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'S OPPOSITION TO DEFENDANT'S 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

TABLE OF CONTENTS

Page No.

TABLE OF AUTHORITIES

Page No.

Cases

I. INTRODUCTION

Disregarding this Court's July 3, 2007 claim construction order, Roche incredibly argues that Lin's '933 and '422 claims should be restricted to a narrower scope of equivalents than the claims literally encompass. But nothing in the claim language or intrinsic record expressly limits the scope of Lin's asserted '933 and '422 claims as Roche would like. Consequently, Roche is forced to contrive an argument based on inferences it concocts based on amendments made during the prosecution of Lin's '933 and '422 patents. It then relies on those inferences to argue that Amgen is estopped from asserting Lin's '933 and '422 claims against peg-EPO under the doctrine of equivalents. Because Roche's accused peg-EPO literally infringes Lin's asserted '933 and '422 claims, the simple response is that any motion for summary judgment regarding the doctrine of equivalents is unripe and need not further consume the Court's limited time and attention.

The fuller answer, however, is that Roche's motion ignores the Court's claim construction. For example, the Court's July 3, 2007 Memorandum and Order emphasized that "human erythropoietin" is an open claim term, and does not preclude the attachment of additional molecules to the claimed EPO. Likewise, nothing in the claim language, specification, or prosecution history requires "human erythropoietin" to be limited to EPO having 1-166 amino acids.

Roche's contention that the history of Lin's claim amendments reflects an intent to exclude peg-EPO from the scope of equivalents to which Lin's pioneering patents are entitled is built on a distortion and mischaracterization of the progression and prosecution of Lin's '933 and '422 claims. By ignoring Lin's full set of claims in prosecution, and selectively citing snippets of Lin's prosecution history out of context, Roche asks this Court to draw inferences regarding the prosecution of Lin's claims, including the purpose and effect of various claim amendments,

that the intrinsic record simply does not support. For example, according to Roche:

> "in order to overcome cited prior art, the applicant rewrote the '933 claims in a product by 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."[1]

The truth, however, is quite different. In actual fact, the '178 application from which the '933 patent issued ***always*** included claims to "polypeptide products of the expression of a DNA sequence encoding erythropoietin."[2] Far from the misimpression Roche seeks to create, Lin did not re-write his pending claims in a product by process format to overcome the prior art. Nor did the examiner reject Lin's claims because they failed to limit his invention to the products of a particular process. Rather, he merely insisted that Lin's claims, including his "product of DNA expression" claims, point out the particular biological activity and physical properties that defined the claimed polypeptides. Each of the succeeding amendments to the claims were designed to address that concern and ultimately did so with the examiner's approval.

Ignoring the difference in claim language between Lin's '933 and '080 claims, Roche also argues that the claims of Lin's '933 and '422 patents should be restricted to EPO polypeptides having the "mature erythropoietin amino acid sequence of FIG. 6." But this Court previously found, and the Federal Circuit previously affirmed, that a 165 amino acid EPO product developed by TKT literally infringed the Lin's '422 claims, precisely because "human erythropoietin" is not limited to EPO polypeptides having 166 amino acids.

Notably, Roche fails to identify any feature of its accused peg-EPO product or the process by which it is made that falls outside the literal scope of Lin's '933 and '422 claims, thus

---

[1] Roche Motion at 1.

[2] *See* '178 application, elected claims 16 and 39: Mammen Decl. Ex. A, '933 Patent File History, paper 1, 10/23/87 '178 Application Specification (AM-ITC 00941039-41); Mammen Decl. Ex. B, '933 Patent File History, paper 2, 02/10/88 Application Under 37 C.F.R. 1.60 (AM-ITC 00941076-77).

requiring this Court's consideration of the doctrine of equivalents. The Court cannot evaluate Roche's estoppel arguments without identifying such an equivalent because the estoppel inquiry requires –on a claim-by-claim basis – a careful comparison of the differences between the accused equivalent and the literal scope of each asserted claim. Only then can the Court determine whether the claims as amended, surrendered that equivalent for reasons of patentability. For example, Roche argues that the '933 claims should be limited to 166 amino acids and then argues, based on its blind reading of the prosecution history, that the claims "should not encompass fragments, analogs or synthetic polypeptides" under the doctrine of equivalents. Not only is Roche wrong on the claim construction, but it utterly fails to identify any feature of its accused peg-EPO product that would make it a "fragment, analog or synthetic polypeptide." Roche's motion is purely hypothetical and should be denied on that basis alone.

