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

JOINT PRETRIAL MEMORANDUM

Amgen, Inc. ("Amgen") and F. Hoffmann-La Roche Ltd., Roche Diagnostics GmbH, and Hoffmann La Roche Inc., (collectively, "Roche") offer the following Joint Pretrial Memorandum.

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I. PARTIES' SUMMARY OF EVIDENCE TO BE OFFERED

A. Summary of Evidence to be Offered by Amgen

Amgen will present evidence demonstrating that the manufacture, use, sale, offer to sell, or importation into the United States of glycosylated recombinant human erythropoietin containing products, including "MIRCERA®," "CERA," "RO0503821," "Ro 050-3821,""R744," "Continuous Erythropoiesis Receptor Activator," "pegserepoetin alfa," "methoxy polyethylene glycol-epoetin beta," (collectively "peg-EPO") by defendants F. Hoffmann-La Roche LTD., Roche Diagnostics GmbH and Hoffmann La Roche (collectively "Roche") has and will infringe, either literally or under the Doctrine of Equivalents, the following claims of the patents-in-suit:

- U.S. Patent No. 5,441,868, claims 1 and 2;
- U.S. Patent No. 5,618,698, claims 6-9;[1]
- U.S. Patent No. 5,756,349, claim 7;
- U.S. Patent No. 5,547,933, claims 3, 7-9, 11, 12, and 14; and
- U.S. Patent No. 5,955,422, claim 1.

Amgen's evidence regarding infringement will consist of Roche's own documents (including Roche's regulatory filings with the Food and Drug Administration describing its product and manufacturing process), the deposition admissions of Roche employees or contractors, and the testimony of Amgen's experts regarding infringement.

Amgen will submit evidence of infringement based on the claim construction adopted to date by the Court as law of the case. It is Amgen's understanding that the Court does not wish

[1] Per the 8/2/07 letter from Day to Ben-Ami, Amgen has advised Roche that it will not assert '698 claims 4 and 5 at trial.

Amgen to present evidence of infringement based on alternative claim constructions which the Court has already rejected. If the Court were to change any of its claim construction rulings, Amgen would request leave to offer additional evidence to address infringement under the changed claim construction.

Amgen seeks a permanent injunction restraining defendants and their officers, subsidiaries, successors, affiliates, contractors, agents and all persons acting in concert with them from making, having made, importing, using, selling, or offering to sell in the United States or any of its territories peg-EPO, or any of the inventions claimed in the claims of the patents-in-suit identified above. Amgen requests leave to present evidence immediately following trial that it is entitled to an injunction under the relevant legal standard. Per the Court's request, Amgen has not included injunction issues in this pretrial memorandum.

Amgen will not seek actual or enhanced damages for defendants' actual or threatened infringement of the claims-in-suit occurring prior to the commencement of trial, but reserves the right to seek damages for any activities of Roche subsequent to the commencement of trial of this matter. Accordingly, Amgen will not present evidence at trial regarding damages it may have suffered to date.

If necessary, Amgen will respond to invalidity or unenforceability arguments properly presented by Roche as well as properly presented arguments related to non-infringement. Amgen expects to rebut such arguments with the testimony of various fact and expert witnesses, including the testimony of the inventor of the patents-in-suit Dr. Fu-Kuen Lin, documents relating to Dr. Lin's inventions, the prosecution history of the patents-in-suit, the state of the relevant art at the time of Lin's inventions, the long-felt but unmet need for Lin's inventions, and other objective evidence demonstrating the non-obviousness of Lin's inventions.

B. Summary of Evidence to be Offered by Roche

This Court has determined that the issues of validity, infringement and unenforceability of the asserted claims of the patents-in-suit will be tried to the jury starting September 4, 2007. Roche will present evidence showing that Amgen's asserted claims[2] are invalid for obviousness type double patenting over two prior Amgen patents that are now expired. Roche expects also to prove that prior to the effective filing date of the asserted claims, November 30, 1984, which is the critical date for determining prior art given that Amgen cannot prove an earlier invention date, the subject matter of the claims was already in possession of the public by virtue of what was publicly known or used, invented by others, or taught in patents or printed publications. Roche expects to prove through documents and the testimony of fact witnesses and expert witnesses that the asserted claims cover subject matter that was obvious to a person of skill in the art as early as October 1983. Roche also expects to offer evidence that will prove that Dr. Lin derived enough of the subject matter of the patents-in-suit from others to render the asserted claims obvious. Roche's evidence will show that, in fact, a number of the product claims read on chemical structures that existed long before Dr. Lin completed his inventions and thus those claims are anticipated, the epitome of obviousness.

Further Roche expects to prove that Amgen's asserted claims do not satisfy the enablement, written description, and definiteness requirement of 35 U.S.C. § 112. The specification filed by Amgen fails to describe the claimed subject matter in such full, clear, concise, and exact terms as to enable any person skilled in the art to make and use it, or to recognize that Dr. Lin had possession of the full scope of the claim at the time of filing. The

[2] As used herein, Amgen's "asserted claims" includes all the claims that are the subject of Roche's pleaded declaratory counterclaims of invalidity, including claims 4 and 5 of the '698 patent, and Roche continues to include said claims.

evidence will show that the asserted claims do not particularly point out and distinctly claim the subject matter which Dr. Lin regarded as his invention.

Roche will present evidence showing Amgen's patents-in-suit are unenforceable as a result of Amgen's inequitable conduct during prosecution of the applications that led to the patents in suit. Specifically the evidence will show that Amgen, and those owing a duty of candor to the PTO, intentionally misled the PTO by omitting, misrepresenting and burying information that would have been important to a reasonable examiner.

Roche will also present evidence at trial rebutting Amgen's contention that Roche infringes the claims of U.S. Patent No. 5,411,868, ("the '868 patent"); U.S. Patent No. 5,547,933, ("the '933 patent"); U.S. Patent No. 5,618,698, ("the '698 patent"); U.S. Patent No. 5,756,349, ("the '349 patent"); and U.S. Patent No. 5,955,422 ("the '422 patent"). The evidence will show that Roche's product MIRCERA™, is formulated with a new, unique chemical molecule, and that the process for making MIRCERA™ in Europe, and the methods of using MIRCERA™, if approved by the FDA will not infringe Amgen's asserted claims, either literally or, if not otherwise dismissed from the case, under the doctrine of equivalents. In addition the evidence will show that MIRCERA™ is a product that has been materially changed by subsequent processes as compared to the product of the processes patented in the asserted claims. The evidence will also show that Roche's product is so far changed in principle from the patented product that it is no longer the same invention as what Amgen claims in the asserted patents. Roche will also show that it has not engaged and will not engage in any culpable conduct directed to encouraging others to infringe any of Amgen's asserted patent claims. A complete explanation of Roche's theories was set forth in its interrogatory responses and expert reports served in this action.

II. STATEMENT OF FACTS ESTABLISHED BY PLEADINGS, STIPULATIONS, OR ADMISSIONS

The parties agree that the following facts have been established by the pleadings, stipulation, or summary adjudication:

1. United States Patent No. 5,441,868 (the '868 patent) issued on August 15, 1995.

2. United States Patent No. 5,547,933 (the '933 patent) issued on August 20, 1996.

3. United States Patent No. 5,618,698 (the '698 patent) issued on April 8, 1997.

4. United States Patent No. 5,756,349 (the '349 patent) issued on May 26, 1998.

5. United States Patent No. 5,955,422 (the '422 patent) issued on September 21, 1999.

6. U.S. Patent Application No. 06/747,119 ("the Lai/Strickland '119 application") was filed on June 20, 1985 and issued as U.S. Patent No. 4,667,016 ("the Lai/Strickland '016 patent") on May 19, 1987.

III. CONTESTED ISSUES OF FACT

A. Amgen's Contested Issues of Fact

Amgen's position is attached as Exhibit A.

B. Roche's Contested Issues of Fact

Roche's position is attached as Exhibit B.

