# EXHIBIT A

**NEW PROPOSED AMENDED PLEADING**

**UNITED STATES DISTRICT COURT**
**DISTRICT OF MASSACHUSETTS**

| | | |
|---|---|---|
| AMGEN INC., | ) | |
| | ) | |
| Plaintiff, | ) | |
| v. | ) | Civil Action No.: 05 Civ. 12237 WGY |
| | ) | |
| F. HOFFMANN-LA ROCHE LTD, ROCHE DIAGNOSTICS GmbH, and HOFFMANN-LA ROCHE INC., | ) | **DEFENDANTS'** |
| | ) | **~~FIRST~~[PROPOSED] SECOND** |
| | ) | **AMENDED ANSWER AND** |
| Defendants. | ) | **COUNTERCLAIMS TO** |
| | ) | **PLAINTIFF'S COMPLAINT** |
| | ) | |
| | | **DEMAND FOR JURY TRIAL** |

In response to the Complaint For Declaratory Judgment Of Infringement ("Complaint") filed in this action by Amgen, Inc. ("Amgen"), F. Hoffmann-La Roche Ltd, Roche Diagnostics GmbH, and Hoffmann-La Roche Inc. (collectively "Roche"), by their attorneys, hereby amend their answer and counterclaims to the Complaint For Declaratory Judgment Of Infringement ("Complaint") of Amgen, Inc. ("Amgen") as follows:

## PART I: ROCHE'S ANSWER AND AFFIRMATIVE DEFENSES

In response to the Complaint of Amgen, defendants Roche, by their attorneys, state as follows:

1. Roche admits that Amgen is a corporation existing under the laws of the State of Delaware with its principal place of business in Thousand Oaks, California. Roche lacks knowledge or information sufficient to form a belief as to the truth of the remaining allegations of paragraph 1 of the Complaint.

2. Admitted.

3. Admitted.

4. Admitted.

5. Roche denies the allegations contained in paragraph 5 of the Complaint.

6. The statement in paragraph 6 of the Complaint is neither an averment nor allegation to which a response is required.

7. Admitted.

8. Roche denies that venue and personal jurisdiction are proper in this Court.

9. Roche denies the allegations contained in paragraph 9 of the Complaint.

10. The statements in paragraph 10 of the Complaint are neither averments nor allegations to which a response is required, and Roche otherwise denies these allegations.

11. Roche lacks knowledge or information sufficient to form a belief as to the truth of the allegations contained in the statements of paragraph 11 of the Complaint, and denies those allegations.

12. Roche denies the allegations contained in paragraph 12 of the Complaint.

13. Roche denies the allegations contained in paragraph 13 of the Complaint.

14. Roche denies the allegations contained in paragraph 14 of the Complaint, except Roche admits that U.S. Patents Nos. 5,441,868 ("the '868 patent"), 5,547,933 ("the '933 patent"), 5,618,698 ("the '698 patent"), 5,621,080 ("the '080 patent"), 5,756,349 ("the '349 patent") and 5,955,422 ("the '422 patent") (collectively "the patents-in-suit") were issued on the dates alleged.

15. The statements in paragraph 15 of the Complaint are neither averments nor allegations to which a response is required, and Roche otherwise denies these allegations.

16. The statements in paragraph 16 of the Complaint are neither averments nor allegations to which a response is required, except Roche admits that this Court has

previously issued certain rulings in other litigations concerning certain of the patents-in-suit, and Roche refers Amgen to the actual decisions and orders of this Court, and any appellate court for the holdings therein, and Roche otherwise denies these allegations.

17. Roche lacks knowledge or information sufficient to form a belief as to the truth of the allegations contained in the statements of paragraph 17 of the Complaint, and denies those allegations.

18. Roche denies the allegations contained in paragraph 18 of the Complaint.

19. Roche denies the allegations contained in paragraph 19 of the Complaint.

20. Roche denies the allegations contained in paragraph 20 of the Complaint.

21. Roche denies the allegations contained in paragraph 21 of the Complaint.

22. Roche denies the allegations contained in paragraph 22 of the Complaint.

23. Roche denies the allegations contained in paragraph 23 of the Complaint.

24. Roche denies the allegations contained in paragraph 24 of the Complaint.

25. Roche repeats and reasserts its responses to and denials of the allegations contained in paragraphs 1- 24 of the Complaint.

26. Roche denies the allegations contained in paragraph 26 of the Complaint, and states that CERA (short for Continuous Erythropoiesis Receptor Activator) was created by Roche and is a unique molecule and has been recognized by the FDA as a new chemical entity containing "no active moiety that [previously] has been approved by the FDA." *See* 21 C.F.R. § 314.108 (2005); *see also id*. § 314.50.

27. Roche denies the allegations contained in paragraph 27 of the Complaint.

28. Roche denies the allegations contained in paragraph 28 of the Complaint.

29. Roche denies the allegations contained in paragraph 29 of the Complaint.

30. Roche denies the allegations contained in paragraph 30 of the Complaint.

31. The statement of paragraph 31 of the Complaint is neither an averment nor allegation to which a response is required, and Roche otherwise denies these allegations.

## AFFIRMATIVE DEFENSES

### FIRST DEFENSE - FAILURE TO STATE A CLAIM

32. The allegations of the Complaint fail to state a claim upon which relief can be granted and should be dismissed under Fed. R. Civ. P. 12(b)(6).

### SECOND DEFENSE - PATENT MISUSE

33. The patents-in-suit are not enforceable, in whole or in part, due to wrongful and improper conduct by Amgen which constitutes patent misuse.

### THIRD DEFENSE - NON-INFRINGEMENT

34. Roche has not infringed and is not infringing any of the claims of the '868, '933, '698, '080, '349 and '422 patents, either directly or indirectly, or literally or under the doctrine of equivalents or due to the reverse doctrine of equivalents.

### FOURTH DEFENSE - SAFE HARBOR

35. Roche's allegedly infringing activities do not constitute infringement as a matter of law under 35 U.S.C. § 271(e)(1) (2006).

### FIFTH DEFENSE - INVALIDITY

36. The claims of the '868, '933, '698, '080, '349 and '422 patents are invalid because they fail to satisfy the conditions for patentability, including as specified in 35 U.S.C. §§ 101, 102, 103, 112, 116 and/or 282.

### SIXTH DEFENSE - DOUBLE PATENTING

37. The claims of the '868, '933, '698, '080, '349 and '422 patents are invalid for double patenting over claims of Amgen's earlier issued and now expired U.S. Patent No.

4,703,008 ("the '008 patent") and U.S. Patent No. 4,667,016; and the claims of the '349, '933, '080, and '422 patents are invalid for double patenting over the claims of the '868 and '698 patents.

**SEVENTH DEFENSE – INEQUITABLE CONDUCT BEFORE THE PATENT OFFICE**

~~**INTRODUCTION**~~

**INTRODUCTION**

38. Applicants for patents have a general duty of candor and good faith in their dealings with the Patent and Trademark Office ("PTO") and an affirmative obligation to disclose to the PTO all information that they know to be material to the examination of a pending application pursuant to 37 C.F.R. § 1.56 (2006). This duty extends to the applicants and their representatives, such as their attorneys, and all others associated with the prosecution, including "every person who is substantively involved in the preparation or prosecution of the application." *Id*.

39. In 1987 Amgen obtained the '008 patent which essentially claimed the isolated DNA sequence encoding EPO, and mammalian host cells transformed with this DNA sequence "in a manner allowing" these cells to express EPO and to glycosylate the biologically active EPO (referred to herein as "the DNA and host cell claims"). *See, e.g.*,'008 patent col. 40 ll. 1-3, 7-10, 60-62 (claims 2, 4, and 24). Amgen has enjoyed the full term of protection of this patent, which expired in 2004.

40. From 1995 to 1999 Amgen obtained new patents, which essentially claimed methods for making EPO protein by utilizing mammalian cells transformed with the DNA sequence encoding EPO (the '868, '698 and '349 patents), and the EPO protein expressed

by the transformed mammalian cells (the '933, '080, and '422 patents). Amgen has asserted these method and product claims against Roche as part of this lawsuit.

41. These six patents all share the same specification and all claim priority to the parent application of the '008 patent. These patents demonstrate that Amgen essentially possessed only a single invention with minor obvious variations.

42. The patents-in-suit are unenforceable because individuals substantively involved with the filing and prosecution of these patents, acting as agents or with the knowledge of plaintiff Amgen, knowingly and willfully concealed and misrepresented material evidence with the intent to deceive the PTO over the 16 years that Amgen prosecuted the '868, '933, '698, '080, '349 and '422 patents, and the now expired '008 patent.

**INEQUITABLE CONDUCT RELATING TO DOUBLE PATENTING**

43. The patents-in-suit are unenforceable because individuals including, but not limited to, Michael Borun, Steven Odre and Stuart Watt, associated with the filing and prosecution of these patents and acting as agents and/or with the knowledge of plaintiff Amgen, misrepresented **and omitted** material facts with the intent to deceive the PTO for purposes of overcoming a double patenting rejection based on Amgen's earlier filed and issued '008 patent.

44. During Amgen's prosecution of application Ser. No. 113,179 (the "'179 application"), which issued as the '868 patent, Amgen faced a double patenting rejection of all its pending claims (70 and 72-75) on grounds that these process claims were not patentably distinct from claims 1-6 of the '008 patent because it would have been obvious to one of skill to use the claimed erythropoietin encoding DNA of the '008 patent in prior art methods for host cell expression. Amgen overcame that rejection only by (1) misleading the examiner into believing that a dispositive judicial determination had already confirmed that none of the '008 patent

claims encompassed subject matter of its pending '179 application process claims, (2) misleading the examiner into believing that the Patent Office in interference proceedings had already determined the subject matter of its pending '179 application process claims to be patentably distinct from any of the '008 claims, and (3) by failing to disclose arguments it made before the Patent Office Board of Patent Appeals and Interferences (the "Board"), as well as in opposition proceedings in Europe involving Genetics Institute's EP 411 678 (the '678 patent) and EP 209 539 (the '539 patent), inconsistent with and refuting its arguments for patentability of its pending '179 application process claims.

45. In particular, during the '179 prosecution, Amgen misrepresented the court's decision in *Amgen, Inc. v. U.S. Int'l Trade Comm'n*, 902 F.2d 1532 (Fed. Cir. 1990), as holding that the "rights in the subject matter of '008 patent claims do not extend to the subject matter of the process claims herein . . . ." ('179 FH, Applicant's Amendment and Remarks Under 37 C.F.R. §§ 1.111 and 1.115 dated 10/7/94, at 7). The Federal Circuit considered only whether the composition claims fell within the ambit of 19 USC § 1337(g), which provides patentees the right to bring actions against foreign companies that allegedly infringe a patented process abroad. Significantly, the Court did not address whether the product claims were patentably distinct from the process Amgen was attempting to claim in the '179 application. The Court held only that the claims of the '008 patent could not be used in Section 1337(g) actions because they were not directed to a process. **Similarly, Amgen asserted that a decision before the European Patent Office Board of Appeals in Amgen's corresponding European Patent 0 148 605 supported the patentable distinction of the process claims. However, the European Board never addressed whether the process claims were patentable in light of Amgen's '008 patent.**

**('179 FH, Paper 43, Applicant's Amendment and Remarks Under 37 C.F.R. §§ 1.111 and 1.115 dated 10/7/94, at 9).**

46. Additionally, during the '179 prosecution, Amgen misrepresented to the examiner that in connection with Interference No. 102,096 (the "Fritsch I interference") (with its sole count identical to claim 2 of the '008 patent) and Interference No. 102,097 (the "Fritsch II interference") (with its sole count identical to then pending '179 application claim 65) "it has thus been the position of the Patent and Trademark Office that the production process subject matter claimed herein was patentably distinct from the DNA-related subject matter claimed in U.S. 4,703,008." ('179 FH, Applicant's Amendment and Remarks Under 37 C.F.R. §§ 1.111 and 1.115 dated 10/7/94, at 7).

47. Not only did this misrepresent the position of the Board, which made no such conclusion, Amgen failed to inform the examiner that in the Fritsch II interference it took the entirely contradictory position that its process claims were inherently part and parcel of the same invention as claimed in its '008 patent.

> While the count is directed to a process for preparing *in vivo* biologically active EPO using a mammalian host cell transfected or transformed with an isolated DNA sequence encoding human EPO [i.e., the process patent claims], and the litigation was directed to the purified and isolated DNA sequence and host cells transfected or transformed thereby [i.e., the '008 DNA claims], **it is evident that these are only different manifestations of the same invention** as acknowledged by Fritsch et al in their Motion Q here (and in Motion G in Interference No. 102,096). Clearly, the whole purpose and intent of the purified and isolated DNA sequence encoding human EPO (and host cells transfected therewith) at issue in the litigation was to express *in vivo* biologically active human EPO. Stated otherwise, the process language of the Lin patent claims at issue in the litigation ("encoding human EPO") [see '008 patent claims] is, for all intents and purposes, a description of the present count.

(*Fritsch v. Lin*, Interference No. 102,097, Brief. for the Senior Party Lin at 25-26. (emphasis added)).

Significantly, not only did Michael Borun submit Applicant's October 7, 1994 Amendment and Remarks in the '179 prosecution, Mr. Borun appears "of counsel" on the Lin Brief, evidencing his obvious familiarity with these contradictory positions that Amgen relied on during the interference and his knowing and intentional misrepresentation of those positions in prosecuting the '179 application.

48. Tellingly, Amgen also failed to inform the examiner that in the Fritsch II interference, it had argued that resolving priority issues in regard to the count for the DNA sequence in the Fritsch I interference would necessarily determine those issues in regard to its process claims:

> The same is true with regard to the count of Interference 102,097 [process for making EPO], **if Lin was the first to invent a host cell containing a DNA sequence in a manner allowing the host cell to express rEPO as determined by the Court [DNA count], he is of necessity the first to invent the process of making rEPO using such the host cell** (see the count of Interference 102,097) [process for making EPO]."

(Interference No. 102,097, Lin Reply Brief at 3 (emphasis in original)).

> "Fritsch [Genetics Institute] errs in saying that the District Court case did not involve the count (process for making EPO) of Interference No. 102,097. **The Court assessed the priority evidence regarding the DNA sequence used to make EPO and the reduction to practice of the sequence necessarily and inherently includes the use of that sequence to make EPO according to the count of Interference No. 102,097."**

(Interference No. 102,097, Lin Reply Brief at 9 (emphasis in original)).

49. Moreover, Amgen failed to disclose arguments it made during opposition proceedings in Europe involving Genetics Institute's EP 411 678 ('678 patent) and EP 209 539 ('539 patent) that were similarly inconsistent with and refuted its arguments for the patentability

of its '179 application process claims.[1] In this regard, Amgen acknowledged that its process and resulting *in vivo* biologically active erythropoietin was merely an obvious and inherent result of expressing the DNA sequence encoding human erythropoietin in a host cell: "the particular type of glycosylation linkages was simply a result of the type of host cell used to produce the recombinant erythropoietin." (EP 411 678 Opposition Proceedings, Statement of Grounds submitted by Amgen 10/8/92). Amgen's consistent pattern of failing to apprise the United States examiners of material information from European proceedings is similarly shown through its failure to disclose arguments that were raised during the opposition proceedings to its Kirin-Amgen European Patent Application No. 0 148 605 regarding the high materiality of errors in the data corresponding to Example 10 of its US patent application.

50. ~~Lastly,~~ Amgen also asserted that it was inappropriate for the Examiner to consider prior art (the Yokota 4,695,542 patent) in conjunction with the claims of the '008 patent to show that the pending claims were obvious ('179 FH Applicant's Amendment and Remarks Under 37 C.F.R. §§ 1.111 and 1.115 dated 10/7/94, at 10). Amgen presented no authority in support of this proposition, and consequently misstated the law, which provides that consideration of prior art may be necessary to determine whether one of skill in the art would

[1] In addition, Amgen also failed to disclose inconsistent arguments made during the following proceedings in Europe: (1) Ortho Pharmaceutical Corp. v. Boehringer Mannheim GmbH (Landgericht Dusseldorf (4 O 150/91)) (Patent infringement action for E 0 148 605), (2) Boehringer Mannheim GmbH v. Janssen-Cilag GmbH (4 O 229/91, Landgericht Dusseldorf) (Cilag I), EP 0 205 564 (3) Boehringer Mannheim GmbH v. Janssen-Cilag GmbH (4 O 58/92, Landgericht Dusseldorf) (Cilag II), EP 0 411 678; (4) Boehringer Mannheim GmbH v Kirin-Amgen, (3 Ni 32/93, Bundespatentgericht (BPG)) and appeals therefrom and (5) Kirin-Amgen and Ortho Pharmaceuticals v. Boehringer Mannheim GmbH and Boehringer Mannheim UK Ltd., The High Court Of Justice Chancery Division, Patents Court (CH 1993-K-No. 937).

deem the later claim to be merely an obvious variation on the earlier one. **Furthermore, when Amgen was faced with a double patenting rejection over the Lai '016 patent, Mr. Borun argued that the two-way test for non-obviousness applied, citing *In re Braat*, 937 F.2d 589 (Fed. Cir. 1991). In seeking to overcome the rejection based on the '008 patent, Mr. Borun again cited *Braat*, but did not explain that the two-way test would not apply. ('179 FH, Paper 43, 10/7/94 Amendment at 4-6).**

51. Throughout its response to the PTO's office action rejection on double patenting, Amgen therefore intentionally misrepresented its own understanding of the claims, misrepresented the facts of prior proceedings and misstated legal standards. This fraud on the PTO was motivated by Amgen's need to improperly extend the life of its EPO invention by maintaining and prosecuting applications that issued into patents, which were obvious over an earlier issued and now expired patent. In response, examiner Martinell allowed all of Amgen's pending claims, plainly demonstrating the examiner's reliance on Amgen's misrepresentations. But for these misrepresentations, the examiner would not have allowed the '179 claims to issue, as they did in the '868 patent, in any patent entitled to a term exceeding that of the earlier commonly owned '008 patent. *See Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 968 (Fed. Cir. 2001).

52. Amgen's misrepresentations during prosecution of the '179 application (which issued as the '868 patent) relating to the patentability of its pending product claims over the '008 patent are just as material to the product claims of the other later issued patents in the '179 family, the '698, '422 and '349 patents. But for such misrepresentations, examiner Martinell would not have allowed the claims of these patents to issue, as they did, in patents having a term exceeding that of Amgen's earlier commonly owned '008 patent.

53. Moreover, Amgen's understanding, (and admissions to the Patent Office) that the claimed product described by the pending '178 claims was merely the inherent product of the process Amgen was attempting to claim in the '179 prosecution renders these misrepresentations just as material to Amgen's prosecution of process claims in the '178 line of applications, which ultimately issued as the '080 and '933 patents, as they were to the claims of the '868 patent. (~~see~~***See*** *infra*, §§ ~~54~~**56**-~~64~~**66**). ~~But for~~**Amgen repeatedly stated during prosecution of the '178 line of applications that product was merely the inherent or obvious result of the claimed process. (*See, e.g.*, '178 FH, Paper 19, 1/10/90 Amendment at 6 ("it is submitted that if Lin was the first to invent the DNA encoding erythropoietin, and the use of that DNA in a host cell to produce recombinant erythropoietin, then clearly he was the first to invent a recombinant erythropoietin product produced using** such **a host cell") (emphasis in original); '178 FH, Paper 11, 6/2/89 Amendment at 3 ("All product claims are now product-by-process claims")). Therefore, but for the** misrepresentations **during the '179 prosecution**, ~~examiner~~**the** ~~Martinell~~**Examiner** would not have allowed the claims of ~~these~~**the '178 line of** patents to issue, as they did, in patents having a term exceeding that of Amgen's earlier commonly owned '008 patent.

**54. To the extent that Amgen asserts that these statements of inherency and obviousness are not admissions by Amgen, but rather recitations of Fritsch's arguments, then Amgen committed inequitable conduct by failing to correct the Board's understanding of its arguments, and the entire basis for the Board's decision in *Fritsch v. Lin* is tainted. The Board made clear that it relied on these arguments that an inventor need not "be personally involved in carrying out process steps" "where implementation does not require the exercise of inventive skill", such as the expression of the EPO gene in**

**mammalian host cells and isolation of the resulting glycoprotein. *Fritsch v. Lin*, 21 USPQ2d 1737, 1739 (Bd. Pat. App. & Interf. 1992). The Board further stated that "[w]e agree with Lin", there is "no evidence that the work done at Amgen relating to the expression of the EPO gene in mammalian host cells and isolation of the resulting glycoprotein product involved anything other than the exercise of ordinary skill by practitioners in that field." *Id.* Therefore, either Amgen's statements during prosecution are binding admissions or conclusive evidence that Amgen committed inequitable conduct during the Interferences to secure unpatentable claims, thus rendering each of the patents-in-suit unenforceable.**

**55. Amgen knowingly made these misrepresentations and omissions to overcome a double patenting rejection over the '008 patent with the intent to deceive the PTO, which relied upon Amgen's statements in determining whether to issue the patents-in-suit. But for Amgen's misconduct, the patents-in-suit would not have issued. Amgen was aware of its fraud and misconduct leading to the issuance of the patents-in-suit when it commenced its infringement suit against Roche.**

**INEQUITABLE CONDUCT RELATING TO FAILURE TO DISCLOSE THE BASIS FOR AN EXAMINER'S REJECTIONS OF SUBSTANTIALLY SIMILAR CLAIMS IN CO-PENDING APPLICATIONS**

**56.** ~~54.~~ Amgen's patents-in-suit all issued from one of two co-pending lines of applications, originating from applications Ser. Nos. 07/113,178 (the '178 application) and 07/113,179 (the '179 application), which Amgen filed on October 23, 1987 as continuations of Ser. No. 675,298, which issued October 27, 1987 as the '008 patent. The '178 line ultimately led to the '080 and '933 patents, while the '179 line ultimately led to the '868, '698, '422 and '349 patents.

**57.** ~~55.~~ As exemplified below, on numerous occasions during the prosecution of these co-pending lines of applications, the examiner in one line of co-pending applications issued rejections to claims that were substantially similar to claims that Amgen was prosecuting in the other co-pending line. The existence and grounds for such rejections in one co-pending line constituted highly material information that Amgen had a duty to disclose in the other co-pending line either under the pre-1992 "reasonable examiner" standard, or the new Patent Office standard set forth in 37 C.F.R. §1.56 (1992). *See Dayco Prods., Inc. v. Total Containment, Inc.*, 329 F.3d 1358, 1367-8 (Fed. Cir. 2003). A prior rejection of a substantially similar claim refutes, or is inconsistent with the position that those claims are patentable. An adverse decision by another examiner, therefore, meets the materiality standard under the amended Rule 56. *Id.*

**58.** ~~56.~~ Here, the patents-in-suit are unenforceable because individuals associated with the filing and prosecution of these patents, in arguing for the patentability of pending claims in one line of applications, knowingly took positions inconsistent with highly material arguments that examiners raised against the patentability of substantially similar claims in the other co-pending line of applications, but nonetheless knowingly and intentionally failed to disclose those rejections.

**59.** ~~57.~~ Amgen's intent to deceive the patent office is further evidenced by the fact that at least Amgen attorneys Steven Odre and Michael Borun were both involved throughout the prosecution of the '178 and '179 lines of applications, and therefore, had intimate knowledge regarding the proceedings of both lines of applications. (*See* '178 FH, Preliminary Amendment dated 10/23/87; '178 FH, Exam'r Interview Summary Record dated 7/20/88; '178 FH, Exam'r Interview Summary Record dated 11/18/93; '774 FH, Exam'r Interview Summary

Record dated 3/14/96; '179 FH, Preliminary Amendment dated 10/23/87; '179 FH, Exam'r Interview Summary Record dated 9/14/88; '179 FH, Exam'r Interview Summary Record dated 9/7/94.) In addition, Mr. Borun was intimately involved in and therefore, aware of material details of the prosecution of the applications which led to the '008 patent. (*See* '179 FH, Decl. Accompanying Petition to Make Special Because of Actual Infringement dated 2/9/88).

**60.** ~~58.~~ In prosecution of the '179 application, Amgen submitted a Second Preliminary Amendment canceling all pending claims and entering five new claims 65-69. Among these the only independent claim (65) recited "a process for the preparation of an *in vivo* biologically active glycosylated polypeptide comprising the steps of:

> (a) growing a mammalian host cell which is capable of effecting post-translational glycosylation of polypeptides expressed therein and which is transformed or transfected with an isolated DNA sequence encoding a polypeptide having a primary structural conformation sufficiently duplicative of that of 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, or the progeny thereof, under nutrient conditions suitable to allow, in sequence,
>
> > (i) transcription within said host cell of said DNA to mRNA in the sequence of transcription reactions directed by the nucleotide sequence of said DNA;
> > (ii) translation within said host cell of said mRNA to a polypeptide in the sequence of translation reactions directed by the nucleotide sequence of said transcribed mRNA;
> > (iii) glycosylation within said host cell of said polypeptide in a pattern directed by the amino acid sequence of said translated polypeptide and sufficiently duplicative of the pattern of glycosylation of naturally occurring human erythropoietin to allow possession by the translated glycosylated polypeptide product of the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells; and
>
> (b) isolating the glycosylated polypeptide so produced.

