UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, vs. F. HOFFMANN-LA ROCHE LTD; ROCHE DIAGNOSTICS GmbH; and HOFFMANN-LA ROCHE INC. Defendants.	CIVIL ACTION No.: 05-CV-12237WGY

STATEMENT OF UNDISPUTED MATERIAL FACTS IN SUPPORT OF DEFENDANTS' MOTION FOR SUMMARY JUDGMENT THAT THE CLAIMS OF PATENTS-IN-SUIT ARE INVALID FOR DOUBLE PATENTING OVER AMGEN '016 PATENT

Defendants F. Hoffmann-La Roche Ltd., Roche Diagnostics GmbH and Hoffmann-La Roche, Inc. (collectively "Roche") submit the following statement of undisputed material facts, pursuant to Local Rule 56.1, in support of their motion for summary judgment that the claims of the patents-in-suit are invalid for double patenting over Amgen's U.S. Patent No. 4,667,016 ("the '016 patent").

The statements of fact set forth herein shall be referred to in Roche's accompanying memorandum by the paragraph number of each fact below. The evidence of record in support of each fact is the Declaration of Dr. Edward Everett Harlow, Jr. ("Harlow Decl."), the Declaration of Michael Sofocleous ("Sofocleous Decl."), and the exhibits attached to the Declaration of Kimberly J. Seluga ("Seluga Decl.").

1. The claims-in-suit include claims 1 and 2 of U.S. Patent No. 5,441,868 ("the '868 patent"), 4-9 of U.S. Patent No. 5,618,698 ("the '698 patent"), 7 of U.S. Patent No. 5,756,349

("the '349 patent"), 1 of U.S. Patent No. 5,955,422 ("the '422 patent"), and 3, 7, 8, 9, 11, 12 and 14 of U.S. Patent No. 5,547,933 ("the '933 patent"), all owned by Amgen. Seluga Decl., Exs. A, B, C, D and E.

2. Prior to obtaining the patents-in-suit, Amgen obtained the now expired U.S. Patent No. 4,667,016 ("the '016 patent"). Seluga Decl., Ex. F. Amgen waited until after the issuance of the '016 patent (on May 19, 1987) – sometimes as long as eight years after – to file the applications that issued as the patents-in-suit. *See* Seluga Decl., Exs. A, B, C, D and E.

3. Amgen's also obtained U.S. Patent No. 4,703,008 ("the '008 patent") before the patents-in-suit, and the '008 patent is also now expired. Seluga Decl., Ex. G.

4. Claim 10 of the '016 patent provides a process for harvesting purified "recombinant erythropoietin from a mammalian cell culture supernatant fluid." Recombinant erythropoietin ("rEPO") was the end product of Amgen's EPO Project, which first identified the amino acid sequence for the erythropoietin ("EPO") gene in the '008 patent. *See* Seluga Decl., Exs. F and G.

5. Amgen applied known techniques to clone the EPO gene to produce rEPO. Once in possession of rEPO, such as claimed in claim 10 of the '016 patent, there is no inventive activity required by one skilled in the art to arrive at each of the claims-in-suit. Harlow Decl. ¶¶ 9-14, 17-19, 21-22, 24-27, 29-34, 47-48 and 124.

6. One skilled in the art in 1983 would have known that rEPO, such as claimed in claim 10 of the '016 patent, could be converted into pharmaceuticals for treatment of a kidney dialysis patient by conventional and well-known means. Harlow Decl. ¶¶ 25-31 and 124.

7. In *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 927 F.2d 1200, 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991), the defendant argued that Amgen's failure to deposit or fully disclose the

"specific genetically-heterogeneous strain of Chinese hamster ovary ("CHO") cells, which produced EPO at a rate greater than that of other cells" rendered the '008 patent invalid under 35 U.S.C. §112 for failing to set forth the best mode, in particular, the best mammalian host cells known to Lin as of November 30, 1984, the date Lin filed his fourth patent application, from which the patents-in-suit claim priority. The Federal Circuit found no violation of the best mode requirement, quoting prior case law that "No problem exists when the microorganisms used are known and readily available to the public." Thus, Amgen's CHO cell strain was known to one skilled in the art and publicly available. Seluga Decl., Ex. H, 927 F.2d at 1211, 18 U.S.P.Q.2d at 1025; *see also* Harlow Decl. ¶ 105 and 124.

