UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

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| AMGEN INC.,<br><br>Plaintiff,<br><br>v.<br><br>F. HOFFMANN-LA ROCHE LTD<br>ROCHE DIAGNOSTICS GmbH<br>and HOFFMANN-LA ROCHE INC.<br><br>Defendants. | CIVIL ACTION No.: 05-CV-12237WGY |

**ROCHE'S OPPOSITION TO AMGEN INC.'S MOTION FOR SUMMARY JUDGMENT OF NO OBVIOUSNESS-TYPE DOUBLE PATENTING**

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## I. INTRODUCTION

Defendants F. Hoffmann-La Roche Ltd, Roche Diagnostics GmbH, and Hoffmann-La Roche Inc. (collectively "Roche") hereby oppose Amgen Inc.'s Motion For Summary Judgment Of No Obviousness-Type Double Patenting. Amgen's motion addresses two separate and distinct bases of invalidity. First, Amgen has failed to satisfy its burden of proving that 35 U.S.C. § 121 protects its '349, '933, and '422 patent claims from an obviousness-type double patenting[1] attack over the Lin '008 patent. Here, the fundamental issue is that because Amgen did not maintain consonance with the restriction requirement, it cannot hide behind the Section 121 safe harbor.

Second, Amgen has also failed to demonstrate on summary judgment that the asserted claims of the patents-in-suit are not invalid for obviousness-type double patenting over the Lai '016 patent. Here, Section 121 cannot provide Amgen with immunity from double patenting based on the Lai '016 patent, and thus the § 121 issues are irrelevant for the Lai '016 patent. On this point, Roche has already submitted its own motion for summary judgment on double patenting over the Lai '016 patent (Docket No. 490) based on the proper application of the one-way test, rather than the two-way test.

## II. AMGEN CANNOT SATISFY ITS HEAVY BURDEN OF PROVING SECTION 121 IMMUNITY ON SUMMARY JUDGMENT FOR THE LIN '349, '933, AND '422 PATENT CLAIMS OVER THE LIN '008 PATENT

Amgen does not dispute that its earlier filed and now expired '008 patent claims render the asserted claims of the '349, '933, and '422 claims obvious. Instead, Amgen moves for summary judgment that these patents should be immune from obviousness-type double patenting ("ODP") because Amgen allegedly adhered to the safe harbor provision of 35 U.S.C. § 121. Section 121 allows patentees to escape ODP attacks when, during the course of patent prosecution, they have

strictly followed the Patent Office's restriction requirement. Amgen has argued that it should be afforded Section 121 protection because the Patent Office issued a restriction requirement that separated the subject matter of the '349, '933, and '422 patent claims from the DNA and process claims of Group II, which resulted in the now expired '008 patent, as well as the '868 and '698 patents. Here, Amgen has failed to meet its heavy burden of proving Section 121 immunity on summary judgment for at least the following reasons.[2]

- During the prosecution of the '349 patent, Amgen violated the Patent Office's restriction requirement when it converted the vertebrate cell claims into the asserted process claim (claim 7);
- As demonstrated by the accompanying Declaration of John Lowe, Ph.D. ("Lowe Decl."), claim 7 of the '349 patent clearly belongs to the DNA and process claims of Group II of the PTO's 1986 restriction requirement, since it claims the same subject matter of the process of producing recombinant human erythropoietin by growing vertebrate cells and using non-human promoters; hence claim 7 violates the restriction requirement;
- During the prosecution of the '933 patent, Amgen again violated the restriction requirement when it amended the pending claims to "non-naturally" occurring glycoproteins of the expression of exogenous DNA sequences, thereby vitiating the basis for the Patent Office's restriction requirement;
- During this same prosecution, Amgen violated the restriction requirement when it combined within the same application polypeptide claims from one restricted group (Group I) with pharmaceutical composition and method of treatment claims from another restricted group (Group V); and
- During the prosecution of the '422 patent, Amgen violated the restriction requirement when it combined a pharmaceutical claim from one group (Group V) with a claim for albumin pharmaceutical compositions from a separate restricted group (Group VII) within the same application.
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By invoking the safeguard provisions of Section 121, Amgen is unfairly seeking to hide behind the very Patent Office restriction requirement that Amgen has so systematically and consciously disregarded. Amgen's motion fails because Federal Circuit precedent precludes such an inequitable result. Patentees can only rely upon Section 121 when they have strictly abided by,

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[1] The judicially created doctrine of obviousness-type double patenting prevents extension of patent rights beyond their terms by barring claims that are different, but not patentably distinct, from claims in an earlier-issued, commonly owned patent. *In re Longi*, 759 F.2d 887, 892-94 (Fed. Cir. 1985).

[2] The patent holder always has the burden of proving Section 121 immunity. *See Geneva Pharms., Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1382 (Fed.Cir.2003).

i.e., stayed consonant with, the Patent Office's restriction requirement. Here, Amgen has not done so, and consequently, Section 121 does not apply.

### A. The Prosecution History Of The Earlier Filed '008 Patent And The Now Asserted '349, '933, and '422 Patents

All of the patents-in-suit stem from continuation applications of the '008 patent. As a result, these patents share the same specification as the earlier filed and now expired '008 patent. During the prosecution of '008 patent, the Patent Office entered a restriction requirement separating the pending claims into the following six groups.