IV. JURISDICTIONAL QUESTIONS

A. Amgen's Position

Amgen contends this Court has jurisdiction to hear Amgen's claims for declaratory judgment of infringement of the patents-in-suit. Amgen also contends this Court has jurisdiction to hear Amgen's claims for infringement of the patents-in-suit and to enter a permanent injunction against Roche if Amgen prevails in the patent case. This Court has previously held that it has jurisdiction to hear Amgen's claims. *See* October 20, 2006 Memorandum and Order (D.I. 121) (holding "the Court will not decline jurisdiction over this case at this time."). Amgen

does not contest jurisdiction to hear Roche's counterclaims given the Court's ruling granting jurisdiction for Amgen's claims.

B. Roche's Position

Roche contends that the Court has jurisdiction over its counterclaims for declaratory judgment, antitrust and other claims.

Amgen had previously commenced an action against Roche in the International Trade Commission based on the same asserted claims of the patents-in-suit here and the same alleged conduct that is the subject of this action. After a thorough investigation, including extensive discovery from Roche, the Commission determined that there was no conduct by Roche that constituted an act of infringement for which an investigation commenced by Amgen could proceed, including a finding that Roche's challenged conduct was exempt from infringement under 35 U.S.C. § 271(e)(1). As the initiator of that action, Amgen is bound by that Commission determination. Before this Court, Roche has pled and maintains the affirmative defense of lack of subject matter jurisdiction for Amgen's action in that all MIRCERA™ imported into the United States is within the safe harbor of 35 U.S.C. § 271(e)(1) and thus cannot infringe, and at the time the complaint was filed in this action, FDA approval of MIRCERA™ was not imminent. Roche reserves its right to appeal the Court's denial of Roche's motion to dismiss on this issue, and Roche maintains that the evidence at trial will be insufficient to maintain this suit regardless of the denial of the motion to dismiss.

V. QUESTIONS RAISED BY PENDING MOTIONS

A. Amgen's Position

Amgen's pending summary judgment motions, if granted, will significantly narrow the issues for trial in this phase of the case.[3] Amgen respectfully relies on the papers submitted in opposition to Roche's motions identified below, as well as oral argument on July 17, 2007, and continues its opposition to Roche's motions.

1. Amgen's Motion for Summary Judgment of No Obviousness-Type Double Patenting (D.I. 499)

Because obviousness type double patenting ("ODP") is a question of law for resolution by the Court, Amgen has moved for summary judgment on Roche's defense. The Court can and should delimit the issues for trial by deciding, as a matter of law, that the safe harbor provision of 35 U.S.C. § 121 immunizes the asserted claims of the '933, '349, and '422 patents from ODP over the claims of the '008 patent. Similarly, the Court should decide the appropriate legal test-the "one-way" or "two-way" test – and that under either test, the claims of the patents-in-suit are patentably distinct over Claim 10 of the Lai/Strickland patent.

Alternatively, as noted herein in Section IX, Amgen respectfully requests that the Court, rather than a jury, act as fact-finder to resolve this issue.

2. Amgen's Motion for Summary Judgment of Infringement of '422 Claim 1, '933 Claim 3, and '698 Claim 6 (D.I. 510)

Amgen seeks summary judgment that Roche's importation, use or sale of peg-EPO in the U.S. will literally infringe claim 1 of the '422 patent, claim 3 of the '933 patent, and claim 6 of the '698 patent. The relevant inquiry is whether each of the claim limitations is present in Roche's accused product. There is and can be no genuine issue of material fact regarding the

[3] Amgen's Motion for Summary Judgment Dismissing Roche's Antitrust Counterclaims is not discussed herein, but would serve to remove the need for an additional trial following the patent

composition and identity of Roche's accused product or the process by which peg-EPO is produced in Germany. The only dispute is purely a legal dispute over the Court's construction of the relevant claim terms and the statutory test for infringement under 35 U.S.C. § 271(g) for imported products made by a process patented in the United States.

3. Amgen's Motion for Summary Judgment that Lin's '933, '422 and '349 Claims are Definite, Adequately Described and Enabled (D.I. 532)

Amgen and Roche have both moved for summary judgment on, and thus agree that there are no genuine issues of material fact regarding, the issue of whether Lin's asserted '933, '422 and '349 claims are definite, and that the issue of definiteness under 35 U.S.C. § 112 presents a question of law for the Court's decision.

B. Roche's Position

Roche respectfully relies on the papers submitted in opposition to Amgen's motions listed above, as well as the oral argument before the Court on July 17, 2007 and continues its opposition to Amgen's motions.

The following is a brief summary of pending motions filed by Roche.

1. **Docket Item 539 - Roche's Motion for Summary Judgment That Claim 7 of U.S. Patent No. 5,756,349 Is Invalid Under 35 U.S.C. § 112 and Is Not Infringed.** Since the test specified in the claim cannot measure EPO, as required by the claim, one of skill in the art cannot identify the boundaries of claim 7, or practice the claim without undue experimentation, and the claim therefore is indefinite, lacks written description and is not enabled. Amgen also cannot prove infringement of this claim as Amgen's testing expert did not grow the cells under "suitable nutrient conditions" as required by claim 7, nor is there any evidence that the material measured by the expert was "EPO."

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case to be tried in September 2007.

2. **Docket Item 614 - Roche's Motion for Summary Judgment that Claim 1 of U.S. Patent No. 5,995,422 Is Invalid For Indefiniteness and Lack of Written Description.**

This Court has previously held that claims which expressly distinguished the claimed EPO from prior art human urinary EPO based on glycosylation differences were invalid for indefiniteness and lack of written description, finding the glycosylation of naturally occurring EPO to be a "standardless standard." This Court's previous decision, affirmed by the Federal Circuit, mandates that claim 1 of the '422 patent is invalid for indefiniteness and lack of written description and Amgen should be precluded from arguing otherwise.

At oral argument on this motion Roche emphasized the fact that if the claim language of the '422 patent "purified from mammalian cells grown in culture" is to limit the structures of human EPO included in the claimed product, the claim is invalid because a person of skill in the art in 1984 has no way to determine what the structure of the human EPO is. (July 17, 2007 Hearing Tr. pp. 21-24). The Court asked counsel for Amgen, more than once, to provide an answer to the question "what is the structure of human erythropoietin?" (Id p. 75). Amgen's counsel, however, failed to provide a meaningful response:

> THE COURT: I really want to hear the structure of human EPO.
>
> MR. DAY: Okay, I understand that. So let me, let me just get to that. I want to be sure to give you that examiner's -- because it shows how you have to check the record. Not everything said in this courtroom is consistent with the record.
>
> With respect to the, with respect to the definiteness of human EPO, Roche makes a straw man argument. The claim '422 claim 1 is to human erythropoietin purified from mammalian cells grown in culture. The Court construes the claim human erythropoietin to mean a polypeptide having amino acid sequence of naturally-occurring human EPO. Roche then says that means it must be 1 to 165 and Roche then uses its interpretation of the Court's construction to say that, and we must find that in the specification. So we've had an abstraction of an abstraction of an abstraction. What Lin must describe is what he invented, human erythropoietin. Column 27 and column 28 describe the product of Example 10 as human erythropoietin. Lin describes and points out very specifically the product that he possessed. That meets the written description requirement.
>
> Is it sufficiently definite that one of ordinary skill in the art would be able to

> figure out what that is? Well, as we pointed out in our opposition to Roche's motion, yes, their own expert Bertozzi testified that it was, that she would understand right away that human erythropoietin would be that polypeptide that's produced by cells which contain a DNA that encodes EPO. And it has the essential or the characteristic amino acid sequence that's encoded by that gene however produced by the cell.
>
> Let me get to the '422 claim 1 which says purified by mammalian cells grown in culture. The Federal Circuit has said that's a source limitation. Going back as far as 1896 when the Commissioner of Patents issued the In re Painter decision, the Patent Office and the Courts have recognized that source or process limitations may be used to describe a novel product where the product, because of the process by which it's produced, the full features or the full structure of the product cannot be captured in words. That's why you resort to product, by process or product by source limitations, to encompass the array or panoply of structures that are obtained by following the process.
>
> There need not be, it's a false premise that there need be in the patent words that set out a formula by which you discern the structure where the claimed invention is claimed as the product of a source or a process.
>
> The last point.
>
> THE COURT: It's three o'clock. I'm sticking to the time schedule rigorously because we need to meet informally.
>
> MR. DAY: Regents of University of New Mexico.
>
> THE COURT: Thank you.