The dependent claims further characterized the claimed process in terms of host cell expression of cDNA (68) or genomic DNA (69) sequences, particularly in a CHO cell (66) or COS cell (67). ('179 FH, Second Preliminary Amendment dated 5/24/88 at 3-4).

**61.** ~~59.~~ In the first Office Action dated August 3, 1988, Examiner Tanenholtz rejected the pending claims to a host cell expression process for making a glycosylated recombinant EPO (~~rEPO~~**r-EPO**) as obvious and unpatentable over Yokota *et al*. (US Pat. No. 4,695,542) which taught production of a glycosylated protein by expressing of a DNA sequence encoding the protein in a mammalian host cell, and also in view of Gething *et al*. 1984 (Modern Approaches to Vaccines pages 263-268), which indicated that eukaryotic cells innately possessed the property of glycosylating proteins. ('179 FH, Office Action dated 8/3/88, at 3). Among other things, the Examiner noted that "it would be expected that where one expresses the cDNA gene encoding erythropoietin using the Yokota *et al*. procedures the resulting erythropoietin would necessarily be glycosylated."

**62.** ~~60.~~ In this same time period, in its co-pending '178 application, Amgen sought to prosecute substantially similar claims directed to the product of the process described by its pending '179 application claims. Significantly, Examiner Tanenholtz was not involved in the '179 prosecution, which was before a different examiner, Jeff Kushan. In particular, in its December 1, 1988 Amendment and Reply, Amgen added new claims 61-66 directed to a human erythropoietin glycoprotein product "having a primary structural conformation 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 further characterized as a product derived "from eukaryotic host cell expression (61) of exogenous cDNA (62) or genomic DNA (63)

sequences, particularly in mammalian host cells (64) such as COS (65) and CHO(66) cells." ('178 FH, Amendment and Reply Under 37 C.F.R. §1.111 and 1.115 dated 10/23/87, at 5-6).

**63.** ~~61.~~ The substantial similarity of these pending '178 claims to the pending process claims of the '179 application (and Amgen's awareness of that fact) is evident through Amgen's response to Examiner Tanenholtz' August 3, 1988 Office Action in the '179 prosecution. There, Amgen argued that pending claims 65-69 were directed to "a novel series of process steps wherein a mammalian host cell (including such non-human, non-kidney cells as COS and CHO cells as specified in claims 66 and 67) capable of glycosylating the expressed polypeptides is first transformed or transfected with a DNA sequence (including, e.g., cDNA and genomic DNA as specified in claims 68 and 69) encoding a specifically delineated polypeptide, i.e., one having a sufficient amino acid sequence homology to natural human erythropoietin to allow it to qualify, amino acid sequence-wise, for potential in vivo biological activity. (The DNA reagent employed in the transformation/transfection process is itself the novel and unobvious subject matter of claim 7 of U.S. Patent 4,703,008 and the resulting host cells are as recited in claim 24 of the Patent)." ('179 FH, Applicant's Reply dated 9/27/88, at 2).

**64.** ~~62.~~ Amgen's characterization of its pending '179 claims strikingly demonstrates that Amgen's '178 application claims were directed to nothing more than the inherent product of '179 claims 65-69. Aware of the high materiality of Examiner Tanenholtz's rejection in the '179 prosecution to the substantially similar claims then pending in the '178 prosecution, Amgen knowingly and intentionally failed to disclose that rejection, or the basis for that rejection to Examiner Kushan in the '178 prosecution.

**65.** ~~63.~~ Amgen's failure to disclose Tanenholtz' August 3, 1988 rejection in the '178 prosecution took on even greater significance in view of Amgen's subsequent actions

in the '178 prosecution. On February 10, 1989, examiner Kushan issued a Final Office Action rejecting all the pending claims on several grounds. Among the rejections, Kushan objected to the claimed description of the glycoprotein product as having "glycosylation sufficiently duplicative of that of a naturally occurring human erythropoietin" as indefinite in "not particularly pointing out what the actual glycosylation comprises." ('178 FH, Office Action dated 2/10/89, at 2). Notably, examiner Kushan never raised the argument that Tanenholtz had raised as to the obviousness of the process used to make the claimed ~~rEPO~~**r-EPO** product, nor did he raise the Yokota or Gething references that Tanenholtz had cited.

**66.** ~~64.~~ In response, Amgen replaced all pending claims with new claims 67-75, which defined the claimed product solely through the process through which it was made. In particular, Amgen noted that "[a]ll product claims in the subject application are now product-by-process claims. Independent claim 67, and thus all of the pending claims, specifically define the erythropoietin of the subject invention as a 'glycoprotein product of the expression of an exogenous DNA sequence in a eucaryotic host cell....' These product-by-process claims are presented in an effort to positively recite the physical properties of recombinant erythropoietin, and 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." ('178 FH, Amendment under Rule 116 dated 6/2/89, at 3-4). Amgen once again failed to disclose the rejection by Tanenholtz as to the obviousness of this process.

**67.** ~~65.~~ In fact, throughout the remainder of the '178 prosecution, Amgen continued to argue the novelty of claims to a glycosylated erythropoietin product knowing that its arguments were wholly inconsistent with the basis of Examiner Tanenholtz' 1988 rejection of

claims directed to that process as obvious, but never bringing that rejection to the attention of the '178 examiners.

**68.** ~~66.~~ In an Amendment dated July 11, 1989, Amgen left all its product-by-process claims pending, amending only claim 67 to specify that the claimed product of host cell expression was one produced through a process using a non-human host cell, in order to distinguish the claimed erythropoietin product from the erythropoietin product produced by using a human cell line in the process taught by Sugimoto. ('178 FH, Amendment dated 7/11/89, at 5). Once again, Amgen failed to disclose the rejection by Tanenholtz as to the obviousness of the process described in the pending claims.

**69.** ~~67.~~ In the subsequent Amendment dated January 10, 1990, Amgen cancelled claims 67-75, replacing them with new claims 76-83, which Amgen indicated "are similar to cancelled claims 67-75, but which specify that the DNA sequences encode human erythropoietin. These new claims parallel claim 2 of U.S. Patent No. 4,703,008 (Lin '008 patent), the parent of the instant application." ('178 FH, Amendment under Rule 116, dated 1/10/90, at 5).

**70.** ~~68.~~ In addition, Amgen argued against suspending prosecution during the co-pending *Fritsch v. Lin* interferences No. 102,096 (Fritsch I) involving the Lin '008 patent and No. 102,097 (Fritsch II) involving the Lin '179 process application, in view of the December 11, 1989 decision in *Amgen, Inc., v. Chugai Pharm. Co., Ltd. and Genetics* ~~*Instit*~~***Inst****., Inc*. Civil Action No. 87-2617-Y. In particular, Amgen indicated that against an anticipation attack based on Dr. Fritsch's work at Genetics Institute, not only had the Court upheld claims of the Lin '008 patent directed to the purified and isolated DNA sequence for human erythropoietin, it had also upheld claims to a host cell transformed with such a sequence. ('178 FH, Amendment under

Rule 116 dated 1/10/90, at 5-6). Amgen asserted the Court's decision was therefore "fully dispositive" not only of any priority issue in both interferences, including the Fritsch II interference involving the '179 application, but also of any priority issue in the subject '178 application, stating: "if Lin was the first to invent the DNA encoding erythropoietin and the use of that DNA in a host cell to produce recombinant erythropoietin, then clearly he was the first to invent a recombinant erythropoietin product produced using such a host cell." *Id*. at 6. Knowing this, Amgen again knowingly and intentionally failed to disclose the rejection by Tanenholtz as to the obviousness of the process, while at the same time arguing that its amendment rendered the claims "in condition for immediate allowance and issuance of a patent." *Id.* at 5.

**71.** ~~69.~~ Amgen continued prosecution of the '178 claims in the '874 application, which Amgen filed on February 28, 1994. On April 8, 1994, Amgen submitted a voluminous Information Disclosure Statement ("IDS"), listing almost 400 references, including references of record in the '178 prosecution, the '179 prosecution, the European Opposition Proceeding involving Amgen's EP 148,605, defendant's section 282 notice from *Amgen v. Chugai*, as well as admitted exhibits from *Amgen v. Chugai*. ('874 FH, IDS dated 4/8/94). Significantly, a biotechnology examiner would only have spent approximately 20 hours examining any individual application, such as the '874 application. (*See, e.g.*, U.S. Gen. Accounting Office, GAO-RCED-89-120BR, Biotechnology, Backlog of Patent Applications, at 20 (1989)). Although the 4/8/94 IDS included the Yokota and Gething references cited in the '179 prosecution by examiner Tanenholtz, had the examiner devoted all his time merely to reviewing the cited references, he would have had only about three minutes for each reference. Amgen's continued failure to bring the rejection by Tanenholtz to the attention of the examiners in the '178 line of applications, or to point out the relevance of the Yokota and Gething

references to that rejection, assured that the material nature of these references would remain buried under a mountain of other art.

**72.** ~~70.~~ Amgen's failure to disclose relevant rejections from its co-pending '179 line continued in its prosecution of the '874 application. In a Preliminary Amendment, Amgen cancelled all pending claims, which it replaced with new claims 84-89 (which going forward were renumbered as claims 87-97). ('874 FH, Preliminary Amendment dated 6/13/94). Among the new pending independent claims, Amgen again included product-by-process claims defining the claimed human erythropoietin glycoprotein solely through the process by which it was produced. For example, claim 86 (renumbered as 89) recited:

> The *in vivo* biologically active human erythropoietin glycoprotein product of the process comprising the steps of:
>
> (a) growing, under suitable nutrient conditions, mammalian host cells transformed or transfected with an isolated DNA sequence encoding the human erythropoietin amino acid sequence set out in FIG 6 or a fragment thereof; and
>
> (b) isolating a glycosylated erythropoietin polypeptide therefrom.

Amgen again failed to raise the 8/3/88 rejection by Tanenholtz that the process of host cell expression incorporated into this claim would have been obvious over Yokota *et al* 4,695,542 and Gething *et al* (Modern Approaches to Vaccines pages 263-268).

**73.** ~~71.~~ Amgen filed both application Ser. No. 468,556, which ultimately issued as the '080 patent, as well as application Ser. No. 487,774, which ultimately issued as the '933 patent, as continuation applications from the '874 application. Amgen's failure to disclose the highly relevant and material rejections it received during the '179 prosecution, as described herein, during prosecution of the '178 and '874 applications, therefore critically tainted the prosecution of both the '080 and '933 patents. Accordingly, on these grounds, both the '080 and '933 patents should be held unenforceable for inequitable conduct before the Patent Office.

**74.** ~~72.~~ Amgen's pattern of intentionally withholding material information from the examiners is further evidenced by its failure conversely to disclose rejections it received in the course of prosecuting claims in the '178 line of applications during its prosecution of the '179 application as well as in further continuations of the '179 application, specifically, application Ser. No. 609,741, Ser. No. 957,073, and Ser. No. 100,197. The '178 application contained pharmaceutical composition claims that were substantially similar to those of the '741, '073 and '197 applications, which eventually issued as the '422 patent. In addition, as also noted, *supra*, in paragraphs ~~58-64,~~**60-66,** the '178 application contained product-by-process claims that were substantially similar to the process claims of the '179 application, which eventually issued as the '868 patent.

**75.** ~~73.~~ In particular, during the prosecution of substantially similar claims in the '179, '741, '073 and '197 applications, Amgen failed to disclose the following rejections made during the prosecution of the '178 application:

(1) The June 2, 1988 rejection by Examiner Kushan rejecting, among others, claim 55 under 35 U.S.C. 103 as being unpatentable over Miyake *et al*, Takezawa *et al*, Chiba *et al* or Sugimoto *et al* in view of Papayannopoulo *et al*. Amgen argued for the patentability of claims substantially similar to rejected claim 55 in the '741, '073 and '197 applications and failed to disclose the prior rejection by Examiner Kushan. (*See* '741 FH, Preliminary Amendment dated 11/6/90; '073 FH; and '197 FH Amendment Under Rule 1.116 dated 12/20/93);

(2) The February 10, 1989 rejection by Examiner Kushan rejecting, among others, claims 61-66 under 35 U.S.C. §103 as being unpatentable over Miyake *et al*, Chiba *et al*, Takezawa *et al* or Sugimoto *et al* and claims 55 and 61-66 under 35 U.S.C. 103 as being unpatentable over Miyake *et al*, Chiba *et al*, Takezawa *et al* or Sugimoto *et al*, in view of ~~Papayannaopoulo~~**Papayannopoulo** *et al*. Amgen argued for the patentability of claims substantially similar to the rejected claims in the '179, '741, '073 and '197 applications and again failed to disclose the prior rejections by Examiner Kushan. (*See* '741 FH, Preliminary Amendment dated 11/6/90; '073 FH; '197 FH Amendment Under Rule 1.116 dated 12/20/93; and '179 FH Applicant's Second Preliminary Amendment dated 5/24/88, Applicant's Amendment and Response Under 37 C.F.R. §§1.115 and 1.111 dated 1/3/94);

(3) The June 20, 1989 rejection by Examiner Kushan rejecting, among others, claims 67-73 under 1) the doctrine of obviousness-type double patenting as being unpatentable over the prior invention as set forth in claim 1 to 11 of U.S. Patent No. 4,667,016, 2) 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over Sugimoto *et al*. and 3) 35 U.S.C. 103 as unpatentable over Sugimoto *et al*. in view of Papayannopoulo *et al*. Amgen argued for the patentability of claims substantially similar to the rejected claims in the '179, '741, '073 and '197 applications and again failed to disclose the prior rejection by Examiner Kushan. (*See* '741 FH, Preliminary Amendment dated 11/6/90; '073 FH; '197 FH Amendment Under Rule 1.116 dated 12/20/93; and '179 FH Applicant's Second Preliminary Amendment dated 5/24/88, Applicant's Amendment and Response Under 37 C.F.R. §§1.115 and 1.111 dated 1/3/94);

(4) The September 18, 1989 rejection by Examiner Kushan rejecting, among others, claims 67-73 under the doctrine of obviousness-type double patenting as being unpatentable over the prior invention as set forth in claim 1 to 11 of U.S. Patent No. 4,667,016. Amgen argued for the patentability of claims substantially similar to the rejected claims in the '179, '741, '073 and '197 applications and again failed to disclose the prior rejection by Examiner Kushan. (*See* '741 FH, Preliminary Amendment dated 11/6/90; '073 FH; '197 FH Amendment Under Rule 1.116 dated 12/20/93; and '179 FH Applicant's Second Preliminary Amendment dated 5/24/88, Applicant's Amendment and Response Under 37 C.F.R. §§1.115 and 1.111 dated 1/3/94).

**INEQUITABLE CONDUCT RELATING TO MISREPRESENTATIONS AND OMISSIONS REGARDING ALLEGED DIFFERENCES BETWEEN R-EPO AND U-EPO**

***Contradictory Statements of Amgen's Scientist***

**76.** ~~74.~~ Amgen, and those acting on its behalf who were substantively involved in the prosecution of the patents-in-suit, **including Drs. Lin, Strickland and Egrie, and Amgen attorneys Messrs. Borun, Odre, Watt and Byrne** knowingly misled the PTO through misstatements and omissions of material information with the intent to deceive and mislead the PTO to obtain the patents-in-suit, thereby tainting all patents sharing the common specification. Accordingly, the patents-in-suit should be held unenforceable for inequitable conduct before the PTO.

**77.** ~~75.~~ In order to obtain allowance for its protein claims, Amgen distinguished its recombinant EPO ("r-EPO") from natural urinary EPO ("u-EPO") by representing that the average carbohydrate composition, glycosylation, and molecular weight of its r-EPO were different from that of naturally occurring human EPO proteins. Amgen incorporated these alleged differences into claims of the '933 and '080 patents as elements of patentability and proceeded to argue to the PTO, even in the face of its own contradictory data, that these elements made these claims patentable over u-EPO.

**78.** ~~76.~~ Amgen and its representatives, in the course of foreign patent proceedings and before the FDA, relied on statements and information regarding the molecular weights and carbohydrate compositions of r-EPO and u-EPO that were inconsistent, and refuted the positions Amgen took during prosecution of its patents before the PTO, and in the *Fritsch et al. v. Lin* patent interference No. 102,334.

**79.** ~~77.~~ Two declarations, which have *never been previously considered by this or any U.S. Court*, contain sworn statements by an Amgen scientist which utterly contradict positions that Amgen took in arguing patentability of its then pending EPO claims to the PTO.

**80.** ~~78.~~ Dr. Thomas W. Strickland became involved in Amgen's EPO project in August 1984 and worked on the purification of r-EPO. Dr. Strickland was also involved in the prosecution of Amgen's protein patents related to EPO. In December 1988, during the prosecution of the '178 application, Amgen submitted a declaration by Amgen's scientist, Dr. Strickland **("the 1988 Strickland Declaration")**, stating that Amgen's recombinant EPO product was chemically distinct, and therefore novel and patentable over natural human EPO that was isolated and purified from urine ~~("the 1988 Strickland declaration")~~. Specifically, Strickland stated:

> recombinant erythropoietin as described by Serial No. 113,178 has a different carbohydrate composition than naturally occurring urinary erythropoietin.

('178 FH, Strickland Decl. dated 11/30/88, at 15).

**81.** ~~79.~~ The prosecution history for the '178 application shows that the assertions made in the 1988 Strickland declaration were crucial for the patentability of Amgen's product claim to EPO. The Examiner Interview Summary Record dated 1/26/89 makes it clear that the Examiner interpreted the declaration to relate to differences in carbohydrate content. As stated by the Examiner:

> [D]iscussed effect of declaration on 102 aspects of the original rejection. Discussed effect on 103-based arguments of the difference in glycosylation (carbohydrate content).

('~~179~~**178** FH, Exam'r Interview Summary Record dated 1/26/89 (emphasis added)). **It is clear that but for the submission of the 1988 Strickland Declaration, the Examiner would not have withdrawn his §102 rejection. (*See* '178 FH, Paper 8, 2/10/89 Office Action at 4-5 ("Applicant has shown through the declaration of Strickland and via the disclosure of Takeuchi *et al.* that there is a difference in the overall carbohydrate composition between the naturally occurring and recombinant species," which was "sufficient to overcome the rejections over 35 USC 102.")).**

**82.** ~~80.~~ Amgen made this argument (both in 1988 in order to obtain the '933 patent, and then later in the Fritsch v. Lin interference proceeding) knowing it was false, and then continued to hide that fact from the patent office. The clear evidence for this is that the 1988 declaration by Strickland was directly contradicted by Dr. Strickland himself in two later declarations filed in connection with two opposition proceedings in Europe to Genetics Institute's erythropoietin patents EP 411 678 ("the '678 patent) and EP 209 539 ("the '539 patent").

**83.** ~~81.~~ In February 1992, Amgen submitted the first declaration by Dr. Strickland in support of Amgen's European opposition proceedings against the Genetics Institute '678 patent ("the 1992 Strickland declaration"). (Strickland European Decl. dated 2/13/92). The '678 patent contained claims drawn to a method for producing glycosylated recombinant EPO, which Amgen opposed by arguing, in part, that r-EPO and u-EPO were the same. Strikingly, the '678 patent reported its r-EPO as being analytically identical to human EPO purified from urine (u-EPO). The 1992 Strickland declaration argued that the '678 patent claims produced a protein that is indistinguishable in terms of carbohydrate composition from a protein that was produced by Amgen in 1985 using the procedures set forth in Example 10 of Amgen's European patent EP 148 605 ("the '605 patent"), which is the European counterpart to the '933 patent. Based on experiments discussed in the 1992 Strickland declaration, Strickland concluded that the carbohydrate composition of the 1985 EPO prepared in accordance with Example 10 of Amgen's '605 patent was the same, within the range of experimental and analytical error, as the EPO of the Genetics Institute '678 patent which in turn, according to that '678 patent was chemically identical to u-EPO. The 1992 Strickland declaration was not disclosed to the PTO.

**84.** ~~82.~~ In May 1994, Amgen submitted another declaration by Dr. Strickland in support of Amgen's European opposition proceedings against Genetic Institute's '539 patent ("the 1994 Strickland declaration"). The Genetics Institute patent had claims directed to a recombinant EPO product, which Amgen again opposed by arguing, in part, that r-EPO and u-EPO were the same. In this declaration, Dr. Strickland stated:

> In order to demonstrate the viability of the specific disclosure of Example 10 of EP 148605 [counterpart U.S. patent], reverse phase HPLC was used to purify rEPO directly from cell culture media in which the rEPO had been expressed from CHO cells as described in Example 10. The results show that by following the disclosure of example 10 homogeneous erythropoietin is obtained that meets

> all the requirements of claim 2 of EP 209539, *i.e.*, ...(b) a molecular weight of about 34,000 daltons on SDS-PAGE ...

(Strickland European Decl. dated 5/14/94, at 2 (emphasis added)). According to this declaration, r-EPO prepared in accordance with Example 10 had a molecular weight of 34,000 daltons, the same as that of u-EPO as reported at Col. 5, line 48 of the '933 patent, and not higher, as reported in Example 10.

**85.** ~~83.~~ Significantly, Amgen submitted an IDS for the U.S. Application Ser. No. 202874 which listed dozens of references that were part of the European proceedings involving EPO. However, the 1992 and 1994 Strickland declarations were not disclosed to the PTO. Amgen's knowing and intentional failure to disclose material information from Amgen's European opposition proceedings is evidenced at least by the direct involvement of Amgen attorneys Steven Odre and Stuart Watt in those proceedings, which included personally attending oral proceedings in Europe. (EP 411 678, EPO Opposition Proceedings , Record of Public Oral Proceedings Before the Opposition Division, dated 12/16/94). Additionally, the claims of the later issued '698, '080, '349 and '422 patents from the same family as the '933 patent, are sufficiently interrelated with the '933 claims and have a substantial relationship with the inequitable acts such that these patents should also be deemed unenforceable under the doctrine of "~~"~~"infectious unenforceability."~~"~~"

***Additional Contradictory Statements***

**86.** ~~84.~~ In addition to the contradictory statements made by Amgen in the 1992 and 1994 Strickland declarations, Amgen and its employees, including even the named inventor of the Amgen EPO Patents, have made numerous statements, in publications and to the FDA, that directly contradict positions Amgen has taken before the PTO during the prosecution of the patents in suit. These additional contradictory statements further evidence Amgen's intent

to deceive the PTO. *See Digital Control Inc. v. Charles Mach. Works*, 437 F.3d 1309, 1319 (Fed. Cir. 2006) ("Intent . . . may be inferred from the totality of the evidence."). Tellingly, Amgen's conduct throughout prosecution reveals a consistent pattern of purposely failing to disclose material information to the examiners. During the prosecution of the '349 and '422 patents, Amgen made no effort to inform the PTO of the then pending litigation against TKT (Civil Act. No. 97-10814-WGY).

**87.** ~~85.~~ Lin, the inventor of the patents in suit, reported in a publication that "[r-EPO] has an apparent [molecular weight] of 34,000 when analyzed in an electrophoretic transfer blot." Lin *et al*, *Cloning and Expression of the Human Erythropoietin Gene*, 82 Proc. Nat'l Acad. Sci., 7580, 7582 (1985). The specification for the '933 patent states that the molecular weight of natural EPO was also ~~"~~"approximately 34,000 dalton.~~"~~" ('933 patent, Col. 5, lines 48-50). Lin, therefore, knew as of 1985 that the molecular weights of r-EPO and u-EPO were the same, yet, as shown in Example 10 of the '933 patent which issued from an application that was filed in 1995, continued to state that the molecular weight of r-EPO was higher than that of u-EPO.

**88.** ~~86.~~ In addition, two Amgen scientists, Dr. Joan Egrie, and Dr. Thomas Strickland, reported in a publication that "Both the purified natural and recombinant EPO preparations were characterized . . . by Western analysis. . . . By Western analysis, the recombinant and human urinary EPO migrate identically." Egrie *et al*,, *Characterization and Biological Effects of Recombinant Human Erythropoietin*, 172 Immunobiology 213 (1986). If r-EPO and u-EPO "migrate identically" that means that the two products have the same apparent molecular weight. Therefore, the finding that r-EPO and u-EPO "migrate identically"

contradicts Dr. Egrie's data reported in Example 10 in the '933 patent. This publication, however, was withheld from the Examiner of the '933 patent.

**89.** ~~87.~~ Additional internal documents from Dr. Egrie provide evidence regarding glycosylation inconsistent with the positions that Amgen took during prosecution of its patents. (*See* AM-ITC 00828987-88). This information was never disclosed to the examiner.