8. Limitations relating to the host cells, including the choice of the "specific genetically-heterogeneous strain of Chinese hamster ovary (CHO) cells, which produced EPO at a rate greater than that of other cells" and limitations relating to the host cell's ability to produce EPO at a greater rate cannot be considered patentable distinctions over the "mammalian cell culture" of claim 10 of the '016 patent. Harlow Decl. ¶¶ 9-14, 98, 105 and 124.

U.S. Patent No. 5,547,933 ("the '933 patent"), Claims 3, 7-9, 11-12 and 14

9. Claim 3 of the '933 patent recites a "non-naturally occurring glycoprotein product" of the "expression in a mammalian host cell." A "glycoprotein product" would have been obvious in light of or inherent in "recombinant erythropoietin" as used in claim 10 of the '016 patent. Erythropoietin grown in a "mammalian cell culture" as required by claim 10 of the '016 patent is a glycoprotein, and one skilled in the art in 1983 would have expected it to have "the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells," as called for in claim 3 of the '933 patent. Harlow Decl. ¶¶ 49-51 and 124.

10. Claim 7 of the '933 patent recites that the host cell is "a non-human mammalian [host] cell," and claim 8 further specifies that the non-human mammalian host cell is "a CHO cell." Claim 10 of the '016 patent explicitly requires "a mammalian cell culture," which was well known in 1983, to produce rEPO with the requisite *in vivo* biological property. CHO cells were also well-known to those of skill in the art in 1983 as a preferred mammalian host cell culture for recombinant procedures in which biological activity was sought. Harlow Decl. ¶¶ 52-55 and 124.

11. Amgen itself and its experts has admitted in prior litigation that the additional limitations of claims 3, 7 and 8 of the '933 patent were well known to those skilled in the art at least as early as 1983. *See* Seluga Decl., Ex. H, 927 F.2d at 1211; Ex. I, Brief for the Senior Party Lin, *Fritsch v. Lin*, Interference No. 102,097 at 25-26; Ex. J, *Fritsch v. Lin*, 21 U.S.P.Q.2d 1737, 1739 (BPAI 1991); Ex. K, Deposition Testimony of Fu-Kuen Lin in *Fritsch v. Lin*, at pages 205-210, 216, 217, 219, and 220, dated April 9, 1991, *Amgen v. Chugai*, at pages 107 and 108, dated August 15, 1989, and *Amgen Inc. v. F. Hoffmann-La Roche Ltd.*, at pages 62-65 and 365 to 368, dated March 28-29, 2007 ("Lin Testimony"); Ex. N, Initial Expert Report of Harvey F. Lodish, Ph.D., August 27, 2004 ("Lodish Report") ¶¶ 55-67, 72, 103, 123, 133, 137, 141-148 and 162-168; Ex. R, Testimony of Dr. Julian Davies in *In the Matter of Certain Recombinant Erythropoietin* ("Davies Testimony") (Investigation No. 337-TA-281), at pages 523-24, dated June 21, 1988; Ex. S, Expert Report of Professor Randolph Wall ("Wall Report"), at pages 36-37, 42, and 47, dated November 9, 2000.

12. Claims 9 and 12 of the '933 patent are directed to a pharmaceutical composition that includes a glycoprotein product effective for erythropoietin therapy and a pharmaceutically acceptable diluent, adjuvant or carrier. As stated above, a "glycoprotein product" would have

been obvious in light of or inherent in "recombinant erythropoietin" as used in claim 10 of the '016 patent. Also, one of ordinary skill in the art in 1983 would have understood that purified rEPO, such as claimed in claim 10 of the '016 patent, was intended for pharmaceutical use and it would be routine for one skilled in the art in 1983 to combine the rEPO with a diluent, adjuvant or carrier. Harlow Decl. ¶¶ 56-57 and 124.

13. Claims 11 and 14 of the '933 patent specify that the rEPO be used for treating kidney dialysis patients to increase a patient's hematocrit level, two uses of EPO well known in the art in 1983. Harlow Decl. ¶¶ 58-59 and 124.

