EXHIBIT 28

PART 2 OF 2

These results demonstrate that Dr. Eschbach used a pharmaceutical composition containing amounts of erythropoietin sufficient to cause increases in reticulocyte count, plasma iron clearance rate (i.e., ferrokinetic effects), erythroid cells in the marrow, and red cell mass. Therefore, the Eschbach Sheep Study discloses the use of a "therapeutically effective amount" of EPO as that term has been construed by the Federal Circuit.

Based on the results of his sheep study, Dr. Eschbach repeatedly predicted the administration of EPO to humans would be effective in treating anemia. See, for example:

> Dr. Eschbach predicted "that if and when human EPO became available in sufficient quantities, it would correct the anemia...." (ESCH 0000022-24 at 24).
>
> "These results predict that Ep therapy should be effective in treating the anemia of CRF in humans." (ESCH 0000025-31 at 26).
>
> "These animal studies suggest that Ep therapy should correct the hypoproliferative anemia of CRF." (ESCH 0000025-31 at 30).
>
> "In addition, the experience with the sheep model suggested that Epo worked equally well in the uremic and normal condition, predicting that it would be effective in uremic humans." (ESCH 0000058).
>
> "...we speculated that Epo would be effective in human CRF if and when Epo became available." (ESCH 0000059).

Amgen confirmed the predictability of using an EPO pharmaceutical composition in humans based on the results of Dr. Eschbach's Sheep Study by referring to the sheep study in its orphan drug application in 1986, stating "the sheep model of stable or progressive ESRD used in Eschbach's study mimics that seen in human disease." Further, Amgen stated in the same application "...Eschbach, et al., (1984) were able to demonstrate the efficacy of erythropoietin in uremic sheep." (AM-ITC 00081295)

Therefore, based on Eschbach's study, it would have been obvious to one skilled in the art to create a pharmaceutical composition comprised of a therapeutically effective amount of human erythropoietin and a pharmaceutically acceptable diluent, adjuvant or carrier.

6. Baron, Goldwasser, Essers, and Eschbach Render The Asserted Claims of the '933 Patent Obvious

In addition to invalidating claim 1 of the '422 patent, the foregoing clinical studies also render claims 3, 7, 8, 9[1], 11, 12, and 14 of the '933 patent obvious. As demonstrated herein, *supra* at subsection C.8, and in the Expert Reports of Dr. John Lowe and Dr. Rodney Kellems, one of skill in the art as of the time of the application of the patents-in-suit would have found it obvious to create a DNA clone encoding human erythropoietin and expressing such a cDNA in a mammalian host cell, such as a CHO cell. Once the skilled worker had recombinant human erythropoietin, it would have been obvious to develop pharmaceutical compositions with a "diluent, adjuvant, or carrier" for use in clinical trials to demonstrate the "in vivo biological property of causing bone marrow cells to increate production of reticulocytes and red blood cells," as well as "treating a kidney dialysis patient...in an amount to increase the hematocrit level of said patient."

For example, the Goldwasser and Baron Hamster study discloses a pharmaceutical composition comprising urinary erythropoietin and human serum albumin, a commonly known diluent. This study demonstrated an increase in hematocrit levels of up to 40% compared to control patients. *See supra.* Similarly, Dr. Eschbach's Sheep Study demonstrated the use of a

[1] The Court in this case has already held that claim 9 of the '933 was invalid for lack of definiteness. *See Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 165 (D. Mass. 2001), *aff'd in part*, 314 F.3d 1313, 1342 (Fed. Cir. 2003). The Federal Circuit in its August 2006 opinion reiterated this holding that claim 9 of the '933 patent was invalid. *See Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1299 n.5 (Fed. Cir. 2006)

pharmaceutical composition containing sufficient amounts of erythropoietin from sheep plasma to cause increases in reticulocyte count, plasma iron clearance rate (i.e., ferrokinetic effects), erythroid cells in the marrow, and red cell mass. *See supra.*

In fact, Dr. Lin testified in his deposition that once recombinant erythropoietin worked in mice, there would be a "reasonable expectation" that it would work in humans. For example, Dr. Lin testified as follows:

> THE WITNESS: By then, we already know the recombinant human erythropoietin is
> biologically active in vivo, which we would expect it would be pharmaceutical --
> therapeutically useful.
> BY MS. BEN-AMI:
> Q Now, when you say that at that point, you knew it was biologically active in vivo,
> under what system?
> A In the animal system.

Lin Tr., dated 3/28/07, at 108-109,

> ...By November 30th, 1984, had you determined that if it worked in a mouse, the
> EPO would work in a human?
> [objection]
> THE WITNESS: I would think so.
> The reason is that -- one would probably worry it would not work in mice because there would be a difference between mice and human. If it work in mice, have a very good chance it would work in human.
> BY MS. BEN-AMI:
> Q So it was your understanding on November 30, 1984, that if EPO would work in
> mice, there would be a reasonable expectation it would work in humans?
> A That's correct.

Lin Tr., dated 3/28/07, at 110.

> Q When you were doing your work on EPO, when did you come to a complete understanding

that you could make a pharmaceutically -- a pharmaceutical composition as is written out in
claim 1 of the '422 patent?
[objection]
THE WITNESS: I'm not expert to --I'm not even qualified to explain the claim.
But let me just put it this way: To say that after probably March, '84, once we have expressed erythropoietin gene that show that it have the in vivo activity, now we could expect that it could be -- would expect it would be useful for use in -- for use in patients which would require erythropoietin treatment such as patient under kidney dialysis, for example.
Q Okay.
So once you did what test?
A After we have obtained the in vivo activity in the animal test.
Q And all I'm asking you is what kind of test are you talking about?
A The mouse test, yeah.
At that time, was tested in mice.
Q Okay.
And once you did that, you conceived -- you had a fixed understanding that the EPO you were producing would be therapeutically effective in humans?
[objection]
THE WITNESS: We -- from those data, we would expect that it would work in the --the human -- the clinical setting

Lin Tr., 3/29/97, at 375-377.

In fact, Dr. Lin also testified that once the EPO gene was expressed in a mammalian host cell, he fully expected that it would have biological activity.

Q My question was, whether you had the expectation when you had the genomic EPO gene
that when put into a mammalian cell and expressed, that the resulting EPO would be
biologically active?
[objection]
THE WITNESS: Of course, we would expect that it -- to be -- to have that activity -- in the biological activity.