I. Claims 1-13, 16, 39-41, 47-54 and 59, drawn to polypeptide, classified in Class 260, subclass 112.
II. Claims 14, 15, 17-36, 58 and 61-72, drawn to DNA, classified in Class 536, subclass 27.
III. Claims 37-38, drawn to plasmid, classified in Class 435, subclass 317.
IV. Claims 42-46, drawn to cells, classified in Class 435, subclass 240.
V. Claims 55-57, drawn to pharmaceutical composition, classified in Class 435, subclass 177.
VI. Claim 60, drawn to assay, classified in Class 435, subclass 6.

(Ex. U at 2)[3] ("1986 restriction requirement"). Although the Group II claims were generically described as "drawn to DNA," the actual claims themselves were also directed towards host cells, including vertebrate cells, (claims 14, 17-36, 58, 61, 63 65, 67), as well as processes for making polypeptides by growing these host cells under suitable nutrient conditions (claims 69-72) (Ex V).

In explaining the basis for separating Invention Group I (polypeptide claims) from Invention Group II (DNA, Host Cells and Processes for Production claims), the Patent Office explained that because the EPO polypeptides of Group I could be made by a process different from the recombinant DNA process of Group II, such as isolation from a naturally occurring source, the inventions were deemed different. The Patent Office stated:

Inventions I and II are related as process of making and product made.

[3] "Ex. _" refers to Exhibits attached to the declarations of Kimberly J. Seluga dated June 7, 2007 and June 28, 2007.

> "The inventions are distinct if either (1) the process as claimed can be used to make another and materially different product, or (2) the product as claimed can be made by another and materially different process." MPEP 806.05(f)
>
> In this case, the product as claimed [Group I] may be made by a materially different product [sic], such as isolation from a naturally occurring source." (emphasis added)

(Ex. U at 2). As a result of the 1986 restriction requirement, Amgen elected to prosecute the DNA and host cell claims within that application, which matured into the '008 patent.

Critically, at the time of the restriction requirement, Amgen chose not to file divisional applications based on the 5 remaining groups. Instead, just prior to the issuance of the '008 patent, after waiting 16 months, Amgen began submitting a series of continuation applications which eventually resulted in the patents-in-suit (Exs. W and X). For example, when Amgen submitted its '178 and '179 continuation applications, which eventually matured into all of the patents-in-suit, it re-filed all of the original claims of the original '008 patent application, rather than adhering to the 1986 restriction requirement. *Id.*

### B. Amgen Broke Consonance With The 1986 Restriction Requirement When Prosecuting Claim 7 of the '349 Patent

During prosecution of the '349 patent, Amgen initially pursued the vertebrate cell product claims of Group IV of the 1986 restriction requirement. For example, pending claim 42 of the application read:

> 42. Vertebrate cells which can be propagated *in vitro* and which upon growth in culture are capable of producing in the medium of their growth in excess of 100 U of erythropoietin per $10^6$ cells in 48 hours as determined by radioimmunoassay.

(Ex. Y at 7). However, Amgen decided to add a new claim within this application, drawn not to the vertebrate cells themselves, but to the recombinant process of using those cells to produce erythropoietin. New Claim 61 read:

> 61. The process of producing erythropoietin using vertebrate cells according to claims 42, 43, 44, or 46.

*Id.* at 8. This claim eventually issued as asserted claim 7 of the '349 patent. Amgen explained in the amendment that it should be entitled to the process claim because such methods were the "intended use" of the pending vertebrate cell claims. *Id.* However, Amgen failed to inform the new patent examiner that 10 years earlier, a different patent examiner issued the 1986 restriction requirement which specifically separated these vertebrate cell claims (Group IV) from the process of using these cells to make erythropoietin (Group II). Thus, Amgen should have placed claim 7 within the Group II claims, because those claims were directed to using vertebrate cells to produce recombinant erythropoietin.

The 1986 restriction requirement included within Group II the claims that eventually matured into the '008 patent, as well as process claims which became the '868 and '698 patent. For example, pending claim 71, which was classified within Group II, was to:

> A process for the production of a polypeptide having part or all of the primary structural conformation and one or more of the biological properties of naturally-occurring erythropoietin, said process comprising:
>
> growing, under suitable nutrient conditions, procaryotic or eucaryotic host cells transformed or transfected with a DNA vector according to claim 65, and
>
> isolating desired polypeptide products of the expression of DNA sequences in said vector.

(Ex. V). Claim 71 and its related claims eventually matured into the '698 patent. As seen below, claim 4 of the '698 patent is a direct descendant of claim 71, and is virtually indistinguishable from claim 7 of the '349 patent:

| Claim 4 of the '698 patent | Claim 7 of the '349 patent |
|---|---|
| 4. **A process for the production of a glycosylated erythropoietin** polypeptide having the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells comprising the steps of:<br>a) **growing, under suitable nutrient conditions, vertebrate cells** comprising **promoter DNA, other than human erythropoietin promoter DNA**, operatively linked to DNA encoding the mature erythropoietin amino acid sequence of FIG. 6; and<br>b) isolating said glycosylated erythropoietin polypeptide expressed by said cells. | 7. **A process for producing erythropoietin** comprising the step of **culturing, under suitable nutrient conditions, vertebrate cells** according to claim 1, 2, 3, 4, 5 or 6.<br>1. **Vertebrate cells** which can be propagated in vitro and which are capable upon growth in culture of producing erythropoietin in the medium of their growth in excess of 100 U of erythropoietin per $10^6$ cells in 48 hours as determined by radioimmunoassay, said cells comprising **non-human DNA sequences which control transcription of DNA encoding human erythropoietin.** |

