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 **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 '698 AND '868 PATENTS

Leora Ben-Ami (*pro hac vice*)
Mark S. Popofsky (*pro hac vice*)
Patricia A. Carson (*pro hac vice*)
Thomas F. Fleming (*pro hac vice*)
Howard S. Suh (*pro hac vice*)
Peter Fratangelo (BBO# 639775)
KAYE SCHOLER LLP
425 Park Avenue
New York, New York 10022
Tel. (212) 836-8000

Lee Carl Bromberg (BBO# 058480)
Julia Huston (BBO# 562160)
Keith E. Toms (BBO# 663369)
Nicole A. Rizzo (BBO# 663853)
BROMBERG & SUNSTEIN LLP
125 Summer Street
Boston, MA 02110
Tel. (617) 443-9292

Counsel for Defendants,
F. HOFFMANN-LA ROCHE LTD,
ROCHE DIAGNOSTICS GmbH, and
HOFFMANN-LA ROCHE INC.

Dated: July 3, 2007

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Page

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 1-2 of U.S. Patent No. 5,441,868 (the '868 patent)[1] and claims 4-9 of U.S. Patent No. 5,618,698 (the '698 patent)[2] under the doctrine of equivalents.

I. INTRODUCTION

Claims 4 and 6 of the '698 patent-in-suit recite processes for producing glycosylated erythropoietin polypeptides produced using DNA encoding "the mature erythropoietin amino acid sequence of FIG. 6." This Court has held that in the claims of Amgen's U.S. Patent No. 5,621,080 ('080 patent) the term "mature erythropoietin amino acid sequence of FIG. 6" means that the polypeptides of the claims "must contain an erythropoietin glycoprotein comprising the fully realized erythropoietin amino acid sequence of Figure 6 which depicts 166 amino acids." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F.Supp. 2d 69, 100 (D. Mass. 2001) (*Amgen I*). The Court further stated that the term "mature erythropoietin amino acid sequence of FIG. 6" "should have the same meaning in both [the '080 and '698 patents]." *Id*. at 86.

The phrase "mature erythropoietin amino acid sequence of FIG. 6" was added to the application for the '080 patent for patentability reasons following a patent office interview. The Federal Circuit held that Amgen was, therefore, estopped from arguing that the phrase "mature erythropoietin amino acid sequence of FIG. 6" in the claims 'of the 080 patent was satisfied

---

[1] Ex. 1, U.S. Patent No. 5,441,868. All Exhibits cited herein are attached to the Declaration of Nicole A. Rizzo 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 '698 and '868 Patents.

[2] Ex. 2, U.S. Patent No. 5,618,698.

under the doctrine of equivalents.[3] *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1316 (Fed. Cir. 2003) (*Amgen II*).

As shown below, the words "mature erythropoietin amino acid sequence of FIG. 6" were added to the application for the '698 patent for patentability reasons at the very same time and as a result of the very same patent office interview that resulted in the addition of those words to the '080 patent. Consequently, Amgen should also be foreclosed from using the doctrine of equivalents to broaden the term "mature erythropoietin amino acid sequence of FIG. 6" in the claims of the '698 patent to capture a "process for the production of glycosylated erythropoietin polypeptides" other than the 166 amino acid residue set forth on Figure 6.[4]

Claims 1 and 2 of the '868 patent-in-suit describe processes for producing a glycosylated erythropoietin polypeptide using cells which are transformed or transfected with "an isolated DNA sequence encoding human erythropoietin." As demonstrated below, that limitation was added to the claims to overcome the rejection of a claim to a process for producing "an *in vivo* biologically active glycosylated polypeptide" using a DNA sequence "encoding a polypeptide having a primary structural conformation sufficiently duplicative of that of naturally occurring human erythropoietin." Having narrowed the claims to the use of DNA "an isolated DNA

---

[3] Having initially alleged infringement of the '080 patent in this case under the doctrine of equivalents, Amgen has dropped that claim in the face of a motion by Roche for summary judgment of noninfringement.