(*Id* p. 81 - 83). Having done nothing more than point generally to Example 10 of the ‘422 patent without raising an a genuine issue of material fact of how one of skill in the art would determine the structure of human EPO beyond an amino acid sequence the Court should grant Roche’s motion as a matter of law.

3. **Docket Item 620 - Roche’s Motion for Summary Judgment That Amgen is Estopped From Asserting Infringement Under the Doctrine of Equivalents of the Asserted Claims of the '933 and '422 Patents.** Amgen is estopped because of prosecution history estoppel from asserting that certain terms in the asserted claims of U.S. Patent Nos. 5,547,933 and 5,955,422 encompass erythropoietin fragments, analogs or synthetic polypeptides, that the product of the claims can be anything other than human EPO, that the claims cover any

molecules that do not have the structure and function of the direct product of the expression of an exogenous DNA sequence, or any product that is not produced *in vitro* by mammalian cells in culture.

4. **Docket Item 624 - Roche's Motion for Summary Judgment That Amgen is Estopped From Asserting Infringement Under the Doctrine of Equivalents of the Asserted Claims of the '698 and '868 Patents.** Amgen is estopped because of prosecution history estoppel from asserting that the term "mature erythropoietin amino acid sequence of FIG. 6" in claims 4-9 of U.S. Patent No. 5,618,698 patent and the term "an isolated DNA sequence encoding human erythropoietin" in claims 1 and 2 of U.S. Patent No. 5,441,868 could cover by equivalents a DNA sequence coding for a 165 amino acid sequence.

5. **Docket Item 724 - Defendants' Motion To Preclude Testimony From Amgen's Belatedly Disclosed Fact Witnesses.** Testimony from proposed Amgen witnesses Arnold Berk, Joseph Eschbach, Stuart Orkin, Axel Ullrich, Dennis Fenton, Eli Friedman, and Nancy Spaeth should be precluded at trial because though Amgen has known the identity of these witnesses for long before fact discovery ended, Amgen first disclosed these individuals on FRCP 26(a) statements served well after the close of fact discovery.

6. **Docket Item 331 - Roche's Motion to Compel Production of Documents, and Deposition Testimony Under Rule 30(b)(6), Relating to Pegylation and Aranesp®.** Amgen placed its second-generation product Aranesp® and pegylation of Aranesp® at issue by contending that Aranesp® is an "EPO product" covered by the patents-in-suit, and should therefore be required to provide a complete copy of Amgen's BLA for Aranesp®, documents, including documents of Thomas Boone, related to pegylation of Aranesp® or other compounds Amgen claims are "EPO products" covered by the patents-in-suit, a knowledgeable 30(b)(6) witness on this topic, and any other documents related to Amgen work on "Peg-EPO."

7. **Docket Item 652 - Roche's Motion Pursuant to Fed. R. Civ. P. 56(f) for Relief from Amgen Inc.'s Motion for Summary Judgment that Dr. Lin's Asserted Claims are Definite, Adequately Described and Enabled.** Roche should be permitted to supplement its opposition to Amgen's motion for summary judgment to add numerous relevant, material statements made by Amgen expert Dr. Harvey Lodish at his deposition conducted just two days prior to the date when Roche's opposition was due in that the transcript of the deposition was not available at the time of the opposition.

8. **Docket Item 741 - Motion to Strike, In the Alternative, Untimely Expert Testimony of Ralph A. Bradshaw Regarding Amgen's Motion for Summary Judgment of No Obviousness-Type Double Patenting.** If the Court grants Amgen's Motion to Strike the Expert Testimony of Roche experts Drs. Lowe and Harlow (Docket Item 504), the Court should strike certain testimony of Amgen expert Dr. Bradshaw contained in a declaration submitted in support of Amgen's Motion for Summary Judgment of No Obviousness-Type Double Patenting (Docket Item 498) as Drs. Harlow and Lowe were responding to never previously disclosed testimony of Dr. Bradshaw.

VI. ISSUES OF LAW, INCLUDING EVIDENTIARY QUESTIONS, TOGETHER WITH SUPPORTING AUTHORITY

A. Amgen's Position

1. Legal Standards and Burden of Proof

Amgen's position is attached as Exhibit C.

2. Evidentiary disputes

Exhibit lists. Roche has indicated that they believe they can introduce new exhibits at any time up to and during trial, which are not listed on the exhibit lists exchanged on July 28, 2007. Amgen believes it will be prejudiced by the late introduction of new exhibits, and intends to object to their use at trial. Amgen also objects to Roche's unilateral supplementation of its

exhibit list on August 3, 2007 and August 9, 2007, well after the parties' agreed-upon exchange date of July 28. Roche's practice of continuously adding to its pretrial disclosures after the agreed-upon exchange dates unfairly prejudices Amgen and makes it impossible for Amgen to prepare for trial in an orderly and predictable manner.[4]

Objections to live witnesses. Roche has indicated in its pretrial filings that it intends to call 11 expert witnesses at trial. Amgen does not agree and has never agreed that Roche is entitled to call 11 expert witnesses. The parties' stipulation and the Court's order on this issue, as reflected in the Clerk's Notes of the proceeding on June 6, 2007, clearly states "[t]he parties agree to 10 trial experts." Amgen objects to Roche's listing of 11 trial experts. Furthermore, Amgen believes that it is entitled to immediate notice of the identity of the 10 particular trial experts Roche is limited to.[5]

Amgen reserves its objection to Roche's use as live witnesses at trial individuals not identified in any of Roche's 26(a) disclosures.

Amgen reserves the right to object to Roche's supplementation of its list of live trial witnesses on August 9, 2007.

On August 9, 2007, Roche indicated that it will call seven (7) of Amgen's fact witnesses to testify in Roche's case-in-chief. This will unnecessarily disrupt the lives and schedules of Amgen's witnesses, and will preclude Amgen from presenting its own case effectively and in an orderly fashion. Amgen objects to Roche calling anyone beyond Dr. Lin in its case-in-chief as unfairly prejudicial to Amgen and unworkable.

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[4] Roche has continued to insist that the parties "agreed" to ongoing supplementation of the exhibit list. The parties have no such agreement. *See* 7/30/07 letter from Brown to Fleming and 8/3/07 letter from Brown to Fleming. Amgen has not supplemented its exhibit list. Roche has already done so twice, and continues to insist it may do so unilaterally through trial.

Trial witnesses not disclosed

Amgen reserves its objections to Roche's use as live witnesses at trial individuals not identified in any of Roche's 26(a) disclosures.

Roche's objection to seven fact witnesses not named in Amgen's original initial disclosure ignores the fact that Roche had notice of and took discovery on all but three of these witnesses during the fact discovery period. Roche's motion ignores that the three additional witnesses were added to replace two witnesses — Joseph Eschbach and George Rathmann — who are each too ill to testify at trial. Amgen incorporates and rests on its Opposition to Roche's Motion to more fully and accurately account why Amgen had substantial justification for adding each of these witnesses to its Rule 26 disclosures and why Roche will not be prejudiced by this addition. (D.I. 781)

Regarding Ms. Spaeth, Roche claims that her testimony goes beyond the scope of Dr. Eschbach's testimony, that it is duplicative of other testimony Amgen intends to offer from Drs. Friedman and Brugnara, and that Roche would be prejudiced by Ms. Spaeth's testimony in a trial in this matter. But Roche's argument fundamentally distorts Dr. Eschbach's prior testimony and ignores the fact that Ms. Spaeth's testimony is admissible and highly relevant to rebutting Roche's argument that Dr. Lin's man-made EPO was obvious.