U.S. Patent No. 5,955,422 ("the '422 patent"), Claim 1

14. Claim 1 of the '422 patent recites a "pharmaceutical composition" that includes "a therapeutically effective amount of human erythropoietin" and "a pharmaceutically acceptable diluent, adjuvant or carrier." Claim 1 further specifies that the "erythropoietin is purified from mammalian cells grown in culture." Claim 10 of the '016 patent explicitly requires "recombinant erythropoietin from a mammalian cell culture." Cloning rEPO from humans would have been obvious to one skilled in the art in 1983. One of ordinary skill in 1983 would have understood that purified rEPO, such as claimed in claim 10 of the '016 patent, was intended for use in a *pharmaceutical composition,* in a *therapeutically effective amount.* It would be routine for one skilled in the art in 1983 to combine the rEPO with *a pharmaceutically acceptable diluent, adjuvant or carrier.* Hence, claim 1 of the '422 patent would have been obvious to one of ordinary skill in 1983 in light of claim 10 of the '016 patent. Harlow Decl. ¶ 60-61 and 124.

U.S. Patent No. 5,618,698 ("the '698 patent"), Claims 4-7

15. Claim 4 of the '698 patent recites a process for the production of a "glycosylated erythropoietin polypeptide having the in vivo biological property" that "increase[s] production of reticulocytes and red blood cells," which is obvious over claim 10 of the '016 patent. The rEPO of claim 10 of the '016 patent is a *glycosylated erythropoietin polypeptide* which inherently has the *in vivo biological property* that *increases production of reticulocytes and red blood cells.* The "suitable nutrient conditions" and "vertebrate cells" of claim 4 of the '698 patent are inherent in the '016 patent claim 10's mammalian cell culture of rEPO. The "promoter DNA, other than human erythropoietin promoter DNA" of claim 4 was routinely used in recombinant protein synthesis in 1983. "DNA encoding the mature erythropoietin amino acid sequence of FIG. 6" would be produced by the process of claim 10 of the '016 patent in the mammalian cells. Claim 4's step of "isolating said glycosylated erythropoietin polypeptide expressed by said cells" corresponds to step 7 of the '016 patent claim 10. Hence, claim 4 would have been obvious to one of ordinary skill in 1983 in light of claim 10 of the '016 patent. Harlow Decl. ¶¶ 15-22, 62-64 and 124.

16. Claim 5 of the '698 patent further recites that the promoter DNA is "viral promoter DNA," which was a routine part of the synthesis of recombinant proteins in 1983. Thus, claim 5 includes a step that would have been obvious to one of ordinary skill in 1983 in light of claim 10 of the '016 patent. Harlow Decl. ¶¶ 15-22, 65-66 and 124.

17. Claim 6 of the '698 patent is similar to claim 4; it adds the limitation of "amplified DNA encoding the mature erythropoietin amino acid sequence of FIG. 6," and drops reference to promoter DNA. Amplified DNA was routinely used in recombinant protein

synthesis in 1983 and one skilled in the art in 1983 would have known to use the claim 10 process of the '016 patent to produce human EPO. Harlow Decl. ¶¶ 15-22, 67-69 and 124.

18. Claim 7 of the '698 patent recites that the vertebrate cells include "amplified marker gene DNA," while claim 8 further specifies that the amplified marker gene DNA is "Dihydrofolate reductase (DHFR) gene DNA." Both amplified marker gene DNA and DHFR gene DNA were routinely used techniques during synthesis of recombinant proteins in 1983 and thus would have been obvious to one skilled in the art in light of claim 10 of the '016 patent. Harlow Decl. ¶¶ 15-22, 70-73 and 124.

19. Claim 9 of the '698 patent recites that the [vertebrate] cells are "mammalian cells," an explicitly covered element of the '016 patent claim 10. Thus, one skilled in the art in 1983 would have found using mammalian cells for the vertebrate cells obvious in light of claim 10 of the '016 patent. Harlow Decl. ¶¶ 9-14, 74-75 and 124.