[4] 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.

sequence encoding human erythropoietin," Amgen should be estopped from contending that the phrase can be used under the doctrine of equivalents to recapture surrendered subject matter.

II. STATEMENT OF FACTS

A. Relevant Prosecution History of U.S. Patent No. 4,703,008

Each of the patents-in-suit arises from the same application as expired U.S. Patent No. 4,703,008 ("the '008 patent") and, through the parent applications of the '008 patent, to an application filed December 13, 1983. The application that yielded the '008 patent was filed on November 30, 1984. The '008 patent issued on October 27, 1987, and expired in 2004.

During prosecution of the application for the '008 patent, the examiner rejected claims to a DNA sequence for use in expressing "a polypeptide having part or all of the primary structural conformation" of naturally occurring EPO and to a DNA sequence "coding for a polypeptide fragment or polypeptide analog" of naturally-occurring EPO. (Ex. 3, '008 patent file history, Paper 13, 2/5/87 Office Action; *see also* Ex. 4, Ser. No. 675,298 at pp. 99-100). In rejecting the claims as not enabled, the examiner stated:

> [T]he disclosure is enabling only for claims limited to the DNA sequence coding for erythropoietin. The recitation "of ***fragments*** thereof" the recitation of and/or "having at least ***a part*** of the primary structural conformation and one or more of the biological activities of naturally-occurring erythropoietin" permits the claims to read on proteins and peptides completely unrelated to erythropoietin.

(Ex. 3 at 3 (emphasis added)).

The application was then amended, but the amended claims still described "a polypeptide product having at least a part of the primary structural conformation" of naturally-occurring EPO and a "a polypeptide fragment or polypeptide analog of naturally-occurring erythropoietin." (Ex. 5, '008 patent file history, Paper 15, Amendment and Reply at 1-2, 4-5). The Examiner again

rejected the claims under § 112 as not enabled, noting that the claims "appear to embrace substantially all known DNA sequences since the isolated DNA sequence is not designated as encoding erythropoietin. One that encodes for a protein having 'a' therapeutic activity of erythropoietin is not the same thing." (Ex. 6, '008 patent file history, Paper 17, 6/18/87 Office Action at 3).

The '008 patent issued with one claim -- claim 7 -- that had language similar to language that had been rejected, *i.e.*, "a DNA sequence encoding a polypeptide having an amino acid sequence sufficiently duplicative of that of erythropoietin." However, that claim was later held invalid. *See Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1213-14 (Fed. Cir. 1991).

B. The Asserted Claims of the '868 Patent

Amgen alleges that Roche infringes claims 1 and 2 of the '868 patent which claim processes for producing a glycosylated erythropoietin polypeptide as follows:

> 1. A process for the production of a ***glycosylated erythropoietin polypeptide*** having the ***in vivo*** biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells comprising the steps of:
>
> > (a) growing, under suitable nutrient conditions, mammalian host cells transformed or transfected with an isolated ***DNA sequence encoding human erythropoietin***; and
> >
> > (b) isolating said glycosylated erythropoietin polypeptide therefrom.
>
> 2. The process according to claim 1 wherein said host cells are CHO cells.

(Ex. 1, (emphasis added)).

This Court has construed the term "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." (July 3, 2007 Order (Docket No. 613) at 15).