Roche misrepresents both the scope and the breadth of Dr. Eschbach's prior testimony. Dr. Eschbach testified in several capacities on several occasions. For example, he testified as a nephrologist (a kidney doctor) and provided relevant testimony from a scientific and medical perspective on the inadequacy of prior art treatments for the anemia of chronic kidney failure and the dramatic change in the care of anemic chronic kidney patients as a result of the advent of Dr.

[5] In addition, Roche has listed 11 additional experts as "possible other experts" in its witness list. Amgen similarly objects that this list of additional experts is improper in light of the Court's

Lin's man-made EPO. Dr. Eschbach also testified as an experimentalist with a good deal of knowledge and experience regarding hematology, ferrokinetics, and experimental design. In particular, he testified as to the deficiencies of the Goldwasser three-patient urinary EPO experiment and other purported prior art references.

But that was not all. Dr. Eschbach, among other things, also testified as a fact witness regarding specific patient anecdotes concerning what it was like for them from their perspective in the world before Dr. Lin's rEPO was available. The Court will recall that Dr. Eschbach specifically related the experience of a patient who so much wanted to share a skiing trip with her son, but the plasma infusion she had received did nothing for her and she had to stay in the ski lodge all day. But when she received rEPO she was able to ski all day with her son. Plainly, the topic of the world before and after rEPO ***from the perspective of a patient*** and not a medical doctor or scientist was addressed as a result of Eschbach the fact witness.

Roche has known about this scope literally for years. Dr. Eschbach's trial testimony has been available since 2000. His testimony on remand presented the same topics and has been available since 2003. All of Dr. Eschbach's prior testimony was produced to Roche at the outset of this case in June of 2006 in the related ITC proceeding.

Given his breadth of experience, knowledge, and expertise, Amgen was not able to replicate and replace it in a single witness. Instead, it identified Dr. Friedman, who is a nephrologist, to address from the medical perspective of a nephrologist various topics, including the inadequacy of the prior art treatments for the anemia of chronic kidney failure and the enormous breakthrough Dr. Lin's man-made EPO has been. Given his position and experience, Dr. Friedman will address what was known to doctors and scientists in the prior art. Dr. Brugnara is a practicing pathologist and the director of the Hematology Laboratory at Boston's

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order on this issue.

Children's Hospital. From that perspective, Dr. Brugnara will analyze the experimental design of and specific data from the various putative prior art references, including the Goldwasser urinary EPO experiment.

Ms. Spaeth is the only individual identified on Amgen's Rule 26(a) list who is able to testify with direct personal experience as to living with the anemia of chronic renal failure before the advent of rEPO and the change in her life as a result of the advent of rEPO. Again, it should be pointed out that in asserting that Dr. Lin has made no invention and that rEPO was obvious in light of the prior art, it is Roche who has made highly probative and directly relevant Ms. Spaeth's testimony. The jury should be permitted to consider Ms. Spaeth's factual experience in the world before and after rEPO in order to evaluate what Roche has placed at issue. As noted above, Roche has known for quite some time that Dr. Eschbach's testimony related specific instances directly from the point of view of a patient. Ms. Spaeth is also properly included on Amgen's supplemental Rule 26 disclosures because Amgen did not learn of her until after the close of fact discovery while searching for a replacement for Dr. Eschbach. Amgen promptly supplemented its Rule 26(a) disclosures as per rule 26(e) and provided notice of Ms. Spaeth to Roche. Furthermore, neither Dr. Friedman's testimony nor Dr. Brugnara's will be redundant of one another or of Ms. Spaeth's testimony; they will testify as to their observations as doctors and scientists within the framework of their specific areas of expertise and knowledge.

Finally, Roche claims that Ms. Spaeth's testimony also should be precluded because it is prejudicial. This is simply another way of saying that her testimony is highly probative and persuasive — hardly a ground for excluding it. If Roche is so concerned about Ms. Spaeth's testimony, it can drop the defenses that make it relevant. Moreover, Roche has known of Amgen's intent to call Ms. Spaeth for over a month. Roche's purported prejudice — if any — is simply the result of its refusal to take her deposition

Eschbach documents

From the outset of this litigation, Roche has known of Dr. Eschbach's testimony as a fact witness. Roche served a subpoena on Dr. Eschbach, and his responsive documents have all been produced and in Roche's possession for over two months. In addition, Dr. Eschbach's prior testimony was produced to Roche in June of 2006 and to the extent it was made public, Roche has been aware of his prior testimony for more than three years now. Dr. Eschbach's deposition, like those of all expert witnesses who were to be deposed on factual knowledge, was postponed per the parties' mutual agreement on this matter. Shortly after expert reports were served, Dr Eschbach became gravely ill. As soon as Amgen learned of it, Amgen informed Roche that Dr. Eschbach's grave condition prevented his participation in the litigation. For a more fulsome description of the events relating to Dr. Eschbach's availability as a fact witness, please see D.I. 781. Plainly these are circumstances well beyond Amgen's control and circumstances for which it should not be blamed.

On July 26, Roche wrote to Amgen asking for a stipulation on admissibility of documents produced from Dr. Eschbach's files as well as certain Amgen documents. In the spirit of compromise, Amgen agreed to waive foundation objections (authenticity and hearsay) with respect to the Eschbach documents. Roche's only complaint is that Amgen has not waived its objections as to relevance, an issue that even Dr. Eschbach's deposition would not have accomplished. To date, Roche has not provided any explanation for the relevance of these documents, nor has it made a motion to the Court for relief regarding these documents. Moreover, Roche's assertions regarding the timing of Dr. Eschbach’s production of documents are at odds with its own conduct.

Roche’s request that Amgen be precluded from offering Dr. Eschbach’s prior testimony ignores both the fact that Amgen complied with its production obligations and that Dr. Eschbach

became unavailable through no fault of Amgen. Roche's request that Amgen's documents (as well as Dr. Eschbach's documents) be deemed admissible for any purpose ignores the fact that Dr. Eschbach, even had he been available for deposition, could not have established the relevance of the documents for any potential argument Roche would make at trial (nor could he have even authenticated most of them). Roche's request should be denied.

Expert Reports

Adopting the adage that the best defense is a good offense, Roche inaccurately suggests that Amgen's experts are relying on and seeking to introduce evidence withheld by Amgen during the discovery period. The only late produced discovery cited by Amgen's experts is third party discovery that was properly sought during the fact discovery period but produced thereafter by third parties and publicly available documents that were not in Amgen's possession, custody or control during the fact discovery period. By contrast, Roche has served expert reports that rely on and seek to introduce into evidence Roche's own documents that it stalwartly refused to produce during the fact discovery period. Amgen will be serving motions in limine as described herein that seek to preclude Roche's attempt to back-door through its expert reports documents that it purposefully withheld during the discovery period.

Objections to witnesses testifying by designation. Roche has designated testimony from numerous witnesses that relates only to the antitrust and injunction issues in this case, which is irrelevant and should not be allowed in the patent portion of this trial. Amgen objects to Roche's designated testimony from Leslie Mirani, Maureen Michael, Anthony Messana, Tracey Mooney, Helen Torley , Kevin Sharer, Robert McGorty of Fresenius and Dennis Kogod of DaVita on these grounds. Furthermore, because Mr. McGorty resides within the subpoena power of the District of Massachusetts, Amgen objects to Roche's designation of Mr. McGorty's deposition transcript. Amgen has provided counterdesignations for this testimony to Roche per

the parties' agreement, but maintains its position that the testimony should be precluded and reserves the right to make additional objections to Roche's designated testimony at trial.

Amgen objects to Roche's overbroad designations for multiple witnesses. Roche has designated virtually entire transcripts of certain witness's testimony. Such overbroad designations do not provide Amgen with the requisite notice of the testimony Roche intends to introduce at trial, prevents Amgen from making meaningful counterdesignations, and encompass entirely irrelevant testimony.