As for its limited discussion of the prosecution history, Roche has also failed to show that the identified claim limitations were added to narrow the claims. Roche's cherry-picking of claims and amendments from the complicated prosecution histories fails to make the showing necessary to invoke the presumption of prosecution history estoppel. For all these reasons, Roche's '933/'422 *Festo* Motion should be denied.

II. FACTUAL BACKGROUND

Roche's account of the prosecution history of the '933 and '422 patents includes a number of distortions, omissions, and misleading statements, as described in detail in Amgen's Response to Roche's Rule 56.1 Statement. The most pertinent mischaracterizations are highlighted below.

A. PROSECUTION HISTORY OF THE '933 PATENT

Contrary to Roche's contention, Amgen did not rewrite the '933 claims to limit Lin's claimed invention to the products of a specified process. In fact, the '178 application from which the '933 patent issued always contained claims to polypeptide products of the expression of a

DNA sequence encoding EPO. For example, as originally filed, claim 16 read:

> "A polypeptide product of the expression of a DNA sequence of claim 14 in a prokaryotic or eukaryotic host."[3]

Original claim 14 read:

> "A DNA sequence for use in securing expression in a prokaryotic or eukaryotic host cell of a polypeptide product having at least a part of the primary structural conformation and one or more of the biological properties of naturally occurring erythropoietin, said DNA sequence selected from among:
>
> (a) the DNA sequences set out in Tables V and VI or their complementary strands;
>
> (b) DNA sequences which hybridize to the DNA sequences defined in (a) or fragments thereof; and,
>
> (c) DNA sequences which, but for the degeneracy of the genetic code, would hybridize to the DNA sequences in (a) and (b)."[4]

In October 1987, prior to any action on the claims by the PTO, Amgen unilaterally amended claim 16 to an independent claim, reading as follows:

> "A polypeptide product of the expression in a prokaryotic or eukaryotic host, said DNA sequence selected from among:
>
> (d) the DNA sequences set out in Figures 5 and 6 or their complementary strands;
>
> (e) DNA sequences which hybridize to the DNA sequences defined in (a) or fragments thereof; and,
>
> (f) DNA sequences which, but for the degeneracy of the genetic code, would hybridize to the DNA sequences in (a) and (b)."[5]

In response to this amendment, the PTO issued its May 18, 1988 Office Action, in which the Examiner rejected Lin's pending claims, including claim 16, stating *inter alia*:

> "The claims must particularly point out the essential aspects of the

[3] Mammen Decl. Ex. A, '933 Patent File History, paper 1, 10/23/87 '178 Application Specification at 99 (AM-ITC 00941039).

[4] *Id.* at 98 (AM-ITC 00941038).

[5] Mammen Decl. Ex. C, '933 Patent File History, paper 3, 02/19/88 Preliminary Amendment at 5 (AM-ITC 00941086).

> claimed 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. The **particular biological activities and physical properties** which can be used to define the rEPO should be reflected in the claim language to adequately define the invention."[6]

Far from the misimpression Roche seeks to create, the examiner did not reject Lin's claims because they failed to limit his invention to the products of a particular process. Rather, he merely insisted that Lin's claims, including his "polypeptide product of DNA expression" claims, point out the particular biological activity and physical properties that defined the claimed polypeptides. Each of the succeeding amendments to Lin's then-pending claims was designed to address **that** concern and ultimately did so to the examiner's satisfaction. For example, immediately following the May 1988 Office Action, Amgen amended pending claim 41 and added new claim 61. As amended, claim 41 read:

> "A glycoprotein 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."[7]

New claim 61 read:

> "A glycoprotein product according to claim 41 further characterized by being the product of expression of an exogenous DNA sequence in a eucaryotic host cell."[8]

Because the examiner continued to object that these claims failed to define the claimed polypeptides with sufficient particularity, Amgen continued to amend Lin's "polypeptide product

---

[6] Mammen Decl. Ex. D, '933 Patent File History, paper 4, Office Action at 5(AM-ITC 00941094) (emphasis added).