U.S. Patent No. 5,441,868 ("the '868 patent"), Claims 1 and 2

20. Claims 1 and 2 of the '868 patent are both process claims for the production of a "glycosylated erythropoietin polypeptide" having the "in vivo biological property" that "increase[s] production of reticulocytes and red blood cells." As stated above, the rEPO of claim 10 of the '016 patent is a *glycosylated erythropoietin polypeptide* which inherently has the utility of the *in vivo biological property* that *increases production of reticulocytes and red blood cells.* Claim 1 further requires using "mammalian host cells transformed or transfected with an isolated DNA sequence encoding human erythropoietin." It was routine in the art in 1983 when synthesizing recombinant proteins in mammalian cells to transform or transfect the cells with the isolated DNA sequence encoding the desired protein. Claim 2 further specifies that the mammalian host cells be CHO cells. CHO cells were also well-known to those of skill in the art

in 1983 as a preferred mammalian host cell culture for recombinant procedures in which biological activity was sought. Harlow Decl. ¶¶ 9-14, 76-80 and 124.

U.S. Patent No. 5,756,349 ("the '349 patent"), Claim 7

21. Claim 7 of the '349 patent recites a process for producing erythropoietin whose elements are either contained in or obvious in the light of claim 10 of the '016 patent. To the various limitations discussed above, it adds the requirement that the cells are chosen that are capable of being propagated *in vitro* and of producing EPO in excess of 100, 500, or 1000 U per 10^6 cells in 48 hours as determined by radioimmunoassay. However, because claim 7 fails to disclose or claim any method for making its rate of production possible, and also appears indefinite, its scope must be limited to what was enabled in the '349 patent, which shares the same specification as the Lin '008 patent, which was in turn incorporated into the '016 patent. If capable of being construed to have a definite scope, claim 7 would have been obvious over claim 10 of the '016 patent. Harlow Decl. ¶¶ 9-14, 81-86 and 124. Furthermore, as discussed in Harlow Decl. ¶¶ 111-121, Dr. Lin did not engage in any inventive activity in choosing the host cells.

Amgen's Admissions that the Claims-in-Suit are Obvious Over the '016 Patent

22. After filing the '008 patent in 1983, Amgen pursued filing multiple continuation applications, many of which were later abandoned, based on the '008 patent. Amgen also filed suit the day the '008 Lin patent issued in 1987, and has pursued litigation involving the '008 patent and its "descendents," the patents-in-suit, from that day to this. During the 16-year prosecution of the patents-in-suit, and in the course of the various litigations, Amgen has made admissions which confirm that the claims-in-suit are obvious over claim 10 of the '016 patent. *See* Seluga Decl., Ex. H, 927 F.2d at 1211; Ex. I, Brief for the Senior Party Lin, ***Fritsch v. Lin***,

Interference No. 102,097 at 25-26; Ex. J, 21 U.S.P.Q.2d at 1739; Ex. K, Lin Testimony; Ex. N, Lodish Report ¶¶ 55-67, 72, 103, 123, 133, 137, 141-148 and 162-168; Ex. R, Davies Testimony at 523-24; Ex. S, Wall Report at 36-37, 42, and 47; *see also* Harlow Decl. ¶¶ 98-100 and 105-111.

23. During interference proceedings (Interference Nos. 102,097 and 102,334) with Genetics Institute involving Application Serial Nos. 07/113,178 ("the '178 application") and 07/113,179 ("the '179 application") – from which all of the patents-in-suit claim priority – Amgen argued that the subject matters claimed in the '178 and '179 applications were just different aspects of the same invention as the '008 patent. *See* Seluga Decl., Ex. I, Brief for the Senior Party Lin, *Fritsch v. Lin*, Interference No. 102,097 at 25-26; *see also* Harlow Decl. ¶¶ 99-100.

24. Amgen equated the pending application claims (relating to rEPO, methods of making rEPO, and uses of rEPO) to the claims in the '008 patent (relating to the DNA sequence for EPO):

> While the count [which represents the pending claims] is directed to a process for preparing *in vivo* biologically active EPO using a mammalian host cell …, and the litigation was directed to the purified and isolated DNA sequence and host cells transfected or transformed thereby, it is evident that these are only different manifestations of the same invention …. 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.

See Seluga Decl., Ex. I, Brief for the Senior Party Lin, *Fritsch v. Lin*, Interference No. 102,097 at 25-26.