Lin Tr., 3/29/07, at 367-368

This is further supported by the fact that all of the method of treatment claims in the patents-in-suit were supported by a specification which contained no data on human clinical trials, but only a single mouse study involving 7 mice. *See* '868 patent, col. 29, ln. 49-62.

Moreover, as detailed in Roche's prior supplemental response to interrogatory regarding double patenting based on the Lin '008 patent, Amgen repeatedly told the Patent Office in Interference Proceedings that the (1) DNA encoding erythropoietin and (2) the process for making a recombinant erythropoietin having in vivo biological properties were "the same invention." Amgen argued that the resolution of the priority and inventorship issues of the count of the DNA sequence, by "necessity," determined these issues for the process for making a recombinant biologically active protein. In particular, Amgen stated in briefing papers that:

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

Reply By Senior Party Lin, Interference Nos. 102,096 and 102,09, dated 1/25/90 at 3 (emphasis added).

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

Id. at 9. Amgen stated the following in its final brief to the Board:

> While the count is directed to a process for preparing in vivo biologically active EPO using a mammalian host cell transfected or transformed with an isolated DNA sequence encoding human EPO [i.e., the process patent claims], and the litigation was directed to the purified and isolated DNA sequence and host cells transfected

> or transformed thereby [i.e., the '008 DNA claims], **it is evident that these are only different manifestations of the same invention** as acknowledged by Fritsch et al in their Motion Q here (and in Motion G in Interference No. 102,096). Clearly, the whole purpose and intent of the purified and isolated DNA sequence encoding human EPO (and host cells transfected therewith) at issue in the litigation was to express in vivo biologically active human EPO. Stated otherwise, the process language of the Lin patent claims at issue in the litigation ("encoding human EPO") [see '008 patent claims] is, for all intents and purposes, a description of the present count. **One cannot be sure he has the sequence until he has successfully expressed in vivo biologically active human EPO.** This involves culturing the transfected cells and isolating the expression product to determine whether or not it has the required in vivo activity. Hence, the priority holding in the litigation is directly on point, notwithstanding the different statutory class of claims involved.

Brief for the Senior Party Lin, Interference No. 102,097, dated 7/29/91 at 25-26 (Ex. J) (emphasis added). Amgen urged the Patent Office Board that the process for making biologically active glycosylated EPO in vivo, (as recited in the process claims of the '868, '698 and '349 patents), ***is the same invention*** as the isolated DNA sequence and host cells, (as claimed by the earlier issued '008 patent). In fact, Amgen insisted that the claims of the '008 patent actually recite process steps, i.e., "encoding human EPO," that are identical to the process steps of the count because skilled workers would not know they had the EPO sequence until it was expressed in vivo to show biological activity. *See also* Brief for the Senior Party Lin, Interference No. 102,097, at 5, 10, 23-24, 27, 34, 57-58).

Thus, once it was obvious to make recombinant human erythropoietin in CHO cells (claims 3, 7, and 8), these foregoing clinical studies also made it obvious for one of skill in the art to create pharmaceutical compositions with adjuvants, diluents, or carriers to treat kidney dialysis patients in an amounts effective to increase hematocrit levels, reticulocytes, and red blood cells (claims 9, 11, 12, and 14).

7. Synthetic Gene

All of the asserted Lin patent claims are invalid under section 103 because it would have been obvious to a person of ordinary skill in the art having a synthetic gene encoding for human erythropoietin to use recombinant DNA cloning techniques known in the art prior to October 1983 to express the EPO gene in a CHO cell to obtain EPO. Therefore, prior to October 1983, each of the claimed processes, products and pharmaceutical compositions recited by each of the asserted Lin patent claims would have been obvious.

Several methods for synthesizing DNA and genes were known prior to October 1983. Specifically, U.S. Patent No. 6,936,694 having a priority date of April 15, 1983, discloses all of the key elements required for producing a gene sequence from a known peptide sequence. Additionally, several genes, such as human pro-insulin, human interferon-alpha 1 and human growth hormone, had been synthesized prior to October 1983 using the techniques known in the art. (Fromm paragraphs 20-50).

Using human urinary EPO, the peptide sequence for EPO could have been determined using the peptide microsequencing methods available in 1983. The introduction of the gas phase sequencer in 1981 reduced the amount of protein required for sequencing. Additionally, the prior art taught how to obtain purified EPO in amounts sufficient for sequencing EPO. (Miyake et al. (1977)). Dr. Goldwasser was able to isolate approximately 8mg of EPO using the method disclosed in Miyake et al. Amgen's scientist, Dr. Strickland was later able to reproduce the Miyake et al. method of purification. Therefore, obtaining the peptide sequence of erythropoietin would have been possible using the peptide microsequencing methods of 1983 assuming sufficient milligram amounts of highly purified EPO were available. In addition, prior to October 1983, the role of signal peptides was widely known and one of skill in the art could

have added an appropriate signal peptide to EPO to express the EPO gene in CHO cells. (Fromm paragraphs 51-71)

8. DNA cloning

All of the asserted Lin patent claims are invalid under section 103 because it would have been obvious to one of skill in the art prior to 1983 to isolate a DNA encoding human erythropoietin and then to produce an *in vivo* biologically active recombinant human erythropoietin by expressing such a DNA in a mammalian host cell, such as a CHO cell. Therefore, prior to October 1983, each of the claimed processes, products and pharmaceutical compositions recited by each of the asserted Lin patent claims would have been obvious.

Prior to October 1983, there were numerous cell lines available which could be used as sources of erythropoietin and erythropoietin mRNA. These cells or supernatant were made available to others prior to October 1983. (See Gaylis, Fisher & Shouval reports)

Prior to October 1983 it would have been obvious for the skilled practitioner with access to sufficient quantities of purified human EPO to construct a cDNA library from one of several EPO producing human cell lines and to isolate a human EPO cDNA by screening such a library with an appropriate oligonucleotide probe based on knowledge of the partial amino acid sequence of the protein. Using techniques known in the art and described in the available literature, the skilled practitioner would have had a reasonable expectation of success in obtaining a cDNA clone encoding EPO. Further, it would have been obvious for the skilled practitioner to use the EPO cDNA clone to clone and characterize the human EPO gene.

Prior to October 1983, one of skill in the art would have had a reasonable expectation of success in cloning the EPO gene using a cDNA library. Techniques for use in cDNA cloning were known in the art and described in available literature prior to 1983. Prior to 1983, scientists were using at least two standard approaches to "clone," or isolate genes from mammalian cells.