Amgen further objects that Roche has failed to provide counterdesignations for many of Amgen's designations, with no explanation or justification being offered. Amgen reserves the right to object should Roche attempt to belatedly introduce additional counterdesignations.

Motions in limine that require resolution prior to the start of trial. [6]

Amgen offers the following preliminary list of *motions in limine* that Amgen intends to file that bear on the opening statement and proceedings and on issues surrounding alleged invalidity. Amgen will file these motions shortly.

1. Motion *in Limine* to exclude argument, testimony or other evidence relating to Roche's attempt to relitigate the obviousness or anticipation of Lin's expired '008 patent, as well as inequitable conduct in the prosecution of the patent applications, or issues raised in relation to any of these.

2. Motion *in Limine* to exclude argument, testimony or other evidence relating to tPA clinical data, because such data cannot constitute prior art to any asserted claim.

3. Motion *in Limine* to exclude argument, testimony or other evidence relating to ODP based on the specification of the previously-issued Lai '016 patent and the Lin '008

[6] Amgen reserves the right to file additional *motions in limine* at any time, and further reserves the right not to file any *motion in limine* on this list.

patent; and to exclude any testimony by Roche's expert Blobel testimony regarding ODP, because his opinions improperly rely upon a comparison of the '008 specification to the specification of the claims-in-suit.

4. Motion *in Limine* to exclude Roche expert Harlow from offering testimony regarding ODP based on the '008 claims, because his opinions are not based upon a claim-by-claim analysis.

5. Motion *in Limine* to exclude Roche's experts Kadesch and Lowe from offering testimony on peptide or protein sequencing because neither has the requisite qualifications.

6. Motion *in Limine* to exclude Roche expert Spinowitz from offering testimony relating to whether it would have been obvious to administer increased amounts of urinary EPO to patients to achieve therapeutic effect, because his opinions are based solely on clinical trials conducted with recombinant EPO made available by Dr. Lin's inventions.

7. Motion *in Limine* in exclude argument, testimony or other evidence relating to the 1986 Lai publication, because that publication cannot constitute prior art to any asserted claim and is not representative of the art of protein sequencing in 1983-1984.

8. Motion *in Limine* to exclude argument, testimony or other evidence regarding Dr. Eschbach's single-patient study of the administration of human EPO, because the study cannot constitute prior art to any asserted claim.

9. Motion *in Limine* to exclude argument, testimony or other evidence relating to the invalidity of the '080 claims, which have been dismissed with prejudice.

10. Motion *in Limine* to exclude argument, testimony or other evidence suggesting that Amgen's conduct that complied with the rules of the PTO was somehow improper.

11. Motion *in Limine* to exclude argument, testimony, or other evidence such as statistical analysis tending to suggest that PTO procedures or capabilities are deficient and accompanying inference that the patents-in-suit were not well examined.

12. Motion *in Limine* to exclude argument, testimony or other evidence relating to Amgen's request for injunctive relief in this case and whether the grant of such an injunction would negatively impact the public if peg-EPO therapy is unavailable.

13. Motion for standing order precluding introduction of opinions or supporting evidence not previously identified in any expert report.

14. Motion *in Limine* to exclude testimony regarding opinions presented in supplemental expert reports that incorporated literally or by reference opinions of experts who had already been deposed.

15. Motion *in Limine* to exclude references to patents as "monopolies."

16. Motion *in Limine* to preclude argument, testimony or other evidence relating to allegations made against Dennis Fenton in unrelated litigation.

17. Motion *in Limine* to preclude argument, testimony or other evidence relating to Amgen's revenues derived from sales of EPOGEN.

18. Motion *in Limine* to preclude argument, testimony or other evidence relating to whether Dr. Goldwasser violated any duty as a recipient of public research funding by his collaboration with Amgen.

19. Motion *in Limine* to preclude argument, testimony or other evidence relating to claims in the patents-in-suit that have previously been found invalid.

20. Motion *in Limine* to limit each opening statement to the subject matter of that phase of the trial.

Objections to claim construction

Amgen agrees with the Court's claim constructions. Amgen reserves the right to present evidence should the Court change its claim construction. To the extent that Roche is seeking to re-litigate claim construction arguments in the guise of validity or infringement arguments at trial, Amgen objects.

B. Roche's Position

1. Legal Standards and Burden of Proof

Roche's position is attached as Exhibit D.

2. Evidentiary disputes

Exhibits

The parties agreed that the lists exchanged on July 28, and thereafter were "preliminary" and could be supplemented and amended up to and including the submission of the Final Pretrial Memorandum ("PTM").[7] Roche and Amgen have also agreed to extend the time for interposing objections to each others' lists, to meet and confer about the admitted/numbered exhibits and to submit the final Exhibit Lists to the Court after the date of the submission of the Final Pretrial Memorandum. Amgen also submitted a revised Exhibit List on August 6, 2007. Amgen cannot complain and has no legitimate prejudice.

Amgen's statements of supplementation are inaccurate. The parties agreed to exchange "preliminary" pretrial documents (witness list, exhibit lists, statements of contested facts, etc. well before the preparation of the Final PTM, which the parties did) with the understanding that they could be supplemented or amended through the creation of this Final Pretrial Memorandum.

[7] Roche has continually confirmed that the parties "agreed" that the pretrial exchanges were "preliminary" and that the lists could be supplemented at least to the point of the submission of this Pretrial Memorandum. The parties had a clear agreement. *See* 7/23/07 letter from Fleming to Brown, 7/24/07 email Brown to Fleming (confirming), 8/2/07 and 8/3/07 letters from Fleming to Brown.

Roche has followed the parties' agreement. Amgen has no complaint.

Roche believes that all exhibits the parties intend to use at trial should be included on the exhibit lists, but that the parties should not be precluded from adding exhibits to the lists they exchanged to deal with documents and other evidence based on the evidence, including, for example, exhibits and documents that may become available or that either party may discover in preparing for trial or based on evidence adduced during trial. Amgen's initial list, unlike Roche's more focused list, contained well over 7,500 entries. Since this Pretrial Memorandum is restricted to the jury trial issues of validity, infringement and unenforceability, Roche submits Amgen's list was unfairly excessively large and not meant to be a meaningful representation of the evidence to be presented to the jury. Roche also objects to many of the items on Amgen's current proposed exhibit list which contains over 4,800 entries, as this list contains materials not previously produced in this action or available to Roche, not identified during discovery as relevant by Amgen or set forth in timely served interrogatory responses, and are otherwise improper.

Amgen and Roche had seemed to agree to the following provision which now does not appear in Amgen's portion of the order, Roche respectfully submits that the Court should have this provision apply in the case:

> "With respect to documents produced in this action from the files of a party that were prepared, created or authored by that party, such exhibits are stipulated to be authentic pursuant to Rule 901 of the Federal Rules of Evidence. The certified copies of the patents-in-suit are presumed to be authentic. This stipulation of authenticity should not be construed to include any marking or writing on any such document."

Roche believes that each party should follow a reasonable and practical method of exchanging the identity of witnesses and provide copies of demonstrative charts and other trial disclosures. Roche was the first to suggest such a process, and proposed a reasonable schedule. Amgen then expanded the dates in Roche's proposal to unreasonable limits making it impossible

given the fluidity of a jury trial. For example, Roche proposed to exchange demonstratives for openings with Amgen, and to identify witnesses and exhibits by 5pm the day before they are to testify. Amgen wants to exchange opening demonstratives five days in advance, where the Court has not even had the chance to rule on motions in limine or other matters, and this is completely impractical. Roche's suggestion is far more reasonable and given that the openings are only 15 minutes, not burdensome at all to the parties. This has been employed with success in many Courts and reduces the need for the Court to micromanage the trial as Amgen suggests. Roche respectfully asks that if the Court is inclined to even address this issue without a motion, which is the proper method, the Court should follow Roche's proposal as set forth in section VIII (B)(1) herein.

Amgen's Abuse as to Documents and Evidence Relating to Dr. Eschbach.

