herein are attached to the Declaration of Keith E. Toms in Support of Defendants' Motion For Summary Judgment That Amgen Is Estopped From Asserting Infringement Under The Doctrine Of Equivalents Of The Asserted Claims Of The '933 And '422 Patents.

> 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.

Id. at col. 40, ll. 7-11.

B. Relevant Prosecution History Of The '933 Patent

The application for the '933 patent Ser. No. 487,774 (the '774 application), filed June 7, 1995, was a continuation of Serial Nos. 202,874, (the '874 application) and 113,178 (the '178 application).

During prosecution of the applications that led to the '933 patent, the applicant first sought claims to:

> 1. A purified and isolated polypeptide *having part or all of the primary structural conformation* and one or more of the biological properties *of naturally-occurring erythropoietin* and characterized by being the product of procaryotic or eukaryotic expression of an exogenous DNA sequence.
>
> 7. A polypeptide according to claim 1 possessing *part or all of the primary structural conformation of human erythropoietin as set forth in Table VI [Figure 6] or any naturally occurring allelic variant thereof*.
>
> 41. A glycoprotein product having a *primary structural conformation sufficiently duplicative of that of a naturally-occurring 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 human erythropoietin.
>
> 48. A *synthetic polypeptide having part or all of the amino acid sequence set forth in Figure 6*, other than a sequence of residues entirely within the sequence numbered 1 through 20, and having a biological property of naturally-occurring human erythropoietin.

(Ex. 1, '178 application file history, application claims at 97, 101, 102 (emphasis added)).

The examiner rejected these claims as indefinite and not enabled, stating:

> The terms "part or all of" [and] "sufficiently duplicative of" . . . do not particularly nor adequately point out the distinctions from

> native erythropoietin (EPO) . . . [T]he "parts" of EPO which are contemplated and supported by the disclosure (in terms of amino acid sequence) . . . should be pointed out.
>
> * * *
>
> The claims must particularly point out the essential aspects of the disclosed invention. The broadest limitations must also be supported by the disclosure. As currently set forth, the claims are indefinite and to an extent, non-enabled.

(Ex. 5, '178 application file history, Paper 4, 6/2/86 Office Action at 3-5). The examiner further stated:

> *Claims to "synthetic polypeptides" are not enabled by this disclosure*. "Synthetic," as opposed to "recombinant," is an art recognized term which indicates a chemically derived rather than genetically engineered protein. *No support for chemical synthesis of EPO or EPO fragments is shown by this disclosure.*

Id. at 5 (emphasis added).

In addition, the examiner rejected application claims 1, 7 and 49 in view of prior art. The examiner stated that the prior art showed production of "human EPO in substantially purified form having EPO activity" which was "inherently identical to the claimed EPO." (*Id.* at 6).

In response, the applicant canceled claims 1, 7 and 48 (as well as other claims). (Ex. 6, '178 application file history, Paper 6, 12/1/88 Amendment and Reply at 3). The applicant also amended claim 41 to read:

> A glycoprotein having a primary structural conformation and glycosylation ***sufficiently duplicative of that of a naturally occurring human erythropoietin*** to allow possession of the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells and having an average carbohydrate composition which differs from that of naturally occurring human erythropoietin.

Id.

After failing to overcome the examiner's §112 rejection (Ex. 7, '178 application file history, Paper 9, 2/10/89 Office Action), the applicant canceled claim 41 without prejudice, and submitted new claim 67:

> A glycoprotein product of the expression of an exogenous DNA sequence in a eucaryotic host cell, said product *having a primary structural conformation* and glycosylation *sufficiently duplicative of that of a naturally occurring human erythropoietin* to allow possession of the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells and having an average carbohydrate composition which differs from that of naturally occurring human erythropoietin.