25. Amgen argued that, because Lin was the first to invent an isolated DNA sequence encoding EPO, Lin was the first to invent the process of expressing and isolating rEPO and the

first to invent rEPO itself, since these were just different aspects of the same invention. Amgen admits that all of the work done at Amgen encompassed in the '178 and '179 applications – beyond isolating the gene sequence of the '008 patent – was obvious and involved no inventive activity once the DNA sequence was isolated. *See* Seluga Decl., Ex. H, 927 F.2d at 1211; Ex. I, Brief for the Senior Party Lin, ***Fritsch v. Lin***, Interference No. 102,097 at 25-26; Ex. J, 21 U.S.P.Q.2d at 1739; Ex. K, Lin Testimony; Ex. N, Lodish Report ¶¶ 55-67, 72, 103, 123, 133, 137, 141-148 and 162-168; Ex. R, Davies Testimony at 523-24; Ex. S, Wall Report at 36-37, 42, and 47; *see also* Harlow Decl. ¶¶ 107, 109, 111-121 and 124.

26. The Board of Patent Appeals and Interferences ("BPAI") agreed and held that the process steps for making glycosylated *in vivo* biologically active EPO after the EPO gene was known "d[id] not require the exercise of inventive skill." Seluga Decl., Ex. J, 21 U.S.P.Q.2d at 1739 (emphasis supplied); *see also* Harlow Decl. ¶ 110.

27. The BPAI, in ruling in Amgen's favor, determined that Amgen's opponent had "adduced no evidence suggesting 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" and that Amgen's opponent even acknowledged "that expression of the EPO gene, once isolated, to obtain a recombinant EPO product would not have required more than ordinary skill." Seluga Decl., Ex. J, 21 U.S.P.Q.2d at 1739 (emphasis supplied).

28. Amgen has listed Lin as the sole inventor of the patents-in-suit, because Lin alone identified the DNA sequence claimed in the '008 patent. Lin asked others at Amgen to perform additional non-inventive tasks, such as choosing host cells, expressing proteins from host cells, isolating rEPO from the host cell material, and preparing pharmaceutical compositions from

purified rEPO. Lin has repeatedly testified under oath that his contributions for these additional tasks was simply to refer his colleagues to prior-art literature. *See, e.g.*, Seluga Decl., Ex. K, Deposition Testimony of Fu-Kuen Lin in *Fritsch v. Lin*, at page 217, dated April 9, 1991; Ex. J, *Fritsch v. Lin*, 21 U.S.P.Q.2d 1739 (BPAI 1991); *see also* Harlow Decl. ¶¶ 111-121.

29. Amgen and inventor Lin admit these additional tasks would have been obvious once the gene sequence for EPO was known. Lin provided no instructions to carry out these additional tasks. The others working with Lin on the Amgen EPO Project relied simply on the identification of the gene sequence by Lin and on techniques and operating conditions known to those of ordinary skill in the art for expressing recombinant proteins in mammalian cells. *See* Seluga Decl., Ex. K, Deposition Testimony of Fu-Kuen Lin in *Fritsch v. Lin*, at pages 205-210, 216, 217, 219, and 220, dated April 9, 1991; *see also* Harlow Decl. ¶¶ 111-121.

30. During the prosecution of the '868 patent, the U.S. Patent and Trademark Office (the "PTO") rejected the pending claims as non-enabled and lacking adequate written description under §112. Amgen traversed this rejection in part by arguing that it would have been obvious to the skilled worker, as of the December 13, 1983, filing date to be able to make glycosylated proteins from available host cells. Amgen argued that "numerous other mammalian cells [in addition to CHO and COS] capable of effecting glycosylation of expressed polypeptides were known to those skilled in the art at the time of the present invention." Thus, Amgen admitted during the prosecution of the '868 patent that using host cells capable of effecting post-translational glycosylation was obvious at the time of the invention. Seluga Decl., Ex. L, '179 File History, Paper 33, 1/31/94 Amendment at 5 (emphasis supplied); *see also* Harlow Decl. ¶ 98.

31. Amgen admitted during prosecution of the '178 application, from which the '933 patent claims priority, that

> both the starting material and final product of the ['016 patent] …are included within (dominated by) the recombinant product claims of the present application.

Seluga Decl., Ex. M, '178 File History, Paper 19, 1/11/90 Amendment at 3 (emphasis added); *see also* Sofocleous Decl. ¶ 10; Harlow Decl. ¶¶ 107-108.

