UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, v. F. HOFFMANN-LA ROCHE LTD., a Swiss Company, ROCHE DIAGNOSTICS GmbH, a German Company and HOFFMANN-LA ROCHE INC., a New Jersey Corporation, Defendants.	Civil Action No.: 05-12237 WGY

AMGEN'S RESPONSE TO ROCHE'S RULE 56.1 STATEMENT OF UNDISPUTED MATERIAL FACTS REGARDING ITS MOTION FOR SUMMARY JUDGMENT OF INVALIDITY FOR DOUBLE PATENTING OVER CLAIM 10 OF THE '016 PATENT

Pursuant to Local Rule 56.1, Amgen submits this opposition to Roche's statement of undisputed facts regarding Roche's motion for summary judgment that all claims-in-suit are invalid for obviousness-type double patenting ("ODP") over claim 10 of the '016 patent (Document Item ("D.I.") 492).

Contrary to the requirements of Local Rule 56.1, Roche's statement of facts is neither "concise" nor limited to "material facts." Instead, Roche's statement is 51 paragraphs long, and includes attorney argument, conclusions of law, and several purported facts that are immaterial to Roche's motion. Although Amgen has responded below to each of Roche's "statements of fact," as explained in Amgen's opposition brief, most of these "facts" (and most of Roche's brief and accompanying declarations) are simply irrelevant once the Court rejects any of the following false ***legal*** premises on which Roche's summary judgment motion depends: (1) that the "one-way" double patenting test applies instead of the "two-way" test; (2) that Roche may base its

ODP analysis on subject matter that is named but not claimed in '016 claim 10; and (3) that Roche may use the specification underlying '016 claim 10 (including the referenced teachings of Dr. Lin's patents-in-suit) as prior art against the claims-in-suit.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 1

Undisputed.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 2

Disputed. Each of the patents-in-suit claims priority to Dr. Lin's '298 application (and earlier applications). *See* D.I. 501, Exs. C-G. The '298 application was filed more than six months ***before*** the application that issued as the '016 patent. *Compare* D.I. 501, Ex. H-1 *with* D.I. 501, Ex. K. The later-filed '016 patent issued on May 19, 1987, and is now expired. The patents-in-suit issued after the '016 patent, but not because of any unreasonable or unexplained delay by Amgen. A restriction requirement imposed by the PTO on July 3, 1986 (over one year after the '119 application was filed) forced Amgen to prosecute the inventions claimed in the patents-in-suit in separate applications from the '298 application. *See* D.I. 501, Ex. H-8. Examination of these new applications leading to the patents-in-suit was delayed several years by PTO interference proceedings**.** *See* D.I. 501, Ex. A.

Roche's "Statement of Fact" No. 3

Amgen's [sic] 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.

Amgen's Response to Statement No. 3

Undisputed. The '008 patent and the patents-in-suit all claim priority to the same applications filed in 1983-84. *See* D.I. 501, Exs. B-G. The '008 patent issued before the patents-in-suit, and is now expired.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 4

Disputed. The proper construction of claim 10 of the '016 patent is an issue of law, not fact. *See Gen. Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1277 (Fed. Cir. 1992). Therefore, this "statement of fact" is nothing more than an argument regarding a legal conclusion. Moreover, the documents cited by Roche do not compel the legal conclusion urged by Roche. *See* D.I. 495, Exs. F, G. Roche's suggestion that "recombinant erythropoietin" is part of the '016 claim 10 invention confuses that which is merely named in '016 claim 10 for what is claimed. *Cf. Astellas Pharma, Inc. v. Ranbaxy Inc.*, 2007 U.S. Dist. LEXIS 11870, at *17-18 (D.N.J. Feb. 21, 2007) ("In order to reach such a conclusion [of ODP], the Court would have to compare the '063 claims with the compounds merely named as part of the claimed processes in the '106 patent, contrary to the law of obviousness-type double patenting."). Claim 10 of the '016 patent is a process claim. It is not a product claim to the recombinant EPO starting material mentioned in the preamble. Nor is it a product-by-process claim to purified recombinant EPO. "It is the combination or sequence of acts or steps that are patented in a process claim, not the

resulting product." DONALD S. CHISUM ET AL., PRINCIPLES OF PATENT LAW, 105 (2d ed. 2001).

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 5

Disputed. The obviousness-type double patenting issue of whether one claim is patentably distinct or non-obvious over another claim is a question of law. *In re Berg*, 140 F.3d 1428, 1432 (Fed. Cir. 1998). Therefore, this "statement of fact" is nothing more than an argument regarding a legal conclusion. Moreover, Roche's argument that '016 claim 10 placed recombinant human EPO in the hands of ordinarily skilled workers prior to Lin's claimed inventions is factually wrong and legally flawed, as explained in Part III.B.3 of Amgen's opposition to Roche's motion for summary judgment of invalidity for double patenting over claim 10 of the '016 patent. *See also* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 1-110. The cloning of the EPO gene, as well as the subsequent inventions of processes to produce EPO in vertebrate host cells and the glycosylated EPO polypeptide products were novel and non-obvious. *Id.* ¶¶16-85. The reference to "recombinant erythropoietin" in the preamble of '016 claim 10 is ***not*** the invention claimed in '016 claim 10. Claim 10 claims a process for recovering a purified product; it does not claim the starting material from which a purified product is to be recovered, nor does it claim the purified product itself. "Recombinant erythropoietin" is a different invention than the recovery process of '016 claim 10. *See generally Gen. Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272 (Fed. Cir. 1992); *cf. Astellas Pharma, Inc. v. Ranbaxy Inc.*, 2007 U.S. Dist. LEXIS 11870, at *17-18 (D.N.J. Feb. 21, 2007) ("In order to reach such a conclusion [of ODP], the Court would have to compare the [later-issued] claims

with the compounds merely named as part of the claimed processes in the [earlier-issued] patent, contrary to the law of obviousness-type double patenting.").

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 6

Disputed. This "statement of fact" is based on an incorrect conclusion of law, namely, that rEPO is claimed in '016 claim 10. It is not. See above response to Roche's "statement of fact" No. 5, which is incorporated herein. Moreover, prior to Dr. Lin's inventions in 1983 (the relevant time of the ODP analysis in this case), the DNA sequence encoding EPO was not known to those of ordinary skill in the art. *See Amgen, Inc. v. Chugai Pharm, Co, Ltd.*, 927 F.2d 1200, 1212 (Fed. Cir. 1991) ("The structure of [the EPO] DNA sequence was unknown until 1983, when the gene was cloned by Lin . . . ."); 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 14-50. Therefore, there was no rEPO in 1983. Although irrelevant to the instant motion, Amgen further disputes any suggestion by Roche that possession of recombinant EPO alone, regardless of the meaning Roche attributes to it, renders obvious Dr. Lin's inventions. *See generally* 6/29/07 Declaration of Harvey F. Lodish, Ph.D.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 7

Disputed. Roche's assertion that "Amgen's CHO cell strain was known to one skilled in the art and publicly available" prior to Lin's inventions is misleading, and absolutely false to the extent Roche suggests that the Federal Circuit in *Amgen v. Chugai* found that Dr. Lin's inventions, or Amgen's "specific genetically-heterogeneous strain of Chinese hamster ovary ("CHO") cells, which produced EPO at a rate greater than that of other cells" were known and available to the public prior to Lin's inventions. The Court made no such finding. *See Amgen, Inc. v. Chugai Pharm, Co, Ltd.*, 927 F.2d 1200, 1209-1212 (Fed. Cir. 1991). Instead, the Federal Circuit affirmed the district court's finding that unmodified CHO cells — i.e., the ***starting material*** used to create the specific, genetically-modified strain of CHO cells described in Dr. Lin's patent — could be obtained from generally available sources, and that the description in Example 10 of how to use that starting material to make Amgen's "specific genetically-heterogeneous strain of Chinese hamster ovary ("CHO") cells" was adequate to satisfy the best mode requirement. *Id.*; *see also* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 68-90.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 8