These two approaches were based on use of two types of large collections of cloned DNA fragments, commonly referred to as DNA libraries. The first approach used genomic DNA libraries, and the second used complementary DNA (cDNA) libraries. (Lowe paragraphs 30-42)

Provided one skilled in the art had a sufficient amount of hEPO protein, one would have had a reasonable expectation of success in isolating cDNA clones for EPO using degenerate oligonucleotide probe screening. Prior to October 1983, direct screening with a mixed pool of oligonucleotide probes, based on a partial amino acid sequence of a desired protein, had been established as a reliable method for screening genomic and cDNA libraries. Therefore, once one had sufficient information about the amino acid sequence of a protein to design appropriate probes, such screening methodology provided the skilled scientist with a reasonable expectation of success in cloning the gene for that protein. With sufficient amounts of protein, one could readily obtain sequence information for any number of different portions of the amino acid sequence using known techniques for protein sequencing. To use this methodology to screen a cDNA library for the EPO gene, one only needed enough information about the erythropoietin amino acid sequence to design a suitable degenerate oligonucleotide probe. Prior to October 1983, the design of suitable degenerate oligonucleotide probes could be obtained with small amounts of protein or peptide. (Lowe paragraphs 43-44)

The availability of purified EPO and EPO tryptic fragments from Dr. Goldwasser was necessary to Lin's cloning of the EPO gene. Without sufficient protein material, it was not possible to construct probes. According to Drs. Lin and Goldwasser, Goldwasser's purified urinary EPO was the only source available that was useful for sequencing. Further, Lin was only able to successfully clone the EPO gene after he received correct sequence information based on Dr. Goldwasser's tryptic fragments sent to Amgen in August 1983. Therefore, had Dr.

Goldwasser made purified EPO protein or tryptic fragments available to the public, the Lin patents would have been obvious. (Lowe paragraphs 45-60)

Additionally, an article published by Amgen's Scientist, Por Lai, prior to the filing of the November 11, 1984 application, disclosed the sequencing of the EPO tryptic fragments used to clone the gene. Por Lai, Technical improvements in protein microsequencing, *Analytica Chimica Acta, Volume 163, 1984, Pages 243-248.*

Prior to October 1983, methods for using highly degenerate oligonucleotide probes to screen libraries were well described in the art. It would have been obvious to one skilled in the art to generate suitable probes for screening a cDNA library from information about the amino acid sequence of tryptic fragments of the EPO protein. Further, it would have been obvious to one skilled in the art to use available EPO producing cell lines to construct a cDNA library from the mRNA of such EPO producing cells and to screen that library using the degenerate probes. (Lowe paragraphs 61-94)

Additionally, it would have been obvious to express the EPO gene in mammalian host cells such as CHO cells to produce a biologically active glycosylated protein. Dr. Lin himself testified that it was known that a COS cell is a quick way to express a gene. Dr. Lin also testified that the use of CHO cells was suggested to him by a curator at the ATCC. (Lowe paragraphs 95-134)

Prior to October 1983, each of the claimed processes, products and pharmaceutical compositions recited by each of the asserted Lin patent claims would have been obvious. None of the particular limitations found in any of the asserted claims define any further distinction that would have rendered the particular claimed products or processes non-obvious to one of skill in the art at the time. This is confirmed by the fact that Genetics Institute expressed rHuEPO in a

mammalian host cell, and purified it from the culture media prior to the filing of Lin's November 30, 1984 application. (Lowe paragraphs 135-171, 219-243)

Listed below is additional support for the assertion that all of the Lin patent claims are invalid under section 103 because it would have been obvious to one of skill in the art prior to 1983 to isolate a cDNA encoding human erythropoietin and then to produce an *in vivo* biologically active recombinant human erythropoietin by expressing such a cDNA in a mammalian host cell, such as a CHO cell:

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- AM-ITC 00364871-72
- AM-ITC 00372555
- AM-ITC 00372067-228
- AM-ITC 00364863-71
- AM-ITC 00367241-42
- AM-ITC 00367237-38
- AM-ITC 00370295
- AM-ITC 00373793
- AM-ITC 00364971-72
- AM-ITC 00364959-60
- AM-ITC 00364959
- AM-ITC 00364956-58
- AM-ITC 00367293
- AM-ITC 00364847-60
- AM-ITC 00364800
- AM-ITC 00369667-847
- AM-ITC 00364953-54
- AM-ITC 00364951-53
- AM-ITC 00373738-42
- AM-ITC 00364985-86
- AM-ITC 00364979-81
- AM-ITC 00364979
- AM-ITC 00364977
- AM-ITC 00370545-667
- AM-ITC 00364947-50
- AM-ITC 00364944-47
- AM-ITC 00364944-45
- AM-ITC 00364951

- AM-ITC 00373601-737
- AM-ITC 00373330-35
- AM-ITC 00364941-42
- AM-ITC 00364927-29
- AM-ITC 00378687
- AM-ITC 00364905-08
- AM-ITC 00373596
- AM-ITC 00364802
- AM-ITC 00374434
- AM-ITC 00174527
- AM-ITC 00113058-60
- AM-ITC 00148954
- AM-ITC 00784965-67
- AM-ITC 00414984-85
- AM-ITC 00145916-18
- AM-ITC 00211739-40
- AM-ITC 00874937-45
- AM-ITC 00172320-24
- AM-ITC 00138784-90
- AM-ITC 00239491-99
- AM-ITC 00347087-094
- AM-ITC 00168239-481
- AM-ITC 00138942-45
- AM-ITC 00050916-22
- AM-ITC 00841410
- AM-ITC 00148961-81
- AM-ITC 00113349-50
- AM-ITC 00113651-54
- AM-ITC 00148971
- AM-ITC 0013655-72
- AM-ITC 00074296
- AM-ITC 00373329
- AM-ITC 00168239-481
- AM-ITC 00113064-66
- AM-ITC 00347087-94
- AM-ITC 00113067
- AM-ITC 00932121
- AM-ITC 00373328
- AM-ITC 0033097
- AM-ITC 00113058-60
- AM-ITC 00113673
- AM-ITC 00051976-1135
- AM-ITC 00057704
- AM-ITC 00057723