Claim 4, '698 patent (Ex. B); Claim 7, '349 patent (Ex. C). As detailed by the Lowe Declaration, a straightforward comparison between asserted claim 7 of the '349 patent and asserted claim 4 of the '698 patent demonstrates that they both claim the same subject matter; namely, the process of using vertebrate cells to make recombinant erythropoietin using non-human promoter DNA (Ex. C). In particular, Dr. Lowe has concluded that both the '698 claim 4 and '349 claim 7 are directed to processes for producing erythropoietin. Both claimed processes use vertebrate host cells under suitable nutrient conditions comprising DNA sequences other than human erythropoietin promoter DNA that control transcription of DNA encoding human erythropoietin. Both claimed processes are directed to making the recited erythropoietin product by growing the host cells under suitable nutrient conditions. In Dr. Lowe's opinion, the process of '349 patent claim 7 includes all of the salient features of '698 patent claim 4, and therefore belongs in the subject matter of restriction Group II.[4]

Therefore, Amgen's prosecution of claim 7 of the '349 patent crossed the dividing lines of the 1986 restriction requirement. Amgen was told by the Patent Office to separate its Group II claims (DNA, host cells, and process of making recombinant EPO) from its Group IV claims (vertebrate cell claims). Amgen ignored this when it added new claim 61 (now claim 7) to the application that matured into the '349 patent.

[4] That claim 7 of the '349 patent contains the limitation "100 (or 500 or 1000) U of the erythropoietin...as determined by radioimmunoassay" ("RIA") does not change this result. Roche has already filed summary judgment papers that this limitation makes claim 7 invalid for, *inter alia*, lack of definiteness and written description (Docket No. 539). Skilled workers confronting this claim would not have known the upper or lower limits of production required of this claim because of the ambiguities of the RIA. However, they would have recognized that the claim required at least some baseline level of production. Claim 4 of the '698 patent clearly contemplates this minimum level of production since it requires the production of an "in vivo biological" protein "causing bone marrow cells to increase production of reticulocytes and red blood cells." The only example of *in vivo* bioactivity disclosed in the '349 patent demonstrates activity of 2040±160 U/ml by *in vivo* assay. Ex. C, ('349 patent, col. 27, ln. 61-67). This same sample, when run on an RIA, showed results of 3089±129 U/ml. *Id.* Thus, the data in the patent indicates that samples showing *in vivo* biological activity will satisfy the baseline production levels of an RIA.

### C. Amgen Broke Consonance With The 1986 Restriction Requirement When Prosecuting The Asserted Claims Of The '933 Patent

In restricting the claims of Group I (drawn towards polypeptides) from those of Group II (drawn towards DNA, host cells, and process claims), the Patent Office reasoned that these were different inventions because the EPO polypeptides could be made by a process that was different from the recombinant DNA process of Group II, "such as isolation from a naturally occurring source." (Ex. U at 2).

However, during the prosecution of the '933 patent, Amgen amended the pending claims such that the claimed EPO polypeptide could not be isolated from natural sources and could only be produced by using the recombinant DNA and host cells of Group II as claimed in the '008 patent. Specifically, following an Office Action rejection where the pending claims were held obvious over prior art disclosing EPO protein isolated from human sources, Amgen amended the claims to add the limitations "non-naturally occurring" and "non-human."

> 67. (Amended) A non-naturally occurring glycoprotein product of the expression of an exogenous DNA sequence in a non-human eucaryotic host cell...

(Ex. Z). Amgen's amendment was clearly motivated by its attempt to overcome prior art which suggested EPO polypeptides isolated from a natural source. Amgen explained as follows:

> Claim 67 has been amended to state "a non-naturally occurring glycoprotein product of the expression of an exogenous DNA sequence in a non-human eucaryotic host cell..." Unlike the glycoprotein product of the subject claims, which results from the expression of an exogenous DNA sequence in a non-human eucaryotic host cell, Sugimoto et al. relates to erythropoietin assertedly produced by a human lymphoblastoid cell line. Applicant submits that there is no evidence or reason to believe that erythropoietin produced by a human lymphoblastoid cell line is identical to the glycoprotein product produced by a non-human transformed or transfected cell line.

*Id.* at 5 (emphasis in original). In order to overcome prior art, Amgen explicitly emphasized throughout the '933 patent prosecution that the polypeptide claims were limited to the expression product of recombinant DNA and host cells, as claimed in Group II of the 1986 restriction

requirement and the original '008 patent. For example, Amgen told the Patent Office that the pending claims were "product-by-process" claims that were specifically defined by the recombinant process.

> These product-by-process claims are presented in an effort to positively recite the physical properties of recombinant erythropoietin, and to further define the product of the subject invention since **the recombinant erythropoietin claimed cannot be precisely defined except by the process by which it is produced**.

(Ex. AA at 4) (emphasis added). In fact, Amgen specifically represented to the Patent Office that the pending claims "**parallel claim 2 of [the '008 patent]"** because they "specify that the DNA sequences encode human erythropoietin." (Ex. BB). As demonstrated above, the '008 patent issued from the Group II claims of the 1986 restriction requirement. Because of arguments such as these, Amgen overcame these prior art rejections and was awarded the '933 patent.