Disputed. This "statement of fact" is based on an incorrect conclusion of law, namely, that "recombinant erythropoietin [in] a mammalian cell culture supernatant fluid" is claimed in '016 claim 10. It is not. See above responses to Roche's "statement of fact" Nos. 5 and 7, which are incorporated herein. Moreover, the legal issue of whether two claims are "patentably distinct" requires comparison of the two claimed inventions ***as a whole***. *See Gen. Foods*, 972

F.2d at 1280. Even if particular aspects of a claimed invention were known in the art at the relevant time or claimed in another patent —which is ***not*** the case here — that does not compel a holding of obviousness-type double patenting. The inventions claimed in the claims-in-suit would not have been obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 91-110.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 9

Disputed. This "statement of fact" is based on an incorrect conclusion of law, namely, that "recombinant erythropoietin" is claimed in '016 claim 10. It is not. See above response to Roche's "statement of fact" No. 5, which is incorporated herein. Moreover, the legal issue of whether two claims are "patentably distinct" requires comparison of the two claimed inventions ***as a whole***. *See Gen. Foods*, 972 F.2d at 1280. Even if particular aspects of a claimed invention were known in the art at the relevant time or claimed in another patent — which is ***not*** the case here — that does not compel a holding of obviousness-type double patenting. The inventions claimed in the '933 asserted claims would not have been obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 91-94, 68-85.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 10

Disputed. This "statement of fact" is based on an incorrect conclusion of law, namely, that "recombinant erythropoietin" is claimed in '016 claim 10. It is not. See above response to Roche's "statement of fact" No. 5, which is incorporated herein. Moreover, the legal issue of whether two claims are "patentably distinct" requires comparison of the two claimed inventions ***as a whole***. *See Gen. Foods*, 972 F.2d at 1280. Even if particular aspects of a claimed invention were known in the art at the relevant time or claimed in another patent — which is ***not*** the case here — that does not compel a holding of obviousness-type double patenting. The inventions claimed in the '933 asserted claims would not have been obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 91-94, 68-85. Although irrelevant to the instant motion, Amgen further disputes any suggestion by Roche that it was known at the time of Dr. Lin's inventions what cells would produce *in vivo* biologically active EPO, as such was clearly unknown. *See, e.g., id.* at ¶¶ 40-42, 83.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 11

Disputed. This "statement of fact" mischaracterizes the cited documents: neither Amgen

nor its experts 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, and none of the many documents cited by Roche contain any such admission.

Claims 3, 7, and 8 of the '933 patent state:

> 3. A non-naturally occurring erythropoietin glycoprotein product of the expression in a mammalian host cell of an exogenous DNA sequence comprising a DNA sequence encoding human erythropoietin said product possessing the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells.
>
> 7. The glycoprotein product according to claim 3, 4, 5 or 6 wherein the host cell is a non-human mammalian cell.
>
> 8. The glycoprotein product according to claim 7 wherein the non-human mammalian cell is a CHO cell.

The cited section of the *Amgen v. Chugai* decision (D.I. 495, Ex. H) affirms that Dr. Lin's best mode was disclosed and adequately enabled in the specification. The only statement by Amgen (Dr. Lin) noted in this section reads: "Lin testified that the isolation of the preferred strain was a 'routine limited dilution cloning procedure[ ]' well known in the art." 927 F.2d at 1211. The mere fact that an inventor may utilize one or more previously known elements and techniques does not render his novel combination or result obvious. Read in context, 927 F.2d at 1209-12, it is beyond genuine dispute that this statement is not an admission that certain 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.

The Brief for Senior Party Lin, *Fritsch v. Lin*, Interference No. 102,097 (D.I. 495, Ex. I), the arguments made therein, and the BPAI's decision pertaining thereto (D.I. 495, Ex. J) had no connection with the '933 patent claims or even the interference count corresponding to the then-pending claims of the '178 patent application (that gave rise to the '933 patent). The '097 Interference Brief and the BPAI's decision also had no connection with and did not discuss the

'016 patent or the purification process claimed therein. The '097 Interference Brief and the BPAI's decision pertained to the issues of priority and patentability raised by Fritsch against Amgen's then-pending process claims of the '179 Application. Nothing whatsoever in the '097 Interference could reasonably be construed as an admission regarding what Roche deems "additional limitations" of claims 3, 7 and 8 of the '933 patent.

Likewise, the cited deposition testimony of Dr. Lin (D.I. 495, Ex. K) does not contain any admissions 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.

The opinions expressed in Dr. Lodish's expert reports in the *Columbia* case likewise do ***not*** contain any such admissions, and do not support Roche's argument that the inventions claimed in Dr. Lin's patents-in-suit were obvious and well known. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 111-124 and Ex. Z; D.I. 495, Ex. N.

The cited testimony of Dr. Julian Davies from *In the Matter of Certain Recombinant Erythropoietin* (Investigation No. 337-TA-281) (D.I. 495, Ex. R.) indicates that CHO cells were known, but it does not discuss any cells (CHO or otherwise) comprising a DNA sequence encoding human erythropoietin or the production of "non-naturally occurring erythropoietin glycoprotein products … possessing the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells." *See id.*

The opinions expressed in the expert report of Professor Randolph Wall (D.I. 495, Ex. S) do not in any way suggest that the '933 claimed inventions were known. Dr. Wall's cited opinions concern the sufficiency of Dr. Lin's specification (i.e., enablement). Dr. Wall is clearly opining about the ability of an ordinarily skilled artisan to practice Dr. Lin's inventions based on the detailed disclosures provided in Dr. Lin's patent. *See, e.g., id.* at ¶ 102.

Finally, the legal issue of whether two claims are "patentably distinct" requires comparison of the two claimed inventions ***as a whole***. *See Gen. Foods*, 972 F.2d at 1280. Even if particular aspects of a claimed invention were known in the art at the relevant time or claimed in another patent —which is ***not*** the case here — that does not compel a holding of obviousness-type double patenting. The inventions claimed in the '933 asserted claims would not have been obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 91-94. Amgen has always considered the claimed inventions of the '933 patent to be unknown as of 1983 and Roche identifies no admissions to the contrary.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 12

Disputed. This "statement of fact" is based on an incorrect conclusion of law, namely, that "recombinant erythropoietin" is claimed in '016 claim 10. It is not. See above response to Roche's "statement of fact" No. 5, which is incorporated herein. Moreover, the legal issue of whether two claims are "patentably distinct" requires comparison of the two claimed inventions ***as a whole***. *See Gen. Foods*, 972 F.2d at 1280. Even if particular aspects of a claimed invention were known in the art at the relevant time or claimed in another patent — which is ***not*** the case here — that does not compel a holding of obviousness-type double patenting. The inventions claimed in the '933 asserted claims would not have been obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 91-94. Thus,

although irrelevant to the instant motion, Amgen disputes any suggestion by Roche that possession of recombinant EPO alone, regardless of the meaning Roche attributes to it, renders obvious Dr. Lin's inventions. *See generally* 6/29/07 Declaration of Harvey F. Lodish, Ph.D.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 13