- AM-ITC 00057735
- AM-ITC 00057708-18
- AM-ITC 0057689-701
- AM-ITC 00057687
- AM-ITC 00057688
- AM-ITC 00050918
- AM-ITC 00050919
- AM-ITC 00784956
- AM-ITC 00174334-35
- AM-ITC 00953205-225
- AM-ITC 00953210
- AM-ITC 00953223
- AM-ITC 00953277
- AM-ITC 00953214
- AM-ITC 00953220-221 (added to list)
- AM-ITC 00953221
- AM-ITC 00953222
- AM-ITC 00953233
- AM-ITC 00953699-700
- AM-ITC 00873694-95
- AM-ITC 00873748
- AM-ITC 00052045
- AM-ITC 00057704
- AM-ITC 00057723
- AM-ITC 00057735
- AM-ITC 00057708-18
- AM-ITC 00057689-701
- AM-ITC 00057687
- AM-ITC 00057688
- AM-ITC 00366019-21
- AM-ITC 00265548
- AM-ITC 00410931-411088
- AM-ITC 00410960-61
- AM-ITC 00410964
- AM-ITC 00368663
- AM-ITC 00364221
- AM-ITC 00378667
- AM-ITC 00378249
- AM-ITC 00368801
- AM-ITC 00364235-36
- AM-ITC 00376971
- AM-ITC 00378117-75
- AM-ITC 00376852
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- AM-ITC 00373325
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- AM-ITC 00364799-800
- AM-ITC 00364901
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- Deposition of Eugene Goldwasser (not on original list)
- Deposition of Eugene Goldwasser (not on original list)
- Deposition of Eugene Goldwasser (exhibits)
- Deposition of Fu-Kuen Lin
- Deposition of Fu-Kuen Lin (exhibits)
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- US Patent No. 4,558,006 - Egrie
- US Patent No. 4,966,843 - McCormick - Expression of Interferon Genes in Chinese Hamster Ovary Cells ('843 Patent)
- US Patent No. 4,766,075 - Goeddel - Human Tissue Plasminogen Activator ('075 Patent)
- US Patent Application - 438,991 (1st application - priority app) - McCormick ('991 app)
- US Patent No. 4,399,216 - Axel - Processes for Inserting DNA into Eucaryotic Cells and for Producing Proteinaceous Materials
- US Patent No. 4,703,008 - Lin - Purified and Isolated DNA sequence / transformed host cells. ('008 Patent)
- US Patent No. 4,757,006 - Toole Jr. - Human factor VIII-C Gene and recombinant methods for production
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- Expert Report Dr. James Fisher
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9. Obviousness-Type Double Patenting

a. The Lai '016 patent

U.S. Patent 4,667,016 ("the Lai '016 patent"), entitled "Erythropoietin Purification," names Amgen employees Por-Hsiung Lai and Thomas Strickland as inventors and Kirin-Amgen, Inc. as assignee. The patent was filed as Ser. No. 747,119 ("the '119 application") on June 20,

1985 and issued on May 19, 1987. It expired in 2004. The obviousness-type double patenting analysis generally applies a one-way test. Under the one-way test, a later issued claim will be invalidated for obviousness-type double patenting where it is found to be obvious in light of an earlier claim in a co-owned patent. Under the two way test, a later issued claim will be invalidated for obviousness-type double patenting only where the later claim is obvious in light of the earlier claim, *and* the earlier claim is obvious in light of the later claim. (*See* MPEP §804 (8th ed. Rev.5, Aug. 2006)).

The one-way test applies in all circumstances, including where the later issued claim was filed before the earlier issued claim, except where both of two conditions are satisfied: 1) the applicant could not have filed the earlier and later claims together, and 2) the PTO is solely responsible for the delay that caused the earlier-filed claims to issue after the later-filed claims. Only in those narrow circumstances should the two-way test apply.

The criteria for applying the two-way test are not met in this case. It is therefore my view that in determining whether any of the claims asserted by Amgen in this litigation is invalid for obviousness-type double patenting over the Lai '016 patent, the traditional one-way test should apply.

The Lai '016 patent and the patents-in-suit are all directed to recombinant erythropoietin, and they describe and claim how Amgen made the EPO glycoprotein. The inventions embodied in the Lai '016 patent and the patents-in-suit are therefore closely related.

In fact, the specification of the Lai '016 patent incorporates by reference the '298 disclosure:

> The disclosures of co-owned, co-pending U.S. patent application Ser. No. 675,298, entitled "Production of Erythropoietin", filed Nov. 30, 1984, by Fu Kuen Lin (corresponding to PCT No. US84/02021, filed Dec. 11, 1984, scheduled for publication June

> 20, 1985 as No. WO85/02610) are specifically incorporated by reference herein for the purpose of relating the background of the present invention, especially with respect to the state of the art regarding recombinant methodologies applied to large scale production of mammalian erythropoietin.
> (Lai '016 patent, col. 2:64-3:6).

The Lai '016 patent also makes explicit reference to Example 10 of the '298 Application:

> Practice of the present invention is believed to be suitably illustrated by the following examples practiced on pooled CHO cell supernatants prepared in the manner described in Example 10 of the aforementioned U.S. patent application Ser. No. 675,298. More specifically, the treated supernatants were derived from cell strain CHO pDSVL-gHuEPO "amplified" by means of MTX and grown in roller bottles in serum-free medium as described at page 62 of the application.

(Lai '016 patent, col. 4:33-42). At the time the Lai '016 patent and the '298 application were filed, the named inventors on those patents were working together on Amgen's EPO project.

There was no legal impediment to filing the Lai '016 patent and the '298 application together, particularly in view of the Patent Law Amendments Act of 1984, which took effect before either of those applications was filed. The 1984 Act 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." 35 U.S.C. §116.

Given PTO rules and applicable patent laws, Amgen could have filed a continuation-in-part application combining the Lin '298 and Lai '016 disclosures and named all of Lin, Lai and Strickland as co-inventors. Alternatively, Amgen could have added the Lin disclosure to the Lai application and included Lin as a co-inventor. (MPEP §201.08 (5th ed. Aug. 1983); MPEP §201.01 (8th ed. Rev. 6, Aug. 2006) ("A joint continuation application may derive from an earlier

sole application."). In either case, neither Lin nor Lai would have lost his asserted effective filing date because each claim in a CIP application may have different priority dates.