(Ex. 2, '178 application file history, Paper 11, 6/2/89 Amendment at 1 (emphasis added)). The applicant explained that "[a]ll product claims in the subject application are now product-by-process claims. . . . These product-by-process claims are presented . . . to further define the product of the subject invention since the recombinant erythropoietin *claimed cannot be precisely defined except by the process by which it is produced.*" (*Id.* at 3).

The examiner nevertheless maintained his rejection under §112 as to the use of the term "sufficiently duplicative" of human erythropoietin:

> *Claim 67 to 75 are rejected under 35 U.S.C. 112, first and second paragraphs. . . .* The claim as presented remain deficient under 35 USC 112 first and second paragraphs. The following modifications are suggested to overcome this rejection.
>
> 1. In claim 67, line 3, the phrase "a primary structural conformation" should be changed to "a primary structure *and* conformation . . . ." *This modification makes it clear that the recombinant protein possess the primary structure (e.g. the amino acid sequence of naturally occurring human EPO)* and the tertiary or spatial conformation of human EPO to the extent that the recombinant EPO retains the biological activity of the human EPO in vivo.
>
> 2. The claim must be limited to recombinant *human* erythropoietin. *As presented, a non human analog which possesses enough similarity to native human erythropoietin is encompassed by the*

> *claims. This breadth is not supported by the disclosure.* Applicant may recite that the exogenous DNA sequence codes for human erythropoietin.

(Ex. 3, '178 application file history, Paper 13, 6/14/89 Office Action at 3).

The applicant ultimately canceled claim 67 in favor of application claim 76 which did not include the "sufficiently duplicative" language:

> A non-naturally occurring glycoprotein product of the expression in a non-human eucaryotic host cell of an exogenous DNA sequence consisting essentially of *a DNA sequence encoding human erythropoietin* said product possessing the in vivo biological property of causing human bone marrow cells to increase production of reticulocytes and red blood cells and having an average carbohydrate composition which differs from that of naturally occurring human erythropoietin.

(Ex. 4, '178 application file history, Paper 19, 1/10/90 Amendment at 1 (emphasis added)). The applicant stated that new claims 76-83 were "similar" to the cancelled claims, but "specify that the DNA sequences encode human erythropoietin." (*Id.* at 5). The applicant also noted that application claim 76 was drafted to parallel claim 2 of the '008 patent which claimed: "A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin." (*Id.* at 6). Claim 2 of the '008 patent that had been held valid in *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd*, No. 87-2617-Y, 1989 U.S. Dist. LEXIS 16110 (D. Mass. Dec. 11, 1989). (*Id.* at *250).[4]

[4] *Chugai* held issued claim 7 of the '008 patent (and its dependent claims) invalid under §112 for lack of enablement. *Chugai*, 1989 U.S. Dist. LEXIS 16110, at 164. Claim 7 of the '008 reads:

> A purified and isolated DNA sequence consisting essentially of a DNA sequence *encoding a polypeptide having an amino acid sequence sufficiently duplicative of that of erythropoietin* to allow possession of the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells, and to increase hemoglobin synthesis or iron uptake.

(continued...)

Application claim 76 was eventually cancelled (Ex. 14, '874 application file history, Paper 37, 6/13/94 Preliminary Amendment). The applicant added claims which described a biologically active human erythropoietin glycoprotein product produced by "mammalian host cells." The examiner rejected the claims, saying that "it is not evident that the process of production defined the product." (Ex. 15, '874 application file history, Paper 38, 8/16/94 Office Action at 9). In response, the applicant argued that "it is in fact 'evident that the process of production defines the product.'" (Ex. 16, '874 application file history, Paper 42, 2/16/95 Amendment and Request for Reconsideration at 11).

The claim which issued as claim 3 of the '933 patent was added to the '774 application in a Second Preliminary Amendment, dated December 20, 1995. (Ex. 13, '774 application file history, 6/20/95 Second Preliminary Amendment and Remarks)

Thus, the applicant chose to prosecute the '933 patent application to issuance without the rejected limitations "having part or all of the primary structural conformation . . . of naturally-occurring erythropoietin," "encoding a polypeptide having an amino acid sequence sufficiently duplicative of erythropoietin," and "a synthetic polypeptide having part or all of the amino acid

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(Ex. 17, '008 patent, claim 7 (emphasis added)). The court found that the "sufficiently duplicative" language—which encompasses (1) "the sequence of erythropoietin or . . . very close to it," (2) "naturally occurring allelic forms of mature EPO," (3) "analogs [having] replacements, substitutions and deletions of the amino acids described in the patent" and (4) "synthetic EPO polypeptides containing portions of the EPO molecule"—did not comply with §112. *Chugai*, 1989 U.S. Dist. LEXIS 16110, at 152-164. Citing the "lack of predictability in the art," the court noted that "the patent specification is insufficient to enable one of ordinary skill in the art to make and use the invention claimed in claim 7 . . . without undue experimentation." *Id.* at 164. The Federal Circuit affirmed the invalidity of claim 7 of the '008 under § 112 reasoning "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. It is not sufficient, having made the gene and a handful of analogs whose activity has not been clearly ascertained, to claim all possible genetic sequences that have EPO-like activity." *Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd*, 927 F.2d 1200, 1214 (Fed. Cir. 1991).

sequence set forth in Figure 6." (Ex. 18, '933 patent). Specifically, Amgen limited the '933 claims to *human erythropoietin* in accordance with the examiner's determination that broader claims were not supported by the disclosure.

The '933 patent discloses "human erythropoietin" as a 166 amino acid sequence. The patent disclosure specifically explains to one of skill in the art that the sequence of "FIG. 6 thus serves to identify the primary structural conformation (amino acid sequence) of mature human EPO as including 166 specified amino acid residues (estimated M.W. = 18,399)." (Ex. 19, '422 patent, col. 20:66-21:2; *see also id.* Fig. 9 & col. 19:28-36, 21:2-5, 35:4-11).

Amgen has further admitted to this Court in prior litigation that "when the written description of Amgen's specification was drafted and submitted [in 1984], the specification did not expressly recite an EPO having the 1-165 sequence." (Ex.22, Amgen's Post-Hearing Memo. at 1 (AM-ITC 00852563)). Amgen also admitted that the 165 amino acid sequence of EPO isolated from human urine would constitute "new matter" and this Court acknowledged that Lin would have been required to file a continuation-in-part application to claim the amino acid sequence. *Amgen v. Hoechst Marion Roussel, Inc.*, 287 F. Supp. 2d 126, 144 & fn.22 (D. Mass. 2003), *aff'd in relevant part*, 457 F.3d 1293 (Fed. Cir. 2006).

The '933 claims should therefore be limited to the 166 amino acid human erythropoietin disclosed by the specification and should not encompass fragments, analogs or synthetic polypeptides under the doctrine of equivalents. However, even applying the Court's construction of human erythropoietin as the 165 amino acid sequence of EPO isolated from human urine, Amgen's narrowing amendments preclude it from claiming products other than that "human EPO." Indeed, having relied on the process of making the '933 product to distinguish the cited

prior art, Amgen should be precluded from claiming under the doctrine of equivalents that the '933 claims encompass products that differ from the direct product of the claimed process.

C. The Asserted Claim Of The '422 patent

Amgen alleges that Roche infringes claim 1 of the '422 patent which provides:

> A pharmaceutical composition comprising a therapeutically effective amount of human erythropoietin and a pharmaceutically acceptable diluent, adjuvant or carrier, *wherein said erythropoietin is purified from mammalian cells grown in culture*.

(Ex. A, col. 38 ll. 36-41) (Emphasis added).

D. Relevant Prosecution History Of The '422 Patent

During the prosecution of the '422 patent, application claim 63 (a dependent claim written below in independent form) was presented by Amgen:

> An erythropoietin-containing, pharmaceutically acceptable composition] containing a therapeutically effective amount of recombinant erythropoietin.