Disputed. The cited paragraphs from Dr. Harlow's declaration (as well as the additional paragraphs referenced therein) provide absolutely no evidence for the assertion that it was well known in the art in 1983 to use EPO for treating kidney dialysis patents to increase a patient's hematocrit level. *See* D.I. 494, at ¶¶ 25-28, 58-59, 124. Dr. Harlow appears to be relying on statements made in this Court's 2004 decision in *Amgen/TKT* which were not directed to the state of the art in 1983. *See id.* at ¶ 25 (quoting *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 339 F. Supp. 2d 202, 214 (D. Mass. 2004)). In the paragraph immediately following those cited by Dr. Harlow, this Court found that "[e]arly attempts to obtain EPO from plasma or urine proved unsuccessful," and that "Amgen is recognized as the pioneer in the production of a therapeutically effective amount of EPO." *Amgen*, 339 F. Supp. 2d at 214. Dr. Harlow is not an expert in the field of nephrology, nor does he claim to have any personal experience treating kidney dialysis patients with EPO. *See* D.I. 494, at ¶¶ 1-8. The inventions claimed in the '933 asserted claims would not have been obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 91-94.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 14

Disputed. The obviousness-type double patenting issue of whether one claim is patentably distinct or non-obvious over another claim is a question of law. *In re Berg*, 140 F.3d 1428, 1432 (Fed. Cir. 1998). Therefore, this "statement of fact" is nothing more than an argument regarding a legal conclusion. Moreover, Roche's argument that '016 claim 10 placed recombinant human EPO in the hands of ordinarily skilled workers prior to Lin's claimed inventions is factually wrong and legally flawed, as explained in Part III.B.3 of Amgen's opposition to Roche's motion for summary judgment of invalidity for double patenting over claim 10 of the '016 patent. The reference to "recombinant erythropoietin" in the preamble of '016 claim 10 is ***not*** the invention claimed in '016 claim 10. Claim 10 claims a process for recovering a purified product; it does not claim the starting material from which a purified product is to be recovered, nor does it claim the purified product itself. "Recombinant erythropoietin" is a different invention than the recovery process of '016 claim 10. *See generally Gen. Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272 (Fed. Cir. 1992); *cf. Astellas Pharma, Inc. v. Ranbaxy Inc.*, 2007 U.S. Dist. LEXIS 11870, at *17-18 (D.N.J. Feb. 21, 2007) ("In order to reach such a conclusion [of ODP], the Court would have to compare the [later-issued] claims with the compounds merely named as part of the claimed processes in the [earlier-issued] patent, contrary to the law of obviousness-type double patenting.").

Moreover, the legal issue of whether two claims are "patentably distinct" requires

comparison of the two claimed inventions ***as a whole***. *See Gen. Foods*, 972 F.2d at 1280. Even if particular aspects of a claimed invention were known in the art at the relevant time or claimed in another patent —which is ***not*** the case here — that does not compel a holding of obviousness-type double patenting. The inventions claimed in '422 claim 1 would not have been obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 95-98. Thus, although irrelevant to the instant motion, Amgen disputes any suggestion by Roche that possession of recombinant EPO alone, regardless of the meaning Roche attributes to it, renders obvious Dr. Lin's inventions. *See generally* 6/29/07 Declaration of Harvey F. Lodish, Ph.D.

Roche's assertion that "[c]loning rEPO from humans would have been obvious to one skilled in the art in 1983" also is incorrect. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 51-67.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 15

Disputed. This "statement of fact" is based on an incorrect conclusion of law, namely, that "recombinant erythropoietin" is claimed in '016 claim 10. It is not. See above response to

Roche's "statement of fact" No. 5, which is incorporated herein. Moreover, the legal issue of whether two claims are "patentably distinct" requires comparison of the two claimed inventions ***as a whole***. *See Gen. Foods*, 972 F.2d at 1280. Even if particular aspects of a claimed invention were known in the art at the relevant time or claimed in another patent — which is ***not*** the case here — that does not compel a holding of obviousness-type double patenting. Prior to Dr. Lin's inventions (the relevant time of the ODP analysis in this case), the DNA sequence encoding EPO was not known to those of ordinary skill in the art. *See Amgen, Inc. v. Chugai Pharm, Co, Ltd.*, 927 F.2d 1200, 1212 (Fed. Cir. 1991) ("The structure of [the EPO] DNA sequence was unknown until 1983, when the gene was cloned by Lin . . . ."); 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 14-50. The inventions claimed in the '698 asserted claims would not have been obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 107-110. Thus, although irrelevant to the instant motion, Amgen disputes any suggestion by Roche that possession of recombinant EPO alone, regardless of the meaning Roche attributes to it, renders obvious Dr. Lin's inventions. *See generally* 6/29/07 Declaration of Harvey F. Lodish, Ph.D.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 16

Disputed. This "statement of fact" is based on an incorrect conclusion of law, namely, that "recombinant erythropoietin" is claimed in '016 claim 10. It is not. See above response to Roche's "statement of fact" No. 5, which is incorporated herein. Moreover, the legal issue of whether two claims are "patentably distinct" requires comparison of the two claimed inventions ***as a whole***. *See Gen. Foods*, 972 F.2d at 1280. Even if particular aspects of a claimed invention

were known in the art at the relevant time or claimed in another patent — which is ***not*** the case here — that does not compel a holding of obviousness-type double patenting. Prior to Dr. Lin's inventions (the relevant time of the ODP analysis in this case), the DNA sequence encoding EPO was not known to those of ordinary skill in the art. *See Amgen, Inc. v. Chugai Pharm, Co, Ltd.*, 927 F.2d 1200, 1212 (Fed. Cir. 1991) ("The structure of [the EPO] DNA sequence was unknown until 1983, when the gene was cloned by Lin . . . ."); 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 14-50. The inventions claimed in the '698 asserted claims would not have been obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 107-110. Thus, although irrelevant to the instant motion, Amgen disputes any suggestion by Roche that possession of recombinant EPO alone, regardless of the meaning Roche attributes to it, renders obvious Dr. Lin's inventions. *See generally* 6/29/07 Declaration of Harvey F. Lodish, Ph.D.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 17

Disputed. This "statement of fact" is based on an incorrect conclusion of law, namely, that "recombinant erythropoietin" is claimed in '016 claim 10. It is not. See above response to Roche's "statement of fact" No. 5, which is incorporated herein. Moreover, the legal issue of whether two claims are "patentably distinct" requires comparison of the two claimed inventions ***as a whole***. *See Gen. Foods*, 972 F.2d at 1280. Even if particular aspects of a claimed invention were known in the art at the relevant time or claimed in another patent — which is ***not*** the case here — that does not compel a holding of obviousness-type double patenting. Prior to Dr. Lin's

inventions (the relevant time of the ODP analysis in this case), the DNA sequence encoding EPO was not known to those of ordinary skill in the art. *See Amgen, Inc. v. Chugai Pharm, Co, Ltd.*, 927 F.2d 1200, 1212 (Fed. Cir. 1991) ("The structure of [the EPO] DNA sequence was unknown until 1983, when the gene was cloned by Lin . . . ."); 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 14-50. The inventions claimed in the '698 asserted claims would not have been obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 107-110. Thus, although irrelevant to the instant motion, Amgen disputes any suggestion by Roche that possession of recombinant EPO alone, regardless of the meaning Roche attributes to it, renders obvious Dr. Lin's inventions. *See generally* 6/29/07 Declaration of Harvey F. Lodish, Ph.D.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 18

Disputed. This "statement of fact" is based on an incorrect conclusion of law, namely, that "recombinant erythropoietin" is claimed in '016 claim 10. It is not. See above response to Roche's "statement of fact" No. 5, which is incorporated herein. Moreover, the legal issue of whether two claims are "patentably distinct" requires comparison of the two claimed inventions ***as a whole***. *See Gen. Foods*, 972 F.2d at 1280. Even if particular aspects of a claimed invention were known in the art at the relevant time or claimed in another patent — which is ***not*** the case here — that does not compel a holding of obviousness-type double patenting. Prior to Dr. Lin's inventions (the relevant time of the ODP analysis in this case), the DNA sequence encoding EPO was not known to those of ordinary skill in the art. *See Amgen, Inc. v. Chugai Pharm, Co, Ltd.*,