**90.** ~~88.~~ Another Amgen scientist, Jeff Browne, corroborated the published findings of Egrie and Strickland, stating in a publication that human u-EPO and CHO-cell derived r-EPO migrate identically in SDS-polyacrylamide gels. Browne *et al*, *Erythropoietin: Gene Cloning, Protein Structure, and Biological Properties*, 51 Cold Spring Harbor Symposia on Quantitative Biology 693-702, 698 (1986). This publication also was not disclosed to the Examiner. Additionally, in order to receive approval for its r-EPO drug, Amgen made statements to the FDA that directly contradict the positions Amgen took in arguing patentability of its EPO claims to the PTO. Significantly, these statements were not submitted to the Examiner of the '933 patent. (*See* Amgen PLA, Vol. 4, pg 762 and Figure 9.C-1 (June 1989)).

***Misrepresentations and Omissions Regarding COS r-EPO***

**91. As noted above, Applicant made many arguments for patentability centering around an alleged difference in glycosylation between urinary EPO and recombinant EPO. Indeed, claims in the '933 and '080 patents contain limitations reflecting a purported difference in glycosylation between urinary EPO and recombinant EPO. (*See, e.g.*, '933 patent, claims 1, 6; '874 FH, Paper 37, 6/13/94 Preliminary Amendment; '774 FH, Paper 50, 12/20/95 Second Preliminary Amendment and Remarks at 2; '178 FH, Paper 6, Amendment and Reply at 3; '080 patent, claim 1; '556 FH, Paper 4, Claims for Discussion). During prosecution of the patents-in-suit, Applicant frequently**

**maintained that the claimed inventions covered recombinant erythropoietin expressed in a variety of host cells, including CHO and COS cells. (*See, e.g.*, '178 FH, Paper 6, Amendment and Reply at 6; '179 FH, Paper 33, 1/3/94 Amendment and Response at 5).**

**92. Applicant was therefore required to show a difference in glycosylation between urinary erythropoietin and recombinant erythropoietin from both CHO and COS cells. Indeed, Examiner Kushan stated in an Office Action that "the sites and extent of glycosylation and how they 'differ' from native EPO should be pointed out." ('178 FH, Paper 4, 6/2/88 Office Action at 4). Mr. Sharp -- a colleague of Mr. Borun -- responded by providing the 1988 Strickland Declaration, discussed above.**

**93. When Applicant submitted the 1988 Strickland Declaration to show differences between u-EPO and r-EPO, Applicant knew that (1) Dr. Strickland's conclusions were based solely on experiments comparing u-EPO to r-EPO expressed in CHO cells and not COS cells, ('178 FH, Paper 7, Strickland Declaration at 2 ("The r-HuEPO for use in the experimental procedures was prepared in accordance with the general procedures described in Example 10")), and (2) there was significant data showing that there was no difference in glycosylation or carbohydrate composition between u-EPO and r-EPO expressed in COS cells. Amgen and its scientists were widely disseminating throughout the scientific community that its COS r-EPO was the same as urinary EPO. Specifically, the following articles and presentations evidence the similarity in u-EPO and r-EPO expressed in COS cells:**

- **Egrie *et al.*, Characterization Of Recombinant Monkey And Human Erythropoietin, *Proc Clin Biol Res.* 1985;191:339-50. (showing identical migration and identical apparent molecular weight)**
- **Egrie *et al.*, Abstract (1984) from 10th Annual Fredrick Stohlman Memorial Symposium on Stem Cell Physiology, Boston, MA, October 2, 1984. (showing identical migration and identical apparent molecular weight)**

- **Egrie *et al.*, Presentation (1984) from 10th Annual Fredrick Stohlman Memorial Symposium on Stem Cell Physiology, Boston, MA, October 2, 1984 (AM-ITC 01073032-42) (showing identical migration)**
- **Egrie, Presentation Transcript "Cloning of Human & Monkey EPO" (1984) from Hemoglobin Switching Meeting, Airlie House, Virginia, September 1984 (AM-ITC 00557610-16) (showing identical migration, apparent molecular weight, size and glycosylation to the same extent).**

**Amgen did not disclose any of this information to the Examiner, and the rejection based on §102 was subsequently withdrawn. (*See* '178 FH, Paper 7, Strickland Declaration; Paper 9, 2/10/89 Office Action).**

**94. Furthermore, Dr, Egrie was responsible for providing information regarding glycosylation and molecular weight for inclusion in the specification of the patents-in-suit. She provided a laboratory notebook to Mr. Borun before the '298 application was filed that showed that COS r-EPO was the same as u-EPO. Indeed, she plainly and unequivocally concluded that "human EPO produced by COS cells have the same molecular weight as native urinary EPO (Goldwasser's EPO). This result indicates that the recombinant EPO is glycosylated to the same extent as the native protein." (AM-ITC 01072494, 97). Mr. Borun has testified that he asked for this information and it was provided to him before he drafted and submitted the '298 application. He has also testified that he had the data in his files and that his normal practice would have been to review the data. Finally, he has affirmatively testified that during the prosecution of the '933 and '080 patents, he was aware of the data. However, none of this data was submitted in the course of prosecuting any of the patents-in-suit. Such conduct manifests an intent to deceive the Patent Office by concealing material data that directly contradicts the patentability of Amgen's claims.**

**95. After Examiner Kushan found that the 1988 Strickland Declaration was sufficient to overcome the §102 rejection, Amgen continued prosecuting the '178 application and continued to argue that there was a difference between r-EPO and u-EPO, described in the 1988 Strickland Declaration, sufficient to overcome a rejection based on Sugimoto *et al.* ('178 FH, Paper 15, Amendment at 5). Again, in this Amendment, Amgen's attorney Mr. Byrne provided none of the contrary information on COS cells.**

**96. At a later point in the prosecution of the '178 line of applications, Mr. Borun submitted an IDS disclosing, among other references, WO 86/03520 ("PCT '520"), which he represented as a reference of record in the parent applications of the '178 application. ('874 FH, Paper 36, 4/8/94 IDS). However, the only application in which this is cited is the '179 application, which is not related to the '178 application. It is cited nowhere in the prosecution of the parent applications, nor is the reference listed on the face of the '008 patent. Because Mr. Borun represented the reference as being "of record", this caused Examiner Martinell to give full faith and credit to the earlier consideration of the reference by other examiners, rather than giving it a thorough review. However, the PCT '520 plainly discloses that "EPO produced by COS cells has a mobility on SDS-polyacrylamide gels which is identical to that of native EPO prepared from human urine." (WO 86/03520, pp. 10, 26-27, and Fig. 6). Mr. Borun did not bring this to the attention of the Examiner. Furthermore, in 1992, when Dr. Strickland submitted a declaration opposing EP 0 411 678, which has the same disclosure as the PCT '520, he concluded that the values were within the range of experimental and analytical error. Therefore, Dr. Strickland was clearly aware of the teachings of the PCT '520 during the prosecution of at least the '933 and '080 patents, but Amgen did not submit this declaration to the PTO.**

**97. When Amgen continued prosecuting the '178 application and faced a rejection based on Sugimoto, it disclosed the Cummings Declaration which similarly only focused on CHO r-EPO. (*See* AM-ITC 00903254-488). The only mention of COS r-EPO was in passing, and was in reliance on the misrepresentations set forth in the Lin application. Dr. Cummings did not discuss any of the literature relating to COS r-EPO. Dr. Cummings did mention "2 articles by Egrie" discussed by Dr. Conradt in an opposing declaration, but provided no identifying information, nor were these articles or Dr. Conradt's declaration attached to his declaration. To the extent that these "2 articles" refer to Egrie articles discussing COS r-EPO, Dr. Cummings misrepresented the conclusions of those articles by stating that the "articles show that the r-EPO and u-EPO samples migrate to similar regions, but they do not precisely comigrate." (AM-ITC 00903276). However, the conclusions drawn in the Egrie articles discussing COS specifically stated that COS r-EPO and u-EPO "migrate[] identically." Along with the Cummings Declaration, Mr. Borun cited an article by Takeuchi that showed a difference in glycosylation, but again, that article relates to CHO r-EPO and not COS r-EPO, which was (and is) covered by Lin's claims. (AM-ITC 00903340-42).**

**98. When prosecution continued after the '334 Interference, Examiner Fitzgerald allowed pending claims 76-83, but Mr. Borun elected to continue prosecution without letting the claims issue. Later in the prosecution, when faced with continuing rejections, Mr. Borun added new claims, arguing that "[n]ew claim 99 has a text identical to claim 76" of the '178 application, which was allowed prior to filing the '874 application, and was identical to the sole count in the '334 Interference. ('774 FH, Paper 45, Preliminary Amendment at 2; '774 FH, Paper 50, 12/20/95 Second Preliminary**

**Amendment at 4). However, claim 99 did not have the identical text to claim 76. Specifically, claim 76 contained a limitation to human erythropoietin that was missing from new claim 99. Mr. Borun and Amgen's in-house counsel, including Mr. Odre, understood the PTO rules regarding patent examination and, specifically, understood that a claim previously made allowable is given full faith and credit and rarely rejected. Mr. Borun, therefore, exploited PTO rules and misrepresented key facts to get a claim to issue. This claim, and related claims, issued without further rejection in the '933 and '080 patents. But for Amgen's continual misrepresentations regarding differences in glycosylation between u-EPO and r-EPO, claims of the '933 and '080 patents would not have issued.**

**99. Furthermore, Applicant relied upon purported differences in glycosylation to distinguish his disclosed r-EPO (including from COS and CHO host cells) from prior art human urinary EPO to secure claim 1 of the '422 patent. (*See* '197 FH, Paper 23, 12/1/94 Request for Reconsideration at 3; Paper 25, Amendment and Declaration of Cummings; Paper 33, 4/28/99 Amendment at 5 ("The application further discloses that the glycosylation of human erythropoietin may differ depending upon the host cell used for production.")).**

**100. Amgen cannot rely on submissions in the '334 Interference file to overcome its overt misrepresentations and omissions regarding differences in r-EPO and u-EPO. Indeed, the Interference file shows that Amgen intentionally directed the Board away from considering the EPO product produced in COS cells because it knew there were no differences compared to the prior art EPO. The '334 Interference file alone comprises approximately 5,500 pages of documents focusing on CHO r-EPO. For example, the following statements appear in the Interference file:**

- **AM-ITC 00295811: "This is based in part on the work done by Dr. Egrie with recombinant human EPO expressed from CHO cells"**
- **AM-ITC 00295812: "Studies conducted by Dr. Egrie involving digestion of the CHO cell produced rHuEPO"**
- **AM-ITC 00295814: "in vivo biologically active recombinant EPO product expressed by CHO cells, had an average carbohydrate composition which was different from the pooled human urinary EPO obtained from Dr. Goldwasser."**
- **AM-ITC 00295815: "I confirm that the rHuEPO produced by CHO cells transfected with the human genomic EPO gene meets all of the limitations of the count of Interference No. 102,334."**

**(*See also* AM-ITC 00339456; AM-ITC 00361603; AM-ITC 00832911; AM-ITC 00832913-15; AM-ITC 00832918-20). To the extent that there was any information in the file regarding COS r-EPO, it was buried among a mountain of CHO r-EPO related evidence. Any such disclosure demonstrates a pattern of misconduct by Amgen and its attorneys to avoid fulfilling the duty of good faith and candor.**

**101. The '334 Interference did not decide patentability under §103, yet Amgen relied on the opinion to argue that the PTO must issue the corresponding claims to Lin. Furthermore, the issues in the '334 Interference centered around a claim limitation "having an average carbohydrate composition which differs from that of human urinary erythropoietin", (AM-ITC 00941235), not issues regarding limitations directed to differences in apparent molecular weight, as this limitation did not appear in any filed claims until after the Board rendered its opinion. Finally, the opinion makes clear that the Board, like the Examiner, focused on CHO r-EPO and not COS r-EPO because of Amgen's filings and arguments. The Board made specific references to CHO cells, Example 10, the Takeuchi reference and Amgen's PLA, all of which were based on CHO r-EPO, and made no reference to COS r-EPO.**

**102. But for Amgen's misconduct, at least claims 1, 2 and 6-14 the '933 and claims 1 and 4-6 of the '080 patent would not have issued. Accordingly, the '933 patent and the related '080 patent are unenforceable for inequitable conduct. The misconduct in securing the '933 patent claims also infects the '080 patent, rendering the '080 patent unenforceable for this reason as well. Additionally, the claims of the later issued '698, '349 and '422 patents are sufficiently interrelated with the '933 claims and have a substantial relationship with the inequitable acts, by relying on purported differences in glycosylation and carbohydrate content, such that these patents should also be deemed unenforceable under the doctrine of infectious unenforceability.**

***Misrepresentations and Omissions Regarding CHO r-EPO***

**103. In addition to the information discussed above, Amgen also withheld and misrepresented material information relating to CHO r-EPO. During prosecution of the '178 application, an Examiner Interview Summary indicated that "Applicant intends to submit declaration evidence to show that r-EPO differs in glycosylation from any of the naturally occurring EPOs known as of the effective date of the instant application and even from the naturally occurring EPOs known since." ('774 FH, Paper 39 (emphasis added)). Mr. Borun subsequently submitted the Cummings Declaration, discussed above.**

**104. Aside from the failings of the Cummings Declaration discussed above, the declaration contained no information about "EPOs known since," particularly the Lot-82 and Alpha Therapeutics u-EPO that Dr. Egrie was working with at the time. Experiments with these two forms of u-EPO showed no differences between CHO r-EPO and u-EPO. Yet, Mr. Borun did not disclose this data to the Examiner nor did Amgen**

**make any additional filings to disclose this information within the file histories, instead relying solely on alleged differences with Goldwasser's u-EPO.**

**105. Furthermore, as discussed above, the Cummings Declaration mentioned two articles by Egrie *et al.*, without further identification information. The only two Egrie articles that discuss CHO r-EPO concluded that there was no difference between CHO r-EPO and u-EPO. (Egrie *et al.*, 1986, Characterization and Biological Effects of Recombinant Erythropoietin, *Immunbiol.*, vol. 172, pp. 213-224 (1986); Eschbach *et al.*, Correction of the Anemia of End-Stage Renal Disease with Recombinant Human Erythropoietin, *NEJM* 316:73-78 (1987) (Egrie, co-author)). These articles were not provided to the Examiner. However, Dr. Cummings' discussion of the Egrie articles states that the "rEPO and uEPO samples migrate to similar regions, but they do not precisely comigrate", (AM-ITC 00903276), which is in direct contravention to the actual conclusions of the articles. Dr. Egrie's 1984 presentation (AM-ITC 01073033), which similarly showed identical migration, was also not submitted to the Examiner.**

**106. Furthermore, as noted above, the Browne article showed similar results regarding identical migration and glycosylation with respect to CHO r-EPO. While Dr. Cummings did cite to the Browne article, it was in reference to O-glycosylation of EPO in support of his argument regarding the Nimtz *et al.* (1993) reference. The articles he relied upon to show a difference between r-EPO and u-EPO were clearly summarized in table form (AM-ITC 00903273), but the Browne article was not included in this table, thus misguiding the Examiner to conclude that it was not relevant to the differences in r-EPO and u-EPO. Furthermore, the Browne article was not submitted in an IDS and was not cited as considered by the Examiner in allowing the '933 patent. However, the reference**

**was cited in later applications leading to the '080 patent, thus, indicating that Amgen appreciated its materiality.**

**107. Mr. Borun also did not submit to the Examiner an article by Vapnek *et al.*, "Comparative Studies of Natural and Recombinant Erythropoietin," *Banbury Reports 29: Therapeutic Peptides and Proteins*, 241-56 (1988), which reported no difference in structure between CHO r-EPO and u-EPO.**

**108. In stark contrast to the positions Amgen took in the Patent Office and argued to numerous Examiners, to receive approval for its CHO r-EPO drug, Amgen made statements to the FDA that materially contradicted its position with respect to patentability. Amgen specifically told the FDA that r-EPO and u-EPO were shown to be identical in carbohydrate structure, and did not disclose this contrary position to the patent Examiners. (*See* AM-ITC 00092853). Furthermore, Amgen never explained to the Examiner(s) that purported differences in glycosylation and carbohydrate composition were not necessarily due to differences in the structure of CHO r-EPO and u-EPO, but rather the use of different purification techniques or even experimental error, as it had told foreign patent offices through the 1992 and 1994 Strickland Declarations.**

**109. Amgen's continual misrepresentations and nondisclosures regarding differences in glycosylation and overall carbohydrate structure between u-EPO and CHO r-EPO directly resulted in Amgen obtaining patents to unpatentable "inventions." But for Amgen's misrepresentations and omissions, claims 1, 2 and 6-14 of the '933 and claims 1 and 4-6 of the '080 patent would not have issued. Accordingly, the '933 and '080 patents are unenforceable for inequitable conduct. In addition, Applicant's misconduct in procuring the '933 patent renders the '080 patent unenforceable by infectious**

**unenforceability. Likewise, the claims of the later issued '698, '349 and '422 patents are sufficiently interrelated with the '933 claims and have a substantial relationship with the inequitable acts, by relying on purported differences in glycosylation and carbohydrate content, such that these patents should also be deemed unenforceable under the doctrine of "infectious unenforceability."**

***Misrepresentations and Omissions Regarding Molecular Weight***

**110. In addition to the misrepresentations and omissions set forth above regarding differences in molecular weight, Amgen and its attorneys, including but not limited to Mr. Borun, made a number of additional misrepresentations and omissions that led to a patent on unpatentable subject matter.**

**111. In 1995, Amgen presented for the first time a claim requiring that "said product has a higher molecular weight than human urinary EPO as measured by SDS-PAGE." ('774 FH, Paper 50, 12/20/95 Amendment). This claim was allowed without rejection or amendment. (*See* '933 patent, claim 2). As noted, Lin's specification states that urinary erythropoietin has a molecular weight of approximately 34,000 daltons. (*See, e.g.*, '933 patent, col. 5:48-52; *see also* AM-ITC 00987639-49 ("The human asialo hormone has an apparent molecular weight of 34,000 in SDS, whereas the native form as an apparent molecular weight of 39,000.")). Amgen's Dr. Egrie, who was responsible for providing information regarding molecular weight for inclusion in the specification, also measured the molecular weight of urinary EPOs and found that Goldwasser's u-EPO "is 34,000 MW + Lot-82 EPO - ~35-36". (AM-ITC 01072482). This is information was not disclosed to the examiners.**

**112. As discussed above, Dr. Strickland filed a declaration in May 1994 in related foreign proceedings that showed that r-EPO produced in accordance with Lin's Example 10 exhibited a molecular weight between 31,000 daltons and 45,000 daltons as measured by SDS-PAGE. Clearly, a molecular weight of 31,000 daltons is not a "higher molecular weight than human urinary EPO as measured by SDS-PAGE." However, Amgen never submitted this contradictory declaration or the underlying information to the PTO.**

**113. During the same foreign proceeding, Cilag GmbH, an opposing party, along with Kirin-Amgen, Inc., filed a declaration by Dr. Thomas Heckler stating that "r-HuEPO migrated identically to the reference standard (which had a molecular weight of 34,000 daltons) …." (AM-ITC 00311606). Dr. Goldwasser, an Amgen consultant who also was involved with the prosecution of the patents-in-suit, also submitted a declaration reporting that the molecular weight of urinary EPO as measured by SDS-PAGE was first reported as 39,000 daltons but later reported at 34,000 daltons. (1/23/93 Declaration of Eugene Goldwasser Ph.D., ¶21).**

**114. Amgen plainly stated in this proceeding that it was relying "without limitation" on the citations and exhibits presented by its opponent, Cilag, and these included the Heckler and Goldwasser Declarations, (AM-ITC 00312411-12), yet this information was not submitted to the PTO.**

**115. Evidence shows that the attorneys responsible for prosecuting the patents-in-suit were fully apprised of events in the European proceedings. Attorneys for Cilag and Johnson & Johnson kept at least in-house Amgen attorneys, Messrs. Watt and Odre, apprised of developments in Europe. (*e.g.*, AM-ITC 0312283; AM-ITC 0312291-92).**

**Mr. Watt was a corporate officer of Kirin-Amgen, Inc. (*e.g.*, AM-ITC 00898341). Indeed, Messrs. Odre, Watt and Borun, as well as Drs. Strickland, Egrie and Goldwasser attended the oral arguments for the foreign proceedings relating to EP 209 539. (AM-ITC 00312754). Additionally, written submissions by Kirin-Amgen, Inc. included confidential information provided by Amgen, Inc. (*e.g.*, AM-ITC 00312455-73) and declarations provided by Amgen employees. (*e.g.*, AM-ITC 00312260-71; AM-ITC 00312441-45). The Strickland, Goldwasser and Heckler declarations were all in the possession of Amgen's patent counsel at Marshall, Gerstein & Borun, including Mr. Borun. (*See, e.g.*, February 20, 2007 Third Party Marshall, Gerstein & Borun LLP's Objections and Responses to Subpoena *Ad Testificandum* and *Duces Tecum*, Objections and Response to Request No. 1; March 27, 2007 Letter from Ross to Rycroft).**

~~116.~~**~~Furthermore, the following documents expressly state that the apparent molecular weight of r-EPO is not higher than that of u-EPO:~~**

- ~~**AM-ITC 01072474-501 at 494: "Recombinant ... human EPO produced by COS cells have the same molecular weight as native urinary EPO (Goldwasser's EPO)."**~~

- ~~**Egrie *et al.*, Characterization Of Recombinant Monkey And Human Erythropoietin, *Proc Clin Biol Res.* 1985;191:339-50: "As seen in Figure 5, recombinant human EPO produced in COS1 cells has a molecular weight of 34,000 daltons and migrates identically to the human urinary standard ..."**~~

- ~~**Egrie *et al.*, Abstract (1984) from 10th Annual Fredrick Stohlman Memorial Symposium on Stem Cell Physiology, Boston, MA, October 2, 1984: "By Western analysis, the recombinant erythropoietin has a molecular weight of 34,000 daltons and migrates identically to the human standard erythropoietin ..."**~~

- ~~**Egrie *et al.*, Presentation (1984) from 10th Annual Fredrick Stohlman Memorial Symposium on Stem Cell Physiology, Boston, MA, October 2, 1984 (AM-ITC 01073032-42): "MW and migration of recombinant EPO is identical to EPO standard ..."**~~

- ~~Egric, Presentation Transcript "Cloning of Human & Monkey EPO" (1984) from Hemoglobin Switching Meeting, Airlie House, Virginia, September 1984 (AM-ITC 00557610-16): "In order to determine the size of the recombinant erythropoietin, we characterized the COS-cell expressed EPO by Western analysis. ... This band has a MW of 34,000 daltons + migrates identically to the human EPO standard. ... It has the same MW as the native hormone [illegible] suggesting that it is glycosylated to the same extent." (AM-ITC 00557616; *see also* AM-ITC 00557617-23).~~

- ~~Egric *et al.*, 1986, Characterization and Biological Effects of Recombinant Human Erythropoietin, *Immunobiol.*, vol. 172, pp. 213-224 (1986): "As seen in Figure 4, purified rHuEPO migrates identically with an apparent molecular weight of approximately 36,000 daltons ...."~~

- ~~Vapnek *et al.*, "Comparative Studies of Natural and Recombinant Erythropoietin," *Banbury Reports 29: Therapeutic Peptides and Proteins*, 241-56 (1988): "As shown in Figure 3, both rh-Epo and urinary Epo have an apparent molecular weight of approximately 36,000."~~

~~None of these documents were provided to the PTO.~~

~~117.~~116. Furthermore, Amgen's own Product License Agreement, filed with the FDA, shows that Amgen's r-EPO does not have a "higher molecular weight" than u-EPO. (AM-ITC 00092870, 80). The product label for Epogen® states that the r-EPO product "has a molecular weight of 30,400 daltons…," which is not higher than u-EPO. (*See* AM-ITC 00092249-60 (10/30/87 Proposed Package Insert); Physician's Desk Reference (44th ed. 1990) at 616; AM-ITC 00601553-60 (6/29/94 Product Label for Epogen®); 3/09/2007 Product Label for Epogen® and Procrit® available at www.accessdata.fda.gov)). These labels were not submitted to the PTO during prosecution of the '933 patent.

~~118.~~117. Furthermore, in September 1985, when the applications leading to the '933 patent were still pending, Amgen submitted its Notice of Claimed Investigational Exemption for Recombinant-Human Erythropoietin (r-HuEPO) to Office of Biologics Research and Review Center for Drugs and Biologics at the Food and Drug

Administration (AM-ITC 00091218) in relation to seeking approval for its CHO r-EPO product. The application was assigned to Amgen's attorney, Mr. Odre, who also prosecuted the applications that resulted in the '933 patent. In that document, Amgen represented that: "The r-HuEPO migrates identically to the pure urinary hormone with an apparent molecular weight of ~ 36,000 daltons" in SDS-polyacrylamide. (AM-ITC 00092135, 00092210-11). Therefore, Amgen's CHO r-EPO covered by the '933 patent does not have a "higher molecular weight than human urinary EPO as measured by SDS-PAGE." Again, Amgen did not submit this information to the PTO.