For at least the reasons stated above, it cannot be said that Amgen was required to file the Lai '016 claims separately from the claims-in-suit. Therefore, the first required condition for applying the two-way test fails, and even if the second required condition were met, *i.e.*, even if the PTO were solely responsible for the delay in issuance of the later claims, the one-way test would still apply.

Amgen, and not the PTO, was responsible for the later issuance of the claims-in-suit. All six of the patents-in-suit are based on applications filed after the '016 patent issued on May 19, 1987. Although the patents-in-suit claim priority going back to 1983-1984, Amgen waited until after the issuance of the '016 patent to file the applications in which it pursued the claims-in-suit to issuance. Therefore, the PTO could not have been responsible for the fact that any of the claims-in-suit issued after the Lai '016 patent.

In addition, as noted below and in the preceding section A, many of the claims-in-suit were not even introduced until years after the Lai '016 patent issued. For this reason as well, the PTO could not have been responsible for the fact that any of the claims-in-suit issued after the Lai '016 patent.

In the prosecution of the '422 patent, Amgen did not introduce prosecution claim 64, which ultimately issued as claim 1 of the '422 patent, until 4/22/1999. At that time, Amgen referred to prosecution claim 64 as a "[n]ewly added" claim. ('197 File History, Paper 33, 4/28/99 Amendment at 4). Accordingly, the PTO was not responsible for the fact that claim 1 of the '422 patent issued after the 5/19/87 issuance of the Lai '016 patent.

Similarly, and as noted in the preceding section A, claim 7 of the '349 patent was first introduced as a new claim on December 24, 1996, when Amgen noted that it was "not included in the original claims of Serial No. 06/675,298." ('369 File History, 12/24/96 Second Preliminary Amendment at 9). Accordingly, the PTO was not responsible for the fact that claim 7 of the '349 patent issued after the 5/19/87 issuance of the Lai '016 patent.

Claims 4-9 of the '698 patent were not filed until 1995. Moreover, claims 4-9 of the '698 patent are similar to the process claims that were voluntarily cancelled from the '298 prosecution and reasserted in application '179, after the '016 Lai patent had issued. Accordingly, the PTO was not responsible for the fact that claims 4-9 of the '698 patent issued after the 5/19/87 issuance of the Lai '016 patent.

Claims 1 and 2 of the '868 patent are process claims originally included in the Group II claims elected for prosecution in the '298 application. In a break with the Examiner's restriction requirement, Amgen voluntarily cancelled those process claims and reasserted them in application '179, after the '016 Lai patent had issued. Accordingly, the PTO was not responsible for the fact that claims 1-2 of the '868 patent issued after the 5/19/87 issuance of the Lai '016 patent.

The file histories that set forth double-patenting rejections based on the Lai '016 patent (see Section V), include the following excerpt:

> 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. (see Ex parte Nesbit, 25 USPQ2d 1817 (1992)). Accordingly, the two-way test for obviousness double patent has been applied (see In re Braat 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991))). In support to this conclusion the examiner notes that the instant application, and its immediate parent, 06/675,298 have been subjected to

> extensive interparty interference and court proceedings which have delayed prosecution."

('179 File History, Paper 34, 2/15/94 Office Action at 2). The Examiner found that the '179 claims were obvious in light of the Lai '016 patent but withdrew the obviousness-type double patenting rejection solely on the basis that the two way test applied.

The Examiner apparently found that the two-way test applied on the ground that interference proceedings were responsible for the delay in prosecution. This finding is erroneous because it failed to apply the proper analysis. First, the Examiner appears to have overlooked the first, necessary prong of the analysis entirely: whether the applications could have been filed together. Second, the Examiner failed to consider factors that prove it was Amgen's prosecution strategy—and not administrative delay at the PTO—that resulted in the prosecution delay of the claims-in-suit. For example, the Examiner failed to consider the fact that the claims at issue—the Group II process claims—had been voluntarily withdrawn from earlier consideration, and could have avoided the interference prior to issuance had they been prosecuted along with the related Group II claims that issued in the '008 patent. Similarly, the Examiner failed to take into account that during the co-pendency period of the Lai '016 patent and the patents-in-suit (and before any interference was declared) Amgen requested and received five extensions of time. For at least these reasons, the Examiner's finding that the two-way test applied was in error.

The one-way test is also the appropriate test for analyzing obviousness-type double patenting of the '080 and '933 claims over the Lai '016 claims. As stated above, Amgen could have filed the patents-in-suit together with the claims of the Lai '016 patent. Therefore, the first necessary condition for applying the two-way test fails.

Both the '080 and the '933 patents stem from the '178 application, which was filed after the Lai '016 patent issued. For that reason alone, the PTO could not have been responsible for the fact that any of the claims-in-suit of these patents issued after the Lai '016 patent.

Furthermore, as noted below, numerous limitations were not introduced until years after the Lai '016 patent issued, even though they were supported by the '298 disclosure. For that reason as well, the PTO could not have been responsible for the fact that those claims issued after the Lai '016 patent.

For example, limitations specifying use for the treatment of kidney dialysis patients that appear in the asserted claims of both the '080 and the '933 patents was not introduced until prosecution claim 98 was entered on 2/22/1995. ('874 File History, 2/22/1995 Amendment after Final Office Action, at 5).

Similarly, in the prosecution of the '080 patent, the limitation directed to "non-naturally occurring" erythropoietin was not introduced until the entry of prosecution claim 68 on 12/24/1996. ('556 File History, 12/24/96 Second Preliminary Amendment at 7). Limitations specifying the in vivo biological activity of erythropoietin ("to increase production of reticulocytes and red blood cells") also were not introduced until 12/24/1996. ('556 File History, 12/24/96 Third Preliminary Amendment at 7-8).

Over the course of the prosecution of the patents-in-suit, Amgen sought thirteen extensions of time totaling over fifteen months. Furthermore, in many instances, Amgen waited until the last possible day to respond to correspondence from the PTO.

Interference proceedings do not account for the delay in issuance of the patents-in-suit. As noted above, the Group II process claims could have issued in the '008 patent before becoming embroiled in interferences but for Amgen's decision to cancel those claims from

prosecution alongside related product claims that issued in '008. Furthermore, the '334 Interference was not initiated until 1990, and after the interference was resolved and numerous claims were allowed, Applicant filed two additional continuation applications before the '933 and '080 patents finally issued. Finally, none of the interferences included counts relating to the '349 or '422 patent claims and, thus, do not account for any delay.