32. Where the subject matter product of the '016 patent claim 10 process is "included within (dominated by)" the later-issued '933 patent claims-in-suit, those claims must be obvious over claim 10 of the '016 patent, as directed to the same product subject matter. Sofocleous Decl. ¶¶ 10-11.

Amgen's Expert, Dr. Lodish, Has Admitted in Prior Litigation that Claim Distinctions Similar to Those in this Case Would Have Been Obvious Prior to 1983

33. In prior litigation (*In re Columbia University Litigation*, No. 09-MD-01592, D. Mass.), Amgen's expert in this case, Dr. Harvey Lodish, provided an expert report challenging the validity of patents owned by Columbia University as obvious in light of an earlier-issued patent also owned by Columbia University. Like the patents-in-suit, the Columbia University patents related to recombinant DNA engineering. In that report, Dr. Lodish admitted that, as of 1980, many of the techniques used in this field were obvious and well known. *See* Seluga Decl., Ex. N, Lodish Report ¶¶ 55-67, 72, 103, 123, 133, 137, 141-148 and 162-168; *see also* Harlow Decl. ¶¶ 87-95.

34. Dr. Lodish admitted that the glycosylation of proteins was obvious and well known in 1980. *See* Seluga Decl., Ex. N, Lodish Report ¶¶ 123, 141, 142, 143 and 145 (stating "… In my opinion, the requirement that a protein have an attached carbohydrate chain does not

make it patentably distinct from the simple requirement that it be a protein."); *see also* Harlow Decl. ¶ 89.

35. Dr. Lodish admitted that, as of 1980, the transformation of mammalian cells with exogenous DNA was obvious and well known. *See* Seluga Decl., Ex. N, Lodish Report ¶¶ 55-64; *see also* Harlow Decl. ¶ 90.

36. Dr. Lodish admitted that, as of 1980, the use of CHO cells for producing recombinant proteins was obvious and well known. *See* Seluga Decl., Ex. N, Lodish Report ¶¶ 64, 144-148; *see also* Harlow Decl. ¶ 91.

37. Dr. Lodish admitted that, as of 1980, the amplification of genes in mammalian cell cultures was obvious and well known. *See, e.g.*, Seluga Decl., Ex. N, Lodish Report ¶¶ 65-67, 103, 133, 137, 162-168; *see also* Harlow Decl. ¶ 92.

38. Dr. Lodish admitted that, as of 1980, the use of dihydroflate reductase (DHFR) was obvious and well known. *See, e.g.*, Seluga Decl., Ex. N, Lodish Report ¶¶ 65-67, 103, 133, 137, 162-168; *see also* Harlow Decl. ¶ 93.

39. Dr. Lodish admitted that, as of 1980, the use of viral promoters was obvious and well known. *See, e.g.*, Seluga Decl., Ex. N, Lodish Report ¶ 72; *see also* Harlow Decl. ¶ 94.

40. These recombinant engineering techniques which were known and obvious in 1980, as admitted by Dr. Lodish, and occurred several years before the December 1983 priority filing date of the patents-in-suit. *See* Harlow Decl. ¶ 95.

Obviousness-type Double Patenting Rejection Based on One-way Determination of Obviousness

41. Obviousness-type double patenting includes rejections based on either a one-way or a two-way determination of obviousness. A two-way obviousness test may be applied to support a double patenting rejection if the application at issue is the earlier filed application and

only if: (A) the applicant could not have filed the earlier and later claims in a single application; and (B) the PTO is solely responsible for the delay that caused the earlier-filed claims to issue after the later-filed claims. *See* Ex. O, MPEP §804 (8th ed. Rev. 5, Aug. 2006); *see also* Sofocleous Decl. ¶ 3.

42. All the patents-in-suit claim priority to Application Serial No. 06/561,024 ("the '024 application") filed December 13, 1983. Thus, the applications that matured into the patents-in-suit are considered the earlier filed applications compared to the '016 patent filed on June 20, 1985. However, the one-way obviousness test should be applied when comparing the patents-in-suit to the '016 patent because Amgen cannot show that (1) the applicant could not have filed the earlier and later claims in a single application; and (2) the PTO is solely responsible for the delay that caused the earlier-filed claims to issue after the later-filed claims. Sofocleous Decl. ¶¶ 2-8 and Ex. 2.

