UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

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

AMGEN'S BENCH MEMORANDUM REGARDING NO OBVIOUSNESS-TYPE DOUBLE PATENTING

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I. INTRODUCTION

On August 27, 2007, this Court granted Amgen's motion for summary judgment that all of the claims-in-suit are not invalid for obviousness-type double patenting ("ODP") over the Lai/Strickland '016 patent claims. The Court also held that the asserted claims of the '933, '422 and '349 patents are exempt from ODP over the '008 patent claims under 35 U.S.C. § 121 — the ODP "safe harbor" statute.

In response to the Court's summary judgment ruling, Roche presses its allegations that the '868 and '698 claims are invalid for ODP over the '008 patent claims. Roche refers to these ODP defenses as Roche's ODP "Theory No. 3." In addition, Roche seeks to add several new ODP defenses that Roche neither disclosed nor developed during discovery. Roche refers to these new allegations, that the '933, '422 and '349 claims are invalid for ODP over the '868 and '698 claims, as Roche's ODP "Theory No. 4." Theory No. 4 is not properly in the case.

The Court has requested additional briefing from the parties concerning these unresolved ODP defenses. For the reasons explained below and in Amgen's summary judgment briefing, the Court should dispose of Roche's remaining ODP defenses as a matter of law.

Roche's new ODP defenses based on the '868 and '698 patent claims ("Theory No. 4") should be dismissed on procedural grounds, not only because Roche concealed these ODP defenses during discovery to the detriment of Amgen, but also because Roche is barred by 35 U.S.C. § 282 from asserting claims of Lin's '868 and '698 patents as prior art against any other claims-in-suit. Pursuant to § 282, Roche was required to disclose to Amgen thirty days before trial every prior art reference on which it relied in support of any defense or claim that the patents-in-suit are invalid. Roche's § 282 Notice lists the Lin '008 and Lai/Strickland '016 patents (Roche's other ODP references), but does not list the '868 and '698 patents as invalidity references. (*See* Docket Item ("D.I.") 799, at 4.) Even now — three weeks into trial — Roche

has not provided any detailed explanation of how and why Roche contends that claims of the '868 and '698 patents render the other claims-in-suit invalid for ODP.[1] ODP is an affirmative defense for which Roche bears the burden of proof. It is entirely improper for Roche to seek a tactical advantage by ambushing Amgen with these new defenses in the middle of trial.

Roche's Theory No. 4 should also be dismissed on substantive grounds, because these defenses are precluded by 35 U.S.C. § 121 for the same reasons that the statutory safe harbor exempts the '933, '422 and '349 claims from ODP over the claims in the '008 patent. As already established on summary judgment, the '933, '422 and '349 patent claims arise from applications filed as a result of the PTO's 1986 restriction requirement and are consonant with the non-elected invention groups of that restriction requirement. None of the '933, '422 or '349 claims belong to the same restriction group as the '868 and '698 patent claims (which belong to the same restriction group as the '008 claims), and for that reason 35 U.S.C. § 121 prevents Roche from asserting Lin's '868 and '698 claims as ODP references against Lin's '933, '422 or '349 claims.

The admissions in Roche's briefing make clear that its latest ODP defenses are nothing more than a transparent attempt to circumvent the Court's summary judgment ruling that the '933, '422 and '349 claims are exempt from ODP over the '008 claims. Assuming, *arguendo*, that Roche's latest ODP defenses were not precluded by § 121, and that these claims were not patentably distinct from the '868 and '698 claims, the terms of the '933, '422 and '349 patents would be co-terminus with the '868 and '698 patents (which are terminally disclaimed to each other). But that is not Roche's end-game, because the '868 and '698 patents do not expire until 2012, a full five years from now. Rather, by combining its Theory No. 4 (the '933, '349 and

[1] Should the Court require any additional information to dispose of Roche's new ODP defenses, Amgen respectfully requests the opportunity to submit additional information once Amgen has

'422 claims are obvious over and coterminous with the '868 and '698 claims) with its Theory No. 3 (the '868 and '698 claims are obvious over and coterminous with the '008 claims), Roche hopes to achieve the very result that this Court rejected in its summary judgment ruling, namely, a ruling that the '933, '422 and '349 claims were obvious over, and therefore coterminous with, Lin's '008 patent. This result is precluded by the Court's summary judgment Order, and the Court should reject Roche's latest gambit for what it is: a contrived end-run around the Court's summary judgment ruling.

Roche's Theory No. 3 defenses should be dismissed because the process inventions claimed in Lin's '868 and '698 patents are patentably distinct from the DNA and host cell inventions claimed in Lin's '008 patent. The Patent Office determined on several occasions that Lin's process claims were patentably distinct from the claims of the '008 patent, including an express determination signed by the Acting Commissioner of the PTO that the DNA and host cells claimed in Lin's '008 patent were "deemed to be patentably distinct" from the processes claimed in the '868 and '698 patents. Indeed, during the prosecution of the '868 claims, the examiners expressly considered many of the very same arguments and the very same prior art that Roche now presents. They did so in the context of a rejection of the pending '868 claims for ODP over the '008 claims. After review of the evidence, the PTO decided to withdraw the rejection and allow the claims to issue precisely because it concluded that the inventions claimed in the '868 patent were in fact patentably distinct from the '008 claimed inventions. Consequently, the burden now falls on Roche to prove by clear and convincing evidence that Dr. Lin's process claims were not patentably distinct from Lin's DNA and host cell claims.

For all of the reasons previously made manifest in the prosecution of Lin's process claims, as well as the reasons explained in the supporting declaration of Dr. Lodish, the PTO's

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had an opportunity to review the details of Roche's not-yet-disclosed ODP arguments.

determination that Lin's process inventions are patentably distinct from Lin's DNA and host cell inventions should be affirmed. The Court should hold as a matter of law that the '868 and '698 asserted claims are not invalid for ODP over the '008 patent claims.

II. STATEMENT OF FACTS

A. ROCHE'S ODP ALLEGATIONS

Based on the information disclosed in Roche's August 31, 2007 Pre-Trial Brief (D.I. 919) and September 7, 2007 Offer of Proof (D.I. 1035), Amgen understands Roche's current allegations of obviousness-type double patenting to consist of the following:

Theory No. 3:

- '868 claims 1 and 2 invalid for ODP over '008 claims 2, 4, 6, 7, 25, and/or 27;
- '698 claims 6-9 invalid for ODP over '008 claims 2, 4, 6, 7, 25, and/or 27;

Theory No. 4:

- '933 claims 3, 7-9, 11-12, and 14 invalid for ODP over '868 claims 1, 2, 4, and/or 5;
- '422 claim 1 invalid for ODP over '868 claims 1, 2, 4, and/or 5;
- '422 claim 1 invalid for ODP over '698 claims 6, 7, 8 and/or 9;
- '349 claim 7 invalid for ODP over '868 claims 1, 2, 4, and/or 5;
- '349 claim 7 invalid for ODP over '698 claims 6, 7, 8 and/or 9.[2]

Roche's Theory No. 4 defenses are not properly in this case.

Roche's ODP allegations have morphed repeatedly and substantially over the course of this action, including after the close of discovery, and even during trial. Roche's original

[2] Roche's September 7, 2007 Offer of Proof (D.I. 1035) — filed in response to this Court's order that Roche specify which '868 and '698 claims it seeks to assert as ODP references — does not identify claim 4 of the '698 patent as a basis for any ODP defense. Thus, Roche's arguments and evidence at the October 1, 2007 ODP hearing purporting to show that claim 7 of the '349 patent is invalid for ODP over '698 claim 4 should be disregarded.

Answer and Counterclaims, filed November 6, 2006, provided nothing more than bare notice of Roche's intent to allege that certain undisclosed claims of the patents-in-suit are invalid for ODP over certain undisclosed claims of Amgen's '008 patent: "The claims of the '868, '933, '698, '080, '349 and '422 patents are invalid for double patenting over claims of Amgen's earlier issued and now expired U.S. Patent No. 4,703,008 ('the '008 patent')." (D.I. 140, at 4, ¶ 37.) No other theories of ODP were mentioned in Roche's original Answer and Counterclaims.

During pretrial discovery, Amgen pressed Roche to disclose the factual bases for its general ODP allegation, but Roche repeatedly declined to do so. Roche provided only incomplete disclosure of its ODP defenses in its interrogatory responses served before the close of fact discovery on April 2, 2007. None of these interrogatory responses identified or discussed ODP based on the '868 or '698 patent claims (*i.e.,* Roche's Theory No. 4).

On December 11, 2006, Amgen served two interrogatories, Nos. 9 and 11, requesting detailed, claim-by-claim information regarding Roche's double patenting allegations. In its first response to Amgen's ODP interrogatories, served January 11, 2007, Roche merely alleged that Amgen's asserted claims were invalid for ODP over certain undisclosed claims of Amgen's '008 patent. (Declaration of Geoffrey M. Godfrey In Support of Amgen's Bench Memorandum and Offer of Proof Regarding No Obviousness-Type Double Patenting (D.I. 1165), Ex. A, at 48.) On February 9, 2007, Roche supplemented its response to Amgen's interrogatories, listing the specific claims of the '008 patent that Roche contended invalidated the claims-in-suit for ODP. Roche identified as ODP references '008 claims 1, 2, 4-8, and 23-27. (D.I. 1165, Ex. B, at 69.) On February 26, 2007, in its second supplemental response to Amgen's interrogatories, Roche did not identify any further allegations of ODP.

On March 2, 2007, Roche sought leave to amend its sixth affirmative defense (double patenting) to plead the Lai/Strickland '016 patent as a basis for ODP and to plead that "the

claims of the '349, '933, '080, and '422 patents are invalid for double patenting over the claims of the '868 and '698 patents." (D.I. 304.) Amgen opposed Roche's motion and requested that the Court preclude Roche from seeking any additional time for discovery. (D.I. 321.) On March 20, 2007, the Court granted Roche's motion, but specifically ordered that "The Time For Discovery and Other Pre-Trial Scheduled Dates Are Not Extended." (3/20/07 Electronic Order.)

Two weeks later, on April 2, 2007 — the close of fact discovery — Roche served its third supplemental response to Amgen's ODP interrogatories. As in its prior interrogatory responses, Roche did not explain its ODP allegations based on any patent other than the '008 patent. Roche made absolutely no mention of ODP based on the '868 or '698 patent claims in these interrogatory responses. (D.I. 1165, Ex. C.)

On April 6, 2007, Roche filed its initial expert reports addressing Roche's ODP and other invalidity defenses. Five different Roche experts submitted reports concerning Roche's ODP defenses: Dr. Lowe, Dr. Harlow, Dr. Kellems, Dr. Blobel, and Mr. Sofocleous. All of these expert reports focused on Roche's ODP defenses based on the '008 or '016 patent claims. None of these expert reports mentioned ODP based on the '868 or '698 patent claims.[3] Nor did any of the numerous "corrected" and supplemental reports submitted by Roche's experts address Roche's current ODP defenses based on the '868 and '698 patent claims.[4] Relying on Roche's

[3] Roche has conceded that Dr. Lowe, Roche's only expert witness at trial regarding ODP issues, never provided any opinions regarding Theory No. 4 (ODP over the '868 and '698 claims) in his expert report. (*See* D.I. 1022, at 2 (quoting 9/6/07 Trial Tr. at 306-307).)

[4] In a supplemental report concerning § 112 validity issues, one of Roche's experts, Dr. Kadesch, recited a conclusory, two-sentence opinion that '349 claim 7 is invalid for double patenting over '698 claim 4: "there is no significant difference between claim 7 of the '349 patent and claim 4 of the '698 patent. Therefore, claim 7 of the '349 patent is invalid for double patenting." (5/1/07 Supp. Expert Rpt. of Dr. Thomas Kadesch, at ¶ 8.) This opinion does not address any of the '868 or '698 claims that Roche now asserts as bases for ODP. (*See* Roche's 9/7/07 Offer of Proof, D.I. 1020, at 1.) Moreover, this unsupported opinion is not the type of clear and convincing evidence required to justify a holding of obviousness-type double patenting.

failure to describe any ODP defenses based on the '868 and '698 claims either in its interrogatory responses or its expert reports, Amgen's experts did not address ODP based on the '868 and '698 claims in their rebuttal expert reports.

On May 1, 2007, a month after the close of fact discovery and weeks after Roche's ODP expert reports were submitted, Roche served a fifth supplemental response to Amgen's ODP interrogatories. In these untimely interrogatory responses, Roche made cursory mention of its new theory that the asserted claims of the '933, '422 and '349 patents are invalid for ODP over certain unspecified claims of the '868 and '698 patents. Like Roche's amended affirmative defense, however, these interrogatory responses lacked any detail or any claim-by-claim comparison and failed to state any of the specifics required to establish a defense of ODP over the '868 and '698 patent claims. (D.I. 1165, Ex. D, at 60-61.)

In June and July 2007, Roche's summary judgment briefs expressly referenced Roche's '008- and '016-based ODP defenses but made no mention whatsoever of any ODP defenses based on the '868 or '698 claims.[5]

On August 2, 2007, Roche filed its 35 U.S.C. § 282 Notice regarding its invalidity contentions. Although Roche listed the Lin '008 and Lai/Strickland '016 patents (Roche's other ODP references) in this statutorily-mandated disclosure, Roche failed to disclose the '868 and '698 patents as invalidity references. (*See* D.I. 799, at 4.) This again signaled Roche's intent not to pursue ODP defenses based on claims in the '868 and '698 patents.

The following week, in response to this Court's Order that the parties meet prior to the final pretrial conference "to narrow the issues to be tried," (D.I. 536, at 1), Roche disclosed in the

[5] *See, e.g.*, Mem. In Supp. of Defendants' Mot. for Sum. Judgment That the Claims of Patents-In-Suit Are Invalid for Double Patenting Over Amgen '016 Patent (D.I. 491), at 1 n.2 (noting that, in addition to Roche's ODP defense based on the '016 claims, Roche also had an additional ODP defense based on the '008 patent claims).

parties' August 10, 2007 Joint Pretrial Memorandum one claim from the '868 and '698 patents as a basis for ODP:

> 72. Whether subject matter covered by the Asserted Claims is obvious in view of claim 1 of the '868 patent.

(D.I. 807, Ex. B, at 8 (emphasis added).) Roche did not disclose any other details regarding this new ODP defense in the Joint Pretrial memorandum.

On August 27, 2007, the Court granted Amgen's Motion for Summary Judgment of No Obviousness-Type Double Patenting, which disposed of most of Roche's ODP defenses based on the '008 and '016 patent claims.[6] In light of this ruling, Roche filed a Pre-Trial Brief on August 31, 2007 — the last business day before trial — stating Roche's new desire to pursue at trial several additional ODP defenses based on claims in the '868 and '698 patents. But even that untimely disclosure failed to identify which claims of the '868 and '698 patents Roche sought to assert as a basis for ODP. Roche's pre-trial brief merely contended that the '933, '422 and '349 claims are invalid for ODP over "the claims of the '868 or '698 patents." (D.I. 919, at 34, 41, 50.)