During the discovery period, Roche subpoenaed Dr. Eschbach as a fact witness for documents and his deposition. Amgen responded that he was to be an Amgen expert and that Roche would have the full opportunity to depose him when he was deposed as an expert. Later, during the expert discovery phase, as Roche repeatedly demanded the Eschbach documents responsive to the subpoena, Amgen was silent. Then at the last minute announced that Dr. Eschbach was too ill to participate in the trial and had to be replaced. This denied Roche the ability to depose Dr. Eschbach as a fact witness. Then, again after the end of fact discovery, Amgen finally produced personal documents from Dr. Eschbach that were the subject of Roche's subpoena. These documents are extremely relevant to Roche's invalidity arguments. By Amgen's delaying tactics, Roche was denied the opportunity to seek meaningful discovery from Dr. Eschbach on his documents and related testimony. Roche then asked Amgen to have the Eschbach documents be admitted in evidence. For example, Dr. Eschbach conducted studies with prior art EPO pharmaceutical compositions, tested in animals and administered to humans,

for which he applied for and received federal grants. Amgen led Roche to believe that they would agree to have the Eschbach documents be admitted and given numbers on the exhibit list. By letter delivered late last night, Amgen has now refused this request. Amgen should be precluded from offering any evidence that Dr. Eschbach as a fact witness would have offered, and further, all of his documents, including Amgen documents relating to Dr. Eschbach be deemed admissible for Roche in this action.

Objections to Live Witnesses

During the pretrial conference, the Court stated that an adverse party can call as a live witness in its case any witness identified to be called live by the other party. The Court acknowledged the practice of calling an adverse, hostile witness in such circumstances. Following that instruction, Roche waited to see Amgen's list of witnesses it would call live, and from that list identified witnesses that Roche would call as live in its case. FRE 611. Dr. Lin will be such a witness who will be called by Roche; Roche believes that there may be others. Amgen cannot complain about this process, as it was expressly ordered by the Court. Roche was entitled to identify Amgen witnesses on its preliminary trial witness to be called live and cross-examined (FRE 611 permits a party to call hostile or adverse witnesses in their case and to also cross-examine them by use of leading questions.) Amgen was aware of this and has no reason to complain. Roche acknowledged that there might be some witnesses of the other party who need not be called live (even though listed as a live witness by the other party) and offered a compromise to Amgen. Roche offered to Amgen to have some witnesses testify by deposition to avoid inconvenience to those witnesses; and asked Amgen to agree. Amgen refused to agree. It appears now that Amgen has changed its mind without informing Roche. Roche continues to hope that Amgen will agree to Roche's proposal, and given the Court's prior ruling, Amgen's proposed restriction is improper.

It was also proper for Roche to add the Amgen witnesses to its preliminary witness list once it learned whom Amgen intended to call live.

Roche's witnesses were properly identified in its initial disclosure, because as acknowledged by Amgen, Roche's initial disclosure states that it also identified witnesses identified in Amgen's initial disclosures. Of the few witnesses of which Amgen complains, Amgen either deposed them, or had the opportunity during discovery to depose them.[8]

Expert Reports

Roche has objected to Amgen's attempts to have its experts rely on and introduce evidence that was denied to Roche during discovery in this action, and also to improperly rely on materials and information in violation of FRE 702 and 703. In response to one of Roche's motions, this Court has ruled that "No Witness May Rely On Evidence Withheld From Discovery." (5/16/07 Order). Roche continues its objections to such opinions and testimony and will interpose those objections should Amgen offer such experts at trial. Also Roche objects to Amgen offering documentary evidence and/or opinion testimony that is contrary to findings in prior litigations including those made by this Court (see Roche MIL No. 1 and section VIII (B)(2), infra) that form the basis for issue preclusion. For example, under that doctrine Amgen is precluded from arguing that differences in glycosylation provide a definite limitation sufficient to distinguish product claims of the '422 patent and the '933 patent from prior art erythropoietin. At least Amgen's expert, Dr. Varki has submitted expert reports that would indicate he intends to offer such contrary opinions. As this Court clearly held: "Dr. Lin's disclosure [in the patents-in-suit] fails adequately to describe an EPO glycoprotein whose glycosylation differs from that of human urinary erythropoietin." ... "[T]he glycosylation of human urinary erythropoietin is a

[8] As to only one witness who Amgen appears to object, who was not deposed, his testimony was explained to Amgen in detail as it relates to a very limited issue.

standardless standard"... [because] (1) the glycosylation of urinary erythropoietin has 'enormous heterogeneity....'" *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 155 (D. Mass. 2001).

Trial Witnesses Not Disclosed on Amgen's Initial Disclosures

Roche objects to Amgen's attempt to identify and list as fact witnesses on Amgen's witness list, witnesses who were not properly disclosed on Amgen's Rule 26 Initial Disclosure during the discovery period. Roche has been prejudiced in not having the appropriate opportunity for full and coordinated discovery of Amgen and these witnesses, and therefore they should not be allowed to testify. Included among these witnesses are those set forth in Roche's pending motion (D.I. 724). In addition, Amgen claims that they need a nurse, anemia patient, and motivational speaker, Ms. Spaeth, to substitute for Dr. Eschbach. However, the subject matter Amgen has identified for which Ms. Spaeth may testify (a purported long-felt need for therapeutically effective treatment for the anemia of chronic renal failure) is duplicative of the testimony Amgen intends to offer from the other two experts it has identified to replace Dr. Eschbach, Dr. Brugnara and Dr. Friedman. The testimony Amgen intends to offer from Ms. Spaeth is also unduly prejudicial and far beyond the subject matter of Dr. Eschbach's original expert report. Given that, and the late disclosure and duplicative nature of Ms. Spaeth's testimony she should not be allowed to testify. Amgen never identified any witness nor disclosed one who was an anemia patient certainly not Dr. Eschbach.

Objections to witnesses testifying by designation

Amgen is simply incorrect that the witnesses identified by Roche do not have relevant testimony in this portion of the jury trial. Amgen's conclusory statements ignores the issues that Amgen itself raised in the contested issues of fact and law that have prompted the need for select testimony from witnesses such as Leslie Mirani, Maureen Michael, Anthony Messana, Tracey

Mooney, Helen Torley, Kevin Sharer, Robert McGorty of Fresenius and Dennis Kogod of DaVita . For Amgen to ask this Court to exclude at this juncture such testimony is improper, the Court need not anticipate what evidence may be offered by Amgen and then by Roche in response at this early juncture.

Amgen has asked the Court to limit the number of experts for each side that will testify before the jury. Amgen then has in its deposition designations, identified testimony of non-testifying experts. There is no evidentiary basis for proffering a non-testifying expert's deposition, and when Roche asked Amgen to explain, Amgen refused. Amgen's designations of such non-testifying experts is improper and inadmissible, and Roche should not be made to offer counterdesignations. The overbreadth of Amgen's own purported contested issues of fact have compelled the deposition designations proffered by both sides. There is no doubt that as the case progresses both sides will pare down what is actually presented to the jury. Roche also believes that the parties should be free to modify their designations and counterdesignations as necessary based on the evidenced adduced at trial.

Fact Witnesses in the Courtroom During Trial

Pursuant to FRE 615, Roche respectfully requests that any witness who may testify as a fact witness should be excluded from the courtroom or access to trial evidence when they are not testifying, other than corporate representatives.

Motions in Limine to Be Decided Prior to Start of Trial

Roche identifies the following preliminary list of *motions in limine* **("MIL")**, relating to the parties' opening or the first two days of evidence in the invalidity portion of the case, that Roche may submit and evidentiary issues that may arise during trial[9]:

[9] The parties have agreed that the listed motions need only relate to those concerning the openings on validity and the evidence for the first two days of trial. Roche reserves the right to

1. Roche MIL No. 1, that Amgen should be judicially estopped from offering argument, evidence or expert testimony that contradicts positions Amgen successfully advocated during prosecution of the patents-in-suit and in related interference and foreign proceedings.

2. Roche MIL No. 2, Amgen should be precluded from offering argument, evidence or expert testimony that contradicts findings of fact and holdings on issues in prior cases to which Amgen was a party.