927 F.2d 1200, 1212 (Fed. Cir. 1991) ("The structure of [the EPO] DNA sequence was unknown until 1983, when the gene was cloned by Lin . . . ."); 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 14-50. The inventions claimed in the '698 asserted claims would not have been obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 107-110. Thus, although irrelevant to the instant motion, Amgen disputes any suggestion by Roche that possession of recombinant EPO alone, regardless of the meaning Roche attributes to it, renders obvious Dr. Lin's inventions. *See generally* 6/29/07 Declaration of Harvey F. Lodish, Ph.D.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 19

Disputed. This "statement of fact" is based on an incorrect conclusion of law, namely, that "recombinant erythropoietin" is claimed in '016 claim 10. It is not. See above response to Roche's "statement of fact" No. 5, which is incorporated herein. Moreover, the legal issue of whether two claims are "patentably distinct" requires comparison of the two claimed inventions ***as a whole***. *See Gen. Foods*, 972 F.2d at 1280. Even if particular aspects of a claimed invention were known in the art at the relevant time or claimed in another patent — which is ***not*** the case here — that does not compel a holding of obviousness-type double patenting. The inventions claimed in the '698 asserted claims would not have been obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 107-110. Thus, although irrelevant to the instant motion, Amgen disputes any suggestion by Roche that possession of recombinant EPO alone, regardless of the meaning Roche attributes to it, renders obvious Dr. Lin's inventions. *See generally* 6/29/07 Declaration of Harvey F. Lodish, Ph.D.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 20

Disputed. This "statement of fact" is based on an incorrect conclusion of law, namely, that "recombinant erythropoietin" is claimed in '016 claim 10. It is not. See above response to Roche's "statement of fact" No. 5, which is incorporated herein. Moreover, the legal issue of whether two claims are "patentably distinct" requires comparison of the two claimed inventions ***as a whole***. *See Gen. Foods*, 972 F.2d at 1280. Even if particular aspects of a claimed invention were known in the art at the relevant time or claimed in another patent —which is ***not*** the case here — that does not compel a holding of obviousness-type double patenting. Prior to Dr. Lin's inventions, the DNA sequence encoding EPO was not known to those of ordinary skill in the art. *See Amgen, Inc. v. Chugai Pharm, Co, Ltd.*, 927 F.2d 1200, 1212 (Fed. Cir. 1991) ("The structure of [the EPO] DNA sequence was unknown until 1983, when the gene was cloned by Lin . . . ."); 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 14-50. Nor is it true that a glycosylated erythropoietin polypeptide will inherently have the in vivo biological property of increasing production of reticulocytes and red blood cells. 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 68-85. The inventions claimed in the '868 asserted claims would not have been obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 103-106. Thus, although irrelevant to the instant motion, Amgen

disputes any suggestion by Roche that possession of recombinant EPO alone, regardless of the meaning Roche attributes to it, renders obvious Dr. Lin's inventions. *See generally* 6/29/07 Declaration of Harvey F. Lodish, Ph.D.

Roche's "Statement of Fact" No. 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 Response to Statement No. 21

Disputed. The obviousness-type double patenting issue of whether one claim is patentably distinct or non-obvious over another claim is a question of law. *In re Berg*, 140 F.3d 1428, 1432 (Fed. Cir. 1998). Indefiniteness also is an issue of law. *Exxon Research & Eng'g Co. v. United States*, 265 F.3d 1371, 1376 (Fed. Cir. 2001). Therefore, this "statement of fact" is nothing more than argument regarding legal conclusions.

Roche's ODP argument is flawed and legally wrong, as explained in Part III.B.3 of Amgen's opposition to Roche's motion for summary judgment of invalidity for double patenting over claim 10 of the '016 patent. The inventions claimed in '349 claim 7 would not have been obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 99-102. Thus, although irrelevant to the instant motion, Amgen disputes any suggestion by Roche that possession of recombinant EPO alone, regardless of the meaning Roche attributes to it, renders obvious Dr. Lin's inventions. *See generally* 6/29/07 Declaration

of Harvey F. Lodish, Ph.D. Roche's indefiniteness argument is also legally wrong, for the reasons explained in Amgen's memorandum in support of its motion for summary judgment that Dr. Lin's claims are definite, adequately described and enabled. *See* D.I. 532, at Part II.A.2.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 22

Disputed. The obviousness-type double patenting issue of whether one claim is patentably distinct or non-obvious over another claim is a question of law. *In re Berg*, 140 F.3d 1428, 1432 (Fed. Cir. 1998). Therefore, this "statement of fact" is nothing more than an argument regarding a legal conclusion.

Moreover, this "statement of fact" grossly mischaracterizes the cited documents: neither Amgen nor its experts admitted in prior litigation that the claims-in-suit are obvious over claim 10 of the '016 patent, and none of the many documents cited by Roche contain any such admission. *See* D.I. 495, 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; Harlow Decl. ¶¶ 98-100 and 105-111. For example, the '097 Interference Brief (D.I. 495, Ex. I) had no connection with and did not discuss the '016 patent or the purification process claimed therein. The decision of the Board

of Patent Appeals & Interferences (D.I. 495. Ex. J) also did not address or discuss the '016 patent or the purification process claimed therein. Dr. Lin's testimony in the '097 and '334 Interferences (D.I. 495, Ex. K) also did not address or discuss the '016 patent or the purification process claimed therein. Nothing whatsoever in the '097 or '334 Interferences could be even considered a basis for arguing that there exist Amgen admissions confirming obviousness over claim 10 of the '016 patent.

Finally, the legal issue of whether two claims are "patentably distinct" requires comparison of the two claimed inventions ***as a whole***. *See Gen. Foods*, 972 F.2d at 1280. Thus, even if particular aspects of a claimed invention were known in the art at the relevant time or claimed in another patent —which is ***not*** the case here — that does not compel a holding of obviousness-type double patenting. The inventions claimed in the asserted claims would not have been obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 91-110.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 23

Disputed. Roche mischaracterizes and misinterprets and takes out of context the interference records involving Dr. Lin's various inventions.

There were three *Fritsch v. Lin* interferences: (1) Interference No. 102,096 in which the count corresponded to DNA encoding erythropoietin, *i.e.* claim 2 of the '008 patent, *see* 21 U.S.P.Q.2d 1731, 1733 (BPAI 1991); (2) No. 102,097 in which the count corresponded to the

process of producing in vivo biologically active erythropoietin, *i.e.* then-pending claim 65 of the '179 application, *see* 21 U.S.P.Q.2d 1737, 1738 (BPAI 1991); and (3) 102,334 in which the count corresponded to a non-naturally occurring erythropoietin glycoprotein, *i.e.* then-pending claim 76 of the '178 application, *see* 21 U.S.P.Q.2d 1739, 1740 (BPAI 1991). To be clear, there was no interference involving the '016 patent, and Roche points to nothing in any of the *Fritsch v. Lin* interferences that even touches upon the purification process claimed by Drs. Strickland and Lai in the '016 patent.

In this instance, Roche takes a single sentence out of context from Lin's '097 interference brief. *See* D.I. 495, Ex. I, at 25-26.[1] Indeed, Roche takes the sentence so far out of context that, as a preliminary matter, it must be pointed out that Roche misrepresents the very claims to which the sentence pertained. Roche states that the argument pertained to the claims of the '178 application, when in fact the sentence clearly has nothing whatsoever to do with the claims of the '178 application or even the count of the '334 Interference, but rather pertains solely to the count of the '097 Interference.