It was not until September 7, 2007 — after the first week of trial — that Roche first identified which claims of the '868 and '698 patents Roche now contends invalidate the other claims-in-suit for ODP. (*See* D.I. 1035, at 1.) These untimely disclosures do not provide any explanation of how or why Roche contends that these claims of the '868 and '698 patents render the '933, '422 and '349 claims-in-suit invalid for ODP.

B. RELEVANT PROSECUTION HISTORY

1. The PTO's 1986 Restriction Requirement Required Amgen To Prosecute Dr. Lin's EPO Inventions In Multiple Applications

[6] *See* Electronic Order, dated Aug. 27, 2007, granting Amgen's Motion for Summary Judgment of No Obviousness-Type Double Patenting (D.I. 498).

Beginning in December 1983, Amgen filed a succession of four applications to patent the path-breaking inventions of Dr. Fu-Kuen Lin relating to erythropoietin ("EPO").[7] The last and most comprehensive of Dr. Lin's four initial and continuation-in-part applications, No. 06/675,298 ("the '298 application"), was filed on November 30, 1984.[8] As originally filed, the '298 application was well over 100 pages, and included 60 claims and multiple tables and figures. (TX 2013.6-142 (AM-ITC 00952292-428).) The '298 application disclosed a breadth of information and teaching regarding Dr. Lin's pioneering inventions, including, among many other things, purified and isolated DNA sequences encoding human and monkey EPO, vertebrate and other cells capable of producing recombinant human EPO in abundance when grown in culture, processes for producing *in vivo* biologically active glycosylated recombinant EPO polypeptides as well as the polypeptides themselves, and the first pharmaceutical compositions effective for the therapeutic treatment of severely anemic patients. At the time of Dr. Lin's '298 application, none of these important inventions were in the prior art, and none of Lin's teachings were publicly available to persons of ordinary skill in the art.[9]

On July 3, 1986, after an initial assessment of Dr. Lin's '298 application, the PTO determined that the '298 application included claims to six different categories or "groups" of patentably distinct inventions. For the convenience of the PTO and its examination, the examiner imposed a "restriction requirement" that required Amgen to select one of the six

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[7] *See generally Amgen Inc. v. Chugai Pharm. Co. Ltd.*, 13 U.S.P.Q.2d 1737, 1746-49 (D. Mass. 1989) (summarizing events leading up to the filing of these applications).

[8] *See generally* D.I. 501, Ex. A (providing a visual overview of the prosecution history of Dr. Lin's patents). The patents-in-suit are filed in the record as Trial Exhibits ("TX") 1-5.

[9] A "person of ordinary skill" or "ordinarily skilled artisan" in the field relevant to Dr. Lin's claimed inventions would have been a research scientist with a Ph.D. or M.D. and at least two years of postdoctoral research experience in the field of molecular biology, cellular biology, or protein expression. (Declaration of Harvey F. Lodish, Ph.D. In Support of Amgen's Bench Memorandum and Offer of Proof Regarding Obviousness-Type Double Patenting (D.I. 1164),

invention groups for further examination in the '298 application, and to file separate applications for examination of the remaining, "non-elected" inventions:

> Restriction to one of the following inventions is required under 35 U.S.C. § 121:
>
> 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 240.
>
> 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.
>
> . . . .
>
> Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

(TX 2013.232-33 (AM-ITC 00952501-02).) The specific claims assigned to each of these restriction groups are set forth at TX 2013.103-111 (AM-ITC 00952389-97) and TX 2013.188-190 (AM-ITC 00952457-58). A table organizing these original claims according to the various restriction groups to which they were assigned by the examiner is provided in the 9/26/07 Godfrey Decl. (D.I. 1165), at Ex. E.

2. Amgen Complied with the PTO's 1986 Restriction Requirement

Amgen complied with the PTO's restriction requirement by selecting the claims of Group II for continued examination in the '298 application. (TX 2013.233 (AM-ITC 00952502).) The other, non-elected claims were cancelled from the '298 application so that they could be

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¶ 17.)

prosecuted in separate applications. (*Id.*) Although Amgen initially elected all of the Group II claims, which included DNA, host cell and process claims, for further prosecution in the '298 application, Amgen later cancelled the process claims after it became apparent that the PTO would not allow issuance of those claims based on *In re Durden*, 763 F.2d 1406 (Fed. Cir. 1985), which the PTO at the time mistakenly interpreted as prohibiting the allowance of any claim to a process that applied known process steps to a novel starting material. (*See* TX 2013.365 (AM-ITC 00952592); TX 2013.369 (AM-ITC 00952596); TX 2013.372 (AM-ITC 00952599).) On October 27, 1987, Dr. Lin's '298 application issued as the '008 patent. (TX 7.) Consistent with Amgen's election to have Group II claims examined in the '298 application, all of the '008 patent claims fall within the scope of restriction Group II. (Declaration of Harvey F. Lodish, Ph.D. In Support of Amgen Inc.'s Motion for Summary Judgment of No Obviousness-Type Double Patenting ("6/14/07 Lodish Decl.") (D.I. 502), at ¶ 25.)

Prior to the issuance of the '008 patent, on October 23, 1987, Amgen filed two new applications — Nos. 07/113,178 ("the '178 application")[10] and 07/113,179 ("the '179 application")[11] — that contained claims to non-elected inventions that the PTO had required be examined separately from the '298 application. The '178 and '179 applications were filed under 37 C.F.R. § 1.60. That provision, and the associated PTO procedures, permitted Amgen to file the '178 and '179 applications by submitting a copy of the prior '298 application (as originally filed) and canceling certain of the original '298 claims that were pending in the '298 application, so that only previously non-elected claims were included in the '178 and '179 applications as filed. *See* M.P.E.P. § 201.06(a) (D.I. 501, Ex. P-1).[12] In keeping with the 1986 restriction

[10] TX 2011.3-143 (AM-ITC 000862-1002).

[11] TX 2012.3-123 (AM-ITC 000003-123).

[12] The filing fee for applications filed under 37 C.F.R. § 1.60 was calculated based on the

requirement and the election of Group II in the '298 application, Amgen canceled all claims belonging to Group II, and selected only claims belonging to the non-elected restriction groups for filing in the '178 and '179 applications. The '178 application as filed contained original claims 1-13, 16, 39-41, 47-49, and 55-57, which the PTO had assigned to restriction Groups I and V. (*Compare* TX 2011.4-8 (AM-ITC 000863-67) *with* TX 2013.232 (AM-ITC 00952501).) The '179 application as filed contained original claim 1, which the PTO had assigned to restriction Group I. (*Compare* TX 2012.113-116 (AM-ITC 000972-75) *with* TX 2013.232 (AM-ITC 00952501).)

The '178 and '179 applications are both "divisional" applications under the PTO's definition because they are "later application[s]" (than the '298 application), "carved out of a pending application" (the '298 application), containing claims to "a distinct and independent invention" (Groups I and V, not Group II), and "disclosing and claiming only subject matter disclosed in the earlier or parent application" (as 37 C.F.R. § 1.60 applications, the disclosure and claim language is identical to that in the parent '298 application). *See* M.P.E.P. § 201.6 (D.I. 501, Exs. P-1 and P-2).

As summarized in the following diagram, the '178 and '179 applications were the first applications giving rise to the patents-in-suit filed after the PTO's 1986 restriction requirement, and all of Dr. Lin's patents-in-suit arise from one of these two applications:

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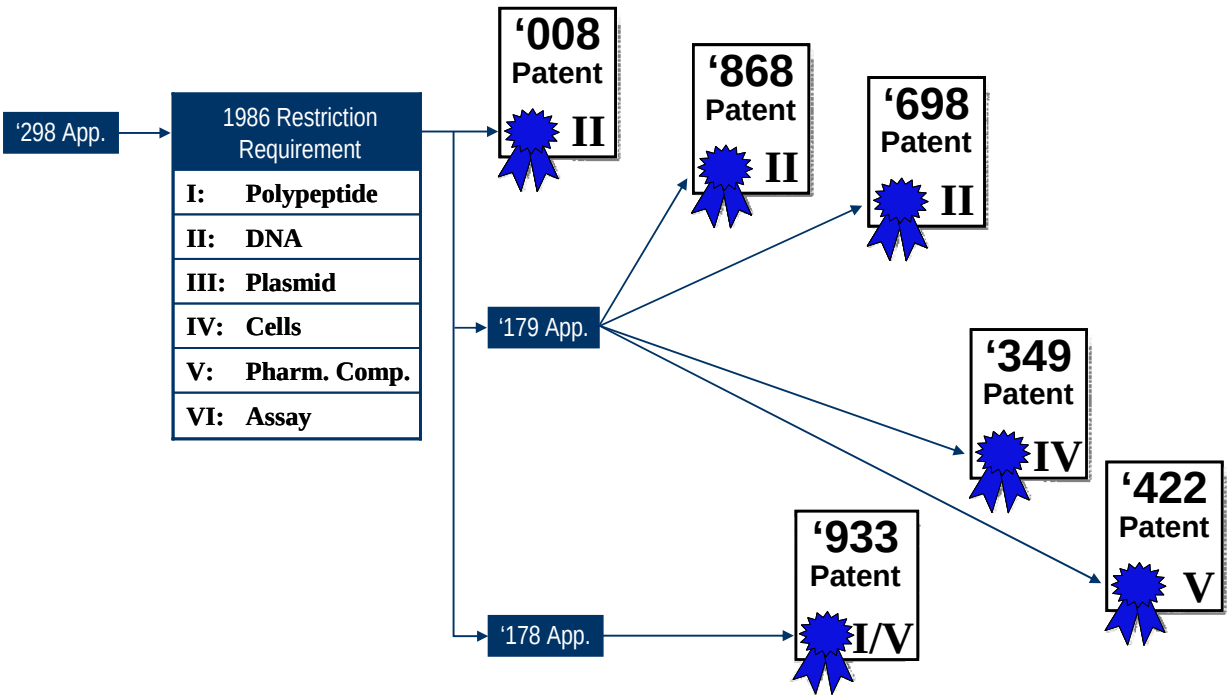
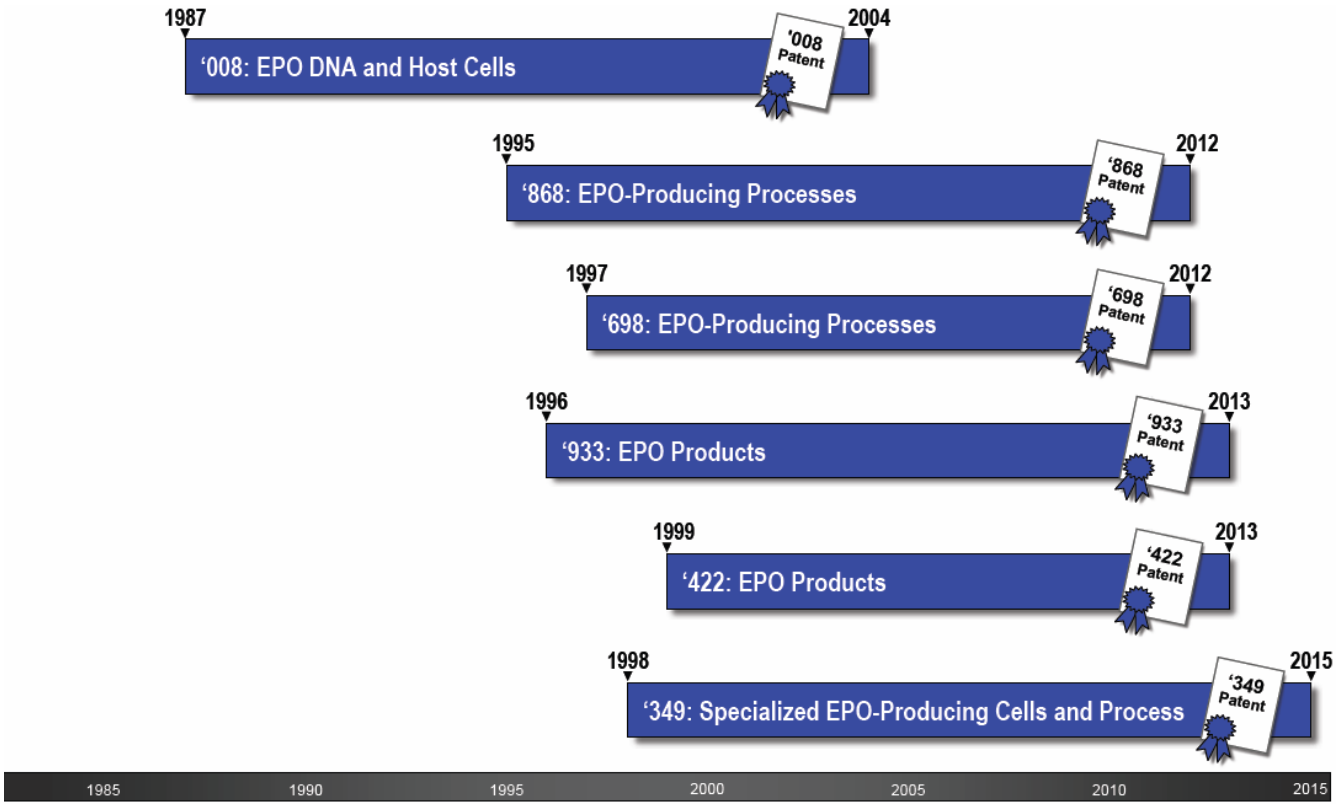
number of claims in the new application (i.e., the non-canceled claims), and not on the number of claims originally filed in the parent application. M.P.E.P. § 201.06 (a) (D.I. 501, Ex. P-1). The filing fee calculation in the '178 and '179 applications makes clear that the canceled claims were not part of the '178 and '179 applications as filed. (*See* TX 2011.5-6 (AM-ITC 000864-65); TX 2012.117-18 (AM-ITC 000117-18).)



During prosecution of the '178, '179, and subsequent applications leading to the patents-in-suit, Amgen canceled claims, amended claims, and added new claims. As a result, the issued claims in the patents-in-suit are not identical to the original claims filed in the '178 and '179 applications. But, importantly, all claims of the '933, '349, and '422 patents fall within the scope of the non-elected restriction groups, and none of these claims fall within the scope of restriction Group II, which was prosecuted to issuance in the '008 patent. (6/14/07 Lodish Decl. (D.I. 502), ¶¶ 26-34.) As shown in the diagram above, the '933 patent claims fall within the scope of restriction Groups I and V, the '422 patent claims fall within restriction Group V, and the '349 patent claims fall within restriction Group IV. (*Id.*) By contrast, the issued claims of the '868 and '698 patents fall within the scope of restriction Group II. (D.I. 568, at 2, 5.)