Importantly, all of the asserted claims of the '933 patent issued with limitations to "non-naturally occurring" EPO (*e.g.*, claims 3-14 of the '933 patent) (Ex. E).[5] By limiting these claims in this manner, Amgen violated the 1986 restriction requirement. While the Patent Office had separated the polypeptide claims from the recombinant DNA and host cell claims, it did so only because it concluded that the polypeptide claims could be made from an alternative source, such as natural tissue. Once Amgen amended the polypeptide claims such that they could not be made from natural sources, but only from recombinant DNA and host cells, Amgen vitiated the Patent Office's rationale for its restriction requirement and broke the consonance requirement of Section 121.

Moreover, Amgen again broke consonance when it combined the polypeptide claims from Group I of the restriction requirement with pharmaceutical composition/method of treatment claims

[5] Pending before the Court is Roche's Motion for Summary Judgment that the asserted claims of the '933 patent are indefinite based on the "non-naturally occurring:" limitation (Docket No. 505), as well as Amgen's motion for summary judgment, *inter alia* that the '933 claims are definite based on this same limitations (Docket No. 531). Resolution of these motions is not a predicate to denying Amgen's summary judgment of no obvious-type double patenting. In fact, Amgen continues to maintain in its summary judgment papers that "non-naturally occurring" is a critical source limitation that cannot be disregarded.

of Group V. As stated above, the Patent Office clearly told Amgen to separate these claims into separate divisional applications (Ex. U). However, Amgen ignored the restriction requirement, and as a result, Amgen has asserted claims from the '933 patent that include both polypeptide claims (claims 3,7, and 8) and claims directed to pharmaceutical compositions and methods of treatment (claims 9, 11, 12 and 14) (Ex. E).

**D. Amgen Broke Consonance With The 1992 Restriction Requirement When Prosecuting Claim 1 Of The '422 Patent**

Amgen also disregarded a second restriction requirement during the prosecution of the '422 patent. Early in the prosecution of that patent, the Patent Office issued a new restriction requirement separating the pending claims into seven categories, including the following:

> V. Claims 55-57, drawn to pharmaceutical compositions comprising EPO, classified in Class 514, subclass 2.
> VII. Claim 61-63, drawn to pharmaceutical compositions comprising EPO and human serum albumin, classified in Class 514, subclass 2.

(Ex. CC) ("1992 Restriction Requirement"). Thus, claims to pharmaceutical compositions containing EPO and human serum albumin (Group VII), were separated from claims drawn towards pharmaceutical compositions comprising just EPO, and without the serum albumin element (Group V).

Amgen elected to pursue Invention Group VII in prosecuting the '422 patent. *Id.* at 4. However, late in the prosecution of this patent, Amgen added the following claim, which is the only claim of the '422 patent presently asserted against Roche.

> A pharmaceutical composition comprising a therapeutically effective amount of human erythropoietin and a pharmaceutically acceptable diluent, adjuvant or carrier, wherein said erythropoietin is purified from mammalian cells grown in culture.

(Ex. DD at 3). Critically, this claim, which matured into claim 1 of the '422 patent, has no reference to human serum albumin, and broadly covers pharmaceutical compositions containing the EPO polypeptide. Amgen stated that this "[n]ewly added Claim 64 is directed to a pharmaceutical

composition of human erythropoietin which is obtained from mammalian cells grown in culture." *Id.* at 4. Amgen never characterizes this claim to include human serum albumin. As further evidence that this new claim was directed to pharmaceutical compositions comprising EPO, without human serum albumin, Amgen concurrently filed a Terminal Disclaimer over the '933 patent, which does not claim human serum albumin (Ex. EE).

However, by filing this new claim in the '422 patent, Amgen again violated the Patent Office's restriction requirement, which separated claims to (1) pharmaceutical compositions containing EPO and human serum albumin from (2) pharmaceutical composition comprising EPO without human serum albumin. Therefore, claim 1 of the '422 patent is the direct result of Amgen's recurring pattern of breaking consonance with Patent Office restriction requirements.

### E. Applicants Must Maintain Strict Consonance In Order To Gain Section 121 Immunity

Pursuant to 35 U.S.C. § 121, claims in a divisional application are immune from an obviousness-type double patenting rejection when the claims were elected in a restriction requirement in the earlier application. The statute reads in relevant part:

> §121. Divisional applications
> ...A patent issuing on an application with respect to which a requirement for restriction under this section has been made, or on an application filed as a result of such a requirement, shall not be used as a reference either in the Patent and Trademark Office or in the courts against a divisional application or against the original application or any patent issued on either of them, if the divisional application is filed before the issuance of the patent on the other application. 35 U.S.C. § 121 (emphasis added)

#### 1. Under The Literal Reading Of The Statute, Section 121 Only Applies To Divisional Applications

Amgen cannot rely upon this statute because the '349, '933, and '422 patents did not issue from divisional applications adhering to the restriction requirements, but rather from continuation

applications which included all of the original claims from the '008 patent application.[6] Each time Amgen re-filed its original claims in the '178 and '179 applications, Amgen never separated its inventions into different divisional application as a result of a restriction requirement, but continued new prosecutions of these claims.[7] After all, the applications resulting in the '349 and '933 patents were filed 9 years after the 1986 restriction requirement. The application resulting in the '422 patent was filed 7 years after the restriction requirement. Quoting the language of Section 121, Amgen's numerous continuation applications were not "filed as a result of" the 1986 restriction requirement. Under these circumstances, the protection of Section 121 should not apply. *See Bristol-Myers Squibb Co. v. Pharmachemie B.V.*, 361 F.3d 1343, 1348 (Fed. Cir. 2004) (In not applying the Section 121, the Federal Circuit stated that "continuation application . . . began a new proceeding in which all of the original claims of the . . . application were once again presented for examination.") (emphasis supplied).