With regard to the '179 application, the claims of which did in fact correspond to the '097 Interference, Roche ignores the express representations by Amgen during the interference, ignores the context for the argument quoted and truncated by Roche, and ignores the express representations by the Patent Office itself.

First, Amgen made clear during the '097 interference that it rejected the notion that the DNA and process claims were the same invention. In fact, the "manifestations of the same

---

[1] The full text of the sentence reads: "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, 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 as acknowledged by Fritsch et al in their

invention" phrase was language used by G.I.'s Fritch in the context of moving to combine the two interferences. In its Opposition G to that motion, Amgen, after quoting Fritch's position, stated:

> Since Fritsch does not even attempt to supply any argument or evidence in support of the bare allegation of "same invention", it is apparent that it was not a serious contention. Suffice it to say that Lin contends that the two counts are not to the "same invention". D.I. 547, Ex. 22, at 81(emphasis in original).

Further, when Amgen actually addressed the issue of obviousness during the '097 interference (as opposed to priority), Amgen expressly stated:

> Furthermore, it was not obvious that in vivo biologically active recombinant human EPO could be made by the claimed process. Until Lin obtained the sequence, Browne used it in expression and Egrie with Dukes found the product had in vivo biological activity, the process at best was only a wish." D.I. 495, Ex. I, at 56.

Thus, there can simply be no dispute that Amgen regarded its DNA invention as separate, distinct and non-obvious from its subsequent process invention.

Second, the sentence Roche cites belonged to a portion of Lin's '097 Brief discussing the issue of who, as between Fritch and Lin, was first to invent the count at issue in the '097 interference (a process claim). In its argument, Amgen referred to this Court's findings in the *Amgen v. Chugai* case, in which Magistrate Saris found not only that Dr. Lin was first to clone the gene for erythropoietin (a necessary starting material for the process count of the '097 Interference), but also first to produce in vivo biologically active polypeptide using that gene sequence. *Amgen, Inc. v. Chugai Pharmaceuticals Co.*, 13 U.S.P.Q.2d 1737, 1748-50 (D. Mass. 1989), *aff'd,* 927 F.2d 1200 (Fed. Cir. 1991). Based on Magistrate Saris' findings and opinion and Fritsch's own arguments, Fritsch could never be first to invent the process count of the '097

Motion Q herein (and Motion G in Interference No. 102,096)."

Interference because he didn't have the starting material (the DNA), because Amgen was first in the race with respect to producing in vivo active erythropoietin, and because Fritsch himself had argued, then conceded, that everything rose and fell with who was first with respect to the DNA. *Fritsch v. Lin*, 21 U.S.P.Q.2d 1737, 1738 (BPAI 1991) ("We note that Fritsch conceded at final hearing that priority in each of the related interferences turns on isolation of the EPO gene.") Amgen made several arguments based on these facts, summarized in the "Summary of Lin's Position" section of the brief (but truncated by Roche), and more fleshed out throughout the remainder of the brief.

To that end, Amgen argued:

> Since the Federal Circuit has found that Lin was the first to have a conception of the DNA sequence (upon reduction to practice), and ***it has not been questioned that Lin produced <u>in vivo</u> biologically active recombinant human EPO before Fritsch et al even conceived of the DNA sequence, it follows that Lin is entitled on the record to priority as to the present count***. The argument presented by Fritsch et al in favor of priority based on his version of a probing method for possible use (FB 21-31) totally disregard the Courts' finding that conception of the purified and isolated EPO gene did not occur until the gene was reduced to practice. ***Fritsch had no concept of the constitution of the gene before the gene was isolated and identified. By that time, Lin had expressed recombinant human EPO and found it to have <u>in vivo</u> biological activity***. D.I. 495, Ex. I, at 36-37 (emphasis added).

And:

> As to why the Federal Circuit decision should govern in an application v. application interference, as here, Lin notes that the Courts' findings on the priority evidence considered in the litigation established that Lin is the prior inventor of not only the DNA sequence and host cells transformed therewith at issue in Interference No. 102,096, ***but that he had used this sequence and transformed mammalian host cells to produce <u>in vivo</u> biologically active recombinant human EPO***. *Id.* at 29 (emphasis added).

And:

> The ***expression*** and isolation of the expression product as required to test for <u>in vivo</u> biological activity clearly meet the limitations of the

> present process count. Hence, it is not necessary to go beyond the undisputed facts as found by the District Court and left unchanged by the Federal Circuit to determine that Lin's expression and determination of in vivo biological activity of the expressed product satisfies all of the limitations of the count of the present interference and represents reduction to practice by Lin well prior to the Fritsch et al conception date. ***However, the present Lin record also includes further confirmation that the expression and testing referred to by the District Court constituted reduction to practice of the process of the count. See, for example, the testimony of Drs. Browne and Egrie that the work which they did on Lin's behalf involved all of the features of the Count (LR 30, 67, 68). Lin also confirmed this (LR 5)***. *Id.* at 39 (emphasis added).

Moreover, the very fact that the Board declared three separate interferences with three separate counts means that the patent office considered these counts to be patentably distinct. "A 'count' defines the interfering subject matter between (1) two or more applications or (2) one or more applications and one or more patents. When there is more than one count, ***each count shall define a separate patentable invention***." 37 C.F.R. § 1.601(f) (1988 and 1990) (emphasis added). And in this case, Examiner Howard Schain, John Kittle, the Director of Group 180, and Jeffrey Samuels, the Acting Commissioner of Patents and Trademarks expressly stated:

> More particularly, Interference No. 102,096 involves a host cell and a DNA sequence encoding EPO. Interference No. 102,097 involves a method of using the host cell to make rEPO. The new interference ['334] will involve rEPO. ***While the subject matter of the three interferences is deemed to be patentably distinct***, that subject matter is nevertheless related.

D.I. 547, Ex. 20, at 2 (emphasis added).

Thus, both Amgen and the patent office consistently maintained that the inventions were separate, patentably distinct, non-obvious inventions.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 24

Disputed. Roche mischaracterizes and misinterprets and takes out of context the interference records involving Dr. Lin's various inventions. See above response to Roche's "statement of fact" No. 23, which is incorporated herein.

Roche's "Statement of Fact" No. 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. & 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.

Amgen's Response to Statement No. 25

Disputed. This "statement of fact" is incorrect. Roche mischaracterizes and misinterprets and takes out of context the interference records involving Dr. Lin's various inventions. See above response to Roche's "statement of fact" No. 23, which is incorporated herein.

Neither Amgen, nor Dr. Lin, nor the Interference Board determined that Dr. Lin's erythropoietin product and process inventions involved in the interferences involved no "inventive activity" once the DNA sequence was isolated. For his part, Dr. Lin explained that

much of the implementation of various aspects of his invention were carried out by others at his request. Nothing in the interference record suggests that the process for making *in vivo* biologically active erythropoietin in heterologous expression systems or the product itself were non-inventive. *See* Response to Statement No. 20 *supra.* Roche makes an illogical and unsupported leap from the fact of an inventor using others as a pair of hands to arguing "no inventive activity." For its part, the Board determined that Dr. Lin was the appropriate named inventor on the grounds that an inventor need not be "personally involved in carrying out process steps defined by the count where ***implementation*** of the steps does not require the exercise of inventive skill." 21 U.S.P.Q.2d 1737, 1739. The Board also expressly found that although Dr. Lin did not personally perform all aspects of his invention, "the expression system of the EPO gene in mammalian host cells using the DNA sequence isolated by Dr. Lin ***was carried out at Lin's request and on his behalf***." *Id.* (emphasis added). The Board made no findings even relating to whether the invention of the '097 Interference Count was non-inventive, and indeed the very declaration of an interference indicates the Board's determination that the Count is patentable subject matter. 37 C.F.R. § 1.601(i) ("An interference may be declared between two or more pending applications naming different inventors when, in the opinion of an examiner, the applications contain claims for the same ***patentable*** invention.") (emphasis added).

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 26

Disputed. Roche mischaracterizes and misinterprets and takes out of context the interference records involving Dr. Lin's various inventions. See above response to Roche's "statement of fact" No. 25, which is incorporated herein.

Roche makes another illogical leap and argues that the BPAI agreed with Amgen's statement at pages 25-26 of its interference brief when the Board held that Lin was the proper inventor. *See also* Roche Br. (D.I. 491) at 9. Roche confuses the legal doctrine of inventorship (which was separately argued by Amgen in the '097 Interference Brief (D.I. 495, Ex. I) starting at page 57) with that of priority (which was argued by Amgen at pages 28-48 of the '097 Interference Brief) and then apparently conflates those with obviousness-type double patenting over the Lai purification patent. The BPAI properly held in the '097 Interference that the inventor himself need not be "personally" involved in the "implementation" of the steps of a claimed process, and that "[t]he expression of the EPO gene in mammalian host cells using the DNA sequence isolated by Dr. Lin was carried out at Lin's request and on his behalf." 21 U.S.P.Q.2d 1737, 1739. The Board did ***not*** hold that the invention claimed by the Count of the '097 Interference required no inventive skill. As accepted by the Patent Office, the fact that Lin was able to achieve production of a recombinant obligate glycoprotein with the proper glycosylation in mammalian host cells so as to obtain an in vivo biological active erythropoietin glycoprotein, warranted a patent, irrespective of whether or not the steps themselves required no more than ordinary skill to implement.

Roche's "Statement of Fact" No. 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).

Amgen's Response to Statement No. 27

Disputed. The suggestions made by Roche regarding this "statement of fact" are incorrect. Roche mischaracterizes and misinterprets and takes out of context the interference

records involving Dr. Lin's various inventions. See above responses to Roche's "statement of fact" Nos. 25 and 26, which are incorporated herein. The Interference Board did ***not*** determine that the Count of the '097 Interference involved no inventive activity or no more than ordinary skill. While it is true that Dr. Lin requested others at Amgen to carry out tasks which, when considered in isolation, required no inventive input, Roche expands this concept beyond its proper scope to a purported admission that somehow the inventions themselves were non-inventive. Each time, Roche fails to consider the claims as a whole, the state of the prior art, and instead focuses on discrete aspects of the claims which Dr. Lin directed others to implement. Roche's approach infuses Dr. Lin's achievements with hindsight and is improper.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 28

Disputed. Roche mischaracterizes and misinterprets and takes out of context the interference records involving Dr. Lin's various inventions. See above responses to Roche's "statement of fact" Nos. 25, 26 and 27, which are incorporated herein. Neither Amgen nor Dr. Lin admitted that the inventions conceived by Lin and implemented at his request would have been obvious. Roche points to nothing other than the fact that certain routine tasks required to implement the inventions conceived by Lin were performed by others at his request. Such routine implementation of another's invention does not render the invention obvious or non-inventive. Even if certain tasks performed at Lin's request to implement his inventions required no further instructions from Lin, that fact does not demonstrate that the combination or result

conceived by Lin was obvious. Roche's argument ignores the inventive conception of Lin and wrongly focuses instead on the routine implementation needed to reduce Lin's conception to practice. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 117, 123.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 29

Disputed. Roche mischaracterizes and misinterprets and takes out of context the interference records involving Dr. Lin's various inventions. See above responses to Roche's "statement of fact" Nos. 25-28 which are incorporated herein. Neither Amgen nor Dr. Lin admitted that the necessary tasks for implementing Dr. Lin's inventions would have been obvious. Roche points to nothing other than that certain of the tasks were implemented by others using routine skill. Even if Dr. Lin had provided no specific instructions regarding certain tasks he requested, he was supervisor of the EPO project and all tasks were performed at his request and on his behalf. Roche's approach infuses Dr. Lin's achievements with hindsight and is improper.

Roche's "Statement of Fact" No. 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 posttranslational 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.

Amgen's Response to Statement No. 30

Disputed. Roche mischaracterizes the Examiner's 9/1/93 rejection (D.I. 501, Ex. N-1, at 5-6) and Amgen's 1/31/94 argument in response (D.I. 495, Ex. L, at 2, 5-6). The Examiner rejected then pending claim 65 on the ground that the claim, as then written, entailed a process involving DNA encoding human EPO, but claimed a process for production of any desired polypeptide having biological activity. "It is noted," the Examiner wrote, "that the instant rejection could be overcome by amending the claim to recite "a process for the production of a biologically active human erythropoietin." Amgen responded by adopting the Examiner's suggestion, cancelling the claim, and submitting new independent claims 70 and 71which restricted the claimed process to the production of biologically active glycosylated erythropoietin polypeptide. Noting that the specification disclosed two different working examples of COS and CHO cells, both shown by Lin to be useful in practicing the claimed process, Amgen properly argued that the teachings of Lin's specification, combined with the knowledge of other mammalian cells capable of effecting glycosylation of expressed polypeptides, enabled the claimed invention. Nothing in that exchange constitutes an admission of Amgen that it would have been obvious, before Lin and without the teaching of his specification, to practice the methods claimed by Lin. It was not known until ***after*** Dr. Lin's inventions that mammalian cell lines would be capable of glycosylating recombinant erythropoietin as claimed in the claims of the '179 application. *See, e.g.,* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., ¶¶ 40-42.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 31

Disputed. This "statement of fact" is a gross mischaracterization of Amgen's actual statement to the PTO. Amgen made no such admission. Amgen's actual statement to the PTO was:

> The fact that both the starting material and the final product of the Lai process ***(neither of which are claimed in the Lai patent)*** are included within (dominated by) the recombinant product claims of the present application is not a basis for a double patenting rejection.

D.I. 501, Ex. M-4, at 3 (underlining in original, other emphasis added).

Roche's "Statement of Fact" No. 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 Response to Statement No. 32

Disputed and immaterial. This "statement of fact" is not a fact at all, but rather an argument regarding a legal conclusion. Moreover, this legal argument is irrelevant because, as Amgen explained to the PTO, neither the starting material nor the final product of the Lai process is claimed in '016 claim 10. D.I. 501, Ex. M-4, at 3; *see also* D.I. 501, Ex. L.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 33

Disputed and immaterial. The opinions expressed in Dr. Lodish's expert reports in the *Columbia* case do ***not*** support Roche's argument that the inventions claimed in Dr. Lin's patents-in-suit were obvious and well known. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 111-124 and Ex. Z; D.I. 495, Ex. N. As Dr. Lodish explains in his accompanying declaration:

> The fact that various techniques were known and practiced in the art hardly means that Lin's particular combination of techniques to solve several long-standing and highly challenging problems that others repeatedly tried but failed to solve would have been obvious. The notion is akin to the argument that a Monet painting would have been obvious because others before Monet had used paint brushes, paint, and canvas to paint water lilies. It is true that workers of ordinary skill in the art had various types of cultured cells that could be used as host cells in transformation experiments and that CHO cells were among the different cell types that could be used as host cells for DNA transformation and recombinant protein production. It was also known that amplified genes could be selected by exposing cells to selection pressure and that the dihydrofolate reductase (DHFR) gene was one of several approaches that could have been used as an amplifiable selectable phenotype. Exogenous promoters, including viral promoters, were known to function in many types of cultured mammalian cells. My opinion that these techniques could be used to express recombinant proteins generally is consistent with my opinions in this case.
>
> . . . .
>
> In this case, it is the novel and inventive way in which Lin combined and used these techniques — techniques that could be used in any number of ways by different artisans for different purposes — that provides the significant difference between the claims-in-suit and claim 10 of the '016 patent. In my opinion, nothing in claim 10 of the '016 patent suggests Lin's claimed use and application of these techniques as claimed in the Lin claims-in-suit.