Where appropriate, Amgen filed terminal disclaimers during prosecution to ensure that the term of any patent which contained claims that were not patentably distinct from claims in an earlier-issued patent would expire on the same date as the earlier-issued patent. The '008 patent (TX 7) issued in October 1987 and expired in October 2004. The '868 patent (TX 2) issued in

August of 1995 and will expire in August of 2012. The '698 patent (TX 3) issued in April of 1997 and, because of a terminal disclaimer over the '868 patent (TX 2007.161-63 (AM-ITC 001782-84)), will also expire in August of 2012. The '933 patent (TX 1) issued in August of 1996 and will expire in August of 2013. The '422 patent (TX 5) issued in September of 1999 and, because of a terminal disclaimer over the '933 patent (TX 2009.766-67 (AM-ITC 003267-68)), will also expire in August of 2013. The '349 patent (TX 4) issued in May of 1998 and will expire in May of 2015. The terms of Amgen's patents are summarized in the following diagram:



3. The PTO Repeatedly Determined That Dr. Lin's Process Inventions Are Patentably Distinct from Lin's DNA and Host Cell Inventions

On multiple occasions during prosecution of Dr. Lin's '868 and '698 patents, the PTO determined that, notwithstanding the fact that they all originated from Group II in the 1986 restriction requirement, the process claims of the '868 and '698 patents are patentably distinct

from (and not obvious over) Dr. Lin's DNA and host cell claims in the '008 patent.

For example, at the urging of Amgen's competitor Genetics Institute, Inc. ("GI"), the PTO declared interference proceedings to determine priority as between Lin/Amgen and Fritsch/GI to various EPO-related inventions. Interference No. 102,096 ("the '096 Interference," declared on May 9, 1989) involved "[a] purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin." (TX 2013.576-78 (AM-ITC 00952797-99).)[13] Interference No. 102,097 ("the '097 Interference," declared on May 9, 1989) involved a multi-step process for preparing a glycosylated polypeptide having "the *in vivo* biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells . . . ." (TX 2012.742-44 (AM-ITC 000297-99).)[14] Interference No. 102,334 ("the '334 Interference," declared on February 9, 1990) involved "[a] non-naturally occurring glycoprotein product . . . possessing the *in vivo* biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells . . . ." (TX 2011.306-08 (AM-ITC 001140-42).)[15]

The fact that the PTO declared three ***separate*** interferences with three ***separate*** counts indicates that the PTO considered the DNA, process, and product inventions corresponding to those counts to be patentably distinct. By rule, each interference count must define a separate patentable invention. M.P.E.P. § 2303 (5th ed., Rev. 9, Sept. 1988) (D.I. 868, Ex. A) ("Each

[13] This "DNA Count" of the '096 Interference is identical to claim 2 in Amgen's '008 patent. The PTO also designated host cell claims of Lin's '008 patent as corresponding to the '096 Interference Count. (TX 2013.578 (AM-ITC 00952799).)

[14] This "Process Count" of the '097 Interference was identical to then-pending claim 65 in Amgen's '179 application which later gave rise to Amgen's '868 and '698 patents. The full text of the '097 Process Count is set forth at TX 2012.744 (AM-ITC 000299).

[15] This "Product Count" of the '334 Interference was identical to then-pending claim 76 in Amgen's '178 application which later gave rise to Amgen's '933 patent. The full text of the '334 Product Count is set forth at TX 2011.308 (AM-ITC 001142).

count shall define a separate patentable invention.") (quoting 37 C.F.R. § 1.603); *see also* 37 C.F.R. § 1.601(f) (1988) (D.I. 868, Ex. B) (same). Importantly, with respect to the subject matter of these three interferences, a determination was signed by Acting Commissioner Jeffrey Samuels, as well as Group Director John Kittle and Examiner Howard Schain, stating that, while related, "***the subject matter of the three interferences is deemed to be patentably distinct*** . . . ." (TX 2011.300 (AM-ITC 001134) (emphasis added).)

Once the '097 Interference was resolved, examination of the '179 application resumed. In a 1994 Office Action, the examiner rejected the pending process claims as obvious over (and not patentably distinct from) the DNA claims of Lin's '008 patent. (TX 2012.1019 (AM-ITC 000422).) In response, Amgen demonstrated that the '008 claims and the pending process claims were patentably distinct inventions. Amgen explained to the axaminer: (1) the expression of a glycosylated EPO product having *in vivo* biological activity was unexpected given the state of the art at the time;[16] (2) a prior ITC decision had determined that Lin's '008 claims did not extend to the process of producing EPO glycoproteins;[17] and (3) the PTO's declaration of separate interference proceedings for the DNA and process counts reflected its determination that Lin's '008 claims and process claims were patentably distinct inventions. (TX 2012.1023-80 (AM-ITC 000426-36, AM-ITC 00455484-530).) The examiner likely was bound by the PTO

[16] Indeed, Amgen had already overcome an obviousness rejection by demonstrating that the *in vivo* biological activity of the erythropoietin polypeptide resulting from the claimed processes was not reasonably expected by the person of ordinary skill in the art at the time. (*See* TX 2012.214-443 (AM-ITC 000191-211, AM-ITC 00454366-574); TX 2012.494-501 (AM-ITC 000262-69); TX 2012.526 (AM-ITC 000294).)

[17] As Amgen explained to the Patent Office during earlier prosecution of the '179 application, the ITC had determined that "the '008 patent covers articles, i.e. host cells, but not processes." (TX 2012.533 (AM-ITC 00953316).) The ITC decision made clear that, unlike Amgen's later '868 and '698 process claims, Amgen's '008 DNA and host cell claims did not provide legal protection against foreign competitors that produced recombinant erythropoietin abroad for importation into the United States. (TX 2012.533-34 (AM-ITC 00953316-17).)

Board's and Acting Commissioner's prior determinations of patentable distinctiveness, but instead of relying solely on those determinations, Amgen also argued the merits that based on the uncertain and highly unpredictable state of the art in 1983-84, there was no reasonable expectation of successfully producing an *in vivo* biologically active EPO product according to the claimed processes.

What is especially significant about Amgen's response to this ODP rejection over the '008 claims is that Amgen disclosed and directed the examiner's attention to a declaration by Dr. Arthur Sytkowski that had been submitted in European Opposition proceedings against Dr. Lin's European EPO patent. (TX 2012.1031 (AM-ITC 000434).) One of the Opponents in this proceeding was Boehringer Mannheim, Roche's predecessor-in-interest. The Sytkowski declaration set forth, in detail, various arguments as to why Dr. Lin's inventions were not patentable,[18] including many of the same arguments Roche now makes in support of its allegations that the process inventions claimed in Lin's '868 and '698 patents were obvious over Lin's '008 claims. For example, the Sytkowski declaration asserts:

- "It was reasonable to expect that the expression of the EPO DNA in COS and CHO cells would yield biologically active rEPO." (TX 2012.1070 (AM-ITC 00455520).)

- "As of 1983, what was the probability of success for the expression of biologically active recombinant EPO? That is, could one introduce exogenous DNA, such as the EPO gene, into a eukaryotic host cell and have a reasonable expectation that this gene would be expressed and that biologically active protein would be produced? The answer is unquestionably 'yes'." (TX 2012.1071 (AM-ITC 00455521).)

- "The successful examples in the prior art pointed the way for Lin: [Genentech's patent], for example, describes the

[18] For example, like Roche and GI before him, Dr. Sytkowski argued that Dr. Goldwasser's supply of purified urinary EPO to Amgen was the reason Lin succeeded and others failed to isolate EPO DNA. (*See* TX 2012.1060-61 (AM-ITC 00455510-11); TX 2012.1068 (AM-ITC 00455518).)

> production of human tissue plasminogen activator which 'comprises expressing a DNA sequence from a transformed host cell . . . . Preferred host cell is a transformed E. coli strain or a mammalian cell line, especially CHO cell line'. . . . Additional examples of production of recombinant proteins in CHO cells using the methods subscribed in [Lin's] patent exist as well. Therefore, it was not only reasonable to try stable transfection and expression in CHO cells, it was the most likely way to succeed, especially if transient expression in COS cells had already yielded a biologically active compound." (TX 2012.877-78 (AM-ITC 00455527-28).)

- "Amgen's inventor Dr. Lin merely followed prior art teachings and, in view of the successful experiments reported on in the prior art, must have had a reasonable expectation of success when he introduced the human EPO gene into COS cells and CHO cells in Example 7 and 10 of the contested patent, respectively, and obtained biologically active glycosylated human erythropoietin protein." (TX 2012.1078 (AM-ITC 00455528).)

After considering Amgen's detailed response to the PTO's rejection of Dr. Lin's process claims for ODP over Lin's '008 DNA and host cell claims, including the ***invalidity*** arguments made by Amgen's competitors in the Sytkowski declaration, the PTO withdrew its ODP rejection, indicating yet again that it viewed the subject matter of the process claims to be patentably distinct from the claims of the '008 patent, and issued a notice of allowability for the '868 patent. (TX 2012.1101 (AM-ITC 000455).) The PTO did not require Amgen to file a terminal disclaimer for the '868 patent over the '008 patent.

After further examination, the PTO also determined that the '698 claims were allowable. (TX 2007.208-210 (AM-ITC 001829-31).) The same senior level examiner, Dr. Martinell, made the determination to allow both the '868 and '698 patents. (TX 2012.1101 (AM-ITC 000455); TX 2007.208 (AM-ITC 001829).) As with the '868 patent, the PTO did not require Amgen to file a terminal disclaimer for the '698 patent over the '008 patent.[19] The '008 patent is listed as a

[19] Amgen did file a terminal disclaimer of the '698 patent over the '868 patent. (TX 2007.161-

cited reference on the face of each of the patents-in-suit, including the '868 and '698 patents. (TX 1-5.)

C. THE COURT'S ODP SUMMARY JUDGMENT ORDER

On August 27, 2007, this Court granted Amgen's motion for summary judgment of no obviousness-type double patenting. (*See* 8/27/07 Electronic Order, granting D.I. 498.) Amgen's summary judgment briefing addressed the two ODP theories that were the focus of Roche's discovery responses and expert reports, namely, ODP over the Lai/Strickland '016 patent claims (Roche's ODP "Theory No. 1") and ODP over the '008 patent claims (Roche's ODP "Theory No. 2"). Amgen did not move for summary judgment on Roche's allegations of ODP over the '868 and '698 patent claims (Roche's ODP "Theory No. 4") because those defenses had not been disclosed or developed by Roche during discovery.[20]

With respect to Roche's ODP defenses based on the Lai/Strickland '016 patent claims, Amgen proved in its summary judgment briefing, under both the two-way and one-way ODP tests, that the claims-in-suit are not invalid for ODP over the '016 claims. (*See* D.I. 499, at 13-20; D.I. 676, at 12-20; D.I. 576, at 1-20.) As to Roche's ODP defenses based on the '008 claims, Amgen proved that 35 U.S.C. § 121 exempts the inventions claimed in Lin's '933, '422 and '349 patents from ODP over the DNA and host cell inventions claimed in the '008 patent. (*See* D.I. 499, at 8-13; D.I. 676, at 2-12.) In particular, Amgen demonstrated that: (1) the '178 and '179 applications that gave rise to the patents-in-suit were "divisional" applications "filed as a result of" the 1986 restriction requirement in the earlier '298 application; and (2) the issued claims in the '933, '422 and '349 patents maintained consonance with the non-elected invention groups in

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63 (AM-ITC 001782-84).)

[20] Also, Amgen did not move for summary judgment on Roche's allegations that the '868 and '698 claims are invalid for ODP over the '008 claims (Roche's ODP "Theory No. 3").

the 1986 restriction requirement. To prove consonance, Amgen demonstrated that the issued claims of the '933, '422 and '349 patents fall within non-elected invention groups of the 1986 restriction requirement (Groups I, IV and V), and do not fall within Group II — the invention group that was elected in the '298 application and prosecuted to issuance in the '008 patent. Although the Court has not yet issued its written opinion addressing these ODP issues, the Court indicated that it agreed with the positions set forth in Amgen's summary judgment briefing.[21]

Roche has filed a motion for partial reconsideration of the Court's summary judgment Order, contending that the Court committed a "clear error of law" by granting summary judgment that Amgen's '349 patent claims are exempt under § 121 from ODP over the '008 patent claims. (D.I. 908.) Amgen maintains that the Court was correct to reject Roche's flawed ODP analysis on summary judgment, and Amgen has filed an opposition to Roche's motion for reconsideration. (D.I. 1000.)

III. ARGUMENT

A. GOVERNING LEGAL STANDARDS

1. The ODP Safe Harbor Statute: 35 U.S.C. § 121

A preliminary step in any obviousness-type double patenting analysis is to determine whether the defense is precluded under 35 U.S.C. § 121, the ODP safe harbor statute. Section 121 routinely protects patentees against ODP attacks where the Patent Office has imposed a "restriction requirement" that required the applicant to prosecute its inventions in separate applications. *See Applied Materials, Inc. v. Adv. Semiconductor Materials Am., Inc.*, 98 F.3d 1563, 1568-69 (Fed. Cir. 1996).[22] Section 121 states in pertinent part:

[21] "I've ruled what I've ruled. She's [Ms. Ben-Ami] correct to assume that, to the extent you [Amgen] have argued, the restriction; I have bought that argument. She's correct to assume that." (9/4/07 Trial Tr. 35:8-11.)

[22] "A restriction requirement is made during the prosecution of a patent application at the

> If two or more independent and distinct inventions are claimed in one application, the Director may require the application to be restricted to one of the inventions. If the other invention is made the subject of a divisional application which complies with the requirements of section 120 of this title it shall be entitled to the benefit of the filing date of the original application. 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. . . . The validity of a patent shall not be questioned for failure of the Director to require the application to be restricted to one invention.

Section 121 "effects a form of estoppel that shields the [patentee] from having to prove the correctness of the restriction requirement in order to preserve the validity of the second patent." *Studiengesellschaft Kohle mbH v. N. Petrochemical Co.*, 784 F.2d 351, 361 (Fed. Cir. 1986) (Newman, J., concurring). In so doing, § 121 "assures that the technicalities of restriction practice are not elevated from their purpose of examination convenience to a potential taint on the validity of the ensuing patents." *Applied Materials*, 98 F.3d at 1568.[23] The final sentence of § 121 provides that the absence of a restriction requirement separating two groups of claims may not be used to argue that the claims are patentably ***in***distinct and therefore invalid: "The validity of a patent shall not be questioned for failure of the Director to require the application to be restricted to one invention." 35 U.S.C. § 121.

Section 121 immunizes a later-issued patent from an obviousness-type double patenting attack if two fundamental requirements are met: (1) the patent arises from an application that was

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discretion of the Commissioner to avoid granting a patent for more than one invention. . . . The restriction requirement also preserves revenue to the PTO and ensures the integrity of the PTO's classification system." *Applied Materials*, 98 F.3d at 1576 (Archer, J., dissenting).