**2. Section 121 Requires Strict Consonance With The Restriction Requirement**

In order to obtain the protection of Section 121, consonance must exist between the earlier restriction requirement and the claims later prosecuted, *i.e.*, the applicant's actions must be consistent with the initial restriction requirement dividing groups of claims into distinct categories. *Gerber Garment Tech., Inc. v. Lectra Sys., Inc.*, 916 F.2d 683, 688 (Fed. Cir. 1990); *Bristol-Myers Squibb Co. v. Pharmachemie B.V.*, 361 F.3d 1343, 1348 (Fed. Cir. 2004); *Geneva Pharms., Inc. v.*

[6] For the '349 patent, Amgen filed continuation applications No. 113,179 in October 23, 1987 and No. 468,369 in June 6, 1995 (Ex. C at 1). For the '933 patent, Amgen filed continuation application No. 113,178 in October 23, 1987, No. 202,874 in February 28, 1994, and No. 487,774 in June 7, 1995 (Ex. E at 1). For the '422 patent, Amgen filed continuation applications No. 113,179 in October 23, 1987, No. 609,741 in November 6, 1990, No. 957,073 in October 6, 1992, and No. 100,197 in August 2, 1993 (Ex. D at 1).

[7] Under statutory interpretation, the literal language of the wording "Divisional" should be followed. *See Reves v. Ernst & Young*, 507 U.S. 170, 177 (1993) (quoting *United States v. Turkette*, 452 U.S. 576, 580 (1981)) ("In determining the scope of a statute, we look first to its language. If the statutory language is unambiguous, in the absence of 'a clearly expressed legislative intent to the contrary, that language must ordinarily be regarded as conclusive.'"); *Northland Cranberries, Inc. v. Ocean Spray Cranberries, Inc.*, 382 F. Supp. 2d 221, 225 (D. Mass. 2004) ("When statutory

*GlaxoSmithkline PLC*, 349 F.3d 1373, 1381 (Fed. Cir. 2003). "Consonance requires that the line of demarcation between 'independent and distinct inventions' that prompted the restriction requirement be maintained. . . .Where that line is crossed the prohibition of the third sentence of Section 121 does not apply." *Gerber*, 916 F.2d at 688. Therefore, restriction requirements must identify the scope of the distinct inventions that have been restricted, and must do so with sufficient clarity to show that a particular claim falls within the scope of the distinct inventions. *Geneva*, 349 F.3d at 1382. Only if such a discernable consonance exists and is maintained throughout continuing applications, the applications are entitled to the protection of Section 121. *Id*. As recognized in *Gerber*, the consonance requirement is consistent with the legislative purpose behind Section 121.

> Congress could not have intended to deny all inquiry into whether the restriction requirement it established in Section 121 had been disregarded during [the] prosecution of a divisional application.

*Gerber*, 916 F.2d at 688 (emphasis added). As detailed *supra*, Amgen engaged in a systematic and deliberate campaign of ignoring and eviscerating the very restriction requirement that it now seeks protection from.

- First, Amgen broke consonance with the 1986 restriction requirement when it added a process claim to the vertebrate cell claims of the '349 patent prosecution. Even though the Patent Office told Amgen to separate its vertebrate cell claims (Group IV) from its process claims (Group II), Amgen disregarded this restriction. As demonstrated by the Lowe Declaration, claim 7 of the '349 patent is virtually indistinguishable from claim 4 of the '698 patent, a Group II claim, since both claim the process for making erythropoietin using "vertebrate cells" under suitable nutrient condition with non human promoter sequences.

- Second, Amgen broke consonance with the 1986 restriction requirement during the prosecution of the '933 patent when it eliminated the very basis for restricting out the polypeptide claims (Group I) from the process claims (Group II). In the restriction requirement, the Patent Office explained that the only reason it was separating such similar claims was because the polypeptides could be made using a different process, "such as isolation from a naturally occurring source." (Ex. U at 2). However, during the course of prosecuting the '933 patent, Amgen amended its claims to add the limitation "non-naturally occurring," thereby vitiating the Patent Office's reasoning for separating these group of claims (Ex. Z at 4-5).

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interpretation is at issue, the plain and unambiguous meaning of a statute prevails in the absence of clearly expressed legislative intent to the contrary."; quoting *In re Alappat*, 33 F.3d 1526, 1531 (Fed. Cir. 1994)).

- Third, during the '933 patent prosecution, Amgen also broke consonance with the restriction requirement when it combined polypeptide claims (Group I) with pharmaceutical claims (Group V) (Ex. E). Thus, even though the Patent Office told Amgen to keep these claims in separate divisional applications, Amgen ignored this directive and prosecuted these claims together in the same application.