The initial '024 application was filed on 12/13/1983, and the last patent-in-suit issued on 9/21/1999. Fewer than three of these almost-sixteen years were attributable to the delay caused by interference proceedings. In my view, the prosecution strategy reflected in the preceding paragraphs—and not administrative delay on the part of the PTO—was responsible for the protracted prosecution of the claims-in-suit.

For all of the reasons stated above, even if Amgen had been required to file the Lai '016 application separately from the patents-in-suit, it cannot be said that the PTO was solely responsible for the delay in prosecution of any of the patents-in-suit. Accordingly, Amgen is not entitled to a two-way test for obviousness with respect to any of the claims-in-suit, and the Examiner's finding that the two-way test applied with respect to certain claims introduced in the '179 application was in error.

b. '868 and '698 Patents

For all the reasons set forth in Roche's prior supplemental response to this interrogatory regarding obviousness-type double patenting based on the earlier issued '008 patent, the asserted claims of the '933 patent, '080 patent, '349 patent, and '422 patent are either invalid for obviousness type double patenting based on the earlier issued claims of the '868 and '698 patent or should be deemed to expire on 8/15/12, the expiration date of the '868 and '698 patents. The claims of the '868 and '698 patents are directed to the process of making recombinant

erythropoietin by expressing DNA encoding the erythropoietin gene in vertebrate and mammalian host cells to make an in vivo biologically active glycoprotein. The various asserted claims of the '933, '080, '349, and '422 patents cover such glycoprotein products, pharmaceutical compositions containing such products, methods of treatment using these pharmaceutical compositions, and the process for using vertebrate cells to produce certain levels of erythropoietin. As a result, these latter claims would have been obvious over the earlier issued process claims of the '868 and '698 patents.

10. Genentech's tPA Work

Recently produced documents from Genentech concerning their work on tissue plasminogen activator ("tPA") provide further support, that one of skill would have had a reasonable expectation of success in using CHO cells to produce a functional, in vivo biologically active recombinant human glycoprotein.

Genentech's product license application (PLA) for recombinant tPA provides a detailed description of the manufacture of a glycosylated recombinant human tPA product that was used for clinical trials and preclinical studies in animals, as well as data relating to its efficacy and in vivo biological activity. See Product License Application Summaries (from PLA vol. 1 and vol. 11) at ROCHE-GNE 00001-00036, 03009-03060. As indicated in these PLA documents, production of this product using CHO cells resulted in a glycosylated protein biologically indistinguishable from human tPA derived from human melanoma cells. ROCHE-GNE 00094-00136 at 00999. These data confirm that the recombinant human tPA glycoprotein made in CHO cells, as described in the '075 patent and in EP '619 published application exhibits biological activity in vivo (when administered in human subjects and in various animal models).

To produce recombinant human tPA, the PLA indicates that a DHFR$^-$ CHO cell line was stably transfected with a plasmid vector encoding human tissue type plasminogen activator and DHFR (dihydrofolate reductase). The transfected cells were maintained in selective media and colonies that arose were isolated individually. Culture media from individual cell lines were tested for recombinant tPA activity. One such stably transfected clone was subjected to growth in media containing increasing concentrations of methotrexate, which allowed selection of cells that had amplified the cDNA sequence encoding human tPA to yield a cell line that secreted high levels of recombinant human tPA product, and was used to prepare a Master Cell Working Cell Bank. See ROCHE-GNE 03025-26, 03046-60. PLA item III.B provides a detailed description of the plasmid and cell line history. ROCHE-GNE 03050-53, figs. 1-4.

The '075 patent and in EP '619 describe the generation of recombinant CHO host cells for production of recombinant human tPA using essentially the same methods as those described in Genentech's PLA, including use of the same CHO-K1-DUX-B11 cell line ('075 patent, col. 25-26, EP '619 at 46-48), essentially the same plasmid expression vector encoding human tPA and DHFR ('075 patent, col. 24-26, fig. 4, fig. 5(a-c), fig. 11, EP '619 at 44-46, fig. 4, fig 5(a-c), fig., 11), and essentially identical methods for amplifying the cDNA sequence encoding human tPA in the transfected CHO host cells ('075 patent, col. 25-27, EP '619 at 46-50).

There are no substantive differences between the methodology described in the later filed (December 13, 1983) asserted Lin patents for producing recombinant human EPO in DHFR$^-$ CHO host cells and the methodology described in Genentech's PLA and in the '075 patent and EP '619 application for producing recombinant human tPA in DHFR$^-$ CHO host cells, including use of the same CHO-K1-DUX-B11 cell line ('868 patent col. 26-29, Example 10), use of a single plasmid expression vector encoding a recombinant human glycoprotein and DHFR as a

means for first selecting stably transfected cell clones, and subsequently for amplification of the linked DNA sequence encoding the recombinant glycoprotein ('868 patent col. 26-29, Example 10), and essentially the same methods for amplifying the linked DNA sequence in the stably transfected CHO-K1-DUX-B11 host cells ('868 patent col. 26-29, Example 10).

The methodology described in the PLA as well as in the '075 patent and EP '619 application, and also in the '868 patent for production of a recombinant human glycoprotein in CHO cells was all widely known and available in the prior art before October 1983, as evidenced by the references cited in these patents. See for example, Lowe April 6, 2007 Expert Report ¶¶ 95-127, Lin '868 patent col. 2-3, 26 (Example 10), Goeddel EP '619 at 16, 21-22, '075 patent col. 9, 11-12, PLA vol. 1, Item III.B at ROCHE-GNE 03050-54, ref. 3-4 (SV40 promoter and replication sequences), 5-6 (polyadenylation sites), 7 (DHFR cDNA sequence), 8 (DNA sequences useful for propagating and selection of plasmid DNA in bacterial host cells), 9-12 (origin and use of DHFR- CHO-K1 DUX B11 cells), 13-14 (methods for transfection of mammalian host cells), 16 (methotrexate mediated gene amplification).

Further documents from Genentech's PLA indicate that the clinical studies described in the PLA, as well as various animal studies described in the PLA, were conducted with recombinant human tPA produced in CHO cells and made using one of two manufacturing processes resulting in either a two chain product (designated by product code G11021) or a predominantly one-chain product (designated by product codes G11035 and G11044). ROCHE-GNE 03025-36, vol. 11 Clinical Summary ROCHE-GNE 0001-36 at 0008-14, 00029-31.