[23] The effect of the § 121 ODP safe harbor is summarized in the legislative history as follows: "neither of the resulting patents can be held invalid over the other merely because of their being divided in several patents." S. Rep. No. 1979, 82nd Cong., 2nd Sess. 20, 1952 U.S.C.C.A.N. 2394, 2413.

filed as a result of a restriction requirement; and (2) the claims in the patent are consonant with that restriction requirement. *See, e.g.*, *Gerber Garment Tech., Inc. v. Lectra Sys., Inc.*, 916 F.2d 683, 687-88 (Fed. Cir. 1990).[24] Additionally, the patent containing the "reference" claim (i.e., the earlier-issued claim asserted as the basis for ODP) must either have issued from the application in which the restriction requirement was made, or arisen from an application filed as a result of the restriction requirement, and must not contain claims belonging to the same restriction group as the later-issued patent.

As applied in the case law, Element (1) — "filed as a result of a restriction requirement" — is satisfied if the first application filed after the restriction requirement that gave rise to the later-issued patent contained claims drawn only to the non-elected inventions, and contained no claims to the invention elected in response to the restriction requirement. *See, e.g.*, *Gerber*, 916 F.2d at 687-88. The Federal Circuit has applied § 121 to patents that issued from continuations of earlier applications filed as a result of a restriction requirement. *See, e.g.*, *Symbol Techs., Inc. v. Opticon, Inc.*, 935 F.2d 1569, 1579-80 (Fed. Cir. 1991) (affirming § 121 protection for patent that issued from an application filed approximately three years after a restriction requirement where the application was a continuation of an earlier application filed as a result of the restriction requirement); *Applied Materials*, 98 F.3d at 1567-69 (affirming § 121 protection for patent that issued from an application filed approximately ten years after a restriction requirement where the application was one in a series of continuations of an earlier application filed as a result of the restriction requirement).[25] Additionally, several cases have indicated that

[24] The requirements for § 121 protection are discussed in detail in Amgen's summary judgment briefing. (*See* D.I. 499, at 10-13; D.I. 676, at 3-12.)

[25] In *Applied Materials*, the Federal Circuit even noted that "the history of these patents shows several refilings, amendments, and continuations-in-part," and nonetheless held that § 121 applied to preclude ODP. *Id.* at 1567.

§ 121 applies to applications that are not formally designated as "divisional" applications.[26]

Element (2) — "consonance" — is satisfied if all claims in the later-issued patent fall within the scope of the non-elected restriction groups and not within the scope of the restriction group elected for prosecution in the original application. That is, the later-issued claims must not "cross the line of demarcation drawn around the invention elected in the restriction requirement." *Symbol*, 935 F.2d at 1579.[27] New or amended claims in the later-issued patent (i.e., claims not originally present in the application filed as a result of the restriction requirement) also are entitled to the protection of § 121, provided all claims in the patent satisfy the consonance requirement. *Id.*[28] One reason for this rule is that "[i]t is almost inevitable that some refinement of the claims will occur after restriction is ordered, since restriction often comes as a preliminary step before the examiner reaches the merits of the patent claims." *Union Carbide Corp. v. Dow*

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[26] *See*, *e.g.*, *Gerber*, 916 F.2d at 684, 686-89 (applying § 121 to continuation-in-part application and finding lack of consonance); *Studiengesellschaft Kohle*, 784 F.2d at 353, 355-56 (stating in dicta that § 121 would have applied to application, which was a continuation-in-part); *id.* at 357-61 (Newman, J., concurring) (agreeing that § 121 applied to application, which was a continuation-in-part, and arguing that case should be decided on § 121 grounds); *Pfizer Inc. v. Teva Pharms. USA, Inc.*, 2007 U.S. Dist. LEXIS 20190 at *234 n.58 (D.N.J. Mar. 20, 2007) (stating in dicta that "[t]he Federal Circuit has applied § 121 to continuation-in-part applications on several occasions"); *cf. Transco Prods. Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 556 (Fed. Cir. 1994) ("[T]he expressions 'continuation,' 'divisional,' and 'continuation-in-part' are merely terms used for administrative convenience.").

[27] Consonance is not violated if a patent contains claims from multiple, ***non-elected*** restriction groups. Consonance is maintained so long as the claims are drawn to the non-elected inventions, and "do not cross the line of demarcation drawn around ***the invention elected in the restriction requirement***." *Symbol*, 935 F.2d at 1579 (emphasis added); *see also Gerber*, 916 F.2d at 688 ("To gain the benefits of Section 121 . . . Gerber must have brought its case within the purview of the statute, *i.e.*, it must have limited the claims in its divisional application to the non-elected invention ***or inventions***.") (emphasis added). This makes sense because a patent that contains claims drawn only to the non-elected inventions, and not to the inventions elected for examination in the earlier patent, does not extend the term of patent protection for the previously elected inventions.

[28] Broadening amendments are permitted, provided consonance is maintained. *See Applied Materials*, 98 F.3d at 1567-69 (affirming § 121 protection notwithstanding amendments that enlarged the claims beyond their scope at the time of imposition of the restriction requirement).

Chem. Co., 619 F. Supp. 1036, 1060 (D. Del. 1985). Testimony from technical experts may be relevant to the consonance determination. *See, e.g.*, *Symbol*, 935 F.2d at 1580 (affirming determination of consonance and § 121 protection based on declaration of technical expert). During prosecution, "[n]oncompliance with the consonance requirement is normally detected by the PTO examiner." *Gerber*, 916 F.2d at 685.

When assessing whether claims are consonant with the non-elected invention groups in a restriction requirement, the proper point of reference is the actual restriction groupings imposed by the examiner (i.e., the substance of the claims in each restriction group), and not the examiner's written descriptions thereof. *Texas Instruments Inc. v. ITC*, 988 F.2d 1165, 1179 (Fed. Cir. 1993); *see also Applied Materials, Inc. v. Adv. Semiconductor Materials Am., Inc.*, 1994 U.S. Dist. LEXIS 7810, at *28-34 (N.D. Cal. Apr. 26, 1994) ("[T]he line of demarcation and its attendant consonance requirement are controlled by the actual claim groupings made by the Examiner, [not] by the Examiner's subsequent explanatory comments."), *aff'd*, 98 F.3d 1563 (Fed. Cir. 1996). Where there are multiple restriction requirements, the relevant restriction requirement for purposes of assessing § 121 protection is the one that first required the applicant to prosecute the later-issued claim separately from the claim asserted as the basis for ODP. *Cf. Geneva Pharms., Inc. v. GlaxoSmithKline, PLC*, 349 F.3d 1373, 1378 (Fed. Cir. 2003) ("Thus, if the [later] patents and the [earlier] patent trace their lineage back to a common parent which was subject to a restriction requirement, then § 121 intervenes to prevent a non-statutory double patenting rejection.").

The applicability of § 121 is a question of law. *Bristol-Myers Squibb Co. v. Pharmachemie B.V.*, 361 F.3d 1343, 1348 n.1 (Fed. Cir. 2004); *Applied Materials*, 98 F.3d at 1567. As such, the § 121 issue is frequently decided on summary judgment. *See, e.g.*, *Gerber*, 916 F.2d at 685; *Bristol-Myers Squibb Co. v. Pharmachemie B.V.*, No. 01-cv-3751, 2002 U.S.

Dist. LEXIS 27230 (D.N.J. July 25, 2002); *Union Carbide*, 619 F. Supp. at 1055-60. Although the heavy burden of proving obviousness-type double patenting remains with the party challenging the validity of the patent at all times (i.e., it never shifts to the patentee), the patentee bears the burden of proving, by a preponderance of the evidence, that the safe harbor provision of § 121 applies. *See Pfizer*, 2007 U.S. Dist. LEXIS 20190, at *215-16.

2. Obviousness-Type Double Patenting

If a claim is not exempt from a particular allegation of obviousness-type double patenting under 35 U.S.C. § 121, it is appropriate to consider whether the defendant has met its burden of proving the ODP defense. Obviousness-type double patenting is a judge-made doctrine, designed "to prevent an inventor from effectively extending the term of exclusivity by the subsequent patenting of variations that are not patentably distinct from the first-patented invention." *Applied Materials*, 98 F.3d at 1568. If the two claimed inventions are "patentably distinct," there is no ODP violation.

As with other affirmative defenses of invalidity, the defendant bears the burden of proving obviousness-type double patenting by clear and convincing evidence, "a heavy and unshifting burden." *Symbol*, 935 F.2d at 1580. Where the asserted grounds for invalidity were reviewed by the PTO (as was the case here for Roche's allegation that the '868 patent claims are invalid for ODP over the '008 patent claims), "the challenger has the added burden of overcoming the deference that is due to a qualified government agency presumed to have properly done its job." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 105 (D. Mass. 2001) (internal quotation omitted); *accord PharmaStem Therapeutics, Inc. v. Viacell, Inc.*, 491 F.3d 1342, 1366 (Fed. Cir. 2007).

Because of the statutory presumption of validity under 35 U.S.C. § 282, ODP must be evaluated separately, on a claim-by-claim basis, for each challenged claim. The invalidity of any

one claim for ODP does not automatically require the invalidation of other claims in the same patent. *Ortho Pharm. Corp. v. Smith*, 959 F.2d 936, 942 (Fed. Cir. 1992).

Obviousness-type double patenting is a question of law for the Court to decide.[29] The reason for this is because "determining what is patented by correct claim interpretation is essential to determination of obviousness-type double patenting issues." *Gen. Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1279 (Fed. Cir. 1992) (capitalization altered). It is the Court's role, not the jury's, to determine the metes and bounds of the claimed inventions. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370 (1996). Accordingly, the Federal Circuit has repeatedly held that, as with claim construction, obviousness-type double patenting is a question of law that is reviewed *de novo*, without deference. *See Gen. Foods*, 972 F.2d at 1277 ("Double patenting is altogether a matter of what is claimed. Claim interpretation is a question of law which we review de novo."); *In re Metoprolol Succinate Patent Litig.*, 494 F.3d 1011, 1015 (Fed. Cir. 2007) ("De novo review is appropriate because double patenting is a matter of what is claimed, and therefore is treated like claim construction upon appellate review.") (quoting *Georgia-Pacific Corp. v. U.S. Gypsum Co.*, 195 F.3d 1322, 1326 (Fed. Cir. 1999)).[30]

In other recent patent jury trials, ODP defenses have been decided by the court, not the jury. *See, e.g.*, *Engineered Prods. Co. v. Donaldson Co, Inc.*, 313 F. Supp. 2d 951, 993 (N.D. Iowa 2004) ("[T]he double-patenting defense will be tried to the court, because it is a question of law . . . . the court will avoid any confusion about which issues are for the jury to decide, and

[29] Not surprisingly, ODP is not addressed in the model patent jury instructions from the Federal Circuit Bar Association, the American Intellectual Property Law Association (AIPLA), or the Northern District of California.

[30] *Cf. Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 344 F.3d 1359, 1368 n.3 (Fed. Cir. 2003) ("We recognize that rebuttal of the presumption may be subject to underlying facts, which we discuss in more detail below. Nonetheless, the resolution of factual issues underlying a legal question may properly be decided by the court.")

which are for the court, by trying the double-patenting defense to the court without the jury present, either by taking pertinent witnesses after the jury is done for the day or after the submission of evidence to the jury is completed, or by deciding the issue on written submissions."), *vacated in part on other grounds*, 147 Fed. Appx. 979 (Fed. Cir. 2005); *Applera Corp. v. MJ Research Inc.*, 363 F. Supp. 2d 261, 262 (D. Conn. 2005) (deciding the ODP issue based on proposed findings of fact and conclusions of law submitted by the parties addressing the patents at issue, prior deposition testimony not introduced at trial, as well as trial testimony and exhibits). For these reasons, the Court's September 7, 2007 Order that ODP is a matter of law for the Court was correct, and Roche's objections to that order (D.I. 1022) are meritless.

At a high level, the Court's ODP analysis entails two steps, which must be performed for each pair of claims alleged by Roche to be patentably indistinct:

> First, as a matter of law, a court construes the claim in the earlier patent and the claim in the later patent and determines the differences. Second, the court determines whether the differences in subject matter between the two claims render the claims patentably distinct. A later claim that is not patentably distinct from an earlier claim in a commonly owned patent is invalid for obvious-type double patenting. A later patent claim is not patentably distinct from an earlier patent claim if the later claim is obvious over, or anticipated by, the earlier claim.

Metoprolol, 494 F.3d at 1016 (quoting *Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 968 (Fed. Cir. 2001)); *cf. Georgia-Pacific*, 195 F.3d at 1326 ("Accordingly, analysis of the claims at issue is the first step in determining if the second invention is merely an obvious variation of the first.").

The determination of whether a later-claimed invention is obvious over an earlier-claimed invention (and therefore not patentably distinct) parallels the determination of

obviousness under 35 U.S.C. § 103 in some respects.[31] *See In re Longi*, 759 F.2d 887, 892 n.4 (Fed. Cir. 1985). First, the "obviousness" of an invention is determined from the perspective of a person of ordinary skill at the time the invention was made. *Takeda Chem. Indus., Ltd. v. Alphapharm, Pty.*, 492 F.3d 1350, 1355 (Fed. Cir. 2007). To avoid improper use of hindsight, one must not consider what was learned from the teachings of the patents-in-suit or the patent applications giving rise to the patents-in-suit, nor may one consider what was learned since the invention. *See KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1742 (2007); *Gerber*, 916 F.2d at 687. For purposes of Roche's ODP defenses, the relevant date for determining whether the later-claimed invention would have been obvious is the date that the later-claimed invention was made. As found by this Court in *Amgen v. Chugai*, Dr. Lin's recombinant human EPO was expressed in mammalian host cells in early 1984 (in 293 cells and in COS cells in January and in CHO cells in May 1984) and its *in vivo* biological activity was determined in March 1984.[32] Expression of recombinant EPO in cells having amplified EPO DNA (as claimed in the '698 patent) was performed in September and October 1984.[33] Dr. Lin's last CIP application — the '298 application — was filed on November 30, 1984. (*See supra* p 9.)

Second, in determining whether the later-claimed invention would have been obvious in view of the earlier-issued claim, it is the later-claimed invention ***as a whole***, not individual limitations, that must be considered. It is improper to deconstruct the later-claimed invention into specific limitations and then determine whether particular elements or limitations of the claims, or particular differences between individual limitations and the prior art, would have

[31] Although a "two-way" obviousness test is used to assess ODP in certain instances (*see generally* D.I. 576 at 11-12), there is no dispute that the "one-way" test applies for purposes of Roche's remaining ODP defenses.

[32] *Amgen Inc. v. Chugai Pharm. Co. Ltd.*, 13 U.S.P.Q.2d 1737, 1748 (D. Mass. 1989).

[33] *Id.* at 1749.

been obvious in isolation from the claimed invention as a whole. *See Carman Industries, Inc. v. Wahl*, 724 F.2d 932, 940 (Fed. Cir. 1983) ("However, rather than focusing on the point of novelty, we wish to clarify that double patenting is determined by analysis of the claims as a whole."); *Gen. Foods*, 972 F.2d at 1278 ("Claims must be read as a whole in analyzing a claim of double patenting.").