(Ex. 11, '422 patent file history, Paper 2, 11/6/90 Preliminary Amendment at p. 9).

In rejecting this claim over the prior art the examiner cited the following disclosure in the specification:

> The present invention provides . . . isolated polypeptide products having part or all of the primary structural conformation . . . and one or more of the biological properties (e.g. immunological properties and The present invention provides . . . isolated polypeptide products having part or all of the primary structural conformation . . . and one or more of the biological properties (e.g. immunological properties and *in vivo* and *in vitro* biological activity of naturally occurring erythropoietin . . . These polypeptides are also uniquely characterized by being the product of prokaryotic or eukaryotic host expression . . . of exogenous DNA sequences obtained by genomic or cDNA cloning or by gene synthesis . . . Depending on the host employed, polypeptides of the invention may be glycosylated with mammalian or other eukaryotic carbohydrates or may be non-glycosylated.

(Ex. 12, '422 patent file history, Paper 20, 5/26/94 office action at 4). The examiner concluded:

> [I]t is apparent that the claimed erythropoietin (EPO) compositions read on any erythropoietin molecule regardless of its source. In particular, the specification indicates that glycosylated erythropoietin that exhibits the characteristic amino acid squence and biological properties of naturally occurring erythropoietin is envisioned. Therefore, the EPO recited the claims reads directly upon natural isolates and the basics of the instant rejection as explained above properly established that the claimed invention would have been *prima facie* obvious.

Id.

The examiner further found claim 63 to be indefinite in using "recombinant" on the basis that it was unclear how that limitation would "modify the physical erythropoietin composition." *Id.* at 2. The examiner "deemed unpersuasive" a declaration submitted by Dr. Richard Cummings purportedly showing that recombinant EPO and urinary EPO are structurally distinct. (Ex. 9, '422 patent file history, Paper 26, 3/31/95 Patent Office Communication; (AM-ITC 00899419)).

In the face of these continued rejections, claim 63 was cancelled and replaced with the claim that issued as '422 claim 1. Acknowledging that the phrase "wherein said erythropoietin is purified from mammalian cells grown in culture" limited the "source of the EPO," the applicant stated that the intent was to "include any EPO produced by mammalian cells (human, CHO, COS etc.) that are grown in culture, which means in vitro." (Ex. 8, '422 patent file history, Paper 33, 4/20/99 Amendment at 5).

III. ARGUMENT

A. The Summary Judgment Standard

As this Court has stated, "[i]f there are no genuine issues of material fact, summary judgment is appropriate in a patent infringement case as in any other." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 93 (D. Mass 2001). "To support a summary judgment of noninfringement it must be shown that, on the correct claim construction, no reasonable jury could have found infringement on the undisputed facts or when all reasonable factual inferences are drawn in favor of the patentee." *Techsearch LLC v. Intel Corp.*, 286 F.3d 1360, 1371 (Fed. Cir. 2002). "[A]lthough equivalence is a factual matter normally reserved for a factfinder, the trial court should grant summary judgment in any case where no reasonable fact finder could find equivalence." *Id.*

B. The Presumption Of Prosecution History Estoppel

This Court has observed, that the Supreme Court has "made clear that a 'presumption' of prosecution history estoppel arises when an amendment is made to secure the patent and the amendment narrows its scope." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 287 F.Supp. 2d 126, 131 (D. Mass. 2003) (citing *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 736 (2002)). "The inventor can overcome the 'presumption' by showing that the amendment does not surrender the particular equivalent in question." *Id.* There are three "narrow ways" of rebutting the presumption of estoppel: (i) "showing that an equivalent was unforeseeable; (ii) demonstrating that the purpose of an amendment was merely tangential to the alleged equivalent; or (iii) establishing 'some other reason' that the patentee could not have reasonably been expected to have described the alleged equivalent." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1310-11 (Fed. Cir. 2006) (*Amgen IV*); *see Cross Med.*

Prods. Inc. v. Medtronic Sofamor Danek Inc., 480 F.3d 1335, 1342 (Fed. Cir. 2007) ("[The t]angential relation criterion for overcoming the *Festo* presumption is very narrow.").