[7] Mammen Decl. Ex. E, '933 Patent File History, paper 6, 12/1/88 Amendment and Reply at 3 (AM-ITC 00941108)

[8] Mammen Decl. Ex. E, '933 Patent File History, paper 6, 12/1/88 Amendment and Reply at 4 (AM-ITC 00941109).

of DNA expression" claims, ultimately adding new claim 76, which the Examiner accepted on February 9, 1990 as overcoming his prior section 112 rejections.[9]

Thus, contary to the false impression Roche seeks to create, the full prosecution history reveals that Lin consistently chose to define polypeptides claimed in the '933 prosecution as the product of the expression in certain cells of DNA sequences encoding EPO. And contrary to the inference Roche asks this Court to draw, nothing in the prosecution history demonstrates that Lin's claim amendments were requested or made for the purpose of excluding compounds, such as peg-EPO, that contain polypeptide products of the expression in a mammalian cell of DNA encoding human EPO.

Roche also states that, following further amendment and substitution of claims, the examiner rejected "the claims" on the basis that "it is not evident that the process of production defined the product." Contrary to the misimpression Roche seeks to create, claim 88, which closely resembles both issued claim 3 and allowed claim 76, was not rejected on that basis.[10] Claim 88 reads:

> "A glycoprotein product of the expression in a eucaryotic host cell of an exogenous DNA sequence comprising a DNA sequence encoding human erythropoietin …."[11]

B. PROSECUTION HISTORY OF THE '422 PATENT

As the Court ruled in its July 3, 2007 Memorandum and Order, and in prior litigation, "human erythropoietin" is not limited to a 166 amino acid sequence. This Court's construction

[9] Mammen Decl. Ex. I, '933 Patent File History, paper 21, 2/9/90 Office Action at 2 (AM-ITC 00941226). *See also*, Mammen Decl. Ex. J, '933 Patent File History, paper 34, 12/29/93 Office Action at 1 (AM-ITC 00941411-412).

[10] *See* Mammen Decl. Ex. N '933 Patent File History, paper 38, 8/16/94 Office Action at 1, 2-6 and *passim* (AM-ITC 00941456-466).

[11] Mammen Decl. Ex. K, '933 Patent File History, paper 37, 6/13/94 Preliminary Amendment at 1 (AM-ITC 00941452).

of "human erythropoietin" is set forth in paragraph 1 of Roche's Rule 56.1 Statement, and Roche admits that it includes a 165 amino acid sequence.[12] In *Amgen, Inc. v. Hoechst Marion Roussel, Inc*., 126 F.Supp.2d 69, 93-96 (D.Mass. 2001), this Court granted summary judgment of literal infringement of claim 1 of the '422 patent by TKT's accused product, which was a 165 amino acid product. As the Court noted in that case, TKT sought, as Roche does here, "to read a 166 amino acid limitation into the claim term 'human erythropoietin.' This the Court cannot do. … [T]his argument drifted far astray from the language of the claim and was therefore unpersuasive."[13] The Federal Circuit affirmed.[14] Thus, as a matter of claim construction, "human erythropoietin" literally includes a 165 amino acid sequence.

In its Rule 56.1 Statement, Roche selectively and misleadingly quotes out of context sentence fragments from proceedings relating to the Court's application of the doctrine of equivalents to a different claim term in the '080 patent. The Amgen brief and court decisions cited in paragraph 24 pertain to the applicability of prosecution history estoppel and the doctrine of equivalents to the '080 patent claim term, "mature human erythropoietin sequence of FIG. 6."[15] This term is a narrower and different claim term which was added to the '080 patent via amendment to distinguish the '080 claims from those of the '933 patent.[16] All of the partial quotations included in paragraph 24 relate to that narrower claim term, not to "human

---

[12] Roche Motion at 9.

[13] *Amgen, Inc. v. Hoechst Marion Roussel, Inc*., 126 F.Supp.2d 69, 95 (D.Mass. 2001).

[14] *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1347-1349, 1358 (Fed. Cir. 2003).

[15] Mammen Decl. Ex. L, *Amgen Inc. v. Hoechst Marion Roussel, Inc*., D.Mass. Case No. 97-10814-WGY, Amgen Inc.'s Post-Hearing Memorandum In Support of Its Fed. R. Civ. P. 52(c) Motion that '080 Claims 2-4 Are Infringed Under the Doctrine of Equivalents, filed 8/18/03, AM-ITC 00852559-580; *see also Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 287 F.Supp.2d 126 (D.Mass. 2003).