- Fourth, Amgen broke consonance again when it prosecuted claim 1 of the '422 patent. During that application, the Patent Office issued a second Restriction Requirement which separated pharmaceutical composition claims (Group V) from claims covering pharmaceutical compositions containing human serum albumin (Group VII) (Ex. CC). Amgen elected to prosecute the albumin claims, but just prior to the application being allowed, Amgen inserted a Group V claim which was directed to a pharmaceutical composition that did not contain human serum albumin (Ex. DD at 3). Thus, Amgen again disregarded the restriction requirement and prosecuted restricted claims within the same application.[8]

- Finally, as stated above, each time Amgen filed its '178 and '179 continuation applications for the '349, '933, and '422 patents, it resubmitted all of the original claims of the '008 patent parent application as they were filed before the 1986 restriction requirement, and did not file divisional applications grouped by the restriction categories (Exs. W and X). Therefore, upon each of these filings of a continuation application, Amgen disregarded the Patent Office's restriction requirement.

Therefore, Amgen's failures are manifest. Amgen failed to maintain the consonance of the restriction requirement during the prosecution of the '349, '933, and '422 patents. As a result, Section 121 cannot shield these patents from ODP as a matter of law. Amgen has also failed to meet its heavy burden of proving Section 121 immunity on summary judgment.

## III. ROCHE, NOT AMGEN, IS ENTITLED TO SUMMARY JUDGMENT ON DOUBLE PATENTING OVER THE '016 PATENT

It is undisputed that the '016 patent claim 10 explicitly requires "recombinant erythropoietin" ("rEPO") from "a mammalian cell culture supernatant fluid." To the person of skill in the art, rEPO means the purified and isolated DNA sequence encoding human EPO and host cells transfected therewith – the subject of the (expired) Lin '008 patent. *See* accompanying Second Declaration of Edward Everett Harlow, Ph.D. ("Second Harlow Decl.") ¶ 3. Amgen long ago

[8] Contrary to Amgen's argument, the 1992 restriction requirement in the '422 patent prosecution is not trumped by the earlier 1986 restriction requirement from the '008 patent prosecution. While Amgen would have the Court simply ignore the 1992 restriction requirement, the Federal Circuit has found that a later issued restriction requirement supersedes an earlier one when they are not necessarily consistent. *See Bristol-Myers Squibb Co. v. Pharmachemie*

admitted that the "process for preparing *in vivo* biologically active EPO using a mammalian host cell," as well as uses of rEPO – the subject matter of the claims in suit – "are only different manifestations of the same invention [as the DNA sequence]." (Ex. I).

Thus, for the reasons set forth in Roche's memorandum in support of its motion for summary judgment on double patenting (Docket No. 491), summary judgment should be granted in Roche's favor and Amgen's motion must be denied. Amgen has not even attempted to explain how one could practice the now-expired '016 claim 10 without infringing the patents-in-suit. Under the properly applied one-way test, or even under the two-way test proferred by Amgen, the claims-in-suit are invalid for obviousness-type double patenting.

**A. The One-Way Test, Not the Rarely Used Two-Way Test, Applies**

In an obviousness-type double patenting analysis, the determination of whether a "one-way" test or a "two-way" test applies is a question of law. *In re Berg*, 140 F.3d 1428, 1432 (Fed. Cir. 1998). The Federal Circuit has repeatedly held that the two-way test is a rare exception to the general rule.[9] *See, e.g., id.; Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 969 n.7 (Fed. Cir. 2001). The two-way test only applies when an applicant can show that (1) the claims of its separate applications could not have been filed in a single application; and (2) the PTO was solely responsible for the delay that allowed the claims of the later-filed application to issue before the claims of the earlier-filed application. *See, e.g.*, *In re Berg*, 140 F.3d at 1437; *Lilly*, 251 F.3d at n.7; *In re Emert*, 124 F.3d 1458, 1461 (Fed. Cir. 1997); *see also* MPEP §804 (8th ed. Rev. 5, Aug. 2006). Amgen wrongly urges this Court to apply a much stricter standard than is required for

*B.V.*, 361 F.3d 1343, 1348-49 (Fed. Cir. 2004) ("In 1977, when the examiner for the '955 application issued the restriction requirement for that application, she did not reinstate or even advert to the 1973 restriction requirement.").

[9] In fact, the Federal Circuit has acknowledged that the reason for using the rare two-way test has all but been eliminated with the Patent Law Amendments Act of 1984 ("the 1984 Act"), which allows related inventions by different employees of the same company to be filed in a single application. *In re Berg*, 140 F.3d at 1432-1433. The '178 and '179 applications, as well as the '016 patent application, were all filed after the 1984 Act took effect, and could have therefore been combined into a single application even though different Amgen employees were named as inventors.

determining whether the one-way test or two-way test applies, a standard that is simply not supported by the case law.

Amgen deliberately misapplies the one-way test/two-way test analysis by erroneously comparing only the claims of the '008 patent application with those of the Lai '016 patent application. The correct analysis, however, is between the Lai '016 patent and the claims of the patents-in-suit. Thus, Amgen cannot meet the first requirement of the two-way test (that the claims could not have been filed in the same application), let alone prove the second (that delay in issuance of the claims in suit was solely the fault of the PTO).