Third, the "obviousness" analysis must consider whether the person of ordinary skill in the art would have had a reasonable expectation of successfully obtaining or practicing the later-claimed invention. In other words, was the level of predictability in the art at the time of the invention such that one of ordinary skill would have had an objectively based expectation of successfully making and using the claimed invention. *See, e.g.*, *Longi*, 759 F.2d at 896-97.[34]

Fourth, the "obviousness" analysis must account for any objective evidence of non-obviousness, such as:

- whether there was a long-felt need for the invention;
- whether others tried but failed to solve the problem addressed by the invention;
- whether the patentee deviated from the accepted wisdom indicated by the prior art;
- whether unexpected results were achieved by the invention;
- contemporaneous expressions of surprise or acclaim by those skilled in the art following the invention;
- praise of the invention by the infringer or others in the field;

[34] The Supreme Court's recent decision in *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007), makes clear that the assessment of a "reasonable expectation of success" requires an objectively based assessment of the state of the art at the time and what one skilled in the art at the time would objectively expect to achieve in view of that art. *See PharmaStem*, 491 F.3d 1342, 1360 (Fed. Cir. 2007) ("[T]he burden falls on the patent challenger to show by clear and convincing evidence that a person of ordinary skill in the art would have had reason to attempt to make the composition or device, or carry out the claimed process, and would have had a reasonable expectation of success in doing so."); *Takeda*, 492 F.3d at 1360-63 (assessing reasonable expectation of success).

- commercial success of products covered by the patent claims or made by a process covered by the patent claims;
- the taking of licenses under the patent by others; and
- copying of the invention by others in the field.

See, e.g., *In re Emert*, 124 F.3d 1458, 1462 (Fed. Cir. 1997); *Longi*, 759 F.2d at 896-97; *In re Gladrow*, 406 F.2d 1376, 1383 (C.C.P.A. 1969).[35]

Notwithstanding these similarities between the obviousness analysis under § 103 and the "patentably distinct" analysis for ODP, there is a crucial distinction between these two invalidity defenses: ODP analysis involves a comparison of two patent ***claims***, and it is impermissible to treat the earlier patent's disclosure as prior art against the later-issued claim. *See Gen. Foods*, 972 F.2d at 1281 ("Our precedent makes clear that the disclosure of a patent cited in support of a double patenting rejection cannot be used as though it were prior art, even where the disclosure is found in the claims."); *Longi*, 759 F.2d at 892 n.4; *In re Kaplan*, 789 F.2d 1574, 1580 (Fed. Cir. 1986).

To avoid violating this fundamental principle of ODP law, it is important to distinguish between "a claim as a written disclosure and a claim as a definition of an invention." *Gen. Foods*, 972 F.2d at 1281. That is, one must not confuse that which is merely named in an earlier-issued claim for that which is claimed. *See id.* at 1281-82; *Astellas Pharma, Inc. v. Ranbaxy*

[35] In *Geneva Pharms., Inc. v. GlaxoSmithKline PLC*, the Federal Circuit, in dictum in a footnote, without citing any authority, suggested that ODP does not require inquiry into a motivation to modify the prior art or objective criteria suggesting non-obviousness. 349 F.3d at 1378 n.1. This idea is contrary to earlier Federal Circuit ODP cases that considered whether there was a motivation to modify the prior art and whether there was objective evidence of nonobviousness. *See, e.g.*, *Ortho*, 959 F.2d at 943; *Emert*, 124 F.3d at 1462; *Longi*, 759 F.2d at 896-97. Several district courts have declined to follow the *Geneva* dictum. *See, e.g.*, *Eli Lilly & Co. v. Zenith Goldline Pharms., Inc.*, 364 F. Supp. 2d 820, 244-46 (S.D. Ind. 2005); *In re Glaxo '845 Patent Litig.*, 450 F. Supp. 2d 435, 438 (S.D.N.Y. 2006); *Pfizer Inc. v. Synthon Holdings BV*, 2006 U.S. Dist. LEXIS 63063, at *56 (M.D.N.C. Aug. 31, 2006). Roche agrees with Amgen that secondary considerations of non-obviousness are relevant to the ODP analysis. (*See* D.I. 1022, at 5.)

Inc., 2007 U.S. Dist. LEXIS 11870, at *17-18 (D.N.J. Feb. 21, 2007); D.I. 576, at 16-20; D.I. 676, at 16-20. ODP analysis is not concerned with "what one skilled in the art would be aware from reading the claims but with what inventions the claims define." *In re Sarett*, 327 F.2d 1005, 1013 (C.C.P.A. 1964); *Metoprolol*, 494 F.3d at 1018 ("The disclosure of the claims forming the basis of a double patenting rejection cannot be used as 'prior art' for a rejection under 35 U.S.C. § 102, 103. . . . what is claimed, as opposed to what is disclosed to one skilled in the art, remains critical.").

For these same reasons, it is impermissible to ***combine*** claims, or elements from multiple claims, in an earlier-issued patent when considering whether a claim in a later-issued patent is patentably distinct. This type of flawed ODP argument was recently confronted and rejected in *Lucent Techs. Inc. v. Gateway, Inc.*, 470 F. Supp. 2d 1163, 1179-80 (S.D. Cal. 2007):

> Microsoft alleges that claim 1 of the *'457 patent* teaches a frequency transform and a masking threshold; claim 4 of the *'457 patent* teaches coding quantized frequency coefficients; and claim 6 of the *'457 patent* teaches an iterative rate loop. According to Microsoft, if all of these elements are combined, all that is missing is the teaching of an AHT, which was known to one of skill in the art.
>
> Microsoft's double patenting contention is problematic. The heart of double patenting encompasses the argument that two patents claim the same thing or an obvious variation of the same. *General Foods Corp. v. Studiengesellschaft Kohle mbH, 972 F.2d 1272, 1280 (Fed Cir. 1992)*. The claims are compared as a whole, claim-by-claim, between the patents, "paying careful attention to the rules of claim interpretation to determine what invention a claim defines and not looking to the claim for anything that happens to be mentioned in it as though it were a prior art reference." Id.
>
> Here, Microsoft has done exactly what the Federal Circuit has forbidden: Microsoft extracts "disclosures" from parts of claims 1, 4, and 6 of the *'457 patent* and amasses them together to arrive at the *'080 claims.* Therefore, Microsoft has not met its burden to demonstrate that the claims of the *'080 patent* when properly compared in their entirety are the same method or an obvious variation of the *'457 claims*.

The reason it is impermissible to apply the earlier commonly-owned patent's disclosure

in assessing ODP is because it is not part of the relevant prior art under 35 U.S.C. § 102. *See Gerber*, 916 F.2d at 687 ("[T]hat disclosure is the applicant's and is not in the 'prior art.'"); *In re Braithwaite*, 379 F.2d 594, 600 n.4 (C.C.P.A. 1967) ("While analogous to the non-obviousness requirement of 35 U.S.C. 103, that section is not itself involved in double patenting rejections because the patent principally underlying the rejection is not prior art."). Here, all of Dr. Lin's patents claim priority to the same set of initial patent applications filed in 1983-84 so none of the disclosures of those applications is prior art to any of the patents-in-suit. Thus, the disclosure of Dr. Lin's '008 patent (which is the same as the disclosure of the patents-in-suit) cannot be used in determining ODP.

The Federal Circuit has also cautioned against confusing "domination" for double patenting. One patent claim dominates another patent claim if the claim of the first patent reads on a device built or a process practiced according to a claim of the second patent. "This commonplace situation is not, per se, double patenting . . . ." *Kaplan*, 789 F.2d at 1577-78; *see also Sarett*, 327 F.2d at 1014 ("[I]t is elementary that readability of a claim on the subject matter of another claim (domination) is neither determinative of the double patenting issue nor demonstrative that claims are directed to the same invention.").

B. THE COURT SHOULD STRIKE ROCHE'S ALLEGATIONS THAT THE '933, '422 AND '349 CLAIMS ARE INVALID FOR ODP OVER THE '868 AND '698 CLAIMS (ROCHE'S "THEORY NO. 4") BECAUSE THESE DEFENSES WERE NOT DISCLOSED DURING DISCOVERY OR IN ROCHE'S § 282 PRETRIAL NOTICE

On September 7, 2007, at the end of the first week of trial, Roche filed an Offer of Proof identifying eight claims from the '868 and '698 patents that Roche now — for the first time — contends render invalid the asserted claims of the '933, '422 and '349 patents. (D.I. 1020.) As described in detail above (*see supra* pp. 4-8), these new ODP defenses based on the '868 and '698 claims were not mentioned in any interrogatory responses served before the close of fact discovery. Nor were these defenses developed in any of Roche's expert reports. While Roche's

summary judgment briefing expressly referenced its '008- and '016-based ODP defenses, it made no mention whatsoever of any ODP defenses based on the '868 or '698 claims, further demonstrating no intent to assert these defenses.

When Roche filed its 35 U.S.C. § 282 Notice on August 2, 2007, Roche again failed to disclose the '868 and '698 patents as invalidity references, even though Roche listed its other ODP references (the '008 and Lai/Strickland '016 patents) in that statutorily-mandated pretrial disclosure. (*See* D.I. 799, at 4.) Pursuant to § 282, Roche was required to disclose to Amgen thirty days before trial every reference on which it relied in support of any defense or claim that the patents-in-suit are invalid. Section § 282, "just as interrogatories, requests for admissions, and the like under the Rules, is intended to do more than alert an adversary to the existence of evidence. It enables the plaintiff to know what sort of defense is going to be asserted. In a very real sense it determines what is to be tried." *Thermo King Corp. v. White's Trucking Serv., Inc.*, 292 F.2d 668, 675 (5th Cir. 1961). Roche listed the '008 and '016 patents as invalidity references in its § 282 Notice but failed to list the '868 or '698 patents as references. This failure to meet its statutory disclosure obligations provides an independent basis to preclude Roche from asserting the '868 and '698 claims as ODP references against the other claims-in-suit. *See Primos, Inc. v. Hunter's Specialties, Inc.*, 451 F.3d 841, 851 (Fed. Cir. 2006) ("It was well within the district court's province [under § 282] to determine that because the Aluminum Flap Call was not identified as potential prior art until after discovery had closed and shortly before trial commenced, it would then be unfair to permit its introduction into evidence."); *Ferguson Beauregard/Logic Controls v. Mega Sys., LLC*, 350 F.3d 1327, 1347 (Fed. Cir. 2003) ("The district court's rulings, rather that being contrary to law, followed the letter of § 282 precisely. The district court simply declined to allow [defendant] to offer up actions not described in the statute as sufficient notification.")

Now, having lost most of its '008 and '016-based ODP defenses on summary judgment, Roche seeks to add these new ODP defenses that it withheld from its pretrial disclosures. But Roche still fails to provide any of the information it was obligated to disclose months ago in discovery. Rather than providing the detailed, claim-by-claim analysis required to support an ODP defense, Roche's Offer simply recites a new list of claims from the '868 and '698 patents to be argued as ODP references against the asserted claims of the '933, '422 and '349 patents. ODP is an affirmative defense for which Roche bears the burden of proof. It is entirely unacceptable that Roche still — more than two weeks into trial — has not provided any detailed explanation of how and why Roche contends that these claims of the '868 and '698 patents render the other claims-in-suit invalid for ODP. Roche's tactics make a mockery of the Federal Rules of Civil procedure and this Court's disclosure requirements and should be rejected.

The distraction and burden of responding to Roche's untimely defenses in the middle of trial has significantly prejudiced Amgen. As Roche recently urged the Court, a party that fails to make the required disclosures should not be permitted to pursue the undisclosed theories at trial. *See* D.I. 1006, at 4 (citing *Klonoski v. Mahlab*, 156 F.3d 255, 269 (1st Cir. 1998); *Cytyc Corp. v. TriPath Imaging, Inc.*, 2007 U.S. Dist. LEXIS, at *13-18 (D. Mass. Aug. 22, 2007)). Amgen respectfully requests that the Court put an end to Roche's improper attempts to expand the invalidity case by striking Roche's untimely ODP defenses based on the '868 and '698 claims for failure to comply with the Court's discovery schedule and 35 U.S.C. § 282.

C. UNDER 35 U.S.C. § 121, THE '933, '422 AND '349 CLAIMS ARE EXEMPT FROM ODP OVER THE '868 AND '698 CLAIMS

Consistent with the Court's Order granting Amgen's Motion for Summary Judgment of No Obviousness-Type Double Patenting, Roche's new ODP defenses ("Theory No. 4") also should be precluded under 35 U.S.C. § 121, the ODP safe harbor statute. As demonstrated in Amgen's summary judgment briefing, the '933, '422 and '349 patents each satisfy the

requirements for § 121 protection. The '178 and '179 applications that gave rise to these patents were both "divisional" applications "filed as a result of" the 1986 restriction requirement in the earlier '298 application. (*See* D.I. 499, at 10-12; D.I. 676, at 3-6.) The issued claims in the '933, '422 and '349 patents maintained consonance with the non-elected invention groups in the 1986 restriction requirement (specifically, Groups I, IV and V), and do not fall within Group II. (*See* D.I. 499, at 12-13; D.I. 676, at 6-12.) The Court has indicated that it agreed with Amgen's position on these restriction requirement issues.[36]

Although Amgen's summary judgment briefing proved that the '933, '422 and '349 claims were not invalid for ODP over the claims of the ***'008 patent***, the same principles and holdings apply with respect to Roche's new defenses that the '933, '422 and '349 claims are invalid for ODP over claims of the ***'868 and '698 patents***. As Roche repeatedly has argued, the '868 and '698 patent claims, like the '008 patent claims, fall within the scope of Group II of the PTO's 1986 restriction requirement.[37] In contrast, the '933, '422 and '349 patents were filed for the purpose of pursuing claims to non-elected (i.e., non-Group II) inventions from the 1986 restriction requirement and all three of those patents contain only claims falling within the non-elected restriction groups. As summarized in the diagram on page 13, above, none of the '933, '422 and '349 claims fall within the same invention group as the '868 and '698 claims (i.e., Group II). Thus, the Court's holding on summary judgment that § 121 exempts the '933, '422 and '349 patent claims from ODP over the Group II inventions in the '008 patent is equally applicable to Roche's new ODP defenses based on the Group II inventions in the '868 and '698

[36] "I've ruled what I've ruled. She's [Ms. Ben-Ami] correct to assume that, to the extent you [Amgen] have argued, the restriction; I have bought that argument. She's correct to assume that." (9/4/07 Trial Tr. 35:8-11.)

[37] *See, e.g.*, Roche's Opp. to Amgen's Mot. For Summary Judgment of No Obviousness-Type Double Patenting (D.I. 568), at 2, 5.

patents. In short, the '933, '422 and '349 claims are protected from ODP over the '868 and '698 claims to the same extent that they are protected from ODP over the '008 claims.