3. Roche MIL No. 3, Amgen should be precluded from offering argument, evidence or expert testimony that the product license between Amgen and J&J (Ortho) which was entered before the issuance of any of the Lin patents is a recognition of the validity of the patents in suit.

4. Roche MIL No. 4, Amgen should be precluded from offering argument, evidence or expert testimony that contradicts its admissions regarding the prior art in the specification to the patents-in-suit.

5. Roche MIL No. 5, pursuant to FRE 703, Amgen's experts should be precluded from relying on inadmissible evidence which is of a type not typically reasonably relied upon by experts in their field of expertise, such as testimony from other judicial proceedings.

6. Roche MIL No. 6, Amgen should be precluded from arguing, maintaining or presenting any evidence to the jury to the effect that statements or actions by other corporations such as Chugai, Genentech, Genetics Institute, or Boehringer Mannheim are admissions by Roche or binding on Roche for any issues regarding non-infringement, invalidity or unenforceability.

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submit such other and further motions in limine or to make such other evidentiary applications to the Court based on the evidence adduced or proposed to be adduced at trial. Roche also reserves the right to file additional *motions in limine* at any time, and further reserves the right not to file any *motion in limine* on this list or to separate out certain motions into other motions.

7. Roche MIL No. 7, Amgen and its experts and other witnesses should be precluded from mentioning to the jury the existence or outcomes of prior litigations relating to Amgen or the patents-in-suit, as Roche was not a party in these litigations and thus these actions in no way bind or estop Roche from any argument, defense, position, etc., and they can have no preclusive effect on Roche and are not admissible evidence.

8. Roche MIL No. 8, Amgen should be barred from arguing or offering any evidence that any prior settlement regarding any Amgen patents is admissible in violation of FRE 408 and applicable common law, or has any preclusive or estoppel effect or is in any way binding on Roche.

9. Roche MIL No. 9, Amgen should be precluded from relying on any evidence regarding pegylation on which Amgen did not provide full and fair discovery to Roche.

10. Roche MIL No. 10, that Amgen should be precluded from prejudicing the jury against Roche by arguing that Roche is a foreign company, since Amgen knows that the only entity that would seek to sell or offer to sell MIRCERA in the United States is the US Roche company in Nutley.

11. Roche MIL No. 11, to preclude Amgen from arguing or submitting evidence of secondary considerations not previously disclosed in discovery as a secondary consideration.

12. Roche MIL No. 12, to preclude Amgen from offering any evidence related to Dr. Eschbach's factual testimony because Amgen denied Roche discovery of this information during the proper period in this case.

Objections to Claim Construction[10]

Where, as here, claim construction has been argued and resolved pre-trial, the Federal

[10] If the Court were to change any of its claim construction rulings, Roche would request leave to offer additional evidence to address issues of infringement, invalidity or other relevant issues under the changed construction.

Circuit has held that further objection to a district court's pre-trial ruling is unnecessary to preserve a party's right to revisit the claim construction ruling on appeal. *See, e.g., Cardiac Pacemakers, Inc. v. St. Jude Medical, Inc.*, 381 F.3d 1371 (Fed. Cir. 2004). However, out of an abundance of caution, Roche respectfully notes some specifics of its objections to the Court's claim constructions and reserves its objections to these constructions, which may be provided as a glossary to the jury during the trial, and further reserves the right to raise arguments at the time that this Court entertains proposed jury instructions and, if necessary, on appeal. Roche's positions were presented in claim construction briefs (docket entry nos. 311, 322) and arguments before the Court on April 17, 2007 (docket entry nos. 401, 428), and were further developed in Roche's summary judgment papers (docket entry nos. 473, 478, 482, 490, 505, 539, 540, 568, 588, 614, 620, 624, and 695) and arguments before the Court on July 17, 2007 (docket entry no. 762), and its objections are to the extent the Court's construction did not adopt and apply Roche's positions.

Disputed Claim Terms:

"*Human erythropoietin*" ('422 patent, claim 1)

Court construction: A protein having the amino acid sequence of human EPO, such as the amino acid sequence of EPO isolated from human urine.

Roche contends that the claim term "human erythropoietin", properly construed, should include all elements of the structure of human erythropoietin, such as glycosylation and higher-order conformation, rather than defined only as an amino acid sequence. For example, the claims should be limited to glycosylated and folded proteins having the amino acid sequence and full structure of human EPO, such as those expressed from the human EPO gene in mammalian cells known as of the date of the invention. This construction is supported by patentee's

definition and use of this term in the specification and prosecution histories, as well as by testimony of Amgen's experts and prior judicial findings.

If "*human erythropoietin*" is to be limited only to an amino acid sequence, it must be the 166 amino acid sequence disclosed in Figure 6 or the fragments of Table I of the specification of the patents-in-suit, because Amgen defined "*human erythropoietin*" in terms of the 166 amino acids of Figure 6 or the fragments of Table I, in the original patent specification. Later acquired knowledge cannot expand the scope of the claims to cover proteins not known at the time of filing. The specification and prosecution history supports Roche's position. (*See* docket entry no. 615).

***"Purified from mammalian cells grown in culture"* ('422 patent, claim 1)**

Court construction: Obtained in substantially homogeneous form from the mammalian cells, using the word from in the sense that it originates in the mammalian cells, without limitation to it only taking it directly out of the interior of the cells, which have been grown in the in vitro culture.

Roche contends that this source limitation does not define any recognizable physical limitation to the recited human erythropoietin. Nothing in the claims or specification supports a construction of the source limitation as imparting limiting structural features to the claimed product. Any structural limitations that distinguish prior art must be shown to be present in the accused product. (*See* docket entry nos. 615, 401, and 428).

***"[A] pharmaceutical composition comprising . . . a pharmaceutically acceptable diluent, adjuvant or carrier"* ('422 patent, claim 1; '933 patent, claims 9 and 12)**

Court construction: A composition suitable for administration to humans, containing a diluent, adjuvant or carrier.

Roche contends that this claim term, properly construed, should reflect the ordinary meaning of "composition" in a patent claim, which the Federal Circuit has recognized as being a mixture of specified components.

Additionally, the "A, B, or C" language (i.e., Markush language) of the second component of this claim indicates that "diluent", "adjuvant", "carrier" are three different alternatives, each of which must be supported by the specification, and only one of which can be present in a pharmaceutical composition meeting the claim limitations. The plain meaning of "or" and the absence of any express term providing for mixtures supports Roche's position. (*See* docket no. 479).

Finally, Roche contends that the claim term "pharmaceutical composition" should not be limited to mean one that is suitable for administration to humans. Rather, as previously held by this Court, this term should additionally encompass pharmaceutical compositions suitable for administration to any mammal, not necessarily humans. This construction is further supported by claim 10 of the '933 patent, which depends on claim 9. Under the Court's current claim construction the scope of dependent Claim 10 is impermissibly broader than the scope of Claim 9. (*See* docket entry no. 474).

***"[C]ells transformed or transfected with an isolated DNA sequence encoding human erythropoietin"* ('868 patent, claims 1 and 2).**

Court construction: Cells that have been genetically modified with isolated DNA containing genetic instructions for human erythropoietin or later generations of these cells that have inherited those instructions.

Roche contends that this claim, properly construed, means that the isolated DNA sequence encoding erythropoietin must be isolated and purified and not be introduced with other genetic material from the cells that produced the vector. This construction is supported by the patent specification, the file history, and the understanding of a person of skill in the art, as well as by Amgen's responses to interrogatories. (*See* docket entry nos. 613 (FN 2) and 489).

***"[A] non-naturally occurring glycoprotein product of the expression in a mammalian host cell of an exogenous DNA sequence comprising a DNA sequence encoding human erythropoietin"* ('933 patent, claims 3, 7-9, 11-12, and 14)**

Court construction: A glycoprotein (not occurring in nature) that is the product of the expression in a mammalian host cell of a DNA sequence that does not originate in the genome of the host,

and which contains the genetic instructions (or a DNA sequence) encoding human erythropoietin. (FN 3: Wherein expression means that the glycoprotein was produced in a cell and recovered from the cell culture.)