C. Relevant Prosecution History of the '868 Patent

The application for the '868 patent initially added claims (numbered 61, 62 and 64) to processes for the production of "a polypeptide having part or all of the primary structural conformation" of naturally-occurring EPO which used the DNA sequences of Figures 5 and 6 of the specification and DNA sequences which hybridize to those sequences, a DNA sequence consisting essentially of a DNA sequence encoding human EPO, and a DNA sequence encoding a polypeptide having a primary structural conformation sufficiently duplicative of that of EPO. (Ex. 8, '868 patent file history, Paper 7, 10/23/87 Preliminary Amendment at 5-7). In a second preliminary amendment, the applicant replaced those claims with a claim (number 65) to a process for producing "an *in vivo* biologically active glycosylated polypeptide" using a DNA sequence "encoding a polypeptide having a primary structural conformation ***sufficiently duplicative*** of that of naturally occurring human erythropoietin." (Ex. 9, '868 patent file history, Paper 8, 5/24/88, Second Preliminary Amendment at 3-4 (emphasis added)).

Ultimately, application claim 65 was rejected on the grounds that a claim to any "*in vivo* biologically active glycosylated polypeptide" was unsupported by a process involving only DNA encoding EPO. (Ex. 10, '868 patent file history, Paper 29, 9/1/93 at 5-6). The examiner stated that "the disclosure is enabling only for claims limited to preparation of human EPO" and that the rejection could be overcome "by amending the claim to recite 'a process for the preparation of a biologically active glycosylated human erythropoietin.'" (*Id*. at 9-10). Applicant responded by cancelling claim 65 and replacing it with file claim 70, which limited the claimed DNA sequence to "an isolated DNA sequence encoding human erythropoietin." That claim ultimately issued as '868 claim 1.

The disclosure of "human erythropoietin" set forth in the '868 patent is a sequence of 166 amino acid residues. 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. 1, at col. 22:6-9; *see also* Fig. 9 & col. 20:30-38, 22:9-13, 36:44-51)

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. 14, Amgen's Post-Hearing Memo. at 5 (AM-ITC 00852567)). 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).

Thus, claim 1 of the'868 patent was narrowed for patentability reasons to a process for producing an erythropoietin polypeptide made with an isolated DNA sequence encoding human erythropoietin. "Human erythropoietin" as defined by the patent is a 166 amino acid protein. As such, claim 1 of the '868 patent should be limited to the 166 amino acid sequence of human erythropoietin disclosed by the specification.

D. The Asserted Claims of the '698 Patent

Amgen alleges that Roche infringes claims 4-9 of the '698 patent which recite processes for producing "glycosylated erythropoietin polypeptide[s]." The independent claims are claims 4 and 6:

> 4. A process for the production of ***a glycosylated erythropoietin polypeptide*** having the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells comprising the steps of:
>
> a) growing, under suitable nutrient conditions, vertebrate cells comprising promoter DNA, other than human erythropoietin

promoter DNA, operatively linked to *DNA encoding the mature erythropoietin amino acid sequence of FIG. 6*; and

b) isolating said glycosylated erythropoietin polypeptide expressed by said cells.

6. A process for the production of *a glycosylated erythropoietin polypeptide* having the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells comprising the steps of:

a) growing, under suitable nutrient conditions, vertebrate cells comprising amplified *DNA encoding the mature erythropoietin amino acid sequence of FIG. 6*; and

b) isolating said glycosylated erythropoietin polypeptide expressed by said cells.

(Ex. 2, (emphasis added)).

E. Relevant Prosecution History of the '698 Patent

The application which resulted in the issuance of the '698 patent was a continuation of the application that resulted in the '868 patent and was filed on June 6, 1995. Subsequent to the August 15, 1995 issuance of the '868 patent, applicant proposed to the Patent Office adding claims in the '698 patent with the phrase "DNA encoding the mature erythropoietin amino acid sequence of Figure 6" to avoid a double patenting rejection in light of the '868 patent's "an isolated DNA sequence encoding human erythropoietin."