**1. Amgen Could Have Filed the '178 and '179 Application Claims and the '016 Patent Claims in a Single Application**

Amgen vehemently denies that the '016 patent claims could have been filed together with the '008 patent claims since the subject matter claimed in the '016 patent was not even conceived as of the November 30, 1984 filing date of Dr. Lin's '298 application. Memorandum, pp. 15-16. The correct inquiry, however, considers whether the claims-in-suit could have been filed in a single application, *e.g.*, in the earlier-filed or later-filed application. *See, e.g., In re Emert*, 124 F.3d at 1461, (discussing *In re Braat*, 937 F.2d 589 (Fed. Cir. 1991), and whether the assignee could have included the claims in the later-filed application in the earlier-filed application or added the earlier-filed claims to the later-filed application); *In re Berg*, 140 F.3d at 1437; MPEP §804 (8th ed. Rev. 5, Aug. 2006). Thus, the question here is whether the '016 patent claims (filed in 1985) could have been filed together with the claims filed in the 1987 '178 and '179 applications that became the patents-in-suit. Under the correct analysis, the answer is undeniably yes.

In determining whether the claims could have been filed in one application, the Federal Circuit has considered several factors. For example, in *Berg*, the Court considered whether the disclosures of the two applications were "totally separate." *In re Berg*, 140 F.3d at 1434. In this

case, the disclosures of both the '178 and '179 applications and the '016 patent application are closely related and not totally separate. Indeed, the '016 patent application explicitly "incorporated by reference" the entirety of the specifications of the '178 and '179 applications, and was filed before the pendency of these applications. *See* Ex. F, '016 patent, col. 2, ln. 64 to col. 3, ln. 6. In addition, Por-Hsiung Lai an inventor of the '016 patent, filed a protest on the grounds that he also invented the patents-in-suit. *See* Ex. FF. In *Berg*, the Court also considered whether the inventions disclosed in both sets of claims had been completed before either application was filed. *In re Berg*, 140 F.3d at 1434. Significantly, Amgen cannot argue that the inventions, disclosed in the claims of '178 and '179 applications filed in 1987, had not been conceived or reduced to practice before June 20, 1985, the filing date of the '016 patent. Thus, clearly, the '178 and '179 application claims could have been filed together with the claims of the '016 patent in a single continuation-in-part application, at any time from the June 20, 1985 filing date of the '016 patent to when the '016 patent issued on May 19, 1987. *See* accompanying Second Declaration of Michael Sofocleous ("Second Sofocleous Decl.") ¶¶ 3, 5-12.

**2. Amgen, Not The PTO, Was Primarily Responsible For The Delay In Prosecution**

During the prosecution of the Lin patents, Amgen made a strategic decision to expedite consideration of the claims of the now-expired '008 patent for the DNA sequence so that it could sue purported infringers (which it did the day the '008 patent issued). In stark contrast, Amgen completely stalled prosecution of all the other claims during the pendency of the '016 patent. Most claims were withdrawn by Amgen in April 1986. Amgen feigned interest in the process claims which formed the basis for the '868 patent and the '698 patent, but cancelled them in March 1987 precluding early issuance along with the other claims of the '008 patent. The filing of the '178 and '179 continuation applications was held back until the last possible moment, just days before the

'008 patent issued (after which point Amgen would have lost its rights to pursue those claims). The claims-in-suit were kept out of the PTO's reach until after the '016 patent had already issued. *See* Second Sofocleous Decl. ¶¶ 3-15. It is therefore Amgen, not the PTO, that is responsible for the delay. If the PTO was not solely responsible for the delay, the one-way test is the proper test. *In re Berg*, 140 F.3d at 1435, 1437.

### B. Because rEPO Is Fully Disclosed In '016 Claim 10, The Patents-in-Suit Are Not Patentably Distinct From The '016 Patent

Amgen takes the remarkable position that the reference to "recombinant erythropoietin" in '016 claim 10 is a "simple mention" that "merely names[s] a thing" and does not disclose to the ordinary artisan how to make or possess the claimed rEPO. Amgen is fundamentally wrong, and cites no legal authority in support of its position.

Claims are presumed to be enabled, and it is therefore presumed that an artisan with knowledge of the '016 patent would know how to create the rEPO claimed in '016 claim 10. *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1327 (Fed. Cir. 2003). Claims are of course not intended to be enabled standing on their own, but are enabled by their specifications. 35 U.S.C. § 112, ¶¶ 1 and 2. In this case, the '016 specification explicitly incorporates by reference the entirety of the specification of the patents-in-suit, thereby giving the artisan all of the information necessary to create the rEPO according to the patents-in-suit. See Ex. Q, '016 patent, col. 2, ln. 64 to col. 3, ln. 6. If there was no reliance on the specifications of the patents-in-suit, the '016 patent could not have satisfied the written description and enablement requirements of 35 U.S.C. § 112. In fact, it was necessary to rely upon the disclosure of the co-pending specifications of the patents-in-suit since this disclosure was an essential part of the invention claimed in the Lai '016 patent. Considering that the support for the '016 claims lies in the co-pending specification of the patents-in-suit and that the invention claimed in the '016 patent was part of the invention of the co-pending

patents-in-suit, Amgen could have filed the '016 patent claims in a single continuation-in-part application of the co-pending application which issued into the '008 patent.