C. Roche Should Be Granted Summary Judgment That Amgen Is Estopped From Asserting Infringement Under The Doctrine Of Equivalents Of The Asserted Claims Of '933 Patent

This Court should grant Roche summary judgment estopping Amgen from asserting that the terms "DNA sequence encoding human erythropoietin" and "wherein said erythropoietin is purified from mammalian cells grown in culture" in claims 3, 7-9, 11-12 and 14 of the '933 patent are met under the doctrine of equivalents.

1. "DNA sequence encoding human erythropoietin"

The asserted claims of the '933 patent all contain, either directly (claim 3) or by dependence (claims 7-9, 11-12 and 14), the term "an exogenous DNA sequence comprising a DNA sequence encoding human erythropoietin." As shown above, during prosecution, the applicant amended the claims of the application for the '933 patent to claim only DNA encoding "human erythropoietin" for patentability purposes, surrendering coverage of erythropoietin fragments and synthetic polypeptides. Amgen should, therefore, be estopped, under *Festo*, from asserting that the claims of the '933 patent cover synthetic polypeptides, polypeptide fragments, or polypeptides containing amino acid residues not found in human EPO.

Amgen has the burden of rebutting the presumption of estoppel. Yet, polypeptides which contained only parts of the human erythropoietin amino acid sequence or which contained synthetic polypeptides were foreseeable when the claims were amended to add what became claim 3 of the '933 patent. Plainly, the applicant could have—and did—recite "parts" or "synthetic polypeptides" when they were to be within the claims. Absent a showing by Amgen to rebut the presumption, summary judgment should be awarded in Roche's favor.

2. The '933 Product Is Defined As The Product Of The Expression

As set forth above, Amgen amended the asserted claims of the ‘933 patent to overcome invalidating prior art by recasting the claims as product-by-process claims and by asserting that “the process of production defines the product.” (Ex. 16, ‘874 application file history, Paper 42, 2/16/95 Amendment and Request for Reconsideration at 11). Having thus elected to define the product of the ‘933 patent claims as “the product of . . . expression in a mammalian host cell”, Amgen should be foreclosed from maintaining that the quoted limitation is met under the doctrine of equivalents.

D. Roche Should Be Granted Summary Judgment That Amgen Is Estopped From Asserting Infringement Under The Doctrine Of Equivalents Of Claim 1 Of The ‘422 Patent

This Court should grant Roche summary judgment that the term “wherein said erythropoietin is purified from mammalian cells grown in culture” in claim 1 of the ‘422 patent is infringed under the doctrine of equivalents.

As explained above, Amgen obtained the ‘422 patent adding the source limitation “wherein said erythropoietin is purified from mammalian cells grown in culture.” Amgen made clear that the language was intended to limit the source of the EPO to mammalian cells grown in culture (in contrast with claim 2 of the ‘422 patent which has no such limitation). (Ex. 8, ‘422 patent file history, Paper 33, 4/20/99 Amendment at 5). Having opted to narrow the scope to a specific source by incorporating an express limitation requiring that the claimed product be “sourced” from mammalian cells, Amgen should be estopped from contending that products, which are not and cannot be produced from mammalian cells grown in culture, satisfy this claim element under the doctrine of equivalents.

IV. CONCLUSION

For all of the foregoing reasons, this Court should grant summary judgment in Roche's favor holding that Amgen is precluded from asserting the doctrine of equivalents with respect to claims 3, 7-9, 11-12 and 14 of the '933 patent and claim 1 of the '422 patent.

DATED: Boston, Massachusetts
July 3, 2007

Respectfully submitted,

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/s/ Keith E. Toms
Keith E. Toms