The claims that issued as claims 4 and 6 of the '698 patent were, in fact, added after a December 11, 1996 patent office interview and were among 5 proposed claims -- all of which employed the term "the mature erythropoietin amino acid sequence of Figure 6" -- that were discussed with the examiner.[5] The summary of the patent office interview included in the '698

[5] Two others of the proposed claims discussed at the patent office interview were then added to the then pending application for the '080 patent and issued as claims 1 and 2 thereof. (See below).

patent file history reflects that the applicant agreed to add the claims which became claims 4 and 6 of the patent to avoid a double patenting rejection, that the applicant agreed to file a terminal disclaimer with respect to the '868 patent and that the examiner was "favorably impressed." (Ex. 11, '698 patent file history, Paper 7, 12/11/96 Interview Summary).

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 I*, 126 F. Supp. 2d at 93. "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.* (quoting *Sage Prods. v. Devon Indus., Inc*., 126 F.3d 1420, 1423 (Fed. Cir. 1997)).

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 (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*); *Cross Medical Prods. Inc. v. Medtronic Sofamor Danek Inc.*, 480 F.3d 1335, 1342 (Fed. Cir. 2007) ("tangential 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 '698 Patent

This Court should grant summary judgment that Amgen is precluded from asserting infringement under the doctrine of equivalents because the term "mature erythropoietin amino acid sequence of FIG. 6" in the claims of the '698 limits the claims to "a process for the production of a glycosylated erythropoietin polypeptide" with the 166 amino acid residue set forth by Figure 6.

The claims of the '698 patent describe a process for producing "a glycosylated erythropoietin polypeptide" which employs "DNA encoding the mature erythropoietin amino acid sequence of FIG. 6." The term "mature erythropoietin amino acid sequence of Fig. 6" was added to the application for the '698 patent at the very same time that the identical phrase was added to the application that became the '080 patent.

Construing the phrase "mature erythropoietin amino acid sequence of FIG. 6" in the claims of the '080 patent, this Court previously held that in order to infringe the '080 patent a pharmaceutical composition "must contain an erythropoietin glycoprotein comprising the fully realized erythropoietin amino acid sequence of Figure 6 which depicts 166 amino acids." *Amgen I* at 100. The Court stated that "because the asserted claims are limited explicitly by the meaning of Figure 6, the specific amino acid sequence displayed therein is significant." *Id.* The Court

noted that the phrase "mature erythropoietin amino acid sequence of FIG. 6" "should have the same meaning in both" the '080 and '698 patents. *Amgen I* at 86.

In *Amgen IV*, the Federal Circuit held that Amgen was foreclosed, under the doctrine of prosecution history estoppel, from maintaining that the "mature erythropoietin amino acid sequence of Fig. 6" limitation in the claims of '080 patent could cover an EPO product containing a 165 amino acid sequence under the doctrine of equivalents. 457 F.3d at 1316. As the Federal Circuit observed, a June 6, 1995 preliminary amendment to the application for the '080 patent had added claims which "broadly encompassed an isolated human EPO product." *Id.* at 1310. A second preliminary amendment had "claimed an EPO product made using the amino acid sequence for EPO set out in Figure 6 'or a fragment thereof.'" *Id.* A third amendment "deleted claims for an EPO product made using 'a fragment' of the amino acid sequence of Figure 6. Instead, as of the third preliminary amendment, the . . . application claimed only a human EPO product having the complete amino acid sequence of Figure 6." *Id.* The applicant argued that the added claims "all differ in scope from glycoprotein claim 1 of U.S. 5,547,933 in specifying that the claimed subject matter comprises the mature human erythropoietin sequence of Figure 6." (Ex. 12, '080 patent file history, Paper 6, 12/20/96 Third Preliminary Amendment). The Federal Circuit thus concluded that the third preliminary amendment "may have been central to overcoming a double patenting rejection in light of claim 1 of the '933 patent." *Amgen IV*, 457 F.3d at 1315.

In determining that the presumption of estoppel was not rebutted, the Federal Circuit pointed out that Amgen amended the claims knowing of the 165 amino acid sequence, and still "chose to limit the claims to the 166 amino acid sequence depicted in Figure 6" of the '080 patent specification. *Id.* at 1316.