Section 121 does not apply as between patents that contain claims belonging to the ***same*** restriction group. That is why there is no § 121 protection for the '868 and '698 patents over the '008 patents — each of those patents contains claims belonging to restriction Group II. But that is not the case with the patents implicated by Roche's new ODP defenses. Here, the line of demarcation drawn by the examiner in the 1986 restriction requirement has been maintained, with the '868 and '698 claimed inventions (elected Group II) on one side and the '933, '422 and '349 claimed inventions (non-elected Groups I, IV and V) on the other. Amgen, therefore, is entitled to protection under § 121.

The fact that the '868 and '698 patents did not issue directly from the '298 application in which the 1986 restriction requirement was imposed does not vitiate § 121 protection for the '933, '422 and '349 patents. The protections afforded by the statute are not limited to ODP allegations based on patents that issue directly from the application in which the restriction requirement was imposed. Section 121 also protects against ODP attacks based on patents arising from other applications filed as a result of a restriction requirement:

> ***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). As shown in Amgen's summary judgment briefing, the '179 application that gave rise to the '868 and '698 patents was "filed as a result of" the 1986 restriction requirement. (*See* D.I. 499, at 10-12; D.I. 676, at 3-6.) Thus, the Court's holding on summary judgment that § 121 exempts the '933, '422 and '349 patent claims from ODP over the

Group II inventions is equally applicable to Roche's new ODP defenses based on the '868 and '698 patent claims.

The fact that the PTO never once rejected claims in the '933, '422 or '349 patent applications for ODP over the Group II claims (e.g., in the '008 patent), even though the same examiner (Dr. Martinell) participated in the examination of all of the patents-in-suit, indicates that the PTO recognized that § 121 insulated Lin's '933, '422 and '349 claims from such an ODP challenge. *See Gerber*, 916 F.2d at 685 ("Noncompliance with the consonance requirement is normally detected by the PTO examiner.") (citing M.P.E.P. § 804.01). By contrast, where there was no § 121 protection between the Group II claims in the '868 patent application and the Group II claims in the '008 patent, the PTO did issue a rejection for ODP. (TX 2012.1019 (AM-ITC 000422).)

Roche tries to mislead the Court by arguing that § 121 does not insulate Lin's '933, '422 and '349 claims from an ODP challenge based on the '868 and '698 patents because, according to Roche, the issued claims in the '868 and '698 patents belong to Group II of the PTO's 1986 restriction requirement and therefore were not forced apart from the other Group II claims that issued in the '008 patent. (*See* D.I. 994, at 6-12.) But that is not the relevant inquiry. Roche's new ODP defenses challenge the validity of the '933, '422 and '349 claims — the same claims that were the subject of Amgen's successful motion for summary judgment. Roche's new ODP defenses do not challenge the validity of the '868 or '698 claims. The relevant inquiry is whether § 121 exempts the inventions claimed in the '933, '422 and '349 patents from ODP. The answer is yes, for the same reasons argued in Amgen's summary judgment briefing. Roche's new ODP defenses are nothing more than a transparent attempt to circumvent the Court's summary judgment order of no obviousness-type double patenting.

D. THE '868 AND '698 CLAIMS ARE NOT INVALID FOR ODP OVER THE '008 CLAIMS (ROCHE'S "THEORY NO. 3")

As explained above, the '868 and '698 claims are not protected by § 121 from an ODP challenge based on the DNA and host cell inventions claimed in the '008 patent, because the '868 and '698 claims fall within the same restriction group as the '008 claims. But this absence of § 121 protection does not establish ODP — it merely means that Roche is not statutorily precluded from raising these particular ODP defenses.

The reason Roche's Theory No. 3 ODP defenses fail as a matter of law is because each of the '868 and '698 asserted claims is "patentably distinct" from the inventions claimed in the earlier '008 patent. The PTO has already made this determination of patentable distinctiveness on multiple occasions. Thus, Roche's burden to prove ODP by clear and convincing evidence is even heavier as to its Theory No. 3 defenses. *See Amgen*, 126 F. Supp. 2d at 105; *PharmaStem*, 491 F.3d at 1366. Since Roche cannot meet its burden, the Court should dismiss these defenses as well.

1. The '868 and '698 Asserted Claims Are Significantly Different from the '008 Patent Claims

The first step in an ODP analysis is to determine what, if any, differences exist between the inventions claimed in the earlier-issued and later-issued claims. *Metoprolol*, 494 F.3d at 1016; *Georgia-Pacific*, 195 F.3d at 1326.[38] A comparison of the '008 claims asserted as ODP references by Roche and the later-issued '868 claims-in-suit is set forth in the following chart:[39]

[38] On July 3, 2007, this Court issued a Memorandum and Order construing a number of disputed terms from the '933, '422, '349, '868 and '698 patent claims. (D.I. 613.)

[39] Italicized claims are not asserted by Roche as ODP references, but are recited to provide context for other '008 claims that are asserted by Roche.

'008 Claims 2, 4, 6, 7, 25, 27	**'868 Claims 1-2**
2. A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin. 4. A procaryotic or eucaryotic host cell transformed or transfected with a DNA sequence according to claim 1, 2 or 3 in a manner allowing the host cell to express erythropoietin. *[5. A biologically functional circular plasmid or viral DNA vector including a DNA sequence according to claim 1, 2 or 3.]* 6. A procaryotic or eucaryotic host cell stably transformed or transfected with a DNA vector according to claim 5. 7. A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding a polypeptide having an amino acid sequence sufficiently duplicative of that of erythropoietin to allow possession of the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells, and to increase hemoglobin synthesis or iron uptake. *[23. A procaryotic or eucaryotic host cell transformed or transfected with a DNA sequence according to claim 7, 8 or 11 in a manner allowing the host cell to express said polypeptide.]* *[24. A transformed or transfected host cell according to claim 23 which host cell is capable of glycosylating said polypeptide.]* 25. A transformed or transfected mammalian host cell according to claim 24. 27. A transformed or transfected CHO cell according to claim 25.	1. A process for the production of 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: (a) growing, under suitable nutrient conditions, mammalian host cells transformed or transfected with an isolated DNA sequence encoding human erythropoietin; and (b) isolating said glycosylated erythropoietin polypeptide therefrom. 2. The process according to claim 1 wherein said host cells are CHO cells.

There are several significant differences between the '008 claimed inventions and the '868 claimed inventions.[40] Of primary importance, the asserted claims of the '868 patent claim ***processes for making*** isolatable quantities of ***a glycosylated EPO polypeptide*** having the ***in vivo biological activity*** of causing bone marrow cells to increase production of reticulocytes and red blood cells.[41] In contrast, the claims of the '008 patent claim certain ***DNA molecules*** and certain ***cells transformed or transfected with said DNA molecules***. None of the '008 claims claim a process for producing anything. While certain '008 claims recite host cells transformed or transfected with DNA encoding a polypeptide in a manner "allowing the host cell to express erythropoietin" (*e.g.*, claim 4) or "capable of glycosylating said polypeptide" (*e.g.*, claims 25, 27), none of the '008 claims ***require*** the ability to produce (1) isolatable quantities of EPO, (2) glycosylated EPO and (3) EPO having *in vivo* biological activity. As Dr. Lodish explains, the difference between equipping a cell with a tool that may be useful to achieve a purpose, and actually accomplishing the stated purpose, are two very different things:

> In 1983-84, inserting DNA into a cell in a manner that ***could*** allow the cell to express EPO was very distinct from claiming a process that ***will*** lead to the production of an *in vivo* biologically active EPO from a cell. Saying "I have a bat that is capable of hitting a 100 mph fastball" is far different than saying "I will swing the bat at a 100 mph fastball in a particular way which will lead to a home run."
> . . . .
> It is one thing to have a DNA that will cause a cell to produce a glycoprotein; it is a very different thing to produce a glycoprotein that will have a desired *in vivo* activity.

(D.I. 1164, ¶¶ 129, 173.)

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[40] A table summarizing the differences between each '008 claim asserted as an ODP reference by Roche and each claim-in-suit from the later-issued '868 and '698 patents is provided in the 9/26/07 Godfrey Decl. (D.I. 1165), at Ex. F.

[41] *See, e.g.*, '868 claim 1 ("A process for the production of ***glycosylated*** erythropoietin polypeptide ***having*** the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cell . . . .") (emphasis added).

The '008 claims are directed to purified and isolated DNA sequences and cells into which such DNA sequences have been introduced. In contrast, '868 claims 1 and 2 are process claims that recite the steps required to produce a glycosylated polypeptide product having specified characteristics. Thus, unlike the asserted claims of the '868 patent, none of the '008 claims require: (1) that the recited host cell actually express any EPO polypeptide; (2) that the recited host cell actually express a glycosylated EPO polypeptide; (3) that the host cell be capable of producing an isolatable amount of a glycosylated EPO polypeptide; and (4) that any glycosylated EPO isolated from cells grown in culture have the stated *in vivo* biological function.

Claim 4 of the '008 patent broadly covers any procaryotic and any eucaryotic cell transformed or transfected with a DNA sequence encoding human erythropoietin as recited in '008 claim 2. Similarly, '008 claim 6 covers any procaryotic and any eucaryotic cell transformed or transfected with a DNA vector including a DNA sequence encoding human erythropoietin as recited in '008 claim 2. In contrast to '008 claims 4 and 6, the asserted '868 claims not only require the use of a much more limited set of host cells, but they also require the actual production of isolatable quantities of a glycosylated polypeptide having the *in vivo* biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells. In seeking to produce isolatable quantities of *in vivo* biologically active human EPO polypeptides, Amgen unexpectedly discovered that the procaryotic cells claimed in '008 claims 4 and 6 would not produce such functional polypeptide products and that only a much more limited subset of eucaryotic cells — vertebrate or mammalian cells — would do so.

Moreover, contrary to Dr. Lowe's testimony, neither '008 claim 4 nor any other '008 claim recites a "growing" or an "isolating" step. Since it is "the combination or sequence of acts or steps that are patented in a process claim," DONALD S. CHISUM ET AL., PRINCIPLES OF PATENT LAW, 105 (2d ed. 2001), these required steps and actual production of a polypeptide product

having the recited *in vivo* biological activity provide critical distinctions that patentably distinguish the '868 claims over the '008 claims.

The remaining '008 cell claims all depend from '008 claim 7. Significantly, these cells may include a myriad set of DNA sequences covered by '008 claim 7 or its dependent claims. The DNA sequences of '008 claim 7 include any DNA sequence that encodes any polypeptide whose amino acid sequence is "sufficiently duplicative" of any erythropoietin (not simply human) to allow possession of the stated biological activity. As the Federal Circuit construed claim 7, it encompasses an "enormous" number of DNAs coding for EPO analogs — "all possible genetic sequences that [encode a polypeptide] hav[ing] EPO-like activity."[42] This Court and the Federal Circuit held '008 claim 7 and the claims that are dependent on it (including claims 25 and 27) to be invalid for lack of sufficient enablement. *See Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 13 U.S.P.Q.2d 1737, 1774-77 (D. Mass. 1989), *aff'd*, 927 F. 2d 1200, 1212-14 (Fed. Cir. 1991). In contrast, the cells used in the claimed '868 processes are limited to a DNA sequence encoding human erythropoietin, and there is no dispute in this case that these asserted claims satisfy the enablement requirement for patentability.

A comparison of the '008 claims asserted as ODP references by Roche and the later-issued '698 claims-in-suit is set forth in the following chart:[43]

[42] *See Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F. 2d 1200, 1214 (Fed. Cir. 1991); *see also id.* at 1213 ("The district court found that over 3,600 different EPO analogs can be made by substituting at only a single amino acid position, and over a million different analogs can be made by substituting three amino acids. The patent indicates that it embraces means for preparation of 'numerous' polypeptide analogs of EPO. Thus, the number of claimed DNA encoding sequences that can produce an EPO-like product is potentially enormous.").

[43] Italicized claims are not asserted by Roche as ODP references, but are recited to provide context for other '008 claims that are asserted by Roche.

'008 Claims 2, 4, 6, 7, 25, 27	**'698 Claims 6-9**
2. A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin. 4. A procaryotic or eucaryotic host cell transformed or transfected with a DNA sequence according to claim 1, 2 or 3 in a manner allowing the host cell to express erythropoietin. *[5. A biologically functional circular plasmid or viral DNA vector including a DNA sequence according to claim 1, 2 or 3.]* 6. A procaryotic or eucaryotic host cell stably transformed or transfected with a DNA vector according to claim 5. 7. A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding a polypeptide having an amino acid sequence sufficiently duplicative of that of erythropoietin to allow possession of the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells, and to increase hemoglobin synthesis or iron uptake. *[23. A procaryotic or eucaryotic host cell transformed or transfected with a DNA sequence according to claim 7, 8 or 11 in a manner allowing the host cell to express said polypeptide.]* *[24. A transformed or transfected host cell according to claim 23 which host cell is capable of glycosylating said polypeptide.]* 25. A transformed or transfected mammalian host cell according to claim 24. 27. A transformed or transfected CHO cell according to claim 25.	6. 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: a) growing, under suitable nutrient conditions, vertebrate cells comprising amplified DNA encoding the mature erythropoietin amino acid sequence of FIG. 6; and b) isolating said glycosylated erythropoietin polypeptide expressed by said cells. 7. The process of claim 6 wherein said vertebrate cells further comprise amplified marker gene DNA. 8. The process of claim 7 wherein said amplified marker gene DNA is Dihydrofolate reductase (DHFR) gene DNA. 9. The process according to claims 2, 4 and 6 wherein said cells are mammalian cells.

Because the process claims in the '698 patent are similar to the process claims in the '868 patent in many respects, every one of the distinctions between the '868 and '008 claims discussed above (*see supra* pp. 40-42), also distinguishes the '698 claims from the '008 claims. To avoid repetition, those distinctions will not be restated here.

There are, however, additional differences between the '698 and '008 claims beyond those already described above. For example, unlike the '008 claims, the '698 asserted claims require "amplified DNA encoding the mature erythropoietin amino acid sequence of FIG. 6." Additionally, '698 claims 7 and 8 further require "amplified marker gene DNA." There are no such requirements in the '008 claims, and indeed, nothing in the '008 claims suggests these features. Again, like the '868 claims, the object of the '698 processes is the production of a glycosylated, *in vivo* biologically active EPO product. To be able to produce such a product from cells containing multiple copies of the EPO DNA would have been even less expected than the result of the '868 claims.[44]

The foregoing distinctions, and their significance, are also addressed in Dr. Lodish's accompanying declaration. (*See* D.I. 1164, ¶¶ 125-183.)