Although the novel aspects of the specification do not constitute prior art, it is entirely appropriate for the Court to consult the specification in order to determine the meaning of claim terms, such as rEPO . In upholding a finding of double patenting, the Federal Circuit in *Geneva Pharmaceuticals* considered whether a patent for a method of using a compound was invalid over a previously issued patent for the compound itself. In analyzing the claims, the Court found it appropriate to look at the specification in order to understand the scope and utility of the claimed compound:

> To review the district court's judgment on this point, this Court examines the disclosure of the Fleming claim. Nonetheless, this court does not consider the Fleming claim in a vacuum, as a simple compound, without considering the compound's disclosed utility...Standing alone, that claim does not adequately disclose the patentable bounds of the invention. Therefore, this court examines the specifications of both patents to ascertain any overlap in the claim scope for the double patenting comparison. *See In re Avery*, 518 F.2d 1228, 1232 (C.C.P.A. 1975); *In re Zickendraht*, 319 F.2d 225, 228 (1963).
>
> A person of ordinary skill in the art reviewing the disclosure of the Fleming patent would recognize a single use for potassium clavulanate, administration to patients to combat bacteria that produce <<beta>>-lactamase...The Fleming patent discloses no other use. The 720 patent simply claims that use as a method.

*Geneva*, 349 F.3d at 1385 (emphasis added).[10] In this case, someone of ordinary skill in the field would have easily understood that the term "recombinant" for a protein meant that the protein was made using recombinant DNA techniques, which were well known by 1983 – and which are basically the techniques claimed in the patents-in-suit for making rEPO. Second Harlow Decl. ¶ 3. *See also* Ex. N (Initial Expert Report of Dr. Harvey Lodish, wherein Dr. Lodish explained that these techniques were well known by 1980). For this reason, among others, Amgen's car wash analogy is

[10] *Accord, Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1373 (Fed. Cir. 2005); *Research Corp. Tech., Inc. v. Gensia Labs., Inc.*, 10 Fed. App'x. 856, 864 (Fed. Cir. 2001).

entirely inapt.[11] Despite the expiration of the '016 patent, the public still cannot practice '016 patent claim 10 without facing infringement suits based on the patents-in-suit. Second Harlow Decl. ¶ 4. The '016 patent claim 10 sets forth the rEPO as claimed and asserted in the Lin patents-in-suit, yet Amgen continues to use the Lin patents to extend its monopoly of rEPO beyond the expiration of the '016 patent. Furthermore, the fact that the '016 patent is of a different class than some of the claims-in-suit is of no moment, as this does not provide a patentable distinction for obviousness-type double patenting.[12]

### C. Amgen is Judicially Estopped From Arguing That Differences in Claim Language Render the Patents-in-Suit Patentably Distinct from the '016 Patent

As the record reflects, Amgen repeatedly (and successfully) argued that the composition claims and the process claims "are only different manifestations of the same invention" and that "the whole purpose and intent of the purified and isolated DNA sequence encoding human EPO (and host cells transfected therewith) ... was to express *in vivo* biologically active human EPO." (Ex. I at pp. 25-26). Amgen's past statements are fundamentally inconsistent with its current assertion that the '016 patent does not disclose *in vivo* biologically active human EPO, thus

[11] When Amgen patented rEPO, it was not like making a car – Amgen's rEPO was more akin to a very specific type of vehicle to which Amgen claimed exclusive rights, and this vehicle needed a very specific type of purification process because otherwise the vehicle would not be useable. Second Harlow Decl. ¶ 6. (For example, while it is true that there is no need for a car wash until the car was invented, there was no need for unpurified EPO as its use in a pharmaceutical composition would pose serious health risks. Also, if the wrong purification process was used, the EPO could be damaged). Thus, rEPO was fully set forth in the '016 patent claim 10 and is presumed enabled (and indeed is enabled to the extent of the Lin specification). Once Amgen made its vehicle – rEPO – the subject of claim 10 of the '016 patent, the rEPO was in the possession of the ordinary artisan and the clock on Amgen's patent monopoly started to tick. The subject matter of the patents-in-suit and the '016 patent are inextricably intertwined, and are indeed two parts of the same invention: to be used as a pharmaceutical, the EPO needs to be purified.

[12] For example, claims directed to methods of using a composition can be obvious in light of claims directed to the composition (*see, e.g., Geneva Pharms., Inc. v. GlaxoSmithKline PLC,* 349 F.3d 1373 (Fed Cir. 2003); *In re Lonardo* 119 F.3d 960 (Fed. Cir. 1997)); claims directed to a product can be obvious in light of claims directed to producing the product (*see, e.g., In re Freeman,* 166 F.2d 178 (C.C.P.A. 1948)); and claims directed to a composition can be obvious in light of claims directed to a method of using the composition (*see, e.g., Research Corp. Techs., Inc. v. Gensia Labs., Inc.*, 10 Fed. App'x. 856 (Fed. Cir. 2001)). *See also, Phillips Petroleum Co. v. U.S. Steel Corp,* 604 F. Supp 555 (D. Del. 1985).

precluding summary judgment in favor of Amgen and requiring summary judgment in favor of Roche because the claims-in-suit are merely obvious variations of '016 claim 10.

### D. Even Under the Disfavored Two-Way Test, Amgen's Patents-in-Suit are Invalid

Even if this Court determined that the rare two-way test applies, Amgen's patents-in-suit are invalid. As set forth in the accompanying declaration of Dr. Harlow, the purification steps claimed in '016 claim 10 employ techniques well known to those in the art, and are obvious in light of the prior art. Second Harlow Decl. ¶ 5. Because there is no patentable distinction in either direction, Amgen's patents are invalid even under the two-way test.

## IV. CONCLUSION

Based on the foregoing, Roche requests that Amgen's motion for summary judgment of no obviousness-type double patenting be denied, and that Roche's motion for obviousness-type double patenting over the Lai '016 patent be granted.

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Respectfully submitted,

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