[16] *Id. a*t p. 10 ¶ 5.

erythropoietin."[17]

In its brief, Roche argues that the addition of the claim language "wherein said erythropoietin is purified from mammalian cells grown in culture" creates an estoppel for products that are not so made. As shown above, however, the claim language characterizing the claimed products as being expressed by particular types of cells was present in the originally filed claims down to the issued claims. Amgen did not surrender any such subject matter.

Roche incorrectly cites to the claims pending in the '422 application prior to the filing of the claim that issued as '422 claim 1 but rewrites dependent claim 63 in a confusing manner. Prior pending claims 61-63 actually read:

> "61. An erythropoietin-containing, pharmaceutically-acceptable composition wherein human serum albumin is mixed with erythropoietin.
>
> 62. A composition according to claim 61 containing a therapeutically effective amount of erythropoietin.
>
> 63. A composition according to claim 61 containing a therapeutically effective amount of recombinant erythropoietin."[18]

Claim 1 of the '422 patent actually broadened the scope of these claims by eliminating the reference to human serum albumin. Without that specific element, Amgen rewrote the claim and included the phrase "purified from mammalian cells grown in culture."

Without so stating, Roche seems to argue that this amendment narrowed the claim from "recombinant erythropoietin" and creates an estoppel for the subject matter between the two terms. But the first question is whether the claim was narrowed given the redrafting of the claim as a whole and the deletion of human serum albumin from the claim. Even if this was a narrowing amendment made for purposes of patentability, Roche has not cited to any feature in

---

[17] *See generally id.*

[18] Mammen Decl. Ex. M, '422 Patent File History, paper 2, 11/6/90 Preliminary Amendment at 9 (AM-ITC 00943124).

its product, the source from which it is obtained, or the method of its making that falls outside the scope of erythropoietin produced by "mammalian cells" as compared to "recombinant erythropoietin." In fact, Roche produces its EPO product in mammalian cells just as described and claimed in Lin's patents.

III. ROCHE'S MOTION FOR SUMMARY JUDGMENT OF PROSECUTION HISTORY ESTOPPEL SHOULD BE DENIED.

A. PROSECUTION HISTORY ESTOPPEL

"[P]rosecution history estoppel limits the range of equivalents available to a patentee by preventing recapture of subject matter surrendered during prosecution of the patent."[19] "Estoppel arises when an amendment is made to secure the patent and the amendment narrows the patent's scope."[20] The burden is on the patentee to establish that the reason for the amendment was unrelated to patentability.[21] "If the patentee fails to meet this burden, the court must presume that the patentee had a substantial reason related to patentability for including the limiting element added by amendment."[22] Even if the amendment were related to patentability, the patentee may nevertheless rebut the presumption of estoppel by establishing that "one skilled in the art could not reasonably be expected to have drafted a claim that would have literally encompassed the alleged equivalent."[23] The patentee can rebut the presumption by "(i) showing that an equivalent was unforeseeable; (ii) demonstrating that the purpose for an amendment was merely tangential to the alleged equivalent; or (iii) establishing "some other reason" that the

---

[19] *Southwall Tech., Inc. v. Cardinal IG Co.*, 54 F. 3d 1570, 1579 (Fed. Cir. 1995).

[20] *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 736 (2002).

[21] *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 2007 U.S. App. LEXIS 15942, *20 (Fed. Cir. July 5, 2007) (citing *Warner-Jenkinson Co. v. Hilton Davis Cheml. Co.*, 520 U.S. 17, 33 (1997)).

[22] *Id.* (internal quotations omitted).

[23] *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1312 (Fed. Cir. 2006).

patentee could not have reasonably been expected to have described the alleged equivalent."[24]

The issue of the doctrine of equivalents is not even reached if there is literal infringement.[25] Prosecution history estoppel is likewise irrelevant to claim construction.[26]

B. THE ASSERTED CLAIMS OF THE '933 PATENT ARE NOT SUBJECT TO PROSECUTION HISTORY ESTOPPEL.

Amgen asserts claims 3, 7-9, 11-2 and 14 of the '933 patent in this action. Independent claim 3 provides:

> "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."[27]

Although Roche's motion is directed to all asserted claims of the '933 patent, its motion is premised only on two limitations of independent claim 3, the "a DNA sequence encoding human erythropoietin" limitation (the "human EPO" limitation) underlined above, and the "product of the expression in a mammalian host cell of an exogenous DNA sequence comprising…" limitation (the "product of the process" limitation) italicized above. Neither of these limitations provides a defensible basis for the estoppel that Roche urges.

1. The "Product of the Process" Limitation Was Not Added As a Narrowing Amendment for Reasons of Patentability, But Rather Was Claimed From the Outset

In its account of the prosecution history of application claim 41 and, ultimately, issuance of claim 3, Roche attempts to create the impression that the "product of the process" limitation

---

[24] *Id.* at 1310-11; *see also Festo*, 2007 U.S. App. LEXIS 15942 at *20-21.

[25] *Fromson v. Advance Offset Plate, Inc.*, 720 F.2d 1565, 1571 (Fed. Cir. 1983) ("If there be literal infringement, the doctrine [of prosecution history estoppel] is irrelevant.").

[26] *Southwall*, 54 F.3d at 1578 ("The limit on the range of equivalents that may be accorded a claim due to prosecution history estoppel is simply irrelevant to the interpretation of those claims.").

was added as a narrowing amendment for reasons of patentability. That conclusion cannot be sustained in view of a careful examination of the prosecution history, as set forth in detail above.

Finally, Roche fails to offer any support for the proposition that the "product of the process" approach to claiming the invention of the '933 patent is in any way narrower than the approach originally taken in claim 41. The two claim formulations reflect two different approaches to claiming of the invention the '933 patent, not a progressive narrowing of the claims. It is Roche's burden, in seeking to establish a presumption of prosecution history estoppel, that the modifications to claims during prosecution are in fact narrowing amendments.[28] Roche's motion simply fails to address, let alone satisfy, this burden.

2. Roche's Proposed Scope of Prosecution History Estoppel Is An Improper Attempt to Import Limitations Into the Claim.

On the false pretext that Amgen shifted to a "product of the process" claim formulation, Roche argues that prosecution history estoppel should apply to preclude Amgen from seeking application of the doctrine of equivalents to "products that differ from the direct product of the claimed process."[29] As demonstrated above, the entire premise of Roche's argument is false. But, even if prosecution history were applicable, Roche impermissibly overreaches by seeking to import additional narrowing limitations into the claim language.[30]

Roche's argument runs afoul of this Court's July 3, 2007 Memorandum and Order, in which this Court expressly held that the definition of "human erythropoietin" in the specification

---

[27] '933 Patent claim 3 (emphasis added).

[28] *See United States Gypsum Co. v. Pacific Award Metals, Inc.*, 2006 WL 496043, *8 (N.D.Cal. 2006) ("The party asserting prosecution history estoppel has the burden to establish that a patentee made a narrowing amendment.").

[29] Roche Motion at 10 (emphasis added).

[30] *E.g., Seachange Int'l, Inc. v. UC-Cor., Inc.*, 413 F.3d 1361, 1376 (Fed. Cir. 2005) ("it is improper to import a limitation into a claim where the limitation has no basis in the intrinsic record").

expressly contemplated that additional molecules might be added to EPO.[31] Just as the addition of molecules, such as peg, to a human EPO product does not render the product no longer "human erythropoietin," the addition of processing steps, such as the step of adding the peg, does not remove the product from being the "product of the process." Thus, for the reasons set forth in Amgen's Motion for Summary Judgment of Infringement of the '933 Patent,[32] once the claimed process has been performed, the performance of additional steps to add additional structure does not vitiate infringement.

3. Because The 165 Amino Acid Sequence Falls Within the Literal Meaning of "Human Erythropoietin" The Doctrine of Equivalents Is Irrelevant

Roche asserts that the term, "a DNA sequence encoding human erythropoietin," as found in '993 patent claim 3 and incorporated into each of the other asserted dependent claims, should be limited to the 166 amino acid human erythropoietin disclosed by the specification."[33]

As Roche itself concedes,[34] this argument is contrary to the Court's claim construction and their own claim construction briefing of the limitation. In its July 3, 2007 Memorandum and Order, this Court construed "human erythropoietin" to mean "a protein having the amino acid sequence of human EPO, such as the amino acid sequence of EPO isolated from human urine."[35] This Court further held that this was an "open construction," based on the specification, and that the specification "does not define 'erythropoietin' by the presence or absence of any attached

---

[31] 7/3/07 Memorandum and Order at 14.

[32] *See* Amgen Inc.'s Memorandum in Support of Its Motion for Summary Judgment of Infringement of '422 Claim 1, '933 Claim 3 and '698 Claim 6 (Docket # 510) at p.8; *see also* Amgen Inc.'s Reply in Support of Its Motion for Summary Judgment of Infringement of '422 Claim 1, '933 Claim 3 and '698 Claim 6 (Docket # 664).

[33] Roche Motion at 9.

[34] Roche Motion at 9 ("even applying the Court's construction of human erythropoietin as the 165 amino acid sequence of EPO isolated from human urine …").

[35] 7/3/07 Memorandum and Order at 15.

molecules, such as the carbohydrate that can be attached to EPO proteins for glycosylated EPO. In fact, the specification expressly contemplates that additional molecules ***may*** be attached to 'human erythropoietin.' By implication, therefore, those additional molecules are not part of the amino acid structure that comprises the claimed product."[36] Nothing in the Court's construction of "human erythropoietin" limits the meaning of that term to a 166 amino acid sequence.

Moreover, Roche's argument for the 166 amino acid sequence limitation is premised upon the conflation of two distinct terms: "human erythropoietin," as found in the asserted claims of the '933 patent, and "mature erythropoietin amino acid sequence of Fig. 6," as found in claims 2-4 of the '080 patent and addressed in *Amgen v. Hoechst Marion Roussel*, 287 F.Supp.2d 126 (D. Mass. 2003). The Federal Circuit has concluded that the narrower term "mature erythropoietin amino acid sequence of Fig. 6" is limited to the 166 amino acid sequence, and that Amgen is estopped from asserting the doctrine of equivalents with respect to that term.[37] All of the materials cited by Roche pertain to this narrower term. However, as noted above, in this action, this Court has construed the broader term "human erythropoietin" in a manner that includes 165 amino acid EPO.[38] Roche acknowledges as much in its Motion, where it says, "even applying the Court's construction of human erythropoietin as the 165 amino acid sequence of EPO isolated from human urine …"[39] This is fully consistent with the Court's claim

---

[36] 7/3/07 Order at 14 (citations omitted, emphasis in original).

[37] Also in *TKT*, this Court held that the same accused 165 amino acid product did not literally infringe claims 2-4 of the '080 patent, since all of those claims included the limitation "erythropoietin glycoprotein comprises the mature erythropoietin amino acid sequence of FIG. 6." Figure 6 of the '080 patent shows a 166 amino acid sequence. Accordingly, this Court, and ultimately, the Federal Circuit, considered whether claims 2-4 of the '080 patent covered a 165 amino acid sequence under the doctrine of equivalents. The Federal Circuit held that it did not. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1316 (Fed. Cir. 2006).

[38] 7/3/07 Memorandum and Order at 15.

[39] Roche Motion at 9.

construction in the *TKT* litigation.[40]

4. Other Arguments

Roche further argues that, because other claims were cancelled following § 112 rejections, Amgen is estopped from asserting that the human EPO limitation covers the following under the doctrine of equivalents:

- fragments[41]
- erythropoietin fragments[42]
- polypeptide fragments[43]
- analogs[44]
- synthetic polypeptides[45]
- polypeptides containing amino acid residues not found in human EPO[46]

Roche provides no further support for its argument that each of these items should be excluded under the doctrine of equivalents, and similarly fails to specify how any of the terms bear upon the facts of the present case. The EPO in Roche's product is 165 amino acid epoetin beta. It is not an EPO fragment, analog, synthetic polypeptide or polypeptide containing amino

[40] In *Amgen, Inc. v. Hoechst Marion Roussel, Inc*., 126 F.Supp.2d 69, 93-96 (D.Mass. 2001), this Court granted summary judgment of literal infringement of claim 1 of the '422 patent by TKT's accused product, which was a 165 amino acid product. Just as Roche argues here, "TKT thus [sought] to read a 166 amino acid limitation into the claim term 'human erythropoietin.' This the Court cannot do. … [T]his argument drifted far astray from the language of the claim and was therefore unpersuasive." *Id.* at 95. The Federal Circuit affirmed. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1347-1349, 1358 (Fed. Cir. 2003). Thus, as a matter of claim construction, "human erythropoietin" literally includes a 165 amino acid sequence.

[41] Roche Motion at 9, 13.

[42] Roche Motion at 13.

[43] Roche Motion at 13.

[44] Roche Motion at 9.

[45] Roche Motion at 9, 13.

[46] Roche Motion at 13.

acid residues not found in human EPO. Thus, there is no actual controversy in this case about these equivalents. Absent a showing by Roche that there is an actual controversy regarding these terms, this Court lacks jurisdiction to pass upon the estoppel questions.

Moreover, Roche has not identified an actual narrowing amendment that would give rise to prosecution history estoppel. Roche appears to argue that, because the original application contained several claims (without counterparts in the issued patent), which were rejected by the examiner as indefinite and not enabled, and covered "a polypeptide having part or all of the primary structural conformation … of naturally-occurring erythropoietin," "a polypeptide … possessing part or all of the primary structural conformation of human erythropoietin…" and "a synthetic polypeptide having part or all of the amino acid sequence set forth in Figure 6," the limitation in claim 3 and its dependents to a "glycoprotein product … comprising a DNA sequence encoding human erythropoietin" is subject to prosecution history estoppel, to exclude each of the terms listed above. However, these limitations from cancelled claims are sufficiently different from any claims that actually issued that Roche has failed to satisfy its burden of demonstrating that there was a narrowing amendment sufficient to trigger the presumption of prosecution history estoppel.[47]

a. EPO Fragments

Apparently based upon Amgen's cancellation of application claims 1, 7 and 48, each of which includes the term "part of the primary structural conformation of erythropoietin," Roche argues that the asserted claims of the '933 patent cannot encompass "fragments" or "erythropoietin fragments" under the doctrine of equivalents. Roche provides no support for its implication that "fragments" and "part of the primary structural conformation of erythropoietin"

[47] *See United States Gypsum Co. v. Pacific Award Metals, Inc.*, 2006 WL 496043, *8 (N.D.Cal. 2006) ("The party asserting prosecution history estoppel has the burden to establish that a patentee made a narrowing amendment.").

mean the same thing, nor does it expressly so assert. Without that connection, there can be no argument that Amgen is estopped from asserting claim coverage for "fragments" or "erythropoietin fragments" under the doctrine of equivalents.

Nor does Roche identify any issue of EPO fragments in this case. Roche may intend to argue that the 165 amino acid sequence is a "fragment" of the 166 amino acid sequence, and is therefore a "fragment" that should be excluded under the doctrine of equivalents. However, under the Court's construction of "human erythropoietin," the 165 amino acid sequence plainly falls within the literal meaning of the term. Therefore, the doctrine of equivalents is irrelevant.[48]

Moreover, the '933 patent must be distinguished from the previously-litigated '080 patent. During prosecution of the '080 patent, a claim containing the limitation "an isolated DNA sequence encoding the human erythropoietin amino acid sequence set out in FIG. 6 or a fragment thereof" was cancelled during prosecution, and Amgen was held to be estopped from asserting the doctrine of equivalents for anything less than the complete sequence "set out in FIG. 6."[49] By contrast, claim 4 of the '933 patent issued with exactly the same wording as the claim that was canceled in the '080 patent.[50] Therefore, "fragments" cannot be deemed to have been surrendered via claim cancellations during prosecution of the '933 patent.

b. Analogs

Roche's argument concerning "analogs" appears to be based on the fact that claim 7 of the '008 patent was invalidated under § 112 due to its inclusion of "sufficiently duplicative," after that term was construed to include, *inter alia*, "analogs." Roche identifies no part of the prosecution history in which Amgen narrowed any claim to exclude "analogs," and offers no

[48] *Fromson v. Advance Offset Plate, Inc.*, 720 F.2d 1565, 1571 (Fed. Cir. 1983) ("If there be literal infringement, the doctrine [of prosecution history estoppel] is irrelevant.").

[49] *Amgen, Inc. v. Hoechst Marion Roussel*, 457 F.3d 1293, 1311 (Fed. Cir. 2006).

[50] *See* '933 patent claim 4.

independent argument to that effect. Accordingly, the doctrine of prosecution history estoppel is inapplicable to "analogs."

c. Synthetic Polypeptides

As Roche itself noted, the examiner explained that "'Synthetic,' as opposed to 'recombinant,' is an art recognized term which indicates a chemically derived rather than genetically engineered protein."[51] Because the EPO in Roche's accused products is generated through recombinant, not synthetic, methods, any question of doctrine of equivalents as to synthetic polypeptides is not at issue in this case, and is therefore not ripe for decision.

d. Polypeptides Containing Amino Acid Residues Not Found In Human EPO

Finally, Roche argues that Amgen should be estopped from asserting that a "DNA sequence encoding human erythropoietin" includes, under the doctrine of equivalents, "polypeptides containing amino acid residues not found in human EPO." Roche identifies no basis in the prosecution history or prior litigation of the Lin patents to support this assertion, and indeed appears to have devised the phrase from whole cloth. To the extent Roche intends it to mean polypeptides including human EPO *plus* additional amino acid residues, it falls squarely within the literal scope of "human erythropoietin" as construed by this Court: "the specification expressly contemplates that additional molecules ***may*** be attached to 'human erythropoietin.'"[52]

C. THE ASSERTED CLAIM OF THE '422 PATENT IS NOT SUBJECT TO PROSECUTION HISTORY ESTOPPEL.

Finally, Roche argues that Amgen should be barred under *Festo* from arguing that claim 1 of the '422 patent covers "products which are not and cannot be produced from mammalian cells grown in culture," due to the addition during prosecution of language providing a source

[51] Roche's Rule 56.1 Statement at ¶ 9.

[52] 7/3/07 Memorandum and Order at p.14. To the extent Roche is referring to polypeptides *not also* containing human EPO in addition to such amino acid residues, it is unclear what, if any

limitation: "wherein said erythropoietin is purified from mammalian cells grown in culture."[53] However, by conflating "products" and "erythropoietin," Roche's argument ignores this Court's July 3, 2007 claim construction ruling. It is not the entire accused *composition* that must be purified from mammalian cells grown in culture, but rather the *erythropoietin* in such a composition. As this Court ruled, "the specification expressly contemplates that additional molecules ***may*** be attached to 'human erythropoietin.'"[54]

IV. CONCLUSION

For the foregoing reasons, Amgen respectfully requests that Roche's 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 be denied.

Respectfully Submitted,

AMGEN INC.,
By its attorneys,

/s/ MICHAEL R. GOTTFRIED

D. DENNIS ALLEGRETTI (BBO#545511)
MICHAEL R. GOTTFRIED (BBO#542156)
PATRICIA R. RICH (BBO#640578)
DUANE MORRIS LLP
470 Atlantic Avenue, Suite 500
Boston, MA 02210
Telephone: (857) 488-4200
Facsimile: (857) 488-4201

LLOYD R. DAY, JR. (*pro hac vice*)
DAY CASEBEER
MADRID & BATCHELDER LLP
20300 Stevens Creek Boulevard, Suite 400
Cupertino, CA 95014
Telephone: (408) 873-0110

Of Counsel:

STUART L. WATT
WENDY A. WHITEFORD
MONIQUE L. CORDRAY
DARRELL G. DOTSON
KIMBERLIN L. MORLEY
ERICA S. OLSON
AMGEN INC.
One Amgen Center Drive
Thousand Oaks, CA 91320-1789
(805) 447-5000

relevance such polypeptides would have to this case.

[53] Roche Motion at 14.

[54] 7/3/07 Memorandum and Order at 14.

Facsimile: (408) 873-0220

WILLIAM GAEDE III (*pro hac vice*)
McDERMOTT WILL & EMERY
3150 Porter Drive
Palo Alto, CA 94304
Telephone: (650) 813-5000
Facsimile: (650) 813-5100

KEVIN M. FLOWERS (*pro hac vice*)
MARSHALL, GERSTEIN & BORUN LLP
233 South Wacker Drive
6300 Sears Tower
Chicago IL 60606
Telephone: (312) 474-6300
Facsimile: (312) 474-0448

July 13, 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 non-registered participants.

/s/ Michael R. Gottfried
Michael R. Gottfried