2. The Significant Differences in Claimed Subject Matter Render Each '868 and '698 Asserted Claim Non-Obvious and Patentably Distinct from Each '008 Patent Claim

The second step in an ODP analysis, after identifying the differences between the claims at issue, is to determine whether those differences in subject matter between the two claims render the later-issued claim patentably distinct from the earlier-issued claim. *Metoprolol*, 494

[44] *See* D.I. 1164, ¶ 180 ("It would have been particularly unexpected in 1983-84 that *in vivo* biologically active recombinant EPO could be produced using a process involving amplified DNA, such as that claimed in '698 claim 6, because the ordinarily skilled artisan would have been concerned that engineering host cells to produce very large quantities of a foreign protein like EPO increases the likelihood of misfolding or mislocalization of the desired recombinant protein.").

F.3d at 1016. A later-claimed invention is patentably distinct (and therefore not invalid for ODP) if that invention as a whole would have been non-obvious over the earlier-claimed invention to a person of ordinary skill in the art at the time just before the later-claimed invention was made. (*See supra* pp. 27-29.) Here, the evidence shows that each invention claimed in the '868 and '698 asserted claims is patentably distinct from each invention claimed in the '008 patent. Thus, Roche's Theory No. 3 ODP defenses should be rejected as a matter of law.

Roche's allegations that the inventions claimed in the '868 and '698 asserted claims would have been obvious over the inventions claimed in '008 claims 2, 4, 6, 7, 25 and/or 27 rest on two central contentions: (1) that once a person of ordinary skill in the art had possession of a purified and isolated EPO DNA sequence (or a host cell transformed or transfected with that DNA sequence), it would have been obvious in 1983-84 to culture a cell containing that DNA sequence and isolate an EPO glycoprotein that had the *in vivo* biological activity of causing bone marrow cells to increase production of reticulocytes and red blood cells, and (2) that the ordinarily skilled artisan would have had a reasonable expectation of successfully doing so at that time. Both contentions were rejected by the PTO on multiple occasions. Because Roche cannot prove its contentions by clear and convincing evidence, Roche's "Theory No. 3" ODP defenses fail.

a) The proceedings in the PTO confirm that Lin's '868 and '698 process claims are patentably distinct from the '008 claims

On several occasions, the Patent Office determined that Dr. Lin's process inventions are patentably distinct from the DNA and host cell inventions claimed in the '008 patent. The PTO even considered and rejected many of the very same arguments and the very same prior art that Roche now relies on.

As explained above (*see supra* pp. 15-16), the Patent Office declared separate interference proceedings to determine priority to the EPO DNA and process inventions. (*See* TX

2013.576-78 (AM-ITC 00952797-99); TX 2012.742-44 (AM-ITC 000297-99).) Under the rules in effect at the time, the fact that the PTO declared ***separate*** interferences with ***separate*** counts for the DNA/host cell and process inventions indicates that the PTO considered those inventions to be patentably distinct. *See* M.P.E.P. § 2303 (5th ed., Rev. 9, Sept. 1988) (D.I. 868, Ex. A) ("Each count shall define a separate patentable invention.") (quoting 37 C.F.R. § 1.603); *see also* 37 C.F.R. § 1.601(f) (1988) (D.I. 868, Ex. B) (same).

When the PTO later declared a third separate interference proceeding to determine priority to the EPO product inventions, the PTO's Acting Commissioner, Jeffrey Samuels, as well as Group Director John Kittle and Examiner Howard Schain, signed a determination stating that, while related, "***the subject matter of the three interferences is deemed to be patentably distinct*** . . . ." (TX 2011.300 (AM-ITC 001134) (emphasis added).) Therefore, it is beyond dispute that the PTO considered Lin's process inventions to be patentably distinct from Lin's DNA inventions.

After the interference proceedings, the PTO again determined — this time in the specific context of a rejection of the '868 claims for ODP over the '008 claims — that Lin's process inventions are patentably distinct from Lin's DNA and host cell inventions. In making its determination that these claims were patentably distinct, the PTO considered many of the same arguments and evidence that the parties rely on in this action. Amgen argued in response to the Examiner's ODP rejection that: (1) the PTO's declaration of separate interference proceedings for the DNA and process counts reflected its determination that Lin's '008 claims and process claims were patentably distinct inventions; (2) a prior ITC decision had determined that Lin's '008 claims did not extend to the process of producing EPO glycoproteins; and (3) a person of ordinary skill in the art at the time would not have had a reasonable expectation of successfully producing a recombinant glycosylated EPO product having the specific *in vivo* biological activity

recited in the claims. (TX 2012.1023-80 (AM-ITC 000426-36, AM-ITC 00455484530).)

As determined by the ITC, real legal consequences attached to the distinction between the process claims of the '868 patent and the DNA and host cell claims of the '008 patent. When Amgen attempted to enforce the '008 patent against Chugai Pharmaceutical Co., a foreign competitor that was making recombinant erythropoietin overseas for importation into the United States, the U.S. International Trade Commission determined that "the '008 patent covers articles, i.e. host cells, but not processes." (TX 2012.533 (AM-ITC 00953316).) Consequently, the '008 patent did not provide Amgen any protection against the importation of Chugai's foreign manufactured EPO glycoprotein product. This limitation in the legal protection afforded by the '008 claims was a primary reason why Amgen made repeated efforts to accelerate examination and issuance of the '868 process claims. (*See, e.g.*, TX 2012.531-34 (AM-ITC 009953314-17).)

Amgen also argued to the examiner that there was no reasonable expectation of success in producing a recombinant EPO having the recited *in vivo* biological activity. Before Lin, it was understood and believed that both the carbohydrate structure and the amino acid sequence of EPO would play an essential role in creating a functional EPO product. But what, if any, recombinant cell would in fact produce and secrete an EPO polypeptide that had the carbohydrate structure needed to achieve the required *in vivo* activity, simply was not known. Indeed, no one even knew what structures or modifications were needed to produce such a functional product. While the DNA of the '008 claims could be used to direct a cell to produce the required amino acid sequence, the DNA was not sufficient to produce a glycosylated EPO protein product that actually possessed the stated *in vivo* biological activity. What more was needed — including proper protein conformation an all necessary carbohydrate side chains — was not known before it was actually achieved and successfully demonstrated. Therefore, even with the purified and isolated DNA sequence claimed in the '008 patent, there was no reasonable

expectation of success in using that sequence to produce a recombinant EPO product that had the *in vivo* biological activity of causing bone marrow cells to increase the production of reticulocytes and red blood cells.

In responding to the PTO's ODP rejection, Amgen directed the examiner to its prior submissions, including an extensive computerized search report of prior recombinantly produced glycoproteins, which showed that the production of *in vivo* biologically active recombinant EPO was unexpected and non-obvious to those skilled in the art at the time of the invention. (*See* TX 2012.1030 (AM-ITC 000433) (citing TX 2012.214-443 (AM-ITC 000191-211, AM-ITC 00454366-574)[45] and TX 2012.494-501 (AM-ITC 000262-69)).) Amgen had previously relied on these references to successfully overcome the PTO's rejection of Lin's process claims for obviousness under § 103. Although the PTO's prior rejection had been for § 103 obviousness, and not ODP, the absence of any "reasonable expectation of success" was the same in both instances.[46] In its response to the examiner's ODP rejection, Amgen explained the significance of these prior submissions to the ODP issue and attached a table summarizing 38 of the previously-disclosed references. (TX 2012.1055-56 (AM-ITC 00455505-06).)

[45] The computerized search reports identified as Exhibit E to "Applicant's Second Preliminary Amendment," dated May 24, 1988 ('179 File History, Tab 8), and referenced at TX 2012.228-29 (AM-ITC 000205-06) are attached as 9/26/07 Godfrey Decl. (D.I. 1165), Ex. I. These search reports were also submitted to the PTO as part of Amgen's September 27, 1988 "Reply Under 37 C.F.R. 1.111." (*See* TX 2012.496 (AM-ITC 000264).)

[46] At the time of the earlier § 103 obviousness rejection, the PTO mistakenly interpreted *In re Durden*, 763 F.2d 1406 (Fed. Cir. 1985), as prohibiting the allowance of ***any*** claim to a process that applied known or obvious process steps to a novel starting material. The false premise underlying the PTO's overbroad application of *Durden* was the assumption that applying known or obvious processes steps to a particular starting material would ***always*** produce an expected result (i.e., if the process itself is obvious, the product of that process can be predicted *a priori*). Amgen eventually overcame the PTO's § 103/*Durden* rejection by demonstrating, among other things, that the ordinarily skilled artisan would not have had any reasonable expectation of successfully producing *in vivo* biologically active recombinant EPO. (*See* TX 2012.214-443 (AM-ITC 000191-211, AM-ITC 00454366-574); TX 2012.494-501 (AM-ITC 000262-69); TX 2012.526 (AM-ITC 000294).)

The references submitted by Amgen showed that recombinant human EPO, unlike the other recombinantly produced glycoproteins reported in the prior art, is an "obligate" glycoprotein. That is, recombinant human EPO requires the attachment of specific carbohydrates (glycosylation) in order to achieve its intended *in vivo* (but not *in vitro*) biological activity. (*See* TX 2012.1030-31 (AM-ITC 000433-34); 2012.221-233 (AM-ITC 000198-210); 2012.496-99 (AM-ITC 000264-68).) Since there did not appear to be any examples in the prior art of recombinant human obligate glycoproteins in *in vivo* biologically active form, there were no relevant guideposts for the problem confronting Lin. (*Id.*)[47] Moreover, because there are numerous variables that impact the glycosylation of proteins, production of an obligate glycoprotein, such as EPO, entailed many more uncertainties than did the recombinant production of proteins whose *in vivo* activity did not depend on the specific attachment of certain carbohydrate structures. And that is why the prior art examples did not provide the ordinarily skilled artisan with a reasonable expectation of successfully producing a recombinant *in vivo* biologically active ***EPO***. (*Id.*)[48] The PTO agreed. Indeed, the PTO had even expressly determined in an earlier office action that the state of the art of heterologous gene expression was

[47] Amgen acknowledged that tPA might also be an "obligate glycoprotein," but noted that there was no published report that an *in vivo* active recombinant form of tPA had been produced in mammalian cells.

[48] Amgen further explained to the examiner that, even if the prior art had included a report of the successful production of *in vivo* biologically active tissue plasminogen activator (tPA) (another obligate glycoprotein), a single disclosure of the recombinant production of an obligate human glycoprotein would not have provided a reasonable expectation of success at recombinant production of all other obligate glycoprotein products, and especially not a glycoprotein product having the *in vivo* biological activity of human EPO. (TX 2012.1030-31 (AM-ITC 000433-34).) As Amgen had previously explained to the PTO, "there did not exist any body of information in the art which would . . . provid[e] a basis for asserting that the transformation/transfection, transcription, translation, glycosylation and isolation as described by [Lin's process] claims could reasonably have been expected to succeed in yielding a human erythropoietin product having the amino acid sequence and glycosylation required for in vivo biological activity." (TX 2012.498 (AM-ITC 000262) (emphasis in original); *see also* TX 2012.232 (AM-ITC 000209) (same).)

"primitive" at the time of Lin's inventions, and that it was "highly unpredictable that a heterologous protein would be produced in a biologically active glycosylated form." (TX 2012.916 (AM-ITC 000319).)

b) Additional evidence shows the unpredictability in the art

The PTO's conclusion as to the state of the art comports with other contemporaneous evidence of the difficulties and uncertainties in the art. As demonstrated in the comments section of Trial Exhibit 2062 ("Comparative Studies of Natural and Recombinant Erythropoietin," presented at the Cold Spring Harbor Symposium[49]), Dr. Lin's recombinant EPO was "one of the first glycoprotein products made by recombinant-DNA technology" (TX 2062, at AM-ITC 00580155), and other scientists, even after the report of Lin's invention, were not only concerned that EPO was so extensively glycosylated, but also expected that the carbohydrates attached to the recombinant protein would necessarily differ from the carbohydrates attached to the natural EPO protein. That, in turn, led to concern over the effect such differences would have on the recombinant molecule and its *in vivo* effect.

> [Dr. Liu:] Well, let us remember that this protein has 40% carbohydrate and that 40% is a big chunk of the molecule. Moreover, that carbohydrate will not be identical in any way between the natural and the r-DNA products. (*Id.* at AM-ITC 00580154.)
> . . . .
> [Dr. Bangham:] . . . r-DNA erythropoietin, one of the first preparations made in animal cells; glycosylation would presumably provide something different from the natural human substance. Therefore, the overall structure and antigenic nature of this product may be different from the natural one. (*Id.* at AM-ITC 00580156.)

One of the references Amgen discussed in overcoming the PTO's ODP rejection related to the contemporaneous work at Genentech on recombinant human tissue plasminogen activator

[49] *See generally* 9/14/07 Trial Tr. 1097:22-1098:17 (discussing Cold Spring Harbor Symposium).

("tPA") — the same work that Roche relies on as prior art in this case. In the prosecution history, Amgen noted that the first report of *in vivo* biologically active tPA was not published until 1984, and Amgen argued that even if this was considered prior art to Lin's work, "a single disclosure of the recombinant production of an obligate human glycoprotein would not have provided a reasonable expectation of success at recombinant production of a glycoprotein having the *in vivo* biological activity of human erythropoietin." (TX 2012.1030 (AM-ITC000433).)

Because tPA was addressed in the prosecution history and is raised as a reference here by Roche, Genentech's characterizations of the state of the art during prosecution of its patents relating to recombinant tPA are instructive. In overcoming obviousness rejections during prosecution of its '075 patent application, filed in 1983, Genentech explained to the Patent Office that there was no reasonable expectation of success at the time that one could produce an *in vivo* biologically active form of the protein using recombinant technology:

> The principal flaw in the Examiner's rejection, even as applied to the non-elected claims, is that ***there is no basis in the art of record for predicting with reasonable certainty that human t-PA could be expressed in a recombinant system, that it would be compatible with recombinant host cells, or that bioactive t-PA of a degree of purity enabled by the present invention could be produced by any practical means***.
>
> It would have been appreciated by those skilled in the art at the time this invention was made that the expression of human t-PA in transformed cells would be fraught with many potential difficulties. ***The art of recombinant DNA technology appears to be deceptively straightforward but is inherently unpredictable.*** . . .
>
> One of the reasons for not being able to reasonably predict the ability of a recombinant cell to successfully produce by expression a heterologous protein concerns the fate of foreign DNA in a host cell system. For example, it is not predictable that mRNA, if produced at all from such DNA, will be stable or that it will be accurately translated into a full-length protein. Even if it is, one cannot be certain that the protein will not be degraded by enzymes, either within the cell or extracellularly, or that the recombinant cell will properly fold the molecule conformationally so that it will exhibit its desired biological activity. The human t-PA of the present invention contains some 527 amino acids, with many potential cleavage sites and some essential conformational

> requirements for biological activity. Thus, ***it would certainly have been unpredictable before the fact that one could obtain by recombinant DNA technology a biologically active protein such as the one forming the basis of the present invention.***

(TX 0045 (10/21/85 Amendment from '075 patent file history), at 24-26 (emphasis added).)

In arguing the non-obviousness of its tPA product claims during the prosecution of its parallel '486 patent, Genentech submitted evidence to the PTO that the recombinant tPA made in CHO cells had glycosylation that differed from the natural protein. Genentech then argued: "The applicants submit that at the time the invention was made [1983], and even today [1996], it would not have been predictable whether such glycosylation differences would, in fact, produce intact, functionally biologically active glycoprotein." (D.I. 1165, Ex. J, at 3.)

Elsewhere during prosecution of its tPA patents, Genentech argued:

> At the time this invention was made [1982-83], it was unknown (a) what effect glycosylation differences would have on the biological activity of a protein, and (b) whether the cell type used for expression of the protein would effect the glycosylation pattern.
> . . . .
> It would not have been predictable whether glycosylation differences would, in fact, produce intact, functionally and biologically active glycoprotein. On this point, even later published papers reiterate this uncertainty.

(TX 0051 (7/3/96 Amendment from file history of '314 patent), at 5-6.)

Similarly, scientists working in the field of protein expression, and specifically erythropoietin expression before Dr. Lin's inventions, did not know whether CHO cells could be successfully used to produce *in vivo* biologically active EPO. (*See*, e.g., Browne Trial Testimony, Trial Tr. at 1910-12, 1935-36; Hood Trial Testimony, Trial Tr. 1993:11-20.)

c) <u>The evidence Roche relies on was all before the PTO</u>

Importantly, in determining that Lin's '868 claims were allowable without any terminal disclaimer over the '008 patent, the Patent Office also considered and rejected the contrary arguments and evidence that Roche now relies on to support its position that Lin's process

inventions would have been obvious over Lin's DNA and host cell inventions. Amgen specifically disclosed and directed the examiner's attention to these contrary arguments, many of which were made in a declaration from Dr. Arthur Sytkowski that had been submitted on behalf of Amgen's competitors during contested proceedings concerning Dr. Lin's European counterpart patent. (TX 2012.1031 (AM-ITC 000434); TX 2012.1058-78 (AM-ITC 00455508-28).) Amgen attached the entire Sytkowski declaration as an exhibit to Amgen's response to the PTO's ODP office action. (*Id.*) The Sytkowski declaration repeatedly asserted that the ordinarily skilled artisan would have had a reasonable expectation of success in using isolated EPO DNA to produce recombinant EPO polypeptides having the stated *in vivo* biological activity. (*See supra* pp. 17-18.) In addition to the Sytkowski declaration, Amgen also disclosed and directed the examiner's attention to the references that Amgen's opponents in Europe had asserted in support of their contention that ordinarily skilled artisans would have had a reasonable expectation of successfully producing recombinant EPO polypeptides having *in vivo* biological activity. (TX 2012.1031 (AM-ITC 000434).)

Many of the references that Amgen submitted to the PTO concern the very same proteins that Roche now relies on. Based on Dr. Lowe's trial testimony, Roche apparently is asserting that references concerning the following proteins are sufficient evidence that the ordinarily skilled artisan would have had a reasonable expectation of success in using isolated EPO DNA to produce recombinant EPO glycoproteins having *in vivo* biological activity:

- tissue plasminogen activator (tPA);[50]
- hemagglutinin surface glycoprotein (HA);[51]

[50] *See* 9/5/07 Trial Tr. 171:24-172:7, 182:2-183:18; 9/6/2007 Trial Tr. 280:9-284:3 (TX 2029, 2030), 323:25-325:9.

[51] *See* 9/6/07 Trial Tr. 230:1-13 (TX 2020).

- human interleukin-2;[52]
- interferon-beta (IFN-β);[53]
- interferon-gamma (IFN-γ).[54]

The PTO considered evidence concerning each of these proteins.[55] Dr. Lowe conceded during trial that Amgen provided all of this evidence to the PTO during examination of Dr. Lin's patents. (9/7/07 Trial Tr. 379:9-380:21.) Because Roche has cited nothing new, Roche has failed to prove that the '868 and '698 claimed inventions would have been obvious over the '008 claimed inventions.

d) Expert evidence shows the unpredictability of the art in 1983-84

Dr. Lodish explains in great detail in his declaration why a person of ordinary skill in the art in 1983-84, without the benefit of the disclosures in Dr. Lin's patent specification, would not have reasonably expected to succeed in using isolated EPO DNA to produce glycosylated EPO polypeptides having the *in vivo* biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells. (*See* D.I. 1164, ¶¶ 18-121.) Dr. Lodish summarized his views as follows:

> Too much was unknown at that time regarding the structure and function of EPO, the role of glycosylation in EPO's function, and

[52] *See* 9/5/07 Trial Tr. 171:12-15.

[53] *See* 9/5/07 Trial Tr. 171:5-11, 182:2-3; 9/6/07 Trial Tr. 272:9-273:16 (TX 2026, 2027).

[54] *See* 9/6/07 Trial Tr. 325:6-9, 274:8-276:4 (TX 2028).

[55] *See, e.g.*, '179 File History, 1/3/94 Information Disclosure Statement, at TX 2012.954 (AM-ITC 000357) and 2012.957 (AM-ITC 000360) (disclosing Goeddel EP '619 Application (TX 2029) and Collen at el., *J. Pharm. & Expt. Therapeutics*, 231:146-152 (1984) regarding tPA); '179 File History, 10/7/94 Information Disclosure Statement, at TX 2012.1083 (AM-ITC 000439) (disclosing Gething et al., *Nature*, 293:620-625 (1981) (TX 2020) regarding HA); *id.* at TX 2012.1084 (AM-ITC 000440) (disclosing Taniguchi et al., *Nature*, 302:305-310 (1983) regarding human interleukin-2); *id.* at 2012.1084 (disclosing McCormick et al., *Mol. Cell. Biol.*, 4(1):166-172 (1984) regarding IFN-β); '179 File History, 9/26/88 Information Disclosure Statement, at TX 2012.1233 (AM-ITC 000587) (disclosing Haynes et al., *Nucleic Acids Res.*, 11(3), 587-706 (1983) (TX 2001) regarding IFN-γ).

> the possibility of differences for EPO produced in cells of different types, or from different species, to lead to a reasonable expectation of success. For example, a person of ordinary skill in the art would not have known whether the particular human kidney cells that make EPO in the human body imparted special glycosylated structures on the EPO molecule that were critical to its biological activity. A person of ordinary skill in the art would not have known whether production of EPO in a cultured mammalian cell might create a form of EPO that would trigger a severe immunological reaction when injected into humans.
>
> Before Dr. Lin's work, a person of ordinary skill in the art would have known that there were many different reasons why a human glycoprotein might not be produced in a biologically active form in cultured cells. Before Lin, there were no reports of successful production of human glycoproteins in mammalian cells with *in vivo* biological activity, with at best, one possible exception. This uncertainty was exacerbated by the absence of any experiment demonstrating that *in vivo* biologically active EPO had actually been successfully made and isolated from recombinant cells. It was only after Dr. Lin's work demonstrating that a biologically active human EPO glycoprotein could be successfully produced in at least CHO cells that one of ordinary skill in the art could begin to expect success for producing *in vivo* biologically active EPO going forward. Dr. Lin's development of methods of producing biologically active EPO glycoprotein, and proof that such methods actually worked were important experimental validations. To say that everything followed predictably once the DNA sequence encoding EPO was isolated ignores the substantial, subsequent work performed by Dr. Lin and his colleagues as well as the unpredictability of the art prior to Dr. Lin's success.

(D.I. 1164, ¶¶ 131-32.) For these reasons, and others explained in his declaration, Dr. Lodish concludes that each of the inventions claimed in the '868 and '698 asserted claims would ***not*** have been obvious to a person of ordinary skill in the art in 1983-84, even in light of claims 2, 4, 6, 7, 25 and/or 27 of the '008 patent. (D.I. 1164, ¶¶ 175, 183.)

Dr. Lodish's opinion is further corroborated by the testimony of Roche's expert, Dr. Harlow. During his deposition, Dr. Harlow testified that different proteins require different kinds of glycosylation, that different cell types produce different kinds of glycosylation, and that it was known in 1983 that small changes in glycosylation produce significant changes in a

protein's biological activity. (6/20/07 Harlow Tr. 195:22-196:22 (D.I. 1165, Ex. H).) Dr. Harlow also conceded that some proteins — even though they are produced in glycosylated form — do not require glycosylation in order to be biologically active *in vivo*. Consequently, as he also conceded, the knowledge that biologically active versions of such proteins had been successfully produced in one cell type would not have provided a reasonable expectation of successfully using the same cell type to produce a different glycoprotein, such as EPO, whose *in vivo* activity required the attachment of certain specific carbohydrates. (*See id.* at 196:23-197:1; 226:15-227:5; 231:19-232:20; *see also* Harlow Trial Testimony, Trial Tr. 1788:24-1789:8.)

Other experts who testified at trial agreed that a person of ordinary skill in the art in 1983-84 would not have reasonably expected to succeed in producing an *in vivo* biologically active EPO glycoprotein in mammalian cells grown in culture. (*See, e.g.*, Varki Trial Testimony, Trial Tr. 2243:8-22.)

e) Roche's additional arguments are meritless

In addition to its primary ODP arguments and evidence, which the PTO considered and rejected, Roche has developed new arguments regarding its Theory No. 3 ODP defenses. Roche's new arguments are meritless and fall far short of the clear and convincing evidence standard. First, Roche argues that the PTO's failure to separate Dr. Lin's DNA and process inventions into different groups in the 1986 restriction requirement is evidence that the PTO considered these inventions to be patentably ***in***distinct. But Roche's interpretation contravenes the statutory mandate of 35 U.S.C. § 121 and is inconsistent with the PTO's repeated determinations, described above, that Lin's process inventions ***are*** patentably distinct from Lin's DNA and host cell inventions. *See* 35 U.S.C. § 121 ("The validity of a patent shall not be questioned for failure of the Director to require the application to be restricted to one invention."). Were it otherwise, the ODP analysis might collapse into the § 121 analysis in cases

where there is a restriction requirement but no § 121 protection (e.g., where consonance was not maintained). ODP and § 121 must not be conflated — they are separate legal issues, with separate burdens of proof borne by different parties.

Second, Roche argues that Genentech's product license application (PLA) regarding tissue plasminogen activator (tPA) is prior art from which a person of ordinary skill in the art in 1983-84 would have derived a reasonable expectation of success in using isolated EPO DNA to produce recombinant EPO glycoproteins having *in vivo* biological activity. Among many flaws in this argument, the most glaring is the fact that Genentech's PLA does not constitute prior art to Dr. Lin's claimed inventions. Genentech's PLA was filed in April 1986 — nearly 17 months after Dr. Lin's '298 application (which was filed on November 30, 1984). (*See* TX 2055.1.) And even after Genentech's PLA was filed with the FDA in 1986, federal regulations in effect at the time prevented the FDA from publicly disclosing the information in that application unless it had already been made public. *See* 21 C.F.R. § 601.51(c) (1986) ("If the existence of a biological product file has not been publicly disclosed or acknowledged, no data or information in the biological product file is available for public disclosure."). Thus, the information in Genentech's PLA was not publicly accessible at the relevant time.

Moreover, even if the Genentech PLA were prior art and did disclose that recombinant tPA expressed in mammalian cells had *in vivo* biological activity, that information would not have created a reasonable expectation of success in using isolated EPO DNA to produce recombinant EPO polypeptides having *in vivo* biological activity. As Dr. Lodish explains in his declaration:

> Even assuming tPA had been expressed and shown to be *in vivo* biologically active before Dr. Lin's inventions, I do not believe that this single example would have given an ordinarily skilled artisan any confidence or reasonable expectation that ***any other*** glycoprotein that required proper glycosylation for *in vivo* biological activity could be expressed in heterologous host cells in

> an *in vivo* biologically active form. I do not believe that this single example is easily generalizable to the expression of EPO. . . . This is particularly so since the role of glycosylation in tPA function had not yet been determined in 1983-84.
>
> In my opinion, knowledge of the significant differences in the nature of tPA as compared to the nature of EPO would have led the ordinarily skilled artisan to discount the tPA results when considering whether expression of EPO in heterologous mammalian cells could reasonably be expected to lead to the production of *in vivo* biologically active EPO. In particular, as I explained above, the ordinarily skilled artisan would have understood that while tPA is an incredibly short-lived enzyme that would be deleterious if it persisted *in vivo*, EPO is a hormone that must persist in the body for extended periods of time before any *in vivo* biological activity can occur and be observed. Therefore, the requirements for proper post-translational modifications, particularly glycosylation, would have been understood to be very different between tPA and EPO. One would not have expected tPA to have the same acute requirement for proper glycosylation in order to function in the few minutes it needs to persist in the blood stream, whereas an ordinarily skilled artisan would have understood that proper glycosylation would be necessary to allow EPO to discharge its function as a hormone, to escape removal from the blood by cell surface receptors that bind abnormal carbohydrates (such as galactose — or mannose — terminated oligosaccharides), and to elicit *in vivo* biological activity.

(D.I. 1164, ¶¶ 115-116.) Thus, the Genentech PLA provides no support for Roche's ODP arguments.

Finally, Roche argues that Amgen "admitted" during prior proceedings, including the *Fritsch v. Lin* interference proceedings, that the '868 and '698 process claims are not patentably distinct from the '008 DNA and host cell claims. In effect, Roche asks the Court to hold the '868 and '698 claims invalid for ODP over the '008 claims as a matter of judicial estoppel. Roche made these same arguments in a motion *in limine* which the Court correctly denied. (D.I. 801.) As Amgen demonstrated in its opposition to Roche's judicial estoppel motion *in limine*, when Amgen's prior statements are considered in their entirety and in context, it is clear that Amgen's past and present positions are not inconsistent. (*See generally* D.I. 867.) Amgen has

always contended that Dr. Lin's process claims are patentably distinct (and not obvious over) Dr. Lin's DNA claims. The purported "admissions" identified by Roche are not even relevant evidence, let alone clear and convincing evidence, of ODP. Therefore, Roche's estoppel arguments are entitled to no weight in the Court's analysis of Roche's Theory No. 3 ODP defenses.

IV. CONCLUSION

For the foregoing reasons, Amgen respectfully requests that the Court hold that Amgen's asserted claims are not invalid for obviousness-type double patenting. In particular, Amgen respectfully requests that the Court hold that:

1. Roche's ODP defenses based on the '868 and '698 claims ("Theory No. 4") are precluded because those defenses were not disclosed during discovery or in Roche's § 282 Pretrial Notice;

2. Section 121 exempts the '933, '422 and '349 claims from ODP over the '868 and '698 claims; and

3. The '868 and '698 claims are patentably distinct from the '008 claims.

October 4, 2007

Respectfully Submitted,

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CERTIFICATE OF SERVICE

I hereby certify that this document, filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of electronic filing and paper copies will be sent to those indicated as non-registered participants on October 4, 2007.

/s/ Patricia R. Rich
Patricia R. Rich