Significantly, the third preliminary amendment of the application for the ‘080 patent was a result of the December 11, 1996 patent office interview which was also a part of the prosecution history of the ‘698 patent. The applicant and the examiner discussed five proposed claims, all of which included the phrase “the mature erythropoietin amino acid sequence of Figure 6.” (Ex. 13, ‘080 patent file history, Paper 4, 12/11/96 Interview Summary). The interview summary which appears in the ‘080 patent file history reflects that two of the 5 proposed claims -- which issued as claims 1 and 2 of the ‘080 patent -- would be added via a preliminary amendment, that a terminal disclaimer would be filed with respect to the ‘933 patent and that the examiner was “favorably impressed.” *Id.*

The Federal Circuit held that Amgen was estopped from asserting that the ‘080 patent claims were infringed under the doctrine of equivalents because the claim had been amended to add the term “mature erythropoietin amino acid sequence of Figure 6” to distinguish over the ‘933 patent. Amgen should similarly be estopped from claiming infringement of the claims of the ‘698 patent infringed under the doctrine of equivalents. The summary of the December 11, 1996 office interview that appears in the ‘698 patent file history reflects that the claim term “mature erythropoietin amino acid sequence of Figure 6” was added to what became the ‘698 patent to distinguish over the ‘868 patent at the very same time as the term was added to the ‘080 patent and as a result of the very same patent office interview that yielded claims 1 and 2 of the ‘080 patent. As mentioned, the interview summary in the ‘698 patent file history reflects that the applicant would add what became claims 4 and 6 of the patent, that the applicant would file a terminal disclaimer with respect to the ‘868 patent and that the examiner was “favorably impressed.” Whereas the ‘868 patent -- like the ‘933 patent -- claims the use of a “DNA sequence encoding human erythropoietin,” the ‘698 patent -- like the ‘080 patent -- was amended

to explicitly narrow the claims to the use of "the mature erythropoietin amino acid sequence of FIG. 6."[6] As with the '080 patent, this limitation was added to the '698 patent to "preempt a double-patenting rejection." *Amgen IV*, 457 F.3d 1293, 1310 (Fed. Cir. 2006); *see also Amgen v. Hoescht Marion Roussel*, 314 F.3d 1313, 1345 (Fed. Cir. 2003) ("The district court correctly found that the amendment, although voluntary, was made to avoid a 'same invention' double patenting rejection.").

Furthermore, Amgen cannot rebut the presumption of estoppel. As the Court pointed out in *Amgen IV*, when the term "mature erythropoietin amino acid sequence of Figure 6" was added to the claims of the '080 patent and the '698 patent, "the 165 amino acid EPO equivalent was foreseeable." 457 F.3d at 1316. Nor was the amendment tangential; it was apparently central to issuance of the claims. Finally, as in *Amgen IV*, applicant cannot point to "some other reason" for failing to particularly claim the alleged equivalent.

Therefore, this Court should grant summary judgment that Amgen is estopped from asserting infringement under the doctrine of equivalents because the term "mature erythropoietin amino acid sequence of FIG. 6" in the '698 claims limits Amgen to "a process for the production

---

[6] As shown above in Section II.C., the Lin specification discloses human erythropoietin, including EPO isolated from human urine, as having a 166 amino acid residue. Indeed, Amgen made clear that the addition of "mature erythropoietin amino acid sequence of Figure 6" was a failed attempt to claim a 165 amino acid sequence to differentiate over "human EPO". *See* Ex. 14, 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 at 2 ("At the date of the amendment, the prosecution history reveals that Amgen intended the sequence limitation to cover human EPO compositions having the 1-165 amino acid sequence." (emphasis added). In fact, the reasonable inference the prosecution history establish that the amended claims [of the '080] were intended to cover human EPO compositions having the 1-165 amino acid sequence."). Furthermore, Roche maintains that the Lin specification does not adequately describe "human erythropoietin" as a 165 amino acid sequence. *See, e.g.*, Roche's Motion for Summary Judgment That Claim 1 of the '422 Patent is Invalid Under 35 U.S.C. §112 (Docket No. 482) and accompanying memorandum of law (Docket No. 483).

of a glycosylated erythropoietin polypeptide" with the 166 amino acid residue set forth by Figure 6.