6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 117, 123.

Moreover, the legal issue of whether two claims are "patentably distinct" requires comparison of the two claimed inventions ***as a whole***. *See Gen. Foods*, 972 F.2d at 1280. Even if particular aspects of a claimed invention were known in the art at the relevant time or claimed in another patent —which is ***not*** the case here — that does not compel a holding of obviousness-type double patenting. The inventions claimed in the asserted claims would not have been

obvious to one of ordinary skill in the art at the relevant time. *See* 6/29/07 Declaration of Harvey F. Lodish, Ph.D., at ¶¶ 91-110.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 34

Disputed and immaterial. The opinions expressed in Dr. Lodish's expert reports in the *Columbia* case do ***not*** support Roche's argument that the inventions claimed in Dr. Lin's patents-in-suit were obvious and well known. See above response to Roche's "statement of fact" No. 33, which is incorporated herein.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 35

Disputed and immaterial. The opinions expressed in Dr. Lodish's expert reports in the *Columbia* case do ***not*** support Roche's argument that the inventions claimed in Dr. Lin's patents-in-suit were obvious and well known. See above response to Roche's "statement of fact" No. 33, which is incorporated herein.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 36

Disputed and immaterial. The opinions expressed in Dr. Lodish's expert reports in the

Columbia case do ***not*** support Roche's argument that the inventions claimed in Dr. Lin's patents-in-suit were obvious and well known. See above response to Roche's "statement of fact" No. 33, which is incorporated herein.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 37

Disputed and immaterial. The opinions expressed in Dr. Lodish's expert reports in the *Columbia* case do ***not*** support Roche's argument that the inventions claimed in Dr. Lin's patents-in-suit were obvious and well known. See above response to Roche's "statement of fact" No. 33, which is incorporated herein.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 38

Disputed and immaterial. The opinions expressed in Dr. Lodish's expert reports in the *Columbia* case do ***not*** support Roche's argument that the inventions claimed in Dr. Lin's patents-in-suit were obvious and well known. See above response to Roche's "statement of fact" No. 33, which is incorporated herein.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 39

Disputed and immaterial. The opinions expressed in Dr. Lodish's expert reports in the

Columbia case do ***not*** support Roche's argument that the inventions claimed in Dr. Lin's patents-in-suit were obvious and well known. See above response to Roche's "statement of fact" No. 33, which is incorporated herein.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 40

Disputed and immaterial. The opinions expressed in Dr. Lodish's expert reports in the *Columbia* case do ***not*** support Roche's argument that the inventions claimed in Dr. Lin's patents-in-suit were obvious and well known. See above response to Roche's "statement of fact" No. 33, which is incorporated herein.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 41

Disputed. This "statement of fact" is not a fact at all. It is an erroneous statement of the requirements for applicability of the two-way double patenting test. The determination of whether the one-way or two-way test applies is a question of law. *See In re Berg*, 140 F.3d 1428, 1432 (Fed. Cir. 1998). The two-way test must be used if: (1) the applicant could not have filed both claims together in the earlier-filed application;[2] and (2) the applicant did not cause the

[2] *See, e.g.*, *Berg*, 140 F.3d at 1434-37; MPEP § 804(II)(B)(1)(a) (D.I. 495, Ex. O, at 14).

later-filed claim to issue first by delaying examination of the earlier-filed claim during the period when both applications were pending before the PTO (the "co-pendency period").[3]

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 42

It is undisputed that "[a]ll the patents-in-suit claim priority to Application Serial No. 06/561,024 ("the '024 application") filed December 13, 1983," and that "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." The remainder of this "statement of fact" is argument regarding a disputed legal conclusion. *See In re Berg*, 140 F.3d 1428, 1432 (Fed. Cir. 1998) (The determination of whether the one-way or two-way test applies is a question of law.). Amgen's response to Roche's flawed legal argument is set forth in Part III.B.1 of Amgen's opposition to Roche's motion for summary judgment. *See also*, D.I. 503, at ¶¶ 11-16 ('016 claimed inventions neither conceived nor reduced to practice as of November 30, 1984 filing date of '298 application); D.I. 501, Ex. H (examination of '298 application not delayed by Amgen during co-pendency period from June 20, 1985 to May 19, 1987).

Roche's "Statement of Fact" No. 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

[3] *See, e.g.*, *In re Emert*, 124 F.3d 1458, 1461 (Fed. Cir. 1997); *Engineered Prods. Co. v. Donaldson Co., Inc.*, 225 F. Supp. 2d 1069, 1111 (N.D. Iowa 2002).

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).

Amgen's Response to Statement No. 43

Disputed and immaterial. This "statement of fact" is not a fact at all, but rather an argument regarding a legal conclusion. The first requirement for application of the two-way double patenting test is that the applicant could not have filed both claims together ***in the earlier-filed application***. *See, e.g.*, *Berg*, 140 F.3d at 1434-37; MPEP § 804(II)(B)(1)(a) (D.I. 495, Ex. O, at 14). Thus, to the extent Roche is arguing that the '016 claims and Dr. Lin's claims could have been combined together in an application filed sometime ***after*** Dr. Lin's earlier-filed '298 application, this argument is legally irrelevant. Any suggestion that the '016 claims could have been included as part of Dr. Lin's earlier-filed '298 application is incorrect and contrary to the undisputed evidence that the '016 inventions were not conceived or reduced to practice as of the November 30, 1984 filing date of Dr. Lin's '298 application. D.I. 503, at ¶¶ 11-16; *see also* D.I. 504, at ¶¶ 32-34 (explaining how the '016 claims "are directed to a new and non-obvious combination"); D.I. 502, at ¶¶ 59-61 (similar). Thus, it was impossible — both as a practical matter and a legal matter under 35 U.S.C. § 112 — for Amgen to have filed the '016 claims as part of the earlier-filed applications that gave rise to the patents-in-suit.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 44

Immaterial. This "statement of fact" is not a fact at all, but rather an argument regarding

a legal conclusion. Moreover, it is legally irrelevant to Roche's summary judgment motion because the first requirement for application of the two-way double patenting test is that the applicant could not have filed both claims ***together in the earlier-filed application***. *See, e.g.*, *Berg*, 140 F.3d at 1434-37; MPEP § 804(II)(B)(1)(a) (D.I. 495, Ex. O, at 14). It is legally irrelevant whether the '016 claims and Dr. Lin's claims could have been combined together in a continuation-in-part application filed sometime ***after*** Dr. Lin's earlier-filed '298 application.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 45

Immaterial. This "statement of fact" is not a fact at all, but rather an argument regarding a legal conclusion. Moreover, it is legally irrelevant to Roche's summary judgment motion because the first requirement for application of the two-way double patenting test is that the applicant could not have filed both claims ***together in the earlier-filed application***. *See, e.g.*, *Berg*, 140 F.3d at 1434-37; MPEP § 804(II)(B)(1)(a) (D.I. 495, Ex. O, at 14). It is legally irrelevant whether the '016 claims and Dr. Lin's claims could have been combined together in a continuation-in-part application filed sometime ***after*** Dr. Lin's earlier-filed '298 application.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 46