~~119.~~118. But for Amgen's misconduct, claims 2 and 9-11 of the '933 patent would not have issued. In addition, the '080 patent is unenforceable by infectious unenforceability due to the inequitable conduct in procuring the parent '933 patent.

~~120.~~119. As demonstrated above at paragraphs 76-119, Amgen knowingly made the misrepresentations and omissions regarding differences in u-EPO and r-EPO with the intent to deceive the PTO which relied upon Amgen's statements in determining whether to issue the '933 and '080 patents. But for Amgen's misconduct, claims of the '933 patent and '080 patent would not have issued. Amgen was aware of its fraud and misconduct leading to the issuance of the '933 and '080 patents when it commenced its infringement suit against Roche.

INEQUITABLE CONDUCT RELATING TO THE STANDARD USED IN RADIOIMMUNOASSAY IN THE '349 PATENT

~~121.~~120. The '349 patent is unenforceable because individuals including, but not limited to, Michael Borun, Steven Odre, Stuart Watt, Joan Egrie and Fu-Kuen Lin, associated with the filing and prosecution of the '349 patent and acting as

**agents and/or with the knowledge of plaintiff Amgen, failed to disclose material facts with an intent to deceive the PTO regarding the standard used in radioimmunoassay.**

~~122.~~**121.** **Every claim of the '349 patent includes a limitation to a measurement of cells grown in culture in excess of a specified amount as "U of erythropoietin per $10^6$ cells in 48 hours as determined by radioimmunoassay" (known as "RIA"). ('349 patent, claims 1-7). Example 2 of the common specification sets forth part of the protocol for conducting the radioimmunoassay. ('868 patent, col. 17:30-68). However, this protocol discloses only "an erythropoietin standard," and not the specific standard employed by Dr. Lin. Similarly, Example 10 of the common specification sets forth experimental results using RIA to determine "effective production rates," but also does not disclose what standard the inventor used. ('868 patent, col. 28:5-25).**

~~123.~~**122.** **Amgen, including at least Drs. Lin, Egrie, Strickland and Browne, knew that there were different urinary erythropoietin standards that could be used and that, depending on which standard was employed, different results would be obtained in RIA. (*See* AM-ITC 00061675, AM-ITC 00550986; AM-ITC 00551040). Amgen also knew that the standard it used, CAT-1, was no longer available as of September 1984, (AM-ITC 00061678), and Amgen's replacement standard, Lot 82, was unavailable to the public.**

~~124.~~**123.** **Amgen also knew that its units ("U") were arbitrary units which did not equate to international units ("IU"). These facts were not disclosed in the patent specification, nor were they disclosed to the Examiner of the '369 application. Amgen's own CEO, Dr. Rathmann, acknowledged in 1990 that Amgen "should be absolutely fastidious in reporting specific activity in arbitrary (Amgen) units until we can**

**establish an excellent correlation with international units. I do not believe such correlation exists today …. I think we have also been careless with respect to what is the precision or uncertainty (accuracy) of our data …. I think we should understand how any standard can deviate from 'parallelism' trying to relate to international units." (3/15/90 Memorandum from George Rathmann to Dan Vapnek, Jeff Browne, Joan Egrie and Tom Strickland re: Erythropoietin Biological Activity; *see also* 7/24/90 Memorandum from Rathmann to Browne, Egrie, Odre, Strickland and Vapnek (AM-ITC 00594730-735) ("Historically ... radio immune assays have been used to measure the activity of erythropoietin containing materials and report the results in international units."; "Amgen units have never been derived from IRP#2.)). This information was withheld from the Examiner.**

**~~125.~~124. Dr. Egrie has testified that that she developed the radioimmunoassay to evaluate recombinant erythropoietin and Dr. Lin has testified that he relied on the RIA protocol and associated test results to demonstrate that his invention fell within the claims of the '349 patent. Mr. Borun has testified that he had frequent contact with both Drs. Lin and Egrie, and both doctors were heavily involved in the prosecution of the patents-in-suit. Therefore, Mr. Borun, Dr. Egrie and Dr. Lin knew or should have known that the information relating to the EPO standard would have been material to the patentability of the '349 claims. However, they did not disclose this information during prosecution of the '349 patent. Amgen's omissions would have been material to the Examiner's determination of best mode, definiteness, enablement and inventorship. But for Amgen's failure to disclose this material information, the '349 patent claims would not have issued. Instead, Amgen now has a patent covering vertebrate cells that is the last of**

its patents to expire, precluding the public from practicing an unpatentable invention until 2015. Accordingly, the '349 patent is unenforceable for inequitable conduct.

~~126.~~125. Amgen knowingly omitted information regarding the standard to be used in RIA with the intent to deceive the PTO, which relied upon Amgen's statements in determining whether to issue the '349 patent. But for Amgen's misconduct, the '349 patent would not have issued. Amgen was aware of its fraud and misconduct leading to the issuance of the'349 patent when it commenced its infringement suit against Roche.

INEQUITABLE CONDUCT RELATING TO AMGEN'S WORK WITH THE 1411 CELL LINE

~~127.~~126. Each of the patents-in-suit are unenforceable because individuals including, but not limited to, Michael Borun, Steven Odre, Joan Egrie and Fu-Kuen Lin, associated with the filing and prosecution of the '298 application, which issued as the '008 patent, and acting as agents and/or with the knowledge of plaintiff Amgen, misrepresented and omitted material facts with an intent to deceive the PTO regarding the Amgen's work with the 1411 cell line.

~~128.~~127. During prosecution of the '298 application, which is a parent application to all of the patents-in-suit, Applicant faced a rejection for obviousness based on the Ullrich *et al.* and Martial prior art references. Examiner Tanenholtz stated that it would be obvious to prepare EPO as a fused peptide by extracting the mRNA for erythropoietin from kidney cells known to be rich therein and using the process taught by Ullrich *et al.* and Martial to convert the mRNA to a cDNA library. ('298 FH, Paper 17, 6/18/87 Office Action).

~~129.~~128. To overcome the rejection, Mr. Borun argued that there was a serious problem at the time in securing cells that produced EPO, let alone high levels of EPO. ('298 FH, Paper 20, 7/10/87 Applicant's Amendment at 20). The pending claims subsequently issued in response to Mr. Borun's remarks. ('298 FH, Paper 21, 7/30/87 Examiner Interview Summary).

~~130.~~129. Mr. Borun failed to disclose that Amgen and Dr. Egrie were working with cells that produced high levels of erythropoietin -- the 1411 cell line. (*See* AM-ITC 00052045, AM-ITC 00057704; AM-ITC 00057723; AM-ITC 00057735; AM-ITC 00057708-18; AM-ITC 00057689-701; AM-ITC 00057687-88; FG 000012-21; FG 000048). Amgen also failed to disclose published literature which plainly supported the Examiner's rejection, including an article by Gaylis. (*See* Gaylis *et al.*, "In Vitro Models of Human Testicular Germ-Cell Tumors", *World J. Urol.*, 2:2-5 (1984) ("We recently detected production of significant amounts of erythropoietin (Ep) by a cell line designated 1411H … Clearly, then, the production of Ep by 1411H is of significant biological interest and may be of clinical value if the gene controlling Ep synthesis can be cloned"); *see also* AM-ITC 00057739 and FG 000051 Ascensao *et al.*, "Inducible Production of Erythropoietin by a Human Yolk Sac Tumor Cell Line", *Am. Fed. Clin. Res.* 31:307A (1983); Ascensao *et al.*, "Erythropoietin Production by a Human Testicular Germ Cell Line", *Blood* 62(5):1132-34 (1983)).

~~131.~~130. Mr. Borun's misrepresentations and omissions regarding the availability of EPO-producing cells directly impacted the Examiner's allowance of the pending claims in the '298 application and resulted in the issuance of the '008 patent. An examiner would have found this information to be material to the patentability of each of

**the patents-in-suit, which all stem from and are related to the invention disclosed and claimed in the '298 application. Accordingly, the patents-in-suit are unenforceable for inequitable conduct under infectious unenforceability.**

**INEQUITABLE CONDUCT TO OVERCOME THE LAI DOUBLE-PATENTING REJECTION**

~~132.~~**131.** **The '868 and '698 patents are unenforceable because individuals including, but not limited to, Michael Borun and Steven Odre, associated with the filing and prosecution of the '179 application and acting as agents and/or with the knowledge of plaintiff Amgen, misrepresented and failed to disclose material facts with an intent to deceive the PTO with respect to the delay in prosecuting the claims of the '868 patent to overcome a double patenting rejection based on U.S. Patent No. 4,667,016 (Lai *et al.*) (the "Lai '016 patent").**

~~133.~~**132.** **The Lai '016 patent issued on May 19, 1987. During prosecution of the '179 application, filed on October 23, 1987 -- after the Lai '016 patent issued -- Applicant faced a rejection of pending claims 65-59 for obviousness-type double patenting over the Lai '016 patent because Lai taught the production of recombinant EPO containing fluid by the same method as was instantly claimed. ('179 FH, Paper 29, 9/1/93 Office Action at 6 (claims 65-59 are "directed to an invention not patentably distinct from claim 9 of commonly assigned Patent No. 4,667,016 (Lai et al.)")). To overcome the rejection, Mr. Borun stated that the two-way test for non-obviousness must be applied and that there would be no timewise extension if the '179 application issued as a patent. ('179 FH, Paper 33, 1/3/94 Amendment and Response).**

~~134.~~**133.** **In reliance on Applicant's remarks, Examiner Hodges withdrew his rejection, noting that Applicant was not responsible for the delay in issuance,**

**and thus, the two-way test for non-obviousness was applied to save the claims from an otherwise proper obviousness rejection. ('179 FH, Paper 34, 2/15/94 Office Action at 2). Examiner Hodges specifically stated that under a one-way test, "the instantly claimed method is an obvious variation of the process of Lai et al…", but the Examiner withdrew his rejection upon applying the two-way test. (*Id.* (emphasis in original)).**

~~135.~~**134.** **The prosecution histories of the patents-in-suit and the '008 patent show that the process claims pending in the '179 application should have been prosecuted in the earlier '298 application (that issued as the '008 patent) and, in fact, substantially similar claims were prosecuted but were voluntarily cancelled by Mr. Borun. (*See* '298 FH, Paper 15, 3/11/87 Amendment and Reply at 27). Furthermore, Applicant did not even file the '179 Application until after the Lai '016 patent issued, so the PTO could not have been responsible for the fact that the '868 patent issued after the '016 patent. Finally, the '096, '097 and '334 Interferences did not commence until years after the 1987 filing date of the '179 application and were, therefore, not responsible for the delay.**

~~136.~~**135.** **Amgen and Mr. Borun failed to correct the Examiner's factual mistakes surrounding the application of the two-way test for nonobviousness, which resulted in application of the wrong test for patentability. This would have been particularly important in light of the Examiner's conclusion that the '179 claims would be invalid for obviousness under a one-way test. (*See* '179 FH, Paper 34, 2/15/94 Office Action). But for Amgen's misrepresentations and failure to disclose the true facts to the Examiner, he would not have issued the '868 and '698 patents in light of the Lai patent. Instead, Amgen continues to have a monopoly which should have ended with the expiration of the '016 patent in 2004. Accordingly, the '868 and '698 patents are unenforceable for**

**inequitable conduct. In addition, Amgen's misconduct in securing the '868 patent renders the '698 patent unenforceable by infectious unenforceability.**

**~~137.~~136. Amgen knowingly misrepresented and omitted material information to overcome a double patenting rejection over the Lai '016 patent with the intent to deceive the PTO which relied upon Amgen's statements in determining whether to issue the '868 patent. But for Amgen's misconduct, the '868 and '698 patents would not have issued. Amgen was aware of its fraud and misconduct leading to the issuance of the '868 and '698 patents when it commenced its infringement suit against Roche.**

**INEQUITABLE CONDUCT RELATING TO THE STATE OF THE PRIOR ART**

**~~138.~~137. The '868 and '698 patents are unenforceable because individuals including, but not limited to, Drs. Lin and Strickland, Michael Borun, Stuart Watt and Steven Odre, associated with the filing and prosecution of the '179 application and acting as agents and/or with the knowledge of plaintiff Amgen, misrepresented and failed to disclose material facts with respect to the teachings of the prior art to overcome a rejection for obviousness.**

**~~139.~~138. During prosecution of the '179 application, Applicant urged the patentability of the pending claims over prior art disclosing general recombinant techniques asserting the claimed processes were one of the first (if not the first) instances of recombinant production of an *in vivo* biologically active human glycoprotein. ('179 FH, Paper 8, 5/24/88 Second Preliminary Amendment at 6, 20; Paper 14, 9/27/88 Reply at 5). Mr. Borun further stated that human erythropoietin was known to be an "obligate" glycoprotein, ('179 FH, Paper 8, 5/24/88 Second Preliminary Amendment at 10), a distinction that Applicant frequently relied upon to support patentability. (*See, e.g.*, '179**

**FH, Paper 10, 9/14/88 Examiner Interview; Paper 14, 9/27/88 Applicant's Reply at 5; Paper 33, 1/3/94 Amendment at 11; Paper 43, 10/7/94 Amendment at 9-10). However, there is no such thing as an "obligate" glycoprotein and it makes no difference in practicing the claimed process. Thus, Applicant presented misleading scientific arguments as fact to remove legitimate prior art.**

~~140.~~**139.** **As part of the prosecution, Applicant was granted "special" status in light of representations that Mr. Borun had taken substantial efforts to become acquainted with the relevant prior art and that he had a good working knowledge of the pertinent prior art, ('179 FH, Paper 3, Declaration Accompanying Petition to Make Special; Paper 8, 5/24/88 Second Preliminary Amendment), and the application was therefore examined on an expedited track. In making such representations, Mr. Borun induced the Examiner to rely on his assertions that he was presenting the full scope of the prior art as part of the examination.**

~~141.~~**140.** **To facilitate expedited examination, Mr. Borun engaged in a computer-assisted prior art search to find references relating to the recombinant production of an *in vivo* biologically active obligate human glycoprotein, and discovered only one reference, Collen *et al.*, J. Pharm. & Expt. Therapeutics, 231, 146-152 (1984), relating to tPA, which Applicant knew was an obligate glycoprotein. ('179 FH Paper 8, 5/24/88 Second Preliminary Amendment at 15-17). Mr. Borun told the Examiner that the Collen reference "does not describe how the recombinant mammalian host cell expression was prepared." ('179 FH, Paper 8, 5/24/88 Second Preliminary Amendment at 17). Mr. Borun conducted further searches in the Derwent World Patent Index database for published patent applications and discovered EP 0 093 619 ("the '619 application"). (*Id.* at**

18). Mr. Borun represented that the '619 application contained no description of the use of mammalian host cell expression systems for tPA production, other than a merely speculative statement that suggested that multiple host cells could be used. ('179 FH, Paper 8, 5/24/88 Second Preliminary Amendment at 18 ("depending upon the host cell")). However, this was a misrepresentation, as the '619 application disclosed use of vertebrate cells and mammalian cells, CHO cells, CHO cells deficient in DHFR activity, use of methotroxate with CHO cells, viral promoters in mammalian cells (including SV40), suitable growth conditions for transfected cells, pharmaceutical compositions of tPA, and that the recombinant techniques enable the production of sufficient material to conduct animal testing unlike prior art tPA. Additional public press releases which Amgen monitored showed that recombinant tPA had *in vivo* biological effects, as disclosed in the '619 application. (2/21/84 Genentech Press Release, accessible at http://www.gene.com/gene/news/press-releases; *see also* 11/13/1987 FDA Press Release, accessible at http://www.fda.gov/bbs/topics/NEWS/NEW00191.html (announcing FDA approval of recombinant tPA)). Therefore, the '619 reference discloses that human glycoproteins could be expressed through recombinant techniques and supports the argument that one would have a reasonable expectation of success in applying those techniques to other obligate glycoproteins. However, in light of Mr. Borun's representations accompanying the petition to make special, the Examiner had reason to rely on his misrepresentations and omissions.

~~142.~~141. Mr. Borun also cited EPO Applications 0 117 059 and 0 117 060 and stated that they were "assertedly" based on January 1983 filings, thus implying that they would not be prior art. ('179 FH, Paper 8, 5/24/88 Second Preliminary

Amendment at 18; Paper 43, 10/7/94 Amendment at 9). To the extent these references were presumed not to be prior art (although they are), that only highlights the materiality of the misrepresentations Mr. Borun made regarding the '619 application and omissions regarding tPA.

~~143.~~142. Furthermore, Mr. Borun did not disclose the U.S. counterpart to the '619 application, U.S. Patent No. 4,766,075. The '075 patent claims an earliest priority date of May 5, 1982, and is therefore prior art. Furthermore, unlike the foreign '619 application, the U.S. patent could have been used as a basis for §102(e)/§103 rejection and, thus, is not cumulative to the '619 application for at least that reason.

~~144.~~143. Mr. Borun also indicated that he attached the '619 application as an exhibit to Applicant's Second Preliminary Amendment and that a form PTO-1449 would be submitted imminently. However, the certified file history only has one IDS (with no accompanying PTO-1449), submitted nearly four months after the Amendment. The IDS does not expressly identify the '619 application or correct Mr. Borun's earlier misstatements regarding its teachings. Only two references relating to "obligate" human glycoproteins were disclosed, neither of which was the '619 application. Therefore, either the '619 application was included among the references cited in the PTO-1449 (which is missing from the file history) and its teachings were again misrepresented, or Amgen simply did not submit this reference. In any event, no steps were taken to correct earlier misrepresentations and omissions.

~~145.~~144. Mr. Borun, and the prosecuting attorneys under his direction, continually misrepresented and failed to disclose the true state of the prior art relating to tPA, and this resulted in the eventual issuance of pending process claims 65-69 as the '868

**patent. ('179 FH, Paper 17, Notice of Allowability). Furthermore, when Mr. Borun elected to continue prosecuting the '179 application despite the notice of allowability, he represented that the '619 application was a reference of record from the '179 application as well as from Defendants' 35 U.S.C. § 282 Notice from *Amgen v. Chugai and G.I.*, C.A. No. 87-2617-Y (D. Mass.), indicating to the Examiner that the reference had been substantively considered and overcome in considering patentability. (*See* '179 FH, Paper 32, 1/3/94 IDS). There is no indication that the '619 was ever substantively considered with respect to the patentability of any process claim. These misrepresentations contributed to the issuance of the claims.**

~~146.~~145. **Furthermore, Amgen failed to disclose material prior art relating to human interferon. Applicant and his attorneys, including Messrs. Borun, Watt and Odre, were aware of work done by McCormick relating to interferon, reflected in U.S. Patent No. 4,966,843 (McCormick *et al.*) ("the '843 patent"), which claims priority to Ser. No. 438,991 ("the '991 application"), filed on November 1, 1982. The McCormick references are entitled to a priority date earlier than any asserted priority date of the Lin patents, and a declaration submitted during prosecution of the '843 patent and '991 application evidences a conception date of December 9, 1981 -- almost two years before the earliest filing date of the patents-in-suit. Both the '843 patent and the '991 application disclosed that human interferon β is a glycoprotein capable of being recombinantly produced in mammalian cells, including CHO cells. Furthermore, the references disclose use of CHO cells deficient in DHFR activity, use of methotroxate with CHO cells, viral promoters in mammalian cells (including SV40), transfecting DHFR deficient CHO cells, amplification with methotroxate, suitable growth conditions for transfected cells,**

pharmaceutical compositions of interferon, and that the disclosed recombinant techniques produce glycosylated products substantially identical to native interferons. Amgen and its attorneys were continuously tracking the activities of its competitors and they were aware that Cetus Corp. was working with recombinant interferon. Yet, Amgen did not disclose the '843 patent or '991 application to the Patent Office.

~~147.~~146. Amgen knowingly misrepresented and omitted material information regarding the state of the prior art with the intent to deceive the PTO which relied upon Amgen's statements in determining whether to issue the '868 patent. But for Amgen's misconduct, the '868 and '698 patents would not have issued. Additionally, misconduct relating to the '868 patent renders the '698 patent unenforceable by infections unenforceability. Amgen was aware of its fraud and misconduct leading to the issuance of the '868 and '698 patents when it commenced its infringement suit against Roche.

INEQUITABLE CONDUCT RELATING TO THE BARON-GOLDWASSER CLINICAL STUDY AND RELATED PRIOR ART

~~148.~~147. The '422, '933 and '080 patents are unenforceable because individuals including, but not limited to, Stuart Watt, Steven Odre, Thomas Byrne, Joan Egrie, Jeffrey Browne, Fu-Kuen Lin and Thomas Strickland, associated with the filing and prosecution of the underlying applications and acting as agents and/or with the knowledge of plaintiff Amgen, misrepresented material facts and failed to disclose prior art material to the patentability of Applicant's pharmaceutical composition claims, including the Baron-Goldwasser clinical study and a 1971 article by J.F. Garcia.

~~149.~~148. Applicant filed the '741 application (which led to the '422 patent) for the purpose of requesting an interference with claims 1-4 of U.S. Patent No. 4,879,272 (Shimoda *et al.*, assigned to Chugai) and to protect Amgen's clinical formulation

of Epogen®, which contained human serum albumin. ('741 FH, Paper 2, 11/6/90 Preliminary Amendment; AM-ITC 00097004-18 at 005, 006). The proposed count for the interference was "An erythropoietin-containing, pharmaceutically-acceptable composition wherein human serum albumin is mixed with erythropoietin." ('741 FH, Paper 2, 11/6/90 Preliminary Amendment at 9-10; Paper 3, Examiner Interview Summary Record). A subsequent interference was also proposed by Amgen with U.S. Patent No. 4,806,524 (Kawaguchi), in which the count added options for bovine serum albumin and gelatin, in addition to human serum albumin. ('197 FH, Paper 18, 12/20/93 Amendment at 2; Paper 17, Examiner Interview Summary Record; Paper 23, 12/1/94 Request for Reconsideration). Applicant requested that file claims 61-63 be designated to correspond to the count in both interferences. ('197 FH, Paper 2, 11/6/90 Preliminary Amendment at 9).

~~150.~~149. In connection with the '741 application filing, Amgen conducted a search for the prior art, including scientific literature, patents, and other documents which included: 1) Erythropoietin plus HSA for therapeutic administration; 2) Erythropoietin plus HSA for other uses; 3) Erythropoietin and BSA for therapeutic administration; 4) Erythropoietin and BSA for other uses; and 5) Other therapeutic proteins plus HSA and/or BSA. Steven Odre, Amgen's in-house patent counsel who bore primary responsibility for patent prosecution and to whom Stuart Watt reported, directed the search and others at Amgen who were substantively involved in the prosecution of the patents-in-suit, including Jeffrey Browne, Joan Egrie and Thomas Strickland, were all aware of the search. (AM-ITC 00097004-00097018 at 006.)

~~151.~~150. A memo dated November 1, 1990 to Steven Odre, Jeffrey Browne, Joan Egrie and Thomas Strickland, among others, entitled "Literature Search to

**Support an Interference Filing Against U.S. Patent 4,879,272," reports that four databases were searched for reports of combinations of erythropoietin plus albumins and that the IND for the Baron-Goldwasser study was discovered in Dr. Egrie's files. The memo reports that the IND taught that HSA stabilizes erythropoietin and that erythropoietin/HSA preparations were suitable for human use. The memo also indicates that the study cannot date later than 1983, although the study began as early as 1979. The also memo cites a 1971 article by J.F. Garcia (Garcia, JF, and JC Schooley, "Disassociation of Erythropoietin from Erythropoietin-Antierythropoietin Complex," *Proc. Soc. Biol. Med.* 138:213-215 (1971)) which disclosed the use of HSA with erythropoietin. (*See* AM-ITC 00097007; AM-ITC 00097005). The November 1 memo further reported that the use of BSA and HSA in erythropoietin preparations is well known in the prior art. (AM-ITC 00097010-AM-ITC 00097011).**

~~152.~~**151.** **Prior to conducting the search, individuals involved in drafting the specification and later prosecuting the '422 patent were well-aware of the Baron-Goldwasser study. By September 1984, Dr. Vapnek, Amgen's Director of Research, had forwarded the Baron-Goldwasser IND -- which disclosed the formulation -- to others at Amgen, including CEO and founder George Rathmann (and Drs. Lin and Egrie), and noted that both Dr. Lin and Dr. Egrie already had a copy of the IND. (AM-ITC 00084770-80). By December 1984, those at Amgen including Drs. Lin, Egrie, Strickland, Browne, Rathmann and Vapnek, were favorably impressed by the information and data generated by the Baron-Goldwasser Study to use the dosing as a guideline for an efficacious dose for its own clinical studies. (AM-ITC 00557514-527 at 518).**

~~153.~~152. Subsequent documents, such as a September 24, 1990 memo, show Dr. Egrie redistributed the Baron-Goldwasser Physician's IND to Dr. Strickland and Browne and Mr. Odre, among others. (*See* AM-ITC 00554114-25). The memorandum plainly states that "[f]or these studies, the EPO was 'diluted in normal serum albumin (Human) ….'" (*Id.* at AM-ITC 00554114; AM-ITC 00554117). On October 31, 1990, Dr. Egrie forwarded additional documents to Dr. Strickland and Browne and Mr. Odre which, again, included information regarding the EPO and HSA formulation (AM-ITC 00573893) as well as "hand-written data summaries of the result of patient response following treatment with urinary EPO." (AM-ITC 00573885-903). Dr. Egrie disclosed that "although no date appeared on the physician's IND for EPO, there is documentation that urinary EPO was formulated for therapeutic use sometime prior to 11/15/78." (*Id.* at 00573885).