As indicated in the PLA documents, CHO produced recombinant human tPA product was administered to patients as early as February 1984, resulting in an "excellent" recanalization rate (opening of occluded arteries feeding the heart muscle). ROCHE-GNE 01447-01959, 01524,

01545, 01568. Subsequent clinical trials demonstrated the biological activity and efficacy of the CHO produced recombinant product in larger groups of patients with occluded coronary arteries. ROCHE-GNE 00383-00578, 01277-01446. TIMI (Thrombolysis in Myocardial Infarction) Study Group, New England J. Med. 312: 932-936 (1985) at ROCHE-GNE 00428-32. See also, ROCHE-GNE 00094-136. In particular, the TIMI study demonstrated that intravenous treatment with recombinant tPA was approximately twice as effective as a thrombolytic agent (for opening the occluded coronary arteries) as intravenous treatment with another clot dissolving protein called streptokinase. ROCHE-GNE 00396-399, 00423-432.

Regarding the above evidence relating to Genentech's work with human recombinant tPA, there is no description whatsoever in either Lin 561,024 application filed on December 13, 1983, as well as the Lin 582,185 application filed as a continuation-in-part on February 21, 1984 of using CHO cells to produce recombinant human EPO, or of any assay of *in vivo* biological activity. The earliest application which mentions CHO cells, the Lin 655,841 application was filed only on September 28, 1984. To the extent that before October 1983 it would have been obvious to use CHO cells to produce a functional, biologically active human glycoprotein, it certainly would have been obvious by September 1984 to use CHO cells for this purpose.

11. Admissions by Amgen's Expert Dr. Katre

Amgen's expert, Dr. Nandini Katre, stated in her expert report that "Davis et al.,...have published patents or patent applications that show how to make pegylated-EPO and all published by 1998." *See* First Expert Report of Nandini Katre, dated April 6, 2007, at ¶ 31. Dr. Katre goes on to state that:

> The earliest of these patents and patent applications was filed in 1977 by Davis et al., and issued in 1979. (Ex. 13, U.S. Patent No. 4,179,337). This patent shows how to make and use many activated PEGs for conjugation to a protein, including PEG

> activated with cyanuric chloride or fluoride, succinate groups. p-diazobenzyl, 3-(p-diazophenyloxy)-2-hydroxypropyloxy, maleimide, and 1-glycydoxy-4-(2'-hydroxy-3'-propyl)butane. Several of these activated PEGs conjugate to proteins with an amide group formed with the primary amino groups of the lysines and/or N-terminus. These activated PEGs were used to pegylate several proteins, including catalase, insulin, and lysozymes. (Ex. 13, U.S. Patent No. 4,179,337). The Davis Patent also contains a number of proposed pegylation reactions with the above reactive PEGs using a variety of other proteins, including EPO. (*Id.*).

Id. at ¶32. Roche does not believe that the Davis patent would have taught one of skill in the art to make a pegylated EPO product. Moreover, Roche does not contend that its CERA product is a PEG-EPO. However, to the extent that Amgen believes that CERA is a PEG-EPO and that the Davis patent would have taught one of skill in the art to make a PEG-EPO as of 1979, all of the asserted claims of the Lin patents would be invalid for being anticipated by a prior publication under Sections 102(a) and 102(b). Under the fundamental axiom of patent law, that which infringes if later, anticipates if earlier. Based upon Dr. Katre's expert report, Amgen contends that Roche is practicing the prior art of the 1979 Davis patent by the manufacture and development of CERA. As a result, all of the asserted claims are invalid for being anticipated.

12. "non-naturally occurring" - claim 3 of the '933 patent

Based on Amgen's proposed claim construction that the expression product is not limited to the product of transcription and translation, claim 3 of the '933 patent should be anticipated by the human urinary erythropoietin disclosed in Miyake, et al., *Purification of Human Erythropoietin*, J. Biol. Chem., Vol. 252, No. 15, pp. 5558-5565 (1977).

"Non-naturally occurring" and "exogenous DNA" are source limitations that imparts no structural distinctions over the prior art. As a result, they can be excised from Claim 3 for the purposes of determining anticipation. (*Amgen II*, at p. 1354 n.20.)

As source and process limitations in a product-by-process claim, these limitations affect anticipation only to the extent the process affects the structure of the product. Moreover, there is no disclosure in the specification that would lead one of skill in the art to determine that these source and process limitations place any limits on the claimed glycoprotein product. Consequently, claim 3 is limited by the biological property defined in the claim. Also, the limitation itself denotes that the DNA sequence encodes "human erythropoietin." As stated above, Amgen has taken the position in *Markman* submissions that "human erythropoeitin" should be defined as the amino acid structure of human erythropoietin.

Miyake, et al.'s product has all the limitations of the glycoprotein product of Claim 3. The Miyake isolate: (a) is a glycoprotein, having an amino acid sequence with glycosylation, (b) has the same amino acid structure as Amgen's recombinant glycoproteins disclosed in the '933 patent, e.g., Example 10 (*Amgen I*, at p. 50), and (c) has the same in vivo activity as Amgen's disclosed recombinant glycoproteins. Therefore, if "non-naturally occurring" and "exogenous DNA" were treated as a pure source limitation, Miyake, et al. would have all Claim 3's structural limitations and anticipate the claim.

D. Lack of Inventorship Under Section 102(f)

To the extent that Amgen argues that the choice of host cells was important in producing the in vivo biologically active erythropoietin of the Lin inventions, then Dr. Lin is not the true inventor of the asserted claims. All of the asserted claims require the use of either mammalian or vertebrate host cells to express DNA encoding human erythropoietin. However, as Dr. Lin testified recently at his deposition, he derived his knowledge over which particular host cells to use from information gathered by scientists at the American Type Culture Collection. Dr. Lin testified as follows:

Q. That's fine. And who suggested using CHO cells for the expression of the EPO gene?
A. I may have suggested -- besides actually CHO cells, I also have actually look
into other cells. I think there's another cell. I talk to the people at ATCC at the
time. There's only two stable cells that can be used -- I mean the stable cell line they could use. One is the other cells. Now I cannot remember. There's another cell. It's
also very stable for the purpose of production. So CHO cells and the other one, yes,
which I -- I talked to one of the guys at ATCC.

Lin Tr. at 63, 3/28/07

Q. So your testimony is that you picked CHO cells because you called the ATCC, and they told you that's what you should use?
[objection]
THE WITNESS: No, no, no. I not call
the ATCC. I was looking for cells of which would be suitable for commercial production. Therefore, the cells -- cell line to be used had to be stable so that's why I would -- try to decide which cell line is to be used. So I call my friend at ATCC and talked to people to see what the -- what the cell line would be good to use. And the CHO cell come up as one. And the other one, I just cannot remember. There's another one that is also very stable.
BY MS. BEN-AMI:
Q. Who is your friend at the ATCC?
A. At the time, I have a friend who's a curator at ATCC. Dr. Tsong, I believe --Dr. Tsong.
Q. Can you spell that?
A. Let me think if I can remember the name. Sung Chang Tsong. It's Chinese. He's senior to me. He's the curator at ATCC.
Q. Can you try to spell that for us? I know you could be wrong, but if you could try. Do you want to write it down?
A. I would spell it probably, S-u-n-g, Sung; Chang, would be, C-h-a-n-g. Something like that; Tsong, would be, like -- Tsong would be T-s-o-n-g. That would be the last name. And I think he may have refer me to
the other guy. The other guy -- what's his
name? I think it's Dr. Cheng -- Dr. Cheng,
C-h-e-n-g. Yeah, he -- at the time, I believe
he was working in the mammalian cell group over
there.
Q. At the ATCC?

A. Yes. One of the --
Q. So you asked them what cell lines would be very stable?
A. That's right, for culture purpose, yeah. Because my concern is for mammalian production, the cell line had to be stable. So I talked to --
Q And they suggested two cell lines to you?
A Definitely one of the cell line was suggested. Yeah.
The other one -- he say that the other cell line may be just as stable or may be even better than CHO cell. That's what he tell me, as I recall.
Q But he suggested CHO cell and one other cell line?
A Yes. He suggest -- I don't know he suggest CHO cell. He basically tell me which cells are stable. It does not mean he suggested -- he did say these other cells are stable.
Q Which cells?
A The CHO and the other one. I forgot what's the other one.
Q Okay.
A Yeah, I forgot the name of the cell now.
Q Okay.
A But if you talk to ATCC people, they probably also still remember what cell line --they probably have information about -- what information what cell lines are stable in the culture.

Id. at 64-67. Therefore, Dr. Lin is not the true inventor to certain aspects of the claimed invention, namely the use of particular mammalian or vertebrate cells to express DNA encoding human erythropoietin, but derived this information by other scientists outside of Amgen, namely the ATCC. As a result, Amgen's asserted claims should be held invalid for lack of inventorship under Section 102(f).

E. Expiration of the Process Claims Based Upon The Earlier Issued Composition Claims Under Section 103(b)(2)

Under Section 103(b)(2), "a biotechnological process using or resulting in a composition of matter that is novel under section 102 and nonobvious under subsection (a) of this section shall be considered nonobvious if -

(2) A patent issued on a process under paragraph 1 -

(B) shall, if such composition of matter is claimed in another patent, be set to expire on the same date as such other patent, notwithstanding section 154."

Applied here, the asserted process claims of the Lin patents, namely, claims 1 and 2 of the '868 patent, claim 4-9 of the '698 patent, and claim 7 of the '349 patent should have all expired on October 27, 2004, because that was the expiration of the claims of the '008 patent, which were directed to host cells transformed or transfected with a purified and isolated DNA sequence encoding human erythropoietin "in a manner allowing the host cell to express erythropoietin." The process claims of the now asserted Lin patents are to "a biotechnological process using or resulting in a composition of matter" that was previously patented, namely the DNA sequences and host cells of the '008 patent. As a result, under Section 103(b)(2), these process claims are required to expire with the '008 patent. Moreover, at least claim 7 of the '349 patent, which has a current expiration date of 5/26/15, and which is directed to the process of making recombinant erythropoietin, should similarly expire on the same date as the asserted claims of the '933 patent, which is 8/20/13. Claim 7 of the '349 patent merely claims the process of making the previously patented composition.

INTERROGATORY NO. 10

Separately, in claim chart form for each claim of Amgen's patents-in-suit that you contend is invalid under 35 U.S.C. § 102, identify and describe on a limitation-by-limitation basis for each claim:

(f) where, on a limitation-by-limitation basis, you contend each claim limitation is disclosed in the prior art;

(g) how each such limitation is disclosed in the prior art, including specific references to pages, claims, columns and/or line numbers (if applicable) in each document supporting such contention;

(h) all evidence on which you rely in support of each contention, including all documents, testimony, prior knowledge, or public uses tending to support your contention(s), and every test, experiment, and/or data upon which you rely in support of each contention that a claim is invalid;

(i) each person, other than counsel, who furnished information or was consulted regarding your response to this interrogatory including the nature and substance of each such person's knowledge or information; and

(j) the three individuals affiliated with Roche, other than counsel, most knowledgeable regarding the subject matter of this interrogatory, stating the nature and substance of each such person's knowledge or information.

RESPONSE:

See Supplemental Objections and Response To Interrogatory No. 9 above.

INTERROGATORY NO. 11

Separately, in claim chart form for each claim of Amgen's patents-in-suit that you contend is invalid under 35 U.S.C. § 103 or for double patenting, identify and describe for each claim and for each asserted defense:

(k) where, on a limitation-by-limitation basis, you contend each claim limitation is found or disclosed in the prior art or earlier Lin patent claims;

(l) why the claim would have been obvious, including where the motivation to combine prior art disclosures or earlier Lin patent claims may be found;

(m) why 35 U.S.C. § 121 does not bar the application of the doctrine of obviousness-type double patenting;

(n) all evidence on which you rely in support of each contention, including all documents, testimony, prior knowledge, or public uses tending to support your contention(s), every test, experiment or data upon which you rely to support your contention(s);

(o) each person, other than counsel, who furnished information or was consulted regarding your response to this interrogatory including the nature and substance of each such person's knowledge or information; and

(p) the three individuals affiliated with Roche, other than counsel, most knowledgeable regarding the subject matter of this interrogatory, stating the nature and substance of each such person's knowledge or information.

RESPONSE:

See Objections and Response To Interrogatory No. 9 above.

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DATED: May 1, 2007

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CERTIFICATE OF SERVICE

I hereby certify that a copy of this document was served upon the attorneys of record for the plaintiff of the law firms listed below via email on the above date.

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