Immaterial. This "statement of fact" is not a fact at all, but rather an argument regarding a legal conclusion. Moreover, it is legally irrelevant to Roche's summary judgment motion because the first requirement for application of the two-way double patenting test is that the

applicant could not have filed both claims ***together in the earlier-filed application***. *See, e.g.*, *Berg*, 140 F.3d at 1434-37; MPEP § 804(II)(B)(1)(a) (D.I. 495, Ex. O, at 14). It is legally irrelevant whether the '016 claims and Dr. Lin's claims could have been combined together in a continuation-in-part application filed sometime ***after*** Dr. Lin's earlier-filed '298 application.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 47

Disputed. All the patents-in-suit claim priority to Dr. Lin's '298 application (and earlier applications). *See* D.I. 501, Exs. C-G. The '298 application was filed several months before the '119 application. *Compare* D.I. 501, Ex. H-1 *with* D.I. 501, Ex. K. A restriction requirement imposed by the PTO on July 3, 1986 (over one year after the '119 application was filed) forced Amgen to prosecute the inventions claimed in the patents-in-suit in separate applications from the DNA inventions elected for prosecuted in the '298 application. D.I. 501, Ex. H-8. Repeated rejections on the same or similar grounds as the patent office struggled to apply new technology to complicated claims took extensive time. PTO interference proceedings delayed examination of the '178 and '179 applications by ***3-4 years.*** *See* D.I. 501, Ex. A. And even Dr. Lin's '008 patent, which issued from the original '298 application, nonetheless issued ***after*** the '016 patent. D.I. 501, Ex. B.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 48

Disputed and immaterial. Roche's expert asserts these "facts" in a conclusory manner, without any citation to supporting evidence in the prosecution history. *See* Sofocleous Decl. (D.I. 493) ¶ 7 and Ex. 2. Even if true, these facts would be legally irrelevant because the only delay relevant to determining applicability of the two-way double patenting test is delay during the co-pendency period that caused the later-filed patent to issue first. As explained in Part III.B.1 of Amgen's opposition to Roche's motion for summary judgment, Amgen did not delay examination of Dr. Lin's '298 application during the co-pendency period from June 20, 1985 to May 19, 1987. *See also* D.I. 501, Ex. H (examination of '298 application not delayed by Amgen during co-pendency period from June 20, 1985 to May 19, 1987). The instances of purported delay identified by Roche are irrelevant because, even if they had not occurred, the '016 claims still would have issued before Dr. Lin's claims-in-suit.

Moreover, the suggestions of intentional delay are completely false. Even though Amgen had claims to DNA and host cells starting in October of 1987, Amgen had ***no*** patent to enforce against foreign manufacturers who might have sought to import a recombinant erythropoietin product for commercial sale. Indeed, Amgen lost a patent-based International Trade Commission action against a Japanese competitor during that time because Amgen was without a process patent. *Amgen, Inc. v. U.S. Int'l Trade Comm'n*, 902 F.2d 1532, 1538 (Fed. Cir. 1990). Repeated rejections on the same or similar grounds as the patent office struggled to apply new technology to complicated claims took extensive time.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 49

Disputed. This "statement of fact" is incorrect and speculative. In response to Examiner's July 1986 restriction requirement, Amgen selected claims to the ***DNA*** (not polypeptide) and process inventions, which had been assigned to restriction Group II, for continued examination in the '298 application. D.I. 501, Ex. H-8, at 3. Amgen was later forced to drop its process claims from the '298 application as a result of the PTO's improper *In re Durden* rejection. *See* D.I. 501, Exs. H-13, at 7, H-14, H-15, at 1, 6. In order to place the '298 application in a condition for allowance, Amgen was forced to choose between appealing the improper rejection by the Examiner to the Board of Patent Appeals and Interferences, or prosecuting the rejected process claims in a separate application to permit the '298 application to issue without the rejected process claims. An appeal would have entailed an indeterminate delay while the appeal was decided and prosecution was thereafter resumed. Thus, any delay was the inevitable result of the PTO's improper application of *In re Durden* to the process claims. Several years later the Federal Circuit overruled the *per se* application of *In re Durden*, whereupon the Patent Office policy regarding such claims changed. *See In re Ochiai*, 71 F.3d 1565, 1570 (Fed. Cir. 1995) (stating that there is no *per se* rule "that a process claim is obvious if the prior references disclose the same general process using 'similar' starting materials"); *In re Brouwer*, 77 F.3d 422 (Fed. Cir. 1996).

Moreover, Roche's suggestion that the '868 patent might have issued before the '016 patent if the process claims had been prosecuted to issuance in the '008 patent is speculation, not "fact." There is no reason to infer — especially on summary judgment — that these claims would have avoided an interference proceeding, or that they would have issued before the '016

patent on May 19, 1987. Even without the process claims, Dr. Lin's '008 patent nonetheless issued ***after*** the '016 patent, on October 27, 1987. *See* D.I. 501, Ex. B.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 50

Amgen demonstrated that Dr. Lin's claims were patentably distinct from the '016 claims under both the "one-way" and "two-way" double patenting tests. D.I. 501, Ex. N-2, at 11-12. The Examiner correctly determined that the two-way test governed the ODP analysis, and that Dr. Lin's claims were patentably distinct from the '016 claims under the two-way test. D.I. 501, Ex. N-3, at 2. For the reasons explained by Amgen's counsel during prosecution of the '179 application (D.I. 501, Ex. N-2, at 11-12), and also in Part III.B.3 of Amgen's opposition to Roche's motion for summary judgment, the Examiner's remark that "the instantly claimed method is an obvious variation of the process of Lai et al." is incorrect as a matter of law.

Roche's "Statement of Fact" No. 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.

Amgen's Response to Statement No. 51

Disputed. The determination of whether the one-way or two-way test applies is a question of law. *In re Berg*, 140 F.3d 1428, 1432 (Fed. Cir. 1998). Therefore, this "statement of fact" is not a fact at all, but rather an argument regarding a legal conclusion. Amgen's response to Roche's flawed legal argument is set forth in Part III.B.1 of Amgen's opposition to Roche's motion for summary judgment. *See also*, D.I. 503, at ¶¶ 11-16 ('016 claimed inventions neither conceived nor reduced to practice as of November 30, 1984 filing date of '298 application); D.I. 501, Ex. H (examination of '298 application not delayed by Amgen during co-pendency period from June 20, 1985 to May 19, 1987).

Dated: June 29, 2007

Respectfully Submitted,

AMGEN INC.,
By its attorneys,

/s/ Patricia R. Rich

D. Dennis Allegretti (BBO#545511)
Michael R. Gottfried (BBO# 542156)
Patricia R. Rich (BBO# 640578)
Christopher S. Kroon (BBO# 660286)
DUANE MORRIS LLP
470 Atlantic Avenue, Suite 500
Boston, MA 02210
Telephone: (857) 488-4204
Facsimile: (857) 488-4201

Lloyd R. Day, Jr. (*pro hac vice*)
DAY CASEBEER, MADRID & BATCHELDER LLP
20300 Stevens Creek Boulevard, Suite 400
Cupertino, CA 95014
Telephone: (408) 873-0110
Facsimile: (408) 873-0220

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

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

Of Counsel:

Stuart L. Watt
Wendy A. Whiteford
Monique L. Cordray
Darrell G. Dotson
Kimberlin L. Morley
Erica S. Olson
AMGEN INC.
One Amgen Center Drive
Thousand Oaks, CA 91320-1789
(805) 447-5000

CERTIFICATE OF SERVICE

I hereby certify that this document, filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of electronic filing and paper copies will be sent to those indicated as non-registered participants.

/s/ Patricia R. Rich
Patricia R. Rich