~~154.~~153. Thus, Amgen, including at least Dr. Lin, Dr. Egrie, Mr. Odre and Mr. Watt, in addition to the other recipients of the Baron-Goldwasser IND and memos, were well aware of prior art describing the use of HSA or BSA (bovine serum albumin) in combination with erythropoietin for therapeutic use during prosecution of the patents-in-suit. (AM-ITC 00097005).

~~155.~~154. With this knowledge and use of the prior art, Amgen nonetheless filed the '741 application on November 6, 1990 in order to protect its commercial formulation and failed to disclose prior art reported in the November 1 memo until over eight years later. Only then did Amgen disclose any of this art and in doing so, selectively disclosed only certain references while knowingly withholding other highly material references. Tellingly, Amgen chose to disclose only those references which,

**according to the November 1 memo, taught HSA or BSA as a carrier for erythropoietin in RIA or for extraction and characterization of erythropoietin, and BSA and erythropoietin for use in animals. Deliberately omitted were any of the references disclosing the use of erythropoietin and HSA in humans or other animals or the use of erythropoietin and BSA in humans.**

~~156.~~**155.** **Specifically, in an Information Disclosure Statement submitted during prosecution of the '422 patent, Amgen failed to disclose the Baron-Goldwasser clinical study or the 1971 Garcia reference. ('197 FH, Paper 34, 4/28/99 IDS and PTO-1449). The IDS listed 1 article by Baron and 11 different articles by Goldwasser, but not the Baron-Goldwasser clinical study. Likewise, Applicant disclosed 3 articles by Garcia, but not the 1971 article uncovered by the literature search requested by Mr. Odre and reported in the November 1 memo. Amgen knew that in light of the Baron-Goldwasser and Garcia references, an Interference would not have been declared with the issued Shimoda patent and that the pending claims of Lin's '741 application were not patentable.**

~~157.~~**156.** **Moreover, before potentially initiating a second interference, this time between the pending application and the Kawaguchi '524 patent, the Examiner rejected file claims 61-63 over the prior art. Specifically, Examiner Stanton noted that the claims at issue are drawn to compositions containing erythropoietin with HSA, and Miyake at al., 1977 (R), Takezawa at al., 1981 (B) or Takezawa at al., 1982 (C) all disclose erythropoietin. The Examiner stated that one would be motivated in view of Bock *et al.* 1982 (D) to prepare a pharmaceutical composition using HSA, a known pharmaceutical excipient. ('197 FH, Paper 20, 6/1/94 Office Action). The Examiner made clear to Applicants that during his search for prior art, he had not discovered a reference that**

expressly disclosed a composition of erythropoietin comprising human serum albumin. Furthermore, in the same Office Action, Examiner Stanton rejected the claims as indefinite based on the term "therapeutically effective." ('197 FH, Paper 20, 6/1/94 Office Action at 2).

~~158.~~157. In response to the prior art rejections, Amgen argued that the previous §103 rejections were improper because none of the cited references suggested a composition, that the Examiner improperly applied hindsight to combine references disclosing urinary erythropoietin (Miyake and Takezawa) with references generally suggesting the use of HSA in pharmaceutical preparations (Bock), and that the cited prior art failed to teach a pharmaceutically acceptable preparation or suggest that "BSA or other stabilizing additive would be necessary once the purified EPO was obtained." Applicant also requested an interference to be declared with the '524 patent. ('197 FH, Paper 23, 12/1/94 Request for Reconsideration at 2-4). In response to the §112 indefiniteness rejection, Applicant argued that the patent specification listed a number of therapeutic responses sufficient to overcome the rejection, including stimulation of reticulocyte response, erythrocyte mass change, stimulation of hemoglobin C synthesis, development of ferrokinetic effects and increasing hematocrit levels in patients. ('197 FH, Paper 23, 12/1/94 Request for Reconsideration at 2). Therefore, Amgen, including at least Mr. Watt, who was involved in prosecuting the '422 patent, was aware that Amgen had interpreted "therapeutically effective" to include these responses.

~~159.~~158. The §103 and §112 rejections were not maintained by the Examiner and, subsequently, the '422 patent issued (based on file claims 64-65) after the Applicant argued that two Goldwasser references "do not disclose a pharmaceutically

acceptable preparation, and there is no indication that BSA or other stabilizing additive would be necessary once the purified EPO was obtained." (*See* '197 FH, Paper 32, 4/21/99 Examiner Interview; Paper 33, 4/28/99 Amendment at 5). Amgen's failure to disclose highly material references identified in the November 1, 1990 memo is particularly egregious in light of these arguments made by Amgen.

~~160.~~159. As confirmed by the November 1, 1990 memorandum, the Baron-Goldwasser clinical study and 1971 Garcia article would have been material to a reasonable examiner examining claims 1 and 2 of the '422 patent and, but for Amgen's failure to submit the information, the '422 patent would not have issued in light of §§102/103. Similarly, the Baron-Goldwasser study also showed many of the therapeutic responses that Applicant pointed to in the specification to overcome the §112 rejection, including that "each patient showed a mild to modest increase in reticulocyte number", "two of the three patients showed increased numbers of nucleated red cells/1000 bone marrow cells and the disappearance of radio-iron from plasma was shortened in two of the three individuals" and "one of the three patients showed an increase in red cell mass following the treatment program." (AM-ITC 00245727-29; *see also* AM-ITC 00084770-80; AM-ITC 00849306-41). This information would have also been important to a reasonable examiner.

~~161.~~160. Motivated by the need to protect the current clinical formulation of Epogen® containing human serum albumin by starting an interference, Amgen had much to gain by withholding these highly material references in order to mislead the PTO and obtain patent protection. A number of individuals at Amgen who were substantively involved with the prosecution of the patents-in-suit knew of these

references yet failed to disclose the information during the lengthy pendency of the '422 patent. Accordingly, the duty of disclosure and the duty of candor was violated in prosecuting the '422 patent to issuance.

~~162.~~161. The highly material information from the Baron-Goldwasser study withheld during the prosecution of the '422 patent would have also been important to a reasonable examiner regarding the patentability of claims 9 and 12 of the '933, which are product-by-process claims. ('178 FH, Paper 11, 6/2/89 Amendment at 3). Claims 9 and 12, depending from claim 3, are directed to pharmaceutical compositions containing "a pharmaceutically acceptable diluent, adjuvant or carrier." ('933 patent, claims 9, 12). Likewise, the information would have been important to a reasonable examiner regarding the patentability of claim 4 of the '080 patent. Amgen and those substantively involved in prosecuting the '933 patent and the '080 patent would have known that if the product claimed in this manner is the same as or obvious from a product in the prior art, the claim is not patentable even though the prior product was made by a different process and, therefore, knew or should have known that the Baron-Goldwasser clinical study and 1971 Garcia article would have been important to a reasonable examiner.

~~163.~~162. Indeed, at least Drs. Lin, Egrie, Strickland and Browne -- who were involved in Amgen's erythropoietin project and in the drafting and prosecution of the patents-in-suit -- and Drs. Rathmann and Vapnek knew of the Baron-Goldwasser study and in fact knew that Amgen used the formulation and dosage information from the study as a guideline to develop its own clinical formulation and dosage. (*See* AM-ITC 00557514-27). Furthermore, the information in the September 24, 1990, October 31, 1990 and November 1, 1990 memoranda was known to the same individuals at the time the '933

**patent and '080 patent claims were pending. Amgen (including Mr. Odre), aware of the September 24, 1990 and November 1, 1990 memoranda and knowing that the prior art disclosed compositions of erythropoietin and HSA (and BSA), nonetheless continued to pursue pharmaceutical composition claims in the application to issuance. (*See, e.g.*, '874 FH, Paper 37, 6/13/94 Preliminary Amendment at 2; Paper 39, 9/7/94 Examiner Interview Summary; Paper 42, 2/16/95 Amendment at 4).**

~~164.~~**163.** **Despite its clear materiality to the pharmaceutical composition claims, at no time during the prosecution of the '933 patent or the '080 patent did Amgen disclose any of the Baron-Goldwasser clinical study documents or the 1971 Garcia article. (*See* '874 FH, Paper 36, 4/8/94 IDS and PTO-1449 Form; '933 Patent, References Cited; '556 FH, Paper 7, 12/20/96 IDS and PTO-1449; '080 Patent, References Cited). Accordingly, Applicant violated the duty of disclosure and the duty of candor during the prosecution of the '933 and '080 patents. Additionally, the inequitable conduct that occurred in prosecuting the '933 patent infects the '080 patent, which claims priority to and is terminally disclaimed over the '933.**

~~165.~~**164.** **Amgen has, in the past, argued that it complied with the duty of disclosure by submitting testimony of Dr. Goldwasser in legal proceedings during the prosecution of the '422 and '933 patents. However, Amgen has admitted that it did not disclose clinical data or study results. Submission of Dr. Goldwasser's testimony before the United States International Trade Commission (Investigation No. 337-TA-281 before Judge Harris) does not constitute disclosure to the Examiners of the '422 patent or the '933 patent, and does not comply with the duty of good faith and candor owed the Patent Office. Similarly, the selected portions of Dr. Goldwasser's testimony that were submitted to the**

**Interference Board (AM-ITC 00900641-648 at 643 (Trial Ex. 102) (identifying only page 5, line 11 to page 44, line 18; page 59, line 17 to page 66, line 4; and page 78, line 3 to page 86, line 18)) failed to disclose the nature of the composition was used in the Baron-Goldwasser clinical study, *i.e.* human erythropoietin and human serum albumin. These portions were buried in interference files totaling over 18,000 pages, and without pointing out specific portions to the Examiner, he would never have known the relevance of the study or where in the mountains of documents to find relevant information. Furthermore, the selected portions of Dr. Goldwasser's testimony that were submitted contained only conclusory statements that insufficient amounts of erythropoietin were available to generate "any result." (*e.g.* AM-ITC 00849306-341 at AM-ITC 00849307; AM-ITC 00245727-29 at AM-ITC 00245728). This testimony contradicts statements made by Dr. Goldwasser and Dr. Baron to the U.S. Public Health Service and the FDA, including the reported increase in reticulocyte number, increase in numbers of nucleated red cells/1000 bone marrow cells and the disappearance of radio-iron from plasma. Amgen was aware of these contradictions.**

~~166.~~**165.** **Dr. Goldwasser's testimony cited by Judge Harris' opinion that was submitted to Patent Office, likewise, does not demonstrate that this important and material information was disclosed. *See* 126 F.Supp.2d at 138 (citing to Trial Ex. 101 at AM 17 027597 (*e.g.* AM-ITC 00900525 - AM-ITC00900640 at 534), Trial Ex.102 at AM 17 027580-81 (*e.g.* AM-ITC 00900641 - AM-ITC 00900648 at 641-642), Trial Ex. 109 at AM 27 015059 (*e.g.* AM-ITC 00900823 - AM-ITC 00900826 at 825) and Trial Ex. 2198 at 214-25 (*e.g.* AM-ITC 00997385-AM-ITC 00997392 at 390-391)). None of these documents disclose the erythropoietin and human serum albumin composition used in the Baron-Goldwasser**

**study or the patient data discussed above, or that Amgen used the Baron-Goldwasser study as a guideline for its dosing in clinical trials.**

**~~167.~~166. Submission of Judge Harris' opinion during prosecution of the '933 patent (*see* '178 FH, Paper 11, 6/2/89 Amendment at 6-7 (Trial Ex. 2198 at 214-215 (AM-ITC 00997385-AM-ITC 00997392 at 390-391)) would not have made the '422 Examiner aware of this information. The '422 patent originated from a different line of continuation applications than the '933 and '080 patents. (*See* AM-ITC 00906488). The Examiners of the '422 patent would not have reviewed the file history of the co-pending '933 patent because it was not a parent application of the '422 patent. (MPEP §609.02 (8th ed. Rev. 5, Aug. 2006)("The examiner will consider information which has been considered by the Office in a parent application...")). Thus, the Examiner's notes in the file history of the '933 patent indicating that he reviewed the file from Interference 102,334, are irrelevant to the '422 prosecution and provide no indication whatsoever that the Baron-Goldwasser clinical study was disclosed during the prosecution of the '422 patent.**

**~~168.~~167. It is clear from the file history that led to the '868 patent that the Examiner could not have substantively considered any alleged submission of the Initial Determination of the ITC during prosecution until years after it was purportedly submitted. Prosecution of the application for the '868 patent was suspended in 1988 ('179 FH, Paper 16, 12/9/88 Letter) and only days after the ITC opinion was submitted, the application was forwarded to the Board of Patent Appeals and Interferences where it stayed until it was returned in early 1992 upon completion of Interference 102,097. ('179 FH, Paper 19, 5/1/89 Request for Withdrawal of Suspension;'179 FH, Paper 21, 5/6/89 Letter; Paper 22, Interference Digest; Paper 27, 2/2/93 Notice of Change of Address). The**

application leading to the '422 patent was filed on November 6, 1990 and according to legible portion of the Search Notes in the prosecution history of the '422 patent by December 1992, the Examiner only "consulted claims in App. No. 07/113,179". (*See, e.g.*, Search Notes at AM-ITC 00899764).

~~169.~~168. Only specific portions of the Initial Determination of the ITC were submitted to the Interference Board and Amgen designated only specific portions of the opinion for the limited purpose of "identification", "patentability of the invention", "priority position" and "background information." Amgen did not designate for any purpose any discussion of the Baron-Goldwasser clinical study. (*See* AM-ITC 00900641-43). Similarly, Amgen referred the Examiner only to pages 49-54 in submitting the opinion during the '933 prosecution. (AM-ITC00900550-55; *see also* AM-ITC 00900629-36; AM-ITC 00900641-43). The referenced pages do not disclose the erythropoietin and HSA composition used or the results of the clinical study. Finally, in submitting the opinion during the prosecution of the '868 patent, the Initial Determination was cited for no more than the fact that after the International Trade Commission reviewed the Initial Determination of the administrative law judge, Amgen's ITC complaint was dismissed for subject matter jurisdiction. (AM-ITC 00900823-26 at 825).

~~170.~~169. Given the workload and the limited time that an examiner has to examine individual applications, it is highly unlikely that any of the Examiners read the entirety of the opinion. However, reading the entirety of the opinion would provide no information beyond the misleading assertions regarding insufficient amounts of EPO, which incorrectly implied that no clinical study occurred when in fact, Drs. Goldwasser

**and Baron had carried out a clinical study that would have been highly material to patentability. (AM-ITC 00900552-553).**

~~171.~~**170.** **In light of Amgen's acknowledged motivation for filing the '741 application and prosecuting the '422 patent to issuance, it is clear that Amgen and those substantively involved in prosecuting the '741 application as discussed above, including Mr. Odre and Mr. Watt, were highly motivated to obtain patent protection through whatever means necessary, including deliberately misleading the PTO by withholding highly material prior art. But for Amgen's misconduct, at least the '422 patent, claims 9-14 of the '933 patent and claims 4-6 of the '080 patent would not have issued. Accordingly, the '422, '933 and '080 patents are unenforceable for inequitable conduct. In addition, the '080 patent is unenforceable as a result of infectious unenforceability due to the inequitable conduct in securing the '933 patent.**

~~172.~~**171.** **Amgen knowingly misrepresented and omitted material information regarding the Baron-Goldwasser clinical study and related prior art with the intent to deceive the PTO, which relied upon Amgen's statements in determining whether to issue the '422, '933 and '080 patents. But for Amgen's misconduct, the '422, '933 and '080 patents would not have issued. Amgen was aware of its fraud and misconduct leading to the issuance of the '422, '933 and '080 patents when it commenced its infringement suit against Roche.**

~~INEQUITABLE CONDUCT RELATING TO DR. STRICKLAND'S INVENTIVE CONTRIBUTIONS AND AMGEN'S VIEW OF OBVIOUSNESS OF EPO/HSA PREPARATIONS~~

~~173.In addition to the intentional withholding of the Baron-Goldwasser clinical study and the 1971 Garcia reference -- which were both determined to be material by those searching for prior art at Amgen -- by 1985, at a company Board Meeting,~~

**individuals at Amgen, including Dr. Browne and Vapnek, had concluded that a formulation with erythropoietin and HSA would be obvious and "not worth" a patent. (AM-ITC 00932278-285 at 279). Amgen had also determined that the use of HSA with erythropoietin was recommended by Dr. Strickland, not Dr. Lin, thus, raising inventorship issues as well. (*Id.*) This information apparently was not disclosed to the Examiner of the '422 patent, the '933 patent or the '080 patent, and would have been material to the patentability of the pharmaceutical composition claims. Failure to disclose this information further demonstrates the pattern of intent to deceive the Patent Office by Applicant to secure additional patent coverage. Accordingly, the '422, '933 and '080 patents are unenforceable for inequitable conduct.**

**INEQUITABLE CONDUCT RELATING TO HUMAN EPO FRAGMENTS**

174.**The '422 patent is unenforceable because individuals, including Mr. Watt and Dr. Lin, associated with the filing and prosecution of the underlying applications and acting as agents and/or with the knowledge of plaintiff Amgen, misrepresented and failed to disclose material facts relating to the recited amino sequence of a human EPO fragment in the common specification with an intent to deceive the PTO, even though they relied on the erroneous sequence to argue for patentability.**

175.**During prosecution of the '422 patent, Applicant argued for the patentability of file claims 64 and 65, stating that "Example 1 discloses the use of human erythropoietin isolated from the urine of patients afflicted with aplastic anemia ('urinary EPO') to produce tryptic fragments and the amino acid sequencing of those fragments." ('197 FH, Paper, 33, 4/28/99 Amendment at 4; *see also* '868 patent, col. 16:7-17:25). Applicant further stated that in light of Examples 7 and 10, disclosing COS-1 and CHO**

~~cells respectively, "human erythropoietin is understood to include any polypeptide having the amino acid sequence of EPO isolated from human urine and may be produced in human cells or in other mammalian cells." ('197 FH, Paper, 33, 4/28/99 Amendment at 5). The Examiner allowed these claims in response to Applicant's representations. ('197 FH, Paper 36, 5/28/99 Notice of Allowability).~~

~~176.By pointing to Example 1 of the common specification as supporting file claim 64, Applicant affirmatively misrepresented to the Examiner that the "invention" disclosed in claim 64 was fully supported by the original specification. Without such support, claim 64 would have been rejected under §112 for the addition of new matter. However, Applicant was aware years before that fragment T28 was wrong.~~

~~177.In the common specification, the sequence for fragment T28 is "E-A-I-S-P-P-D-A-A-M-A-A-P-L-R." ('868 patent, col. 16:33). However, when Amgen provided the amino acid sequence of human urinary EPO to the FDA in 1985, the "M" was replaced by a glycosylated "S." (*See* AM-ITC-00596041-42 at Figure 4B-7). Furthermore, a 1986 scientific article published by Dr. Goldwasser and Amgen scientists, including Por Lai, who worked at the direction of Applicant Lin and provided information for the common specification regarding tryptic fragments, demonstrates that T28 sequence in described in the patent was incorrect. (Lai *et al.* 1986; Figure 1). This publication, like the sequence given to the FDA, indicates that T28 has a serine and not a methionine, and that Applicant was aware by at least August 26, 1985 that the disclosed sequence of T28 in the patents-in-suit was not correct. The authors from Amgen and Dr. Goldwasser concluded that the amino acid in position 126 of erythropoietin isolated from human urine is serine, not methionine as suggested by the patent. Regarding this amino acid, the authors stated:~~

> **Sequence analysis peptides T28 and 2S63 indicated a serine at position 120 and no identifiable PTH for position 126. However, amino acid composition analysis revealed the presence of 2 serine residues in this fragment. Analysis of the DNA sequence indicated that a serine is present at position 126 (10, 11). One possible explanation for these results is that position 126 is a glycosylated serine.**

178.**Drafts of this publication indicate that Amgen originally believed that human urinary erythropoietin contained a methionine at position 126 (numbering provided in Figure 1 of Lai *et al*). (*See, e.g.*, AM-ITC 00072323-44; AM-ITC 00072302-27; AM-ITC 00072538-59; AM-ITC 00138725-55; AM-ITC 00145452-534; AM-ITC 00071306-31; AM-ITC 00071332-61; AM-ITC 00071642-56; AM-ITC 00071657-79; AM-ITC 00071995-2010; AM-ITC 00072060-96; AM-ITC 00072249-95). A partial manuscript accompanying a letter to Por Lai from Eugene Goldwasser, dated October 9, 1984, contains no discussion of amino acid 126. (AM-ITC 00072274 – 83). What appears to be a early version of the manuscript, containing numerous hand-written comments, states**

> **Comparison of the sequence determined from the protein with that determined from the cloned gene shows only one difference, at residue 126; the DNA sequence indicates a serine at that position whereas the protein has a methionine. We do not yet know the reason for this difference but it may be related to the fact that the EPO used was prepared from urine collected in Japan while the genomic DNA was probably from the kidney of a Caucasian.**

**(AM-ITC 00072262). This same statement appears in another version of the manuscript. (*See, e.g.*, AM-ITC 00072302-22 at 11). Fig. 1 of this version of the manuscript shows the amino acid sequence of both "Cloned EPO" and Urinary EPO" where the amino acid residue at position 126 is shown as Ser in the former, and Met in the latter. (AM-ITC 000723315, AM-ITC 00072320). Thus, at this point in time, the authors believed urinary EPO to have a methionine at position 126.**

~~179.~~**~~On March 8, 1985 Dr. Goldwasser informed Dr. Lai about a publication from Genetics Institute, which may have been Amgen's first indication that T28 was incorrect. In a letter to Dr. Lai, Dr. Goldwasser suggested adding a paragraph at the end of the paper explaining that they discovered a report by Jacobs *et al.* at a very late stage, which revealed that Jacobs' amino acid sequence was exactly like Goldwasser's with the exception of a serine in the place of the methionine. (AM-ITC 00211638). The statement proposed by Dr. Goldwasser appears in a version of the manuscript which accompanies a hand written draft of a letter from Dr. Lai to the editor of the Journal of Biological Chemistry. (AM-ITC-00071306-331 at 320; *see also* AM-ITC 00072538-559 at 547 (acknowledging that position 126 may be a serine)). Similarly, the document entitled "Supplemental Material to Structural Characterization of Human Erythropoietin" contains a figure showing only the sequence of urinary EPO and has a serine at position 126. (AM-ITC 00138725-755 at 729).~~**

~~180.~~**~~Another version of the manuscript accompanies a letter dated July 31, 1985 from Eugene Goldwasser to Por Lai. The letter states "Finally here is the figure for the paper. I hope we can get it out without too much more delay." This manuscript further confirms that Applicant knew that the sequence was wrong. (AM-ITC 00071995-2010 at 2002).~~**

~~181.~~**~~Despite the numerous documents that show Dr. Lin and colleagues working at his direction knew that the sequence disclosed in Example 1 of the specification was wrong, Applicant never disclosed this error to the Examiner. Had Applicant disclosed the material error, this would have resulted in a rejection for the addition of new matter. Even if the recited sequence was a typographical error, a subsequent correction would~~**

~~nonetheless be the addition of new matter unless it was an obvious error. It is clear, however, that the error was not obvious. The common specification states that erythropoietin is "a substance for which no substantial amino acid sequence information has been published." ('868 patent, col. 9, ll. 4-7). Therefore, without that information, nothing about the particular amino acid sequence could have been obvious. In any event, additional documents confirm that the recited sequence for T28 was not an error. (*See, e.g.*, AM-ITC 00415129). Furthermore, even if Applicant knew of two different forms of human urinary EPO, one with an "M" and one with a glycosylated "S" -- and, thus, there was not a true "error" to disclose -- this information was material and should have been disclosed to the Examiner, especially in light of Applicant's argument that its claimed invention differed in glycosylation from human urinary EPO. Applicant would have then been obligated to show a difference in glycosylation as compared to two different forms of urinary EPO.~~

~~182.By failing to disclose material information regarding the amino acid sequence of T28 and misrepresenting that fragments of human erythropoietin supported claim 1 of the '422 patent, Applicant and his attorneys, including Mr. Watt, misled the Examiner as to the existence of proper support in the specification for the claimed invention. As a direct result, Amgen obtained claim 1 of the '422 patent. Had Applicant disclosed this information, the claim would not have issued because new matter had been added under 35 U.S.C. §112, ¶1. Accordingly, the '422 patent is unenforceable for inequitable conduct.~~

~~INEQUITABLE CONDUCT RELATING TO THE SULFATE CONTENT OF EPO~~

183. As discussed earlier, Applicant submitted the 1988 Strickland Declaration during prosecution of the '933 patent to show differences between u-EPO and r-EPO. The declaration concludes that "u-EPO contains sialidase resistant negative charges not found in r-HuEPO". ('178 FH, Paper 7, Strickland Declaration at 15). Furthermore, in his Declaration, Dr. Strickland cited an article by Dr. Takeuchi, whom he had direct contact with prior to filing his declaration. Dr. Strickland, and Mr. Borun and Mr. Odre who prosecuted the application, never disclosed his relationship with Dr. Takeuchi

184. Prior to filing the 1988 Strickland Declaration, Amgen received information from Dr. Takeuchi indicating that the sialidase resistant negative charges could be removed from u-EPO "when more substrate and fresher enzyme were used", (AM-ITC 00067214-259 at 241), thus potentially refuting Dr. Strickland's conclusion that the sialidase resistant negative charges supported a difference between u-EPO and r-EPO. However, Amgen and its attorneys, including Mr. Borun, never disclosed this information to the Patent Office. This information would have been material to claims 1, 2 and 6-14 the '933 and claims 1 and 4-6 of the '080 patent because it refuted Amgen's alleged evidence that its claimed product was somehow patentable over the prior art. However, Applicant knew that there were no patentable differences and therefore withheld material information. Because of Applicant's misconduct, claims 1, 2 and 6-14 of the '933 and claims 1 and 4-6 of the '080 patent issued, giving Amgen greater patent protection than its process patents. Accordingly, the '933 and '080 patents are unenforceable for inequitable conduct. In addition, the '080 patent is unenforceable by infectious unenforceability due to the inequitable conduct in procuring the parent '933 patent.

**INEQUITABLE CONDUCT RELATING TO INVENTIVE CONTRIBUTION**

***Inventive Contributions Regarding Use of CHO Cells***

185. **Amgen has asserted that the use of chinese hamster ovary ("CHO") cells to express erythropoietin was routine and did not involve any inventive contribution. If Amgen changes its position and asserts that the use of CHO cells was inventive, then Messrs. Borun and Odre and Dr. Lin affirmatively withheld highly material information relating to individuals who contributed to the invention of the patents-in-suit. Dr. Lin has admitted that at the time of the invention, individuals at the American Type Culture Collection ("ATCC") contributed the idea to use CHO cells. (3/28/07 Lin Tr.).**

186. **Amgen was indisputably aware that information regarding those responsible for inventive contributions to any claim of the patents-in-suit would have been material to prosecution of its patents. With each application filed, Dr. Lin submitted a sworn declaration stating that he was the sole inventor of claimed subject matter. (*See* SN 06/675,298 "Declaration for Patent Application, signed 11/29/84; '179 FH (*e.g.* AM-ITC 00953127); '381 FH (*e.g.* AM-ITC 00898283); '741 FH (*e.g.* AM-ITC 00899006); '556 FH (*e.g.* AM-ITC 00868031); '369 FH (*e.g.* AM-ITC 00898596)). At no time did Dr. Lin or Amgen disclose any contribution made by Drs. Tsong or Dr. Cheng at the ATCC.**

187. **A protest under 37 C.F.R. § 1.291(a) was filed on July 23, 1993 during the prosecution of the 07/119,179 application, which resulted in the '868 patent. In that protest, Dr. Por Lai asserted that he made a critical contribution to the invention claimed. Included in the claims at issue were claims drawn to the production of erythropoietin in CHO cells. ('179 FH, Paper 8, 6/1/88 Second Preliminary Amendment at 4). At no time**

~~during the course of the PTO's consideration of that protest did Amgen or Dr. Lin disclose the contribution by anybody other than Dr. Lin.~~

~~188.Amgen repeatedly misrepresented and failed to disclose the true facts regarding the inventive contribution of the ATCC relating to CHO cells with deceptive intent. Such information would have been material to the patentability of claim 2 of the '868 patent and claims 7 and 12-14 of the '933 patent, and those patents are unenforceable for inequitable conduct. Furthermore, Amgen maintained throughout prosecution of both the '178 and '179 applications that the claimed invention covered recombinant erythropoietin expressed in a variety of host cells including CHO cells. (*e.g.* '178 FH, Paper 6, Amendment and Reply at 6; '774 FH, Paper 50, Second Preliminary Amendment at 5; *see also* '179 FH, Paper 33, 1/3/94 Amendment and Response at 5). Accordingly, by way of infectious enforceability, each of the patents-in-suit are unenforceable for inequitable conduct.~~

~~*Inventive Contributions Regarding Use of Probes*~~

~~189.Amgen has recently taken the position in its rebuttal expert reports that "one of ordinary skill would not have had a reasonable expectation of success that (i) one could successfully obtain correct amino acid sequence(s) that would yield useful degenerate sets of oligonucleotide probes." (Rebuttal Expert Statement of Randolph Wall at ¶ 33; *see also* Rebuttal Expert Report of Harvey Lodish at ¶ 191 ("In 1983, it was neither simple nor obvious to obtain human EPO amino acid sequences that would be useful for making useful sets of degenerate probes to screen a library for human EPO clones, for a number of reasons"); Rebuttal Expert Statement of Stuart H. Orkin at ¶ 49 ("This confirms my belief that in 1983, even with access to the protein, one of ordinary skill in the art would believe it~~

highly likely that the protein sequence information would contain errors that might prevent the design of effective probes to screen a library.")). Assuming this is true and that Amgen, including Dr. Lin, Mr. Borun, Mr. Odre and Mr. Watt, believed this to be the case during the prosecution of the patents-in-suit, this would have constituted inequitable conduct because Amgen intentionally failed to raise this belief when this issue was squarely being addressed by the Patent Office.

190. Specifically, as discussed above, during the prosecution of the '933 patent, Dr. Lai submitted a Protest Regarding Inventorship Under 37 C.F.R. Section 1.291. ('178 FH, Paper 31). Dr. Lai maintained that he should be an inventor to the pending patent application, because among other things, he developed "novel protein microsequencing techniques necessary for working with minutely available proteins such as urinary EPO and its tryptic fragments." (*Id.* at 1-2). Even though Amgen apparently believed that this sequencing work was not routine and therefore inventive, as confirmed by Amgen's rebuttal expert reports, Amgen did not support Dr. Lai's protest for inventorship and name him as an inventor. As a result, the Patent Office determined that Dr. Lai's contribution was not "novel and unobvious" and consequently not inventive. (*See* '178 FH, Paper 34, 12/29/93 Office Action at 3). Therefore, Amgen breached its duty of candor to the Patent Office because, despite the fact that Amgen believed that sequencing of fragments of u-EPO protein was beyond the level of ordinary skill in the art, Amgen failed to inform the Patent Office of this contention, which would have resulted in the Dr. Lai being named as an inventor to the patents-in-suit. Amgen omitted this material information with deceptive intent. Accordingly, each of the patents-in-suit is unenforceable for inequitable conduct.

**INEQUITABLE CONDUCT RELATING TO "PEG-EPO" PRIOR ART**

191. **Amgen asserts that U.S. Patent No. 4,179,337 ("the '337 patent") by Davis *et al.*, which issued in 1979, discloses pegylated erythropoietin compounds or "Peg-EPO". It is Amgen's position that the claims of the patents-in-suit cover "Peg-EPO." Roche does not agree with Amgen's improper characterization of Roche's CERA product. However, based on Amgen's assertions, the '337 patent would have been highly material prior art, which Amgen failed to disclose during prosecution of the patents-in-suit. As Dr. Lin recently testified at this deposition, he was aware of pegylation at the time that the patents-in-suit were filed.**

192. **Dr. Lin and the prosecuting attorneys, Mr. Borun, Mr. Odre and Mr. Watt, knew or should have known of the '337 patent, which is highly relevant prior art to the claims of the patents-in-suit, if those claims are construed as Amgen contends. Thus, Applicant's failure to disclose the '337 patent constitutes yet another failure to disclose material information that Amgen knew about and should have disclosed. Accordingly, to the extent that Amgen asserts that any of the patents-in-suit cover "Peg-EPO," each of those patents are unenforceable for inequitable conduct.**

**AMGEN'S PATTERN OF MISCONDUCT EVIDENCES AN INTENT TO DECEIVE THE PTO**

193. **The file histories of the patents-in-suit evidence an intentional pattern to deceive the U.S. Patent Office to secure additional patents and claims to extend Amgen's monopoly beyond the original '008 patent which expired on October 27, 2004. For example, Amgen secured the '349, '933, '080 and '422 patent claims to protect a product that was already in nature (35 U.S.C. §101) and now asserts that its product claims are not limited by their method of manufacture. (*See, e.g.*, AM-ITC 00906512). By violating the**

~~duty of candor and disclosure, Applicant, including all the individuals named above, successfully secured dozens of additional patent claims, extending Amgen's monopoly against potential competition and, in turn, unfairly shielding its billions of dollars in annual sales (and will continue to do so through 2015).~~

~~194.~~ ~~Plainly, sales in the United States have been lucrative for Amgen, and Amgen expects a continuing increase in patient demand for its products. (*See, e.g.*, 1/25/07 Amgen Press Release at http://www.amgen.com/media/media_pr_detail.jsp?year=2007&releaseID=954402 ("Underlying demand in free-standing dialysis clinics remained consistent with an annual patient population growth of 3-4 percent")). Given the annual revenue generated by Epogen® after its approval by the U.S. Food and Drug Administration in 1989, Amgen had every reason to secure additional patent claims to extend protection beyond the '008 patent term. Since approval for Epogen®, Amgen has reported sales of approximately $25,186,300,000 in the United States. (Amgen Inc., 10K Filings 1991-2006; *see also* AM 44 1508568). Even after the expiration of the '008 patent, Amgen reported approximately $2,455,000,000 in U.S. sales for 2005 and $2,511,000,000 in U.S. sales for 2006. Similarly, its Aranesp® product -- which Amgen asserts is covered by the '698 patent-in-suit -- has generated over approximately $7,718,600,000 in sales since 2001 with approximately $4,894,000,000 of the total amount due to sales since the '008 patent expired. (Amgen Inc., 10K Filings 1991-2006).~~

~~195.~~ ~~Accordingly, Amgen has kept its monopoly alive by filing numerous continuation applications over many years in an attempt to add claims to prevent competitors from entering the U.S. with products. But for Amgen's misconduct there (1)~~

~~would be no patent claims currently in force, including Amgen's numerous product claims and its process claims (that should have at a minimum been disclaimed over the expired '008 patent to gain allowance) and (2) competitive products would be available. Given the commercial environment and Amgen's sales figures, it had every reason to secure its additional claims and patents by whatever means deemed necessary.~~

~~196.~~172. ~~This motivation, along with the material misrepresentations and omissions set forth above, evidences a pattern to intentionally deceive the Patent Office into issuing each of the patents-in-suit.~~

**EIGHTH DEFENSE - UNCLEAN HANDS**

~~197.~~173. ~~89.~~ The asserted patents are unenforceable due to Amgen's unclean hands.

**NINTH DEFENSE - PUBLIC HEALTH AND WELFARE**

~~198.~~174. ~~90.~~ Amgen's request for an injunction precluding Roche from importing into, making, using, or selling CERA in the U.S. is contrary to the public health and welfare.

**TENTH DEFENSE - AMGEN IS ESTOPPED FROM SEEKING DAMAGES**

~~199.~~175. ~~91.~~ Amgen has taken the position that it is not seeking damages against Roche related to the accused product in this action.

~~200.~~176. ~~92.~~ Amgen contends that it is only seeking declaratory and injunctive relief against Roche's alleged acts of infringement.

~~201.~~177. ~~93.~~ Amgen has alleged that there are current acts of infringement in the United States in connection with the accused product.

~~202.~~178. ~~94.~~ Based on its decision to forgo damages, Amgen has argued to the Court that Roche is not entitled to a jury trial on Amgen's claims.

~~203.~~179. ~~95.~~ At the conclusion of the litigation, in the event that Amgen is successful in its claims against Roche and the asserted claims are found to be infringed, valid and enforceable, the Court must undertake an analysis mandated by the United States Supreme Court's decision in *eBay, Inc. v. MercExchange, L.L.C.*, 126 S. Ct. 1837 (2006), to determine if a permanent injunction would be appropriate.

~~204.~~180. ~~96.~~ Based on Amgen's decision to waive any damages, compensatory or otherwise, as a tactic to deprive Roche of its constitutional right to a jury trial on Amgen's claims (even though Roche contends that they are entitled to a trial by jury), Amgen is estopped and precluded from seeking, asserting or maintaining a claim for damages, compensatory or otherwise, for any damages, whether past, current or future, in the event that Amgen is successful on its claims and the Court determines that a permanent injunction is not warranted in this case.

**ELEVENTH DEFENSE - FILE WRAPPER ESTOPPEL**

~~205.~~181. ~~97.~~ Amgen's claims for infringement of the '868, '933, '698, '080, '349 and '422 patents are barred by file wrapper estoppel.

**TWELFTH DEFENSE - OMITTED**

~~206.~~182. ~~98.~~ OMITTED

**THIRTEENTH DEFENSE - PROSECUTION LACHES ESTOPPEL**

~~207.~~183. ~~99.~~ Amgen's claims for infringement of the '868, '933, '698, '080, '349 and '422 patents are barred by prosecution laches and estoppel.

**PART II: ROCHE'S COUNTERCLAIMS**

F. Hoffmann-La Roche Ltd, Roche Diagnostics GmbH, and Hoffmann-La Roche Inc. (collectively "Roche"), as Counterclaim-Plaintiffs, by their attorneys, allege the following counterclaims on information and belief:

## SUMMARY OF COUNTERCLAIMS

1. Roche counterclaims against Amgen under Sections 4 and 16 of the Clayton Act, 15 U.S.C. §§ 15, 26, and the Declaratory Judgment Act, 28 U.S.C. §§ 2201-2202, for violations of Sections 1 and 2 of the Sherman Act, 15 U.S.C. §§ 1 and 2, by reason of Amgen's actions to unreasonably restrain trade in, and monopolize, and/or attempt to monopolize a number of relevant markets, including markets for the sale of Erythropoiesis Stimulating Agent ("ESA") drugs sold for particular indications. Roche also counterclaims against Amgen for a declaratory judgment of patent invalidity, non-infringement, and unenforceability pursuant to 28 U.S.C. §§ 2201 and 2202.

2. Amgen's patent case against Roche is part of a broad, anticompetitive scheme by Amgen to unlawfully maintain or secure monopoly power in violation of the antitrust laws. Amgen possesses monopoly or substantial market power over the sales of ESA drugs sold for particular indications. Amgen's Epogen® and Aranesp® products have been, and today remain, the only such drugs available for patients suffering from End Stage Renal Disease who are on dialysis ("ESRD"). Similarly, Amgen's Aranesp® is the leading ESA medicine administered to patients with non-dialysis Chronic Kidney Disease ("CKD"). Ortho Biotech Products, L.P. ("Ortho") offers the only other ESA drug available to CKD patients, Procrit®, which Ortho sells only because of a license from Amgen and that has the same active ingredient as Epogen®.

3. Roche's CERA drug (to be marketed under the trade name MIRCERA®) presents the first credible challenge to Amgen's dominance over ESAs sold for ESRD and CKD, the two relevant markets here **and, in the alternative, in an All ESA market**. Recognizing that its patents are not likely to block Roche's eventual entry with CERA, Amgen has embarked on a course of anticompetitive conduct designed to hinder Roche's ability to enter or compete

effectively in these markets. Among other conduct, Amgen has: (a) engaged in unlawful and anticompetitive litigation before this Court by, including but not limited to, seeking to enforce patents that were knowingly obtained through willful fraud on the United States Patent and Trademark Office ("PTO"); (b) engaged in sham litigation before the International Trade Commission ("ITC") in a failed effort to hinder CERA's entry; and (c) blocked Roche's access to customers for CERA by (i) recently cementing a long-term exclusive dealing arrangement with the largest single ESA customer, (ii) engaging in other exclusionary contracting practices, and by (iii) threatening customers that purchasing CERA will result in Amgen's retaliating by raising prices, denying those customers access to Amgen's ESA products or denying those customers critical discounts on those products.

4. Amgen's anticompetitive scheme, if not invalidated by this Court, will hinder or eliminate the competition that Roche's CERA is poised to create, limit the ability of patients and physicians to choose an alternative medicine that would provide benefits to patients not currently available, and saddle consumers, patients and those who pay for their medicines with supracompetitive prices and the American public health system with greater expenses. Accordingly, Roche seeks under the antitrust laws monetary damages, a declaration that Amgen's conduct is unlawful, and other appropriate relief, including attorneys' fees and costs.

## THE PARTIES

5. Counterclaim-Plaintiff F. Hoffmann-La Roche Ltd is a foreign corporation existing under the laws of Switzerland with a principal place of business in Basel, Switzerland.

6. Counterclaim-Plaintiff Roche Diagnostics GmbH is a foreign corporation existing under the laws of Germany with principal places of business in Penzberg, Germany and Mannheim, Germany.

7. Counterclaim-Plaintiff Hoffmann-La Roche Inc. is a New Jersey corporation with a principal place of business at 340 Kingsland Street, Nutley, NJ 07110-1199.

8. Roche is a leading healthcare organization that has been active in the discovery, development, manufacture and marketing of novel healthcare solutions for over 100 years. Using innovative technologies, Roche develops medications and other products to prevent, diagnose and treat life-threatening diseases.

9. Counterclaim-Defendant Amgen is a Delaware corporation with its principal place of business at One Amgen Center Drive, Thousand Oaks, California 91320-1799.

## JURISDICTION AND VENUE

10. This Court has jurisdiction over the counterclaims asserted herein under 28 U.S.C. §§ 1331, 1337(a), 1338(a), 1367 and 2201.

11. This Court has personal jurisdiction over Amgen by virtue of its appearance as a plaintiff in this action.

12. Venue is proper in this district under Sections 4 and 12 of the Clayton Act, 15 U.S.C. §§ 15 and 22, as Amgen is subject to personal jurisdiction in this district. Venue is also proper in this district pursuant to the provisions of 28 U.S.C. §§ 1391(b), 1391(c) and 1400(b).

## FACTUAL ALLEGATIONS

### I. ERYTHROPOIETIN STIMULATING AGENTS USED IN THE TREATMENT OF ANEMIA

13. Erythropoietin ("EPO") is a naturally occurring hormone found in human blood. EPO is produced in the kidneys and stimulates red blood cell production in the bone marrow.

14. ESAs are drugs that are used to treat anemia patients by promoting the production of red blood cells. Anemia is the condition of having less than the normal number of

red blood cells or less than the normal quantity of hemoglobin in the blood, which decreases the oxygen-carrying capacity of the blood.

15. The principal uses of ESAs are in the treatment of anemia associated with ESRD (*i.e.*, dialysis patients), CKD, and cancer (oncology). ESAs are also used for the treatment of anemia associated with HIV, pediatric renal disease, surgery, hepatitis C and stroke.

## II. AMGEN'S MONOPOLY OR MARKET POWER IN THE MARKET FOR THE SALE OF ESA DRUGS FOR THE TREATMENT OF ESRD

16. Part of the interstate trade and commerce adversely affected and restrained by the unlawful Amgen acts described herein, and one of the relevant markets in this case, is the sale in the United States of ESAs for the treatment of ESRD ("ESRD ESA").

17. Approximately 400,000 patients have ESRD in the United States. Patients with ESRD receive regular treatments at dialysis centers to filter their blood through hemodialysis machines to remove toxins. The vast majority of ESRD patients have been diagnosed with anemia and require treatment with an ESA to achieve normal hemoglobin levels.

18. No drug other than an ESA is safe and effective for the treatment of anemia in ESRD patients, and no ESA may be marketed for the treatment of anemia in ESRD patients in the United States unless the FDA has approved it for use as a treatment for (*i.e.*, is "indicated for") anemia in dialysis patients (that is, for treating ESRD anemia).

19. Accordingly, the sale in the United States of ESA drugs for the treatment of ESRD is a relevant market.

20. Since 1989, Amgen has sold an ESA under the brand name Epogen® which is indicated for the treatment of anemia in ESRD patients (that is, patients with chronic renal failure on dialysis). Amgen sold more than $2.4 billion worth of Epogen® in 2005.

21. In 2001, Amgen introduced a different ESA under the brand name Aranesp®, which is also indicated for the treatment of anemia in ESRD patients (that is, patients with chronic renal failure on dialysis). Amgen sold more than $2.1 billion worth of Aranesp® in 2005, although on information and belief only a relatively small proportion of sales are for ESRD use.

22. Epogen® and Aranesp®, both Amgen products, are the only ESAs that have been approved by the FDA for the treatment of anemia in ESRD patients and that are currently sold for such treatment in the United States. Although Procrit®, a product sold by Ortho Biotech Products, L.P. ("Ortho") which has the same active ingredient as Epogen®, is also indicated for the treatment of anemia in ESRD patients, Amgen's long-term license with Ortho prevents Ortho from marketing Procrit® for that purpose.

23. Amgen, as the supplier of the only two ESRD ESA products approved for and available for sale in the United States, has 100% market share and monopoly power in the ESRD ESA market.

24. Approximately sixty-five percent (65%) of ESAs used to treat ESRD patients in the United States are purchased directly from Amgen by two Large Dialysis Organizations ("LDOs"). These two LDOs operate numerous facilities throughout the United States at which ESRD patients receive their dialysis treatment and, when necessary, are administered their ESA medications. ESRD patients receive ESA medications during their dialysis visits. The two LDOs historically have purchased ESA medications under centralized contracts with Amgen.

25. Beyond the two LDOs, the remaining thirty-five percent (35%) of ESRD ESA customers consist of small and medium chain dialysis centers, independent dialysis centers and hospitals.

26. Because of Amgen's monopoly power, each and every dialysis center and other ESRD ESA customer in the United States must purchase ESRD ESA drugs from Amgen. There are no products currently on the market that can be substituted for Amgen's ESRD ESA products. Evidencing Amgen's monopoly power, Amgen has steadily raised the prices of Epogen® over time. Also evidencing Amgen's monopoly power, to bolster sales of the distinctly-priced Epogen®, Amgen has refused to make Aranesp® available to many customers for ESRD use at an attractive price.

27. Amgen's monopoly power is protected by high barriers to entry. Amgen alone owns at least twenty-eight U.S. patents with claims related to erythropoietin, and owns many more concerning related technologies. Although Roche now plans to enter the market through a product, CERA, that is not blocked or covered by those patents, Amgen has vigorously enforced its patent portfolio against other companies for the past twenty years. In addition to the numerous patents owned by Amgen and others, barriers to entry include the rigorous FDA approval process to test the safety and efficacy of drug products. Other entry barriers include dialysis centers' long-standing agreements and relationships with Amgen. A new entrant faces these and other significant switching costs, which include convincing personnel to learn new methods for administering different ESA products and convincing formularies to place new medications on their approved drug lists. The preference for some customers to contract with a single ESA provider, and the providers' consequent need to compete "for the contract," also constitutes a substantial entry barrier, as do Amgen's contracting practices and other factors.

28. In light of the foregoing, Amgen has monopoly power — that is, the power to raise prices or exclude competition — in the ESRD ESA market.

**29. In the alternative, the relevant market is all ESAs sold in the United States (the "All ESA market"). There are no reasonably interchangeable substitutes for ESAs for the treatment of anemia. Amgen has monopoly power in the alternative All ESA market because it has a market share of over 70%, and the same high entry barriers in the ESRD ESA and CKD ESA markets exist in the alternative All ESA market.**

## III. AMGEN'S SUBSTANTIAL AND EXPANDING MARKET POWER IN THE MARKET FOR THE SALE OF ESA DRUGS FOR THE TREATMENT OF CKD

**30.** ~~29.~~ Another part of the interstate trade and commerce adversely affected and restrained by the unlawful Amgen acts described herein, and the second relevant market in this case, is the sale in the United States of ESA drugs for the treatment of CKD ("CKD ESA").

**31.** ~~30.~~ In addition to patients whose kidney disease is so severe that they require dialysis (that is, ESRD patients), millions more suffer from a less severe although serious condition known as CKD. CKD patients do not receive dialysis. Instead, they have been diagnosed with some level of reduced kidney function by their personal care physician or nephrologist.

**32.** ~~31.~~ CKD patients, too, are treated with ESAs because CKD patients commonly also suffer anemia. There is no substitute for ESAs in the safe and effective treatment of anemia associated with CKD. Moreover, no ESA may be marketed for the treatment of anemia in CKD patients in the United States unless the FDA approves its use to treat (is "indicated for") anemia associated with CKD.

**33.** ~~32.~~ Accordingly, the sale of ESAs for the treatment of anemia in CKD patients in the United States is a relevant market.

**34.** ~~33.~~ Amgen's Aranesp® is indicated for the treatment of anemia in CKD patients. The only other product available for the treatment of anemia in CKD patients in the United States is Procrit®, which is sold by Ortho under a license from Amgen. Procrit® is a branded version of epoetin alfa which is chemically identical to Amgen's Epogen® product. Although Amgen's Epogen® is also indicated for the treatment of anemia in CKD patients, Amgen's license with Ortho precludes Amgen from marketing Epogen® for such use. No other ESA is currently approved by the FDA for use in treating anemia in CKD patients.

**35.** ~~34.~~ Procrit® and Aranesp® are distributed for use in the CKD market through traditional channels including specialty distributors, hospitals and their general purchasing organizations and retail pharmacies. In contrast to the ESRD ESA market, the customers for CKD ESA drugs are highly diffuse. These drugs are administered at doctors' offices, hospitals and at patients' homes. Accordingly, individual doctors and patients make the decisions concerning the purchase of particular ESA products to treat anemia in patients with CKD, and purchasers of CKD ESA drugs include hospitals, individual medical practices, and specialized clinics.

**36.** ~~35.~~ Since Aranesp® was introduced in 2001, Amgen has steadily increased Aranesp® sales to the point where it is, or soon will be, the leading product sold in the CKD ESA market. On information and belief, Aranesp®'s share of the CKD market has skyrocketed to approximately 50% of CKD ESA sales since it was first introduced in 2001. On information and belief, Aranesp® has obtained its now leading and near-dominant position not

exclusively on the merits, but rather in part through anticompetitive Amgen contracting practices with hospitals, an important ESA customer class.

**37. ESAs approved by the FDA to treat CKD are also approved for other indications, such as chemotherapy induced anemia (CIA). CKD ESAs are sold for and employed for such other uses and could be diverted in certain circumstances to CKD use. The above market shares for CKD ESA sales thus conservatively include all sales of Aranesp and Procrit for these other uses. Accordingly the CKD market, considering such supply substitution, can also be termed the non-ESRD market.**

**38.** ~~36.~~ Amgen's substantial and expanding market power in the CKD ESA market is protected by high entry barriers. As discussed above, Amgen has a substantial patent portfolio that it has enforced against competitors for the past 20 years. The need for new entrants to obtain FDA approval for indications related to the safe and effective treatment of CKD is also a substantial entry barrier. There are also substantial barriers to switching. Entrants must convince doctors and nephrologists to switch from Aranesp® or Procrit® to their new product. Hospitals must also be persuaded to add a new product to their formularies. Entrants must also overcome Amgen's anticompetitive contracting practices, which include (as described below) conditioning discounts to hospitals with respect to Amgen's blockbuster oncology drugs on taking certain volumes of Amgen's ESA drugs across indications.

**39.** ~~37.~~ Amgen accordingly possesses substantial, increasing market power in the CKD ESA market. Amgen's conduct directed against Roche, as described herein, dangerously threatens to expand that power into monopoly power by hindering a new product, CERA, that is poised to derail Amgen's march to monopoly.

40. In the alternative, Amgen possesses monopoly power in another relevant market, all ESAs sold in the United States (the "All ESA market"). There are no reasonably interchangeable substitutes for ESAs for the treatment of anemia. Amgen has monopoly power in the alternative All ESA market because it has a market share of over 70%, and the same high entry barriers in the ESRD ESA and CKD ESA markets exist in the alternative All ESA market.

## IV. AMGEN'S MONOPOLY OR MARKET POWER IN THE MARKET FOR THE SALE OF WHITE BLOOD CELL STIMULATORS

41. White Blood Cell stimulators ("WBC Stimulators") are drugs that are used in oncology to stimulate the production of infection-fighting white blood cells called neutrophils that chemotherapy depletes.

42. There are no reasonably interchangeable substitutes for WBC Stimulators for the treatment of depleted neutrophils in patients undergoing chemotherapy.

43. Only WBC Stimulators approved for sale in the United States by the FDA as safe and effective can be marketed in the United States.

44. Accordingly, the sale in the United States of WBC Stimulators to treat depleted neutrophils in patients undergoing chemotherapy is a relevant market.

45. Amgen has monopoly power in WBC Stimulators sold in the United States. Amgen sells two WBC Stimulator products Neulasta® and Neupogen® which account for over 95% of the WBC Stimulator market. The only other product in the WBC Stimulator market is Leukine, sold by Berlex Laboratories, which has the remaining share of the WBC Stimulator market.

**46. Amgen has demonstrated its ability to exercise monopoly power in the WBC Stimulator market by conditioning discounts on Neulasta® and Neupogen® on purchaser's agreement to exclusionary contract terms regarding the purchase of ESAs.**

**47. There are high barriers to entry in the WBC Stimulator market including substantial patent portfolios, FDA approval, and switching costs.**

**48. In light of the foregoing, Amgen has monopoly power — that is, the power to raise prices or exclude competition — in the WBC Stimulator market.**

## ~~IV~~V. CERA'S THREAT TO AMGEN'S ESA DOMINANCE

**49.** ~~38.~~ Roche is seeking FDA approval to introduce CERA into the United States. CERA is the result of years of research aimed at developing a unique anemia medication that could provide better patient outcomes. Amgen confronts in Roche's CERA a major threat to its dominance in the ESRD ESA and CKD ESA markets**, and the alternative All ESA market**.

**50.** ~~39.~~ During ESA development work, Roche experimented to create an entirely new molecule. The result was CERA — a chemical entity different from recombinant human EPO (rHuEPO) in both its chemical and biological activity.

**51.** ~~40.~~ Because of the differences between CERA on the one hand, and all other ESAs currently on the market, CERA promises to offer physicians and patients the first true alternative that, for at least a significant portion of patients, would prove more appropriate either medically or as a matter of convenience and compliance.

**52.** ~~41.~~ CERA's introduction threatens to end the 17-year monopoly that Amgen has enjoyed in the ESRD ESA market **(and, alternatively, in the All ESA market)**. Similarly, it threatens to end Amgen's and its licensee Ortho's control over the CKD ESA market, and endangers the monopoly power that Amgen otherwise threatens to achieve in that market. CERA offers customers for the first time a legitimate choice of an alternative type of

ESA for the treatment of anemia. This will likely lead to enhanced competition where there has been limited (CKD ESA **and All ESA**) or no (ESRD ESA) such competition.

**53.** ~~42.~~ After years of research and development, Roche started the FDA approval process for CERA. That process included, among other activities, engaging LDOs and other ESA customers to obtain access to anemia patients in order to conduct clinical trials. Roche's CERA product is currently undergoing FDA review for approval.

## ~~V~~VI. AMGEN'S ANTICOMPETITIVE SCHEME TO UNLAWFULLY MAINTAIN ITS ESA DOMINANCE

**54.** ~~43.~~ Amgen recognizes and has asserted that FDA approval of CERA is likely; Amgen itself has alleged that approval of CERA is imminent. Amgen is also well aware that CERA will provide an alternative product choice for customers and providers, and will affect Amgen's monopoly and near-monopoly over the ESRD and CKD ESA markets, respectively**, as well as the alternative All ESA market**. As described below, Amgen has taken, and continues to take, numerous steps to hinder, delay or completely stop the sale of CERA in the United States.

**55.** ~~44.~~ Amgen's anticompetitive scheme to impede or block CERA's entry is multifaceted. Among other conduct, Amgen has (a) engaged in unlawful and anticompetitive litigation before this Court, including but not limited to, by seeking to enforce patents that were knowingly obtained through willful fraud on the PTO; (b) engaged in sham litigation by filing an objectively baseless ITC suit for no reason other than to hinder CERA's entry; and (c) sought to block Roche's access to customers for CERA through, among other conduct, (i) exclusive dealing or higher restrictive arrangements, (ii) other anticompetitive contracting practices, and (iii) threats to customers that purchasing CERA will lead to higher prices, lost Amgen discounts or no Amgen ESA products. Absent action by this Court, Amgen's

anticompetitive course of conduct may well achieve its objective of thwarting CERA's entry, thereby harming Roche, competition, patients and those who pay for their treatment (consumers), and American taxpayers.

**A. Sham Litigation**

**56.** ~~45.~~ Amgen's anticompetitive scheme includes bringing a baseless action in the International Trade Commission ("ITC") against Roche solely for the purpose of hindering, delaying, and raising the costs of CERA's introduction. Amgen has repeated its cost-imposing litigation tactics in this Court, maintaining patent infringement assertions with respect to three claims of U.S. Patent No. 5,621,080 (the "'080 patent") *even though* the Federal Circuit has already rejected the basis for those claims and *even though* Amgen admits that it has no basis to believe Roche infringes that patent. Amgen's objectively baseless litigations, brought for the sole purpose of harming Roche through the litigation *process* rather than its *outcome*, has raised entry barriers and facilitated Amgen's anticompetitive maintenance of its monopoly and near-monopoly power in the relevant markets by raising rivals' costs, distracting and harassing key individuals involved in Roche's effort to obtain FDA approval for CERA, and burdening Roche's potential customers.

1. *Amgen's Sham Litigation Before The ITC*

**57.** ~~46.~~ Amgen initiated a sham litigation against Roche in April 2006, when Amgen requested that the ITC open an investigation of Roche activity that, Amgen asserted, infringed certain Amgen patents. Amgen's ITC litigation was objectively baseless, for two reasons.

**58.** ~~47.~~ *First*, ***unlike this Court***, the ITC can only award relief based upon a finding of either (i) actual importation of an infringing product; or (ii) a commercial sale for

importation of an infringing product. Amgen had no basis for asserting that Roche engaged in *any* infringing activities or made any commercial CERA sales. Indeed, Amgen had no basis to assert that *any* Roche importation of CERA fell outside 35 U.S.C. § 271(e)(1)'s safe harbor for conduct relating to Roche's obtaining FDA approval for CERA. Tellingly, even before Amgen filed its Complaint with the ITC, the ITC Commission requested Amgen to provide briefing on the issue of how an ITC investigation can be maintained in view of the fact that all of the alleged infringing activities are protected under the safeguard provision of 35 U.S.C. § 271(e)(1). In that briefing, Amgen did not deny that there was no current infringement, but instead pointed to four factors supposedly demonstrating "imminent" or "incipient" infringement as a basis for relief:

- Hiring regional sales directors and regional medical liaisons;
- Allocating a marketing budget for product launch;
- Preparing potential physician customers by renting space at a trade show, providing grants to relevant associations, and sponsoring meetings for doctors;
- Completing construction and commencing operations of an overseas manufacturing plant.

Amgen Briefing Memorandum, dated April 27, 2006, at 15. Conspicuously, none of these activities constitute an actual alleged infringing use of the patented technology.

**59.** ~~48.~~ That Amgen's initiation of an ITC action based on an *actual* infringement theory was objectively baseless is confirmed by its outcome: After far-reaching discovery that, as explained below, significantly harmed Roche, the Administrative Law Judge ("ALJ") summarily rejected Amgen's Complaint. The ITC itself then rejected summarily Amgen's subsequent appeal and terminated the investigation.

**60.** ~~49.~~ *Second*, Amgen lacked any objective basis for seeking relief based on an argument for extending or changing the law. Knowing that it could not demonstrate actual importation of infringing product, Amgen argued that the ITC could award relief based on "imminent" or "incipient" non-exempt infringement. Amgen had no objective basis for seeking ITC relief based on such a theory. The ITC by statute cannot find a violation unless there is an actual infringing "importation" or commercial "sale for importation." So-called "imminence" relief cannot be granted when neither circumstance is present. Indeed, as the ALJ explained in rejecting Amgen's "imminence" argument, *no* case had *ever* awarded relief on an "imminence" theory *absent* such a commercial "sale for importation." Tellingly, Congress added "sale for importation" to the statute in 1988 in reflection of courts' granting of "incipiency" or "imminence" relief *in that circumstance* -- that is, when there is a commercial "sale for importation" of infringing product. The limitations on available relief in ITC cases is in sharp contrast to the powers of this Court, which may issue injunctive or declaratory relief in patent matters without reference to those limitations. As explained before Congress's 1988 amendment of the statute: "the Commission lacks authority to issue a declaratory judgment before the products at issue have been imported." *In re Certain Fluidized Bed Combustion Sys.*, No. 337-TA-213, ITC LEXIS 8013 (U.S.I.T.C. Mar. 21, 1985).

**61.** ~~50.~~ As Amgen, of course, had no basis for asserting that Roche had made any *commercial* CERA sales, Amgen could not legitimately seek imminence relief. Nor did Amgen have an objectively reasonable ground for seeking a change in the law based on *Certain Variable Speed Wind Turbines and Components Thereof*, No. 337-TA-376, Initial Determination, 1996 ITC LEXIS 251 (May 30, 1996), which suggested in *dicta* the possibility of extending "imminence" relief where no decision had previously extended it -- where there is no

commercial sale but the defendant had executed a contract for sales in addition maintaining a large stockpile overseas that it threatened imminently to import. *See id.* at *31. Amgen knew full-well when it brought its ITC action that Roche was in no such position. Moreover, while Congress in adding "sale for importation" to the statute in 1988 did not intend to *limit* the scope of the ITC's power, the language Congress used surely evidenced no intent to *expand* "imminence" relief beyond where it actually had been granted in the past (*e.g.*, commercial sales for importation).

**62.** ~~51.~~ The baselessness of Amgen's imminence argument is evidenced by the back-of-the-hand manner in which the ITC rejected it. The ITC Commission, in its Notice of Investigation, dated May 9, 2006, specifically refused to even consider Amgen's "imminence" argument. Rather, the ITC in its May 9, 2006, notice of investigation directed the ALJ to focus solely on Amgen's equally baseless argument of present infringing activity:

> In instituting this investigation, the Commission is mindful of the provision of 35 U.S.C. § 271(e), which states that 'it shall not be an act of infringement to make, use, offer to sell, or sell within the United States...a patented invention...solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drug...' Accordingly, the Commission directs the presiding administrative law judge to consider at an early date any motions for summary determination based upon 35 U.S.C. § 271(e).

**63.** ~~52.~~ The baselessness of Amgen's suit, and Amgen's subjective intent to harm Roche through the ITC *process* rather than any favorable *outcome* from that process, are further evidenced by the course the matter took. Roche, on May 19, 2006, filed for summary determination of no infringement based on Section 271(e)(1). In response, Amgen successfully petitioned the ALJ for broad-reaching discovery into Roche's current acts of importing CERA into the U.S. in order to oppose Roche's motion. As a result, Roche provided to Amgen within a

period of a few weeks, close to half a million pages of documents, and offered 16 deponents in three countries for more than 100 hours of testimony.

**64.** ~~53.~~ Yet when confronted with specific interrogatory requests seeking information about non-exempt acts of alleged infringement, Amgen made only conclusory statements that there were uses within the U.S. unrelated to FDA approval, and again reiterated its baseless position that hiring a sales force and soliciting potential customers warranted relief on an "incipient" infringement theory. *See* Amgen's Objections and Responses To Respondents' First Set of Interrogatories, dated May 30, 2006, at 24. When it came time to actually respond on the merits to Roche's motion for summary determination, Amgen could only point to two alleged instances of non-exempt use: (1) a University of Iowa Pharmacokinetic Study; and (2) future Phase IIIb studies which were to be submitted to the FDA. These allegations were particularly suspect in view of the fact that the discovery record showed that both these studies were intended for submission to the FDA and therefore exempt under Section 271(e)(1).

**65.** ~~54.~~ The ITC Commission Staff accordingly supported Roche's Motion for Summary Determination of No Infringement and opposed Amgen's position of current and incipient infringement. The ITC Commission Staff found that (1) Roche "satisfied their summary determination burden and h[ad] made out a *prima facie* case that the imported CERA was solely for uses reasonably related to the FDA approval process and thus within the Section 271(e)(1) safe harbor;" and (2) the Staff was "not aware of any contrary information and Amgen must do more than rely on only attorney argument and speculation that there may be other undisclosed importations or uses of CERA." Commission Investigative Staff's Response to Respondents' Motion for Summary Determination of No Violation of Section 337, dated June

26, 2006, at 7-8. The ITC Commission Staff also outright rejected Amgen's theory of incipient infringement based on the *Wind Turbines* case. The Staff stated in relevant part:

> As it did in its motion to compel, Amgen is also expected to argue that infringement is "imminent"...The Staff does not expect, however, that Amgen will be able to identify any accused product currently in the United States targeted for these imminent infringing uses. Amgen relies on the Commission's opinion in [*Wind Turbines*] for the proposition that the Commission may consider incipient infringement. However, as set forth in the Staff's response to the parties' motions regarding the scope of discovery, *Wind Turbines* does not mandate a consideration of incipient infringement (potential future importation outside the Section 271(e) exemption) with respect to the pending motion. Respondents' early motion for summary determination on the Section 271(e) issue was clearly contemplated by the Commission, as evidenced by the specific direction to the Judge in the Notice of Investigation...As set forth above, Respondents have shown that do date there have been no non-exempt imports and hence no violation of Section 337. Amgen is not expected to successfully counter this showing. The pending motion should not be denied based on speculation concerning future uses of the accused product that may fall outside the Section 271(e) safe harbor. This course of conduct would needlessly waste the resources of the parties and the Commission.

*Id.* at 9 (emphasis added).

**66.** ~~55.~~ As expected, the ALJ agreed with Roche and the ITC Commission Staff and granted Roche's Motion for Summary Determination. Specifically, the ALJ "reject[ed] [Amgen's] contention that the issue before [him] is whether 'importation for a non-exempt use is imminent." Order No. 6, Initial Determination, dated July 7, 2006. Instead, the ALJ reviewed the comprehensive record and determined that all of Roche's uses of CERA fell within the safe harbor provision of Section 271(e)(1). With respect to the two alleged non-exempt uses identified by Amgen, the University of Iowa Study and the Phase IIIb studies, the ALJ categorically ruled that these activities were reasonably related to FDA approval, and therefore

protected by the safe harbor. *Id.* at 16-17. Finally, the ALJ rejected Amgen's incipiency argument as a matter of law:

> Hence, in Wind Turbines there was a contract for commercial sale of the accused product to a customer in the United States which associated to a "sale for importation" within the meaning of section 337. The administrative law judge finds no evidence put forth by [Amgen] which establishes that there exists a contract entered into by [Roche] for commercial sale of CERA to a customer in the United States. Thus, the administrative law judge rejects [Amgen's] contention that these are the "exact circumstances here" as was in Wind Turbines.

*Id.* at 20.

**67.** ~~56.~~ On August 31, 2006, the ITC Commission adopted the ALJ's Initial Determination and terminated the investigation.

**68.** ~~57.~~ Amgen's sole purpose of bringing the baseless ITC action was to increase Roche's costs and delay CERA's entry, regardless of the suit's outcome. Amgen succeeded in its anticompetitive objective. Amgen's sham ITC action caused substantial anticompetitive effects by raising already high barriers to entry in the relevant markets, hindering and imposing costs on a new entrant, and interfering with that entrant's FDA approval process and customers.

**69.** ~~58.~~ Amgen's sham ITC litigation raised already high entry barriers by imposing substantial litigation costs on Roche, the only firm today poised to challenge Amgen's ESA dominance of the relevant markets. Amgen's imposing of substantial defense costs also caused anticompetitive effects by imposing unnecessary costs on a new entrant into the relevant monopolized and near-monopolized ESA markets, thereby hindering that entry and harming competition and consumers.

**70.** ~~59.~~ Amgen also harmed Roche and competition by using the baseless ITC action to interfere with Roche's clinical trials. Amgen employed third-party subpoenas and other litigation tactics in the ITC case in an effort to intimidate potential clinical investigators and hinder Roche's efforts to obtain FDA approval. Amgen served subpoenas on at least the following dialysis center customers or potential customers of Roche: Dialysis Purchasing Alliance; Fresenius Medical Care; Gambro Inc., and Davita Inc.

**71.** ~~60.~~ Amgen's scorched-earth tactics in its baseless ITC action also harmed Roche and competition by distracting key Roche employees from company business, including business related to the FDA approval and launch of CERA. These included the depositions of Dr. Buch, Dr. Char, Ms. Conte, Dr. Dinella, Mr. Englesbe, Dr. Farid. Dr. Franzino, Dr. Joseph, Dr. Kingma-Johnson, Mr. Knickmeier, Mr. Kokino, Dr. Marcopulos, Dr. Much, Dr. Schorle, Dr. Shah. and Dr. Van Der Auwera -- Roche employees with duties relating to CERA's FDA approval efforts, CERA clinical trials, or otherwise involved in planning CERA's launch.

2. *Amgen's Sham Litigation Before This Court*

**72.** ~~61.~~ Amgen's sham litigation practices extend to the current case before this Court. Amgen's assertion of baseless patent claims in this action is both itself independently unlawful and highlights Amgen's subjective intent to harm Roche regardless of outcome in the ITC case.

**73.** ~~62.~~ Amgen has asserted at least the following claims of U.S. Patent No. 5,621,080 ("the '080 patent ") against Roche's CERA, even though Amgen knows that its allegations are objectively baseless.

> 3. A non-naturally occurring erythropoietin glycoprotein having the in vivo biological activity of causing bone marrow cells to increase production of reticulocytes and red blood cells, wherein

> said erythropoietin glycoprotein comprises the mature erythropoietin amino acid sequence of FIG. ~~6.~~
>
> **6.**
>
> 4. A pharmaceutical composition comprising a therapeutically effective amount an erythropoietin glycoprotein product according to claim 1, 2 or 3.
>
> ~~6.~~
>
> **6.** A method for treating a kidney dialysis patient which comprises administering a pharmaceutical composition of claim 4 in an amount effective to increase the hematocrit level of said patient.

**74.** ~~63.~~ Each of these claims require that the erythropoietin glycoprotein comprises the 166 amino acid sequence of Figure 6 of the patent specification. However, the Federal Circuit in *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1308 (Fed. Cir. 2006), held that a glycoprotein comprising the mature 165 amino acid sequence could not infringe these claims either literally or by the doctrine of equivalents. With respect to the doctrine of equivalents, the Federal Circuit determined that Amgen surrendered any claims to the mature 165 mature amino acid sequence during the prosecution of the '080 patent, and, as a result, was barred from claiming this equivalence based upon the prosecution history estoppel doctrine enunciated by *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 344 F.3d 1359, 1372 (Fed. Cir. 2003). The Court reasoned:

> In sum, we uphold the district court's finding that the 165-amino acid EPO equivalent was foreseeable at the time of the third preliminary amendment. The district court erred, however, in finding that Amgen successfully rebutted the *Festo* presumption of surrender of equivalents under both the tangentially related rebuttal argument and the "some other reason" rebuttal argument. This means that HMR/TKT cannot be found to have infringed the claims 2-4 of the '080 patent under the doctrine of equivalents. Accordingly, the judgment of infringement of claims 2-4 is reversed.

*Hoechst*, 457 F.3d. at 1316.

**75.** ~~64.~~ Amgen's claims that Roche infringes the '080 patent in this case, however, presuppose that Roche's CERA "contains" the mature 165 amino acid sequence of EPO. Specifically, Amgen has maintained these claims despite the fact that Roche's BLA for CERA, which Amgen has had access to since June 2006, discloses that the EPO starting material consists of 165 amino acids. ITC-R-BLA-00004029. This, of course, is the very theory that the Federal Circuit told Amgen that it could not maintain, and demonstrates that Amgen's claim of infringement of the '080 patent is objectively baseless. The Federal Circuit has already determined that the '080 patent cannot be infringed by a 165 amino acid protein, either literally or by the doctrine of equivalents.

**76.** ~~65.~~ Amgen has also asserted claim 9 of the '933 patent against Roche in the current suit, even though this Court, and the Federal Circuit on at least two occasions, stated that this claim was invalid for lack of definiteness. This Court in *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 126 F.Supp.2d 69, 165 (D. Mass. 2001) held that:

> For the reasons set forth above, the Court declares:
> Claims 1, 2, and 9 of the '933 patent are not infringed, and, if this finding is error, those claims are invalid for lack of an adequate written description, indefiniteness, and lack of enablement.