Roche contends that this claim's construction should reflect the clear assertion of the patent specification that the expression product of DNA encoding human erythropoietin produced in mammalian cells has the amino acid sequence of Fig. 6 wherein naturally occurring sugars are attached to only specific residues. This construction is further supported by the claim language and the prosecution history. Roche's position is supported by the fact that Amgen used "non-naturally occurring" during the prosecution history in and attempt to distinguish prior art from the claimed products. Non-naturally occurring must therefore be interpreted to mean having a structure not occurring in nature. (*See* docket entry no. 506).

Roche contends that "expression," properly construed, is the two cellular processes, transcription and translation. This definition comports with the accepted meaning of "expression" to persons of ordinary skill in the art (including Dr. Lin), and is supported by the specification. The product of expression in a mammalian host cell of DNA encoding human erythropoietin is therefore the product as it exists at the completion of transcription and translation, without further modification(s) by subsequent processes, such as proteolytic cleavage after translation or secretion. (*See* docket entry no. 588).

The process claims of the '698 patent recite: "*isolating said glycosylated erythropoietin polypeptide* ***expressed*** *by said cells*" ('698 patent, claims 4-9). To the extent the Court's definition of expression given for claims of the '933 patent also is meant to apply to claims of the '698 patent, Roche respectfully objects. (*See* docket entry no. 588).

VII. REQUESTED AMENDMENTS TO THE PLEADINGS

A. Amgen's Position

Amgen does not request any amendments to the pleadings. The Court has already allowed Roche to amend its pleadings once. This Court has twice rejected Roche's attempts to further amend its pleadings. *See* June 7, 2007 Order Denying [445] Motion to Amend its Answer to Amplify Allegations of Amgen's Inequitable Conduct and to Define Relevant Markets for Purposes of Antitrust Counterclaims; *see also* July 18, 2007 Order Denying [631] Motion to Amend Pleadings to Conform to the Evidence. Amgen will object to any further attempt by Roche to Amend its Answer before trial, because such an amendment at this late date would unfairly prejudice Amgen.

B. Roche's Position

Roche anticipates that it will seek to amend its pleadings (including without limitation its affirmative defense of inequitable conduct) to conform to the evidence introduced at trial. Such amendments are to be liberally allowed under the Rules, and will cause no unfair surprise to Amgen, particularly with respect to evidence that was set forth in Roche's Responses to Amgen Interrogatories served on April 2, 2007, during fact discovery and also was considered by the Court in connection with the parties' motions for summary judgment and was otherwise previously disclosed in Roche's interrogatory responses and expert reports. Roche will present to the jury the evidence concerning Amgen's inequitable conduct as properly and timely disclosed by Roche in its Interrogatory Answers, expert reports, and materials filed in opposition to Amgen's motion for summary judgment on this issue. In particular, Roche submitted its evidence disclosed during the discovery period in opposition to Amgen's motion for summary judgment of no inequitable conduct, including its counter Rule 56.1 Statement, supporting Declarations and exhibits, and brief, which motion the Court denied. The Court stated at the

hearing on that motion (Tr. July 17, 2007, p.32, ln14-33, ln22) that it would consider all the evidence submitted by the parties on that motion.

VIII. ANY ADDITIONAL MATTERS TO AID IN THE DISPOSITION OF THE ACTION

A. Amgen's Position

1. Exchanges during trial

The parties have not been able to reach agreement on a procedure for exchanging information during the trial as to the names of witnesses who will testify on direct examination, and any evidence and demonstratives to be used with those witnesses. Amgen believes that it is critical to a smooth and orderly progression of the case to allow sufficient time for the parties to exchange evidence to be used at trial and to meet and confer, prior to asking the Court to resolve objections. Amgen has proposed the following schedule:

Opening Statements and Closing Arguments

a. By 5 PM on August 31, 2007, the parties will exchange their demonstratives for their openings on validity. On September 1, 2007, the parties will meet and confer in an attempt to resolve objections to each others' opening demonstratives. By 5 PM on September 2, 2007, the parties will exchange final versions of the demonstratives that were exchanged.[11]

b. By 5 PM two (2) days prior to the openings for the other phases of the trial, the parties will exchange their demonstratives for their openings. By 5 PM one (1) day prior, the parties will meet and confer in an attempt to resolve objections to each others' opening demonstratives.

Witnesses Appearing Live at Trial

a. If either party intends to call a fact witness of the opposing party in their case, the party will provide two (2) weeks advance notice of their intent to do so, as well as specify a 3-day window in which that witness is expected to testify.

[11] Roche's complaint about Amgen's proposed 5-day advance notice for the demonstratives exchange for validity openings is meritless. Amgen has proposed this schedule because of the holiday weekend.

b. Except as set forth above, by 5 PM three (3) days before a party intends to call a witness live, the party will identify that witness by name to the opposing party.

c. By 5 PM two (2) days before a party intends to call a witness live, the party will provide to the opposing party the name of the witness who will testify, identify the exhibit number/letter of any exhibits to be used with that witness, provide copies of any demonstratives to be used with that witness, and exchange or make available for inspection physical exhibits and photographs to be used with that witness

d. The requirements and timing of exchanges identically apply when a party calls a fact witness of the opposing party in their case.

Roche has refused to disclose exhibits and demonstratives to be used on direct examination with Amgen's fact witnesses that it intends to call in its case-in-chief. Amgen believes that if Roche is permitted to call an Amgen fact witness during Roche's case-in-chief, Roche's refusal to disclose the exhibits and demonstratives to be used with that witness will result in unfair prejudice to Amgen, and that Amgen is entitled to notice of the evidence that Roche intends to use to examine Amgen's fact witnesses in Roche's case-in-chief.

Furthermore, Roche has indicated that it believes exhibits to be used with a witness should be exchanged ***no earlier than*** either the night before a witness is to testify, or during the actual examination of the witness. Amgen disagrees and believes this will needlessly waste the Court's time by forcing all evidentiary objections to such exhibits to be raised and ruled upon "on the fly" during trial with no meaningful opportunity for the parties to confer to resolve or narrow any such evidentiary issues prior to the introduction of the exhibits. It would be far more efficient for the parties to disclose exhibits and demonstratives at least two days before they are to be used with a witness so that the Court will be able to rule upon any objections to such demonstratives and exhibits during the afternoon of the day before the evidence is to be introduced.

Consequently, Amgen respectfully requests that the Court direct the parties to exchange witness names, an identification of exhibits to be used on direct examination with a witness, and

copies of any demonstratives to be used with a witness on direct examination ***no later than*** two (2) days before a witness is to testify. This requirement should apply equally to any fact witness of the opposing party.

2. Prior Findings and Alleged Admissions

Amgen will submit a bench memorandum addressing Roche's contentions that certain selectively chosen findings and conclusions from other litigations and portions of the '868 patent specification have binding effect and should be treated as Undisputed Facts. Roche's insistence, over Amgen's objections, on burdening this pretrial memorandum with more than 25 pages of selected findings and alleged admissions is inappropriate.

B. Roche's Position

1. Exchanges During Trial and Other Logistical Issues Raised by Amgen

Amgen's characterization of Roche's position is both incorrect and incredible. Roche proposed basically the same procedures its counsel used in another trial in this District, Ariad v. Eli Lilly, last year, which was agreed upon by the parties and the Court. Roche's proposal has been used by counsel in several trials prior to that case. It has been shown to balance the desires of the parties to know what its adversary intends to do, which is not required on a day to day basis, but is general practice to allow for the orderly and fair use of the jury's time. These types of agreements are intended to be neutral, but Amgen's proposal clearly favors Amgen. One cannot help but notice that Amgen seeks five days for demonstratives exchanges for validity openings, so it can change its own presentation, but does not offer the same for its infringement opening where Amgen goes first. The time for this type of jockeying has passed. Roche first proposed to Amