EXHIBIT A

TO AMGEN'S REPLY IN SUPP. OF ITS MOT. TO STRIKE

42. The patents-in-suit are unenforceable because individuals **— [*must identify "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, **— [*must delete open-ended language*]** 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 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

> 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 ***— [must identify "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

[1] In addition, Amgen also failed to disclose inconsistent arguments ***— [must identify "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).

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 ***— [must identify "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 deem the later claim to be merely an obvious variation on the earlier one.

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

to the '080 and '933 patents, while the '179 line ultimately led to the '868, '698, '422 and '349 patents.

55. As exemplified below ***[described in ¶¶ ___]***, on numerous ***— [must delete open-ended language]*** occasions during the prosecution of these co-pending lines of applications, the examiner in one line of co-pending applications issued rejections ***— [must identify "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 ***— [must identify "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*.

56. Here, the patents-in-suit are unenforceable because individuals ***— [must identify "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 ***— [must identify "positions"]*** inconsistent with highly material arguments ***— [must identify "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 ***— [must identify "rejections"]***.

57. Amgen's intent to deceive the patent office is further evidenced by the fact that at least ***— [must delete open-ended language]*** Amgen attorneys Steven Odre and Michael Borun were both involved throughout the prosecution of the '1 78 and '179 lines of applications,

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

70. Amgen's failure to disclose relevant rejections **— [*must identify "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).

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 **— [*must identify "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

72. Amgen's pattern of intentionally withholding material information from the examiners is further evidenced by its failure conversely to disclose rejections **— [*must identify "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, 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.

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 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 REGARDING ALLEGED DIFFERENCES BETWEEN R-EPO AND U-EPO

Contradictory Statements of Amgen's Scientist

74. Amgen, and those acting on its behalf **— [*must identify "those acting on its behalf"*]** who were substantively involved in the prosecution of the patents-in-suit, 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, **[*described below in ¶¶ ___*]** thereby tainting all patents sharing the common specification. Accordingly, the patents-in-suit should be held unenforceable for inequitable conduct before the PTO.

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.

76. Amgen and its representatives, **— [*must identify "representatives"*]** in the course of foreign patent proceedings and before the FDA, relied on statements and information **— [*must identify "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.

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 **— [*must identify "positions"*]** that Amgen took in arguing patentability of its then pending EPO claims to the PTO.

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, 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).

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.

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.

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 **— [*must delete open-ended language*]** by the direct involvement of Amgen attorneys Steven Odre and Stuart Watt in those proceedings,

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

84. In addition to the contradictory statements made by Amgen in the 1992 and 1994 Strickland declarations, Amgen and its employees, **— [*must identify “employees”*]** including even **— [*must delete open-ended language*]** the named inventor of the Amgen EPO Patents, have made numerous statements, **— [*must identify “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).

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.

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.

87. Additional internal documents **— [*must identify "additional internal documents"*]** from Dr. Egrie provide evidence regarding glycosylation inconsistent with the positions **— [*must identify "the positions"*]** that Amgen took during prosecution of its patents. (*See* AM-ITC 00828987-88) **— [*must delete open-ended language*]**. This information was never disclosed to the examiner.

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 **— [*must identify "statements to the FDA"*]** that directly contradict the positions **— [*must identify "the positions"*]** Amgen took in arguing patentability