*Id.* The Federal Circuit on appeal affirmed this Court's decision of lack of definiteness of claims 1,2, 9 of the '933 patent. *See Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1342 (Fed. Cir. 2003) ("Applying these legal maxims to the facts of this case, we agree with the district court that the claims requiring "glycosylation which differs" are invalid for indefiniteness."). Moreover, as recently as August 2006, the Federal Circuit once again reiterated its position that claims 1,2, 9 of the '933 patent were invalid for lack of definiteness. *See Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, n.5 (Fed. Cir. 2006) ("As noted

above, in *Amgen II*, we affirmed the ruling of the district court in *Amgen I* that claims 1, 2, and 9 of the '933 patent are invalid. *Amgen II*, 314 F.3d at 1342.”). Nevertheless, Amgen continues to assert claim 9, *which was invalidated by the Federal Circuit as early as 2003*, against Roche in this case.

**77.** ~~66.~~ Accordingly, Roche expected at the very least that, following the Federal Circuit’s August 2006 decision in the *Hoechst Marion Roussel* case, that Amgen would withdraw its claims of infringement of the ‘080 patent and claim 9 of the ‘933 patent . But demonstrating Amgen’s subjective intent to harm Roche through the litigation process rather than any expected favorable outcome, Amgen has *maintained* its ‘080 infringement claims and claim 9 of the ‘933 patent, and, astoundingly, continues to *press* them. In so doing, Amgen has demonstrated both that it had and continues to have no basis for bringing those claims and revealed that it’s sole objective in maintaining those claims is to harass Roche and raise its costs. Without explaining *how* Roche could infringe the ‘080 patent given Amgen’s contention that CERA contains a mature 165 amino acid sequence, Amgen has asserted that the Federal Circuit decision is not final and that it wants discovery to determine the matter (Plaintiff’s Response to First Set of Interrogatories, dated January 9, 2007, at 4). Amgen also could not explain how claim 9 of the ‘933 patent, which was invalidated by the Federal Circuit, could still be asserted in this case.

**78.** ~~67.~~ The only reason Amgen is pressing the ‘080 claims and claim 9 of the ‘933 patent, therefore, is to raise Roche’s already high costs of entering with CERA by running up Roche’s litigation bill and potentially delaying CERA’s launch through baseless proceedings. The effect of Amgen’s sham infringement claims based on the ‘080 and ‘933 patents is to harm Roche, competition, and consumers by raising already high entry barriers in the relevant ESA

markets and shackling a new entrant, Roche, that might reduce Amgen's monopoly and near-monopoly power, with higher litigation costs from defending three baseless claims, discovery-related burdens, and other anticompetitive obstacles to its eventual entry.

**B. Attempted Enforcement of Fraudulently Obtained Patents**

**79.** ~~68.~~ Amgen not only engaged in sham litigation before the ITC, but also persists in doing so before this Court. Counterclaim-Defendant Amgen asserts that it is the assignee and owner of record of the '698, '868, '349, '933, '080, and '422 patents. As alleged above with particularity in Paragraphs 38-~~53~~**55, 76-126, 132-172 and 193-196** of Roche's Answer above, these patents were obtained through knowing and willful fraud on the PTO by Amgen and/or its agents, and are invalid and unenforceable. The present patent infringement suit to enforce these patents against Roche was brought by Amgen with knowledge that these patents were obtained by fraud on the PTO and/or not infringed, and with the intent to injure Roche, and impair competition, by delaying or preventing Roche's entry with CERA.

**C. Interference With, and Locking Up of, Customers**

**80.** ~~69.~~ Anticipating FDA approval for CERA, Roche has begun to develop relationships with potential customers for its CERA product through its clinical trials and through other means.

**81.** ~~70.~~ As the dominant seller of ESA products, Amgen knows the identity of Roche's potential customers for CERA.

**82.** ~~71.~~ On information and belief, Amgen has engaged in a pattern of threats and intimidation designed to deny Roche customers for CERA and to foreclose CERA from the ESRD ESA and CKD ESA markets**, and the alternative All ESA market**. Amgen has intentionally and maliciously interfered with potential business relationships of Roche and has

damaged Roche's prospective business relationships by causing ESA providers to not consider entering business relationships with Roche.

**83.** ~~72.~~ On information and belief, Amgen has offered potential customers research grants and other financial incentives solely for the purpose of intentionally and maliciously interfering with potential business relationships of Roche and has damaged Roche's prospective business relationships by causing ESA providers to not consider entering business relationships with Roche.

**84.** ~~73.~~ On information and belief, Amgen has also threatened numerous ESA customers that, if they order CERA, Amgen may raise the price of, or refuse to sell them, Amgen ESA products, or just as importantly deny those customers discounts on those products that otherwise would be made available, if Amgen prevails in its patent infringement claims against Roche. A provider's inability to receive rebates and/or favorable pricing on the purchase of ESA drugs will likely have severe, detrimental economic consequences. A reduced discount means a higher effective price, and thus fewer funds available to cover ever-increasing provider expenses. The loss of discounts, or the threatened withholding of discounts, is accordingly a credible threat to many ESA customers.

**85.** ~~74.~~ On information and belief, Amgen has also entered long-term sole source and supply agreements with key ESA customers to foreclose those customers from contracting with Roche for CERA. Prior to the threat posed by CERA's entry, Amgen had no need for exclusive dealing arrangements. Amgen recently entered into one or more long-term sole sourcing arrangements solely to block CERA from obtaining economies of scale critical to eroding Amgen's ESA dominance.

**86.** ~~75.~~ On information and belief, Amgen has also engaged in anticompetitive contracting with hospital purchasers in the ESA markets. These contracts conditioned discounts on Amgen's blockbuster oncology medications, Neulasta® and Neupogen®, on the hospitals' purchases of Amgen's ESA drugs. The importance of obtaining discounts on Amgen's monopoly oncology medications leaves hospitals with little choice but to take Amgen's ESA drugs across indications, including for CKD and ESRD, thereby (i) impeding competition on the merits in the ~~CKD ESA and ESRD CKD~~**relevant** markets for those hospitals' ESA requirements and (ii) making successful entry into those markets for entrants, and effective competition by incumbents, more difficult.

### D. Amgen's Anticompetitive Purpose and Lack of Legitimate Business Justification

**87.** ~~76.~~ Amgen has engaged in the above-described conduct with the specific intent to maintain or obtain monopoly power in the ~~ESRD ESA and CKD~~**relevant** ESA markets, with the specific purpose to hinder Roche's ability to enter those markets successfully with CERA, and without any legitimate business purpose or justifiable cause.

## ~~VI~~VII. HARM TO PATIENTS, CUSTOMERS, ROCHE AND COMPETITION

**88.** ~~77.~~ As Amgen has anticipated and intended, its actions have caused, and absent action by this Court will continue to cause, substantial anticompetitive effects.

**89.** ~~78.~~ Amgen's sham litigation and attempted enforcement in this Court of patents obtained through fraud on the PTO harm competition in the relevant ESA markets by improperly raising already high barriers to entry into those markets and anticompetitively imposing higher costs on a new entrant, Roche.

**90.** ~~79.~~ Amgen's denial to Roche of CERA customers through long-term exclusive dealing arrangements, payments, anticompetitive contracting practices, and outright

threats unreasonably restrains trade and harms competition, and threatens to continue to do so, in the ~~ESRD ESA and CKD ESA~~**relevant** markets. Amgen's tactics threaten either to block Roche's entry with CERA or to make that entry less robust than it otherwise would be.

**91.** ~~80.~~ Roche has no effective means to counteract Amgen's anticompetitive conduct aimed at denying Roche important customers. One of two LDOs that together control 70% of the purchases in the ESRD ESA market is foreclosed from Roche through a newly minted long-term exclusive dealing arrangement. In addition, while Roche is confident that it will prevail against Amgen's baseless infringement claims, it is unlikely to convince vulnerable dialysis center customers, whose patients must have access to ESAs to treat their anemia and who depend on product discounting in order to remain in business caring for such patients, to adopt CERA and take the risk that Amgen will punish them and their patients by making discounts or ESA products unavailable to them in the unlikely event that Amgen's patent case blocks CERA. The smaller potential customer base greatly reduces the chance that Roche can obtain the economies it needs to make CERA a serious alternative to Amgen's dominance.

**92.** ~~81.~~ Amgen's anticompetitive, strong-arm tactics with customers, its sham litigation before the ITC and this Court, and its knowing attempt to enforce in this Court patents obtained through fraud on the PTO threaten to maintain Amgen's monopoly over the ESRD ESA market **(as well as in the alternative All ESA market)**, and to help Amgen achieve monopoly power in the CKD ESA market. At the very least, Amgen's conduct will hinder the introduction of additional competition into the highly concentrated CKD and ESRD ESA**, and alternative All ESA,** markets. Amgen's course of conduct also amounts to a misuse of its patents.

**93.** ~~82.~~ Amgen's conduct has harmed, and will continue to harm, not only Roche and competition, but also ESRD and CKD patients and those who pay for their treatment. Amgen's anticompetitive raising of Roche's costs of entering with CERA threatens insurers, patients, and immediate purchasers of drugs with higher prices. Amgen's anticompetitive course of conduct, moreover, threatens to delay, hinder, or outright block the successful entry of an alternative ESA drug, CERA, that offers patients and doctors the first real choice of an alternative, and potentially better, ESA. Consumers also will suffer higher prices than otherwise may well be available if Roche can enter the ESA market unsaddled by anticompetitively increased costs and hindered access to customers. Amgen's anticompetitive conduct also threatens to burden American taxpayers with higher government Medicare and Medicaid expenses as the lack of competition enables Amgen to keep ESA prices artificially high.

## COUNT I

**(Monopolization And Attempted Monopolization (15 U.S.C. § 2))**
**(Walker Process Antitrust Claim — ESRD ~~ESA~~, CKD and ~~CKD~~All ESA Markets)**

**94.** ~~83.~~ The allegations of paragraphs 1 through ~~82~~93 are incorporated in this count as if fully set forth herein.

**95.** ~~84.~~ As detailed with particularity in ~~paragraphs 38-53~~**Paragraphs 38-55, 76-126, 132-172 and 193-196** of Roche's Answer above, among other paragraphs of Roche's Answer and Counterclaims, the patents-in-suit are unenforceable because individuals associated with the filing and prosecution of these patents acting as agents and/or with knowledge of plaintiff Amgen intentionally and willfully misled the PTO by misrepresenting and omitting material information, which, if known by the PTO, would have resulted in the PTO not allowing these patents. In particular, Amgen knowingly misled the PTO ~~to overcome a double patenting objection that~~**as described in paragraphs 38-55, 76-126, 132-172 and 193-196 of Roche's**

**Answer above, but for which the PTO** would have ~~led the PTO to deny~~**denied** each of the six patents-in -suit in this action.

**96.** ~~85.~~ As alleged in ~~paragraphs 38-53~~**Paragraphs 38-55, 76-126, 132-172 and 193-196** of Roche's answer above, in issuing each of the six patents-in-suit, the PTO justifiably relied on the misrepresentations **and omissions** that Amgen made before it, and on the assumption that Amgen had acted in accordance with its duty of candor in bringing to the attention of the PTO any information material to the prosecution of the six patents-in-suit.

**97.** ~~86.~~ Knowing that the patents-in-suit were obtained by fraud and the commission of inequitable conduct before the PTO, Amgen nonetheless commenced the present action for infringement of the patents-in-suit against Roche.

**98.** ~~87.~~ Amgen has (i) publicized the litigation to potential CERA purchasers; and (ii) engaged in a campaign to threaten and intimidate potential customers of Roche by (a) informing them of this litigation and asserting to them that Roche's activities and ESA product infringe the patents-in-suit, or (b) threatening such customers with suit for contributory patent infringement, all while knowing that these patents were obtained by fraud and are, invalid, unenforceable and not infringed.

**99.** ~~88.~~ Such conduct constitutes a knowing, willful and intentional attempt to enforce patents procured by fraud and to improperly maintain and/or obtain monopoly power (which the conduct dangerously threatens) in the ~~ESRD ESA and CKD~~**relevant** ESA markets in violation of Section 2 of the Sherman Act, 15 U.S.C. § 2.

**100.** ~~89.~~ Amgen has acted with specific intent to unlawfully monopolize the relevant markets, as evidenced by the anticompetitive conduct alleged herein, and without legitimate business justification.

**101.** ~~90.~~ As a direct and proximate result of the foregoing, competition in the relevant markets has been, and will continue to be, injured to the detriment of consumers who will be subject to reduced choice, retarded quality in terms of product attributes, and likely higher prices.

**102.** ~~91.~~ As a direct and proximate result of the foregoing, Roche has been injured in its business and property, and is threatened with additional losses from Amgen's conduct.

## COUNT II

## OMITTED

**103.** ~~92.~~ OMITTED

**104.** ~~93.~~ OMITTED

**105.** ~~94.~~ OMITTED

**106.** ~~95.~~ OMITTED

**107.** ~~96.~~ OMITTED

**108.** ~~97.~~ OMITTED

**109.** ~~98.~~ OMITTED

## Count III

**(Monopolization of ESRD ESA ~~Market~~and All ESA Markets (15 U.S.C. § 2))**

**110.** ~~99.~~ The allegations of paragraphs 1 through ~~98~~109 are incorporated in this count as if fully set forth herein.

**111.** ~~100.~~ Amgen has monopoly power in the market for ESAs sold for ESRD in the United States. Amgen long has possessed 100% of the market, which is protected by high entry barriers. **Alternatively, Amgen possesses 70% of the alternative all ESA market, which too is protected by high barriers to entry that confer upon Amgen monopoly power.**

**112.** ~~101.~~ Amgen's conduct alleged herein amounts to willful acquisition and/or maintenance of monopoly power in the relevant market in violation of Section 2 of the Sherman Act, 15 U.S.C. § 2. Amgen's conduct is anticompetitive and lacks any legitimate business justification.

**113.** ~~102.~~ As a direct and proximate result of the foregoing, competition in the relevant ~~market~~**markets** has been and will continue to be injured, to the detriment of consumers who will be subject to reduced choice, retarded quality in terms of product attributes, and likely higher prices.

**114.** ~~103.~~ As a direct and proximate result of the foregoing, Roche has been injured in its business and property, and is threatened with additional losses from Amgen's conduct designed to foreclose and exclude Roche from the relevant ~~market~~**markets**.

## COUNT IV

**(Attempted Monopolization of CKD ESA ~~Market~~and All ESA Markets (15 U.S.C. § 2))**

**115.** ~~104.~~ The allegations of paragraphs 1 through ~~103~~**114** are incorporated in this count as if fully set forth herein.

**116.** ~~105.~~ Amgen has the specific intent to monopolize the **CKD ESA (non-ESRD)** market ~~for~~**and** the ~~sale of ESA Drugs sold for CKD in the United States~~**alternative All ESA market**. Amgen's anticompetitive conduct, as alleged herein, has been undertaken to achieve, maintain, and extend monopoly power and lacks any legitimate business justification. Amgen has a dangerous probability of achieving monopoly power in the ~~market~~**relevant markets**, which is protected by high entry barriers, to the extent it does not already possess monopoly power in the relevant ~~market~~**markets**.

**117.** ~~106.~~ Amgen's conduct alleged herein constitutes the unlawful attempt to monopolize the relevant ~~market~~**markets** in violation of Section 2 of the Sherman Act, 15 U.S.C. § 2.

**118.** ~~107.~~ As a direct and proximate result of the foregoing, competition in the relevant ~~market~~**markets** has been and will continue to be injured, to the detriment of consumers who will be subject to reduced choice, retarded quality in terms of product attributes, and likely higher prices.

**119.** ~~108.~~ As a direct and proximate result of the foregoing, Roche has been injured in its business and property, and is threatened with additional losses from Amgen's conduct designed to foreclose and exclude Roche from the relevant market.

## COUNT V

**(Unreasonable Restraints of Trade in the ESRD ESA ~~and~~, CKD ESA and All ESA Markets (15 U.S.C. § 1))**

**120.** ~~109.~~ The allegations of paragraphs 1 through ~~108~~119 are incorporated in this count as if fully set forth herein.

**121.** ~~110.~~ Amgen, as alleged herein, has entered into one or more contracts, combinations, or conspiracies with third parties that are in and/or affect interstate commerce among the several States.

**122.** ~~111.~~ The effect of Amgen's agreement(s) are, and will be, to restrain trade, cause anticompetitive effects, and expand and reinforce Amgen's market power in the relevant markets alleged herein. Amgen's agreement(s) lack any legitimate business justification. Accordingly, Amgen's agreement(s) comprise unreasonable restraints of trade in violation of Section 1 of the Sherman Act, 15 U.S.C. § 1.

**123.** ~~112.~~ As a direct and proximate result of the foregoing, competition in the relevant market has been and will continue to be injured, to the detriment of consumers who will be subject to reduced choice, retarded quality in terms of product attributes, and likely higher prices.

**124.** ~~113.~~ As a direct and proximate result of the foregoing, Roche has been injured in its business and property, and is threatened with additional losses from Amgen's conduct designed to foreclose and exclude Roche from the relevant market.

## COUNT VI

**(Tortious Interference With Prospective Business Relationships)**

**125.** ~~114.~~ The allegations of paragraphs 1 through ~~113~~**124** are incorporated in this count as if fully set forth herein.

**126.** ~~115.~~ Roche had prospective advantageous business relationships with third parties, including but not limited to distributors, customers, and LDOs.

**127.** ~~116.~~ Amgen had knowledge of Roche's prospective business relations as set forth above.

**128.** ~~117.~~ Amgen knowingly interfered with Roche's business relations as set forth above.

**129.** ~~118.~~ Amgen's interference with Roche's prospective business relations was improper in motive and means. Upon information and belief, Amgen has purposefully engaged in such conduct to improperly and unjustifiably interfere with Roche's relationships as set forth above and damage its business relationships and goodwill.

**130.** ~~119.~~ The acts and conduct of Amgen complained of herein constitute the tort of intentional interference with prospective business relations.

**131.** ~~120.~~ As a result of Amgen's intentional interference with Roche's potential business relations, Roche has suffered monetary damages in an amount yet to be determined.

## COUNT VII

**(Discouraging Competition In Violation Of California's Cartwright Act)**

**132.** ~~121.~~ The allegations of paragraphs 1 through ~~120~~**131** are incorporated in this count as if fully set forth herein.

**133.** ~~122.~~ Amgen's anticompetitive activities described above constitute violations of California's Cartwright Act, Cal. Bus. & Prof. Code § 1670 *et seq.*

**134.** ~~123.~~ As a direct and proximate result of the foregoing, Roche has been injured in its business and property.

## COUNT VIII

**(Discouraging Competition In Violation Of The New Jersey Antitrust Act)**

**135.** ~~124.~~ The allegations of paragraphs 1 through ~~123~~**134** are incorporated in this count as if fully set forth herein.

**136.** ~~125.~~ Amgen's attempted monopolization and anticompetitive activities constitute violations of N.J.S.A. §§ 56:9-3 and 56:9-4 of the New Jersey Antitrust Act.

**137.** ~~126.~~ As a direct and proximate result of the foregoing, Roche has been injured in its business and property, and is threatened with additional losses from Amgen's conduct designed to foreclose and exclude Roche from the relevant market.

## COUNT IX

**(Unfair and Deceptive Business Practices in Violation of the Massachusetts Consumer and Business Protection Act, Mass. Gen. Laws ch. 93A)**

**138.** ~~127.~~ The allegations of paragraphs 1 through ~~126~~**137** are incorporated in this count as if fully set forth herein.

**139.** ~~128.~~ Amgen is engaged in trade or commerce within the meaning of Mass. Gen. Laws ch. 93A.

**140.** ~~129.~~ Roche is engaged in trade or commerce within the meaning of Mass. Gen. Laws ch. 93A.

**141.** ~~130.~~ The conduct of Amgen, as set forth above, constitutes unfair or deceptive acts or practices.

**142.** ~~131.~~ The conduct of Amgen, as described above, was knowing and willful.

**143.** ~~132.~~ Roche has been damaged in an amount to be determined at trial by Amgen's unfair and deceptive business practices.

## COUNT X

**(Declaratory Judgment of Patent Invalidity)**

**144.** ~~133.~~ The allegations of paragraphs 1 through ~~132~~**143** are incorporated in this count as if fully set forth herein.

**145.** ~~134.~~ On August 15, 1995, August 20, 1996, April 8, 1997, April 15, 1997, May 26, 1998, and September 21, 1999, the PTO issued to Amgen the '868, '933, '698, '080, '349, and '422 patents respectively, upon one or more applications filed in the name of Fu-Kuen Lin.

**146.** ~~135.~~ There is an actual and justiciable controversy within the meaning of 28 U.S.C. §§ 2201 and 2202 between Roche and Counterclaim-Defendant Amgen with respect to the validity of the '868, '933, '698, '080, '349, and '422 patents.

**147.** ~~136.~~ The '868, '933, '698, '080, '349, and '422 patents are invalid because they fail to satisfy the conditions for patentability specified in 35 U.S.C. §§ 101, 102, 103, 112, 116 and 282, and because of obviousness-type double patenting.

## COUNT XI

**(Declaratory Judgment of Non-Infringement)**

**148.** ~~137.~~ The allegations of paragraphs 1 through ~~136~~**147** are incorporated in this count as if fully set forth herein.

**149.** ~~138.~~ There is an actual and justiciable controversy within the meaning of 28 U.S.C. §§ 2201 and 2202 between Roche and Counterclaim-Defendant Amgen with respect to the infringement of the '868, '933, '698, '080, '349, and '422 patents.

**150.** ~~139.~~ Roche has not infringed and is not infringing any claim of the '868, '933, '698, '080, '349, and '422 patents. Moreover, the activities alleged in the Complaint do not constitute infringement under 35 U.S.C. § 271(e)(1).

## COUNT XII

**(Declaratory Judgment of Unenforceability)**

**151.** ~~140.~~ The allegations of paragraphs 1 through ~~139~~**150** are incorporated in this count as if fully set forth herein.

**152.** ~~141.~~ There is an actual and justiciable controversy within the meaning of 28 U.S.C. §§ 2201 and 2202 between Roche and Counterclaim-Defendant Amgen with respect to the unenforceability of the '868, '933, '698, '080, '349, and '422 patents.

**153.** ~~142.~~ The patents-in-suit are unenforceable because of all the foregoing allegations including that individuals associated with the filing and prosecution of these patents acting as agents and/or with knowledge of plaintiff Amgen misrepresented **and failed to disclose** material facts with the intent to deceive the PTO ~~for purposes~~**, as detailed with particularity in Paragraphs 38-196** of ~~overcoming a double patenting rejection based on Amgen~~**Roche**'s ~~earlier filed and issued '008 patent~~**Answer above**.

~~143. Among Amgen's inequitable acts, are that the '933 and '080 patents are unenforceable because individuals associated with the filing and prosecution of these patents acting as agents and/or with knowledge of the plaintiff Amgen misrepresented and failed to disclose material inconsistencies regarding alleged differences between r-EPO, which Amgen received patent claims on, and u-EPO, which was in the prior art.~~

**154.** ~~144.~~ Wholly apart from Amgen's fraud on the PTO, the patents-in-suit are unenforceable because Amgen misused those patents in initiating sham litigation before the ITC and because Amgen misused those patents by engaging in an anticompetitive scheme to coerce or otherwise induce ESA customers to forgo CERA.

## PRAYER FOR RELIEF

WHEREFORE, Roche prays for judgment in its favor and against Plaintiff Amgen as follows:

A. Dismissal of Amgen's Complaint with prejudice, and denial of each and every prayer for relief contained therein;

B. A judgment declaring that Amgen's conduct as alleged herein is unlawful;

C. A judgment awarding to Counterclaim-Plaintiff Roche the damages it has sustained as a result of the illegal conduct of Amgen, in an amount to be proven at trial, to be trebled by law, plus interest (including pre-judgment interest), attorneys' fees and costs of suit;

D. A judgment declaring that the ’868, ’933, ’698, ’080, ’349, and ’422 patents are invalid;

E. A judgment declaring that Roche has not infringed and is not infringing the ’868, ’933, ’698, ’080, ’349, and ’422 patents in violation of 35 U.S.C. § 271;

F. A judgment declaring that the ’868, ’933, ’698, ’080, ’349, and ’422 patents were obtained by knowing and willful fraud on the PTO and are unenforceable;

G. A judgment declaring that this is an exceptional case, pursuant to 35 U.S.C. § 285, and awarding Roche its reasonable attorneys’ fees;

H. Awarding Roche all costs, interest (including prejudgment and postjudgment interest), etc. as to which it is legally entitled; and

I. Granting such other and further relief as the Court deems just and proper.

**DEMAND FOR JURY TRIAL**

Roche demands a trial by jury on all issues so triable.

Dated: ~~March 30,~~ **May 23, July 5,** 2007
Boston, Massachusetts

Respectfully submitted,

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

*By their Attorneys*,

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**CERTIFICATE OF SERVICE**

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/s/ Alfred H. Heckel
Alfred H. Heckel

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