43. There was no legal impediment to Amgen filing Application Serial Number 06/747,119 ("the '119 application"), the application that matured into the '016 patent, and Application Serial Number 06/675,298 ("the '298 application"), the application that all of the patents-in-suit claim priority to as continuation applications, together in one application. The Patent Law Amendments Act of 1984, which took effect before either of those applications were filed, specifically provides that "[i]nventors may apply for a patent jointly even though (1) they did not physically work together or at the same time, (2) each did not make the same type or amount of contribution, or (3) each did not make a contribution to the subject matter of every claim of the patent." Ex. P, 35 U.S.C.A. §116 (Thomson/West 2007).

44. Amgen could have filed a continuation-in-part (CIP) application combining the disclosures of the '298 application by Lin and the '119 application by Lai and Strickland and

named all of the inventors as co-inventors. This CIP application could have claimed priority to the '298 application and the '119 application and could have included all the claims-in-suit as well as the claims of the '016 patent. Sofocleous Decl. ¶ 6.

45. Alternatively, Amgen could have added the Lin '298 application disclosure to the Lai et al. '119 application at the time of filing the '119 application and included Lin as a co-inventor. All the claims-in-suit as well as the claims of the '016 patent could have been included in this CIP application. Sofocleous Decl. ¶ 6.

46. In either case, neither Lin nor Lai et al. would have lost his asserted effective filing date because each claim in a CIP application may have different priority dates. Sofocleous Decl. ¶ 6.

47. Amgen delayed filing all of the applications that matured into the patents-in-suit until after the '016 patent issued—in most cases as long as eight years after—even though these applications could have been filed at the same time or before the '119 application was filed. Sofocleous Decl. ¶ 4 and Ex. 2.

48. During the course of the prosecution of the patents-in-suit, Amgen sought and received thirteen extensions of time totaling over fifteen months of additional delay. In many instances, Amgen waited until the last possible day to respond to PTO correspondence. Amgen further delayed the issuance of the claims-in-suit by filing multiple continuation applications, many of which were later abandoned. Sofocleous Decl. ¶ 7 and Ex. 2.

49. During the prosecution of the '298 application, the application that matured into U.S. Patent No. 4,703,008 ("the '008 patent"), Amgen voluntarily chose to cancel claims directed to processes for the production of polypeptides while pursuing related claims directed to the polypeptides themselves. An examiner's restriction requirement had grouped both sets of

these claims together as one invention, the Group II claims elected for prosecution. These cancelled process claims, which were reintroduced in the '868 patent could have avoided the interference proceeding that delayed the issuance of these claims had they been prosecuted along with the related Group II claims that issued in the '008 patent. Thus, the PTO was not at all responsible for the delay that caused these claims in the '868 patent to issue after the claims in the '016 patent. Sofocleous Decl. ¶ 8.

50. During the prosecution of the '179 application – from which the '868 patent, the '349 patent, the '698 patent and the '422 patent claim priority – the Examiner made an obviousness-type double patenting rejection based on the '016 patent, applying a one-way obviousness test. Amgen argued that a two-way obviousness test applied and succeeded in getting the Examiner to withdraw the double patenting rejection of the '179 application. The Examiner still found, however, that the pending claims of the '179 application were obvious in light of the claims of the '016 patent:

> … And while the instantly claimed method is an obvious variation of the process of Lai et al. it is considered that applicant is not responsible for the delay in the prosecution of the instant application which resulted in the prior patenting of a later filed application to an invention derived from the instant invention. …

Seluga Decl., Ex. Q, '179 File History, Paper 34, 02/15/94 Office Action at 2 (emphasis added); *see also* Sofocleous Decl. ¶ 9.

51. The Examiner should have properly applied the one-way obviousness test, rather than the rarely used two-way obviousness test, in rejecting the '178 and '179 applications because Amgen could have filed these applications together with the '119 application even though the applications named different inventors. In addition, as stated above, the PTO was not

solely responsible for the delay that caused the claims-in-suit from issuing before the '016 patent claims issued. *See* Sofocleous Decl. ¶ 3-13.

Dated: June 12, 2007
Boston, Massachusetts

Respectfully submitted,

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