D. Roche Should Be Granted Summary Judgment That Amgen Is Estopped From Asserting Infringement Under The Doctrine of Equivalents Of Claims 1 and 2 Of The '868 Patent

This Court should grant Roche summary judgment that Amgen is estopped from asserting infringement under the doctrine of equivalents because cancelled claims and amendments relating to the claim limitation "encoding human erythropoietin" precludes it from arguing that its "process for the production of a glycosylated erythropoietin polypeptide" covers anything but a process for making the 166 amino acid residue disclosed by the Lin specification.

During prosecution of the '868 patent, the examiner rejected a claim to "an in vivo biologically active glycosylated polypeptide" using "an isolated DNA sequence encoding a polypeptide having a primary structural conformation ***sufficiently duplicative*** of that of naturally occurring human erythropoietin." (Ex. 9 at 3-4 (emphasis added)). In response to the examiner's assertion that "the specification provides guidance for and a working example of only the production of EPO" (Ex. 10 at 9-10) the applicant substituted a claim which issued, to "a glycosylated erythropoietin polypeptide" using cells transformed or transfected with "an isolated DNA sequence encoding human erythropoietin." Amgen specifically surrendered a claim to the use of DNA "sufficiently duplicative" of that coding for naturally occurring erythropoietin in favor of a narrower claim to the use of "an isolated DNA sequence encoding human erythropoietin," which is disclosed by the patent to be 166 amino acids. The examiner expressly held that the claimed process would only be allowable if it were limited to "a process for the preparation of biologically active glycosylated human erythropoietin" and not a process of producing any polypeptide. (Ex. 10 at 5-6) Amgen should, therefore, be estopped, pursuant to the Supreme Court decision in *Festo,* from reclaiming the surrendered coverage. In other words,

this Court should grant summary judgment foreclosing Amgen from arguing that the limitation "an isolated DNA sequence encoding human erythropoietin" can be satisfied 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 estopped from asserting the doctrine of equivalents because of cancellations and narrowing amendments relating to the limitation "the mature erythropoietin amino acid sequence of FIG. 6" in claims 4-9 of the '698 patent and to the limitation "DNA sequence encoding human erythropoietin" in claims 1 and 2 of the '868 patent.

DATED: Boston, Massachusetts
July 3, 2007

Respectfully submitted,

F. HOFFMANN-LA ROCHE LTD,
ROCHE DIAGNOSTICS GMBH, and
HOFFMANN-LA ROCHE INC.

By their Attorneys,

/s/ Nicole A. Rizzo
Lee Carl Bromberg (BBO# 058480)
Julia Huston (BBO# 562160)
Keith E. Toms (BBO# 663369)
Nicole A. Rizzo (BBO # 663853)
BROMBERG & SUNSTEIN LLP
125 Summer Street
Boston, MA 02110
Tel: (617) 443-9292
nrizzo@bromsun.com

Leora Ben-Ami (*pro hac vice*)
Mark S. Popofsky (*pro hac vice*)
Patricia A. Carson (*pro hac vice*)
Thomas F. Fleming (*pro hac vice*)
Howard S. Suh (*pro hac vice*)
Peter Fratangelo (BBO# 639775)
KAYE SCHOLER LLP
425 Park Avenue
New York, NY 10022
Tel: (212) 836-8000

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 (NEF) and paper copies will be sent to those indicated as non registered participants on the above date.

/s/ Nicole A. Rizzo
Nicole A. Rizzo

03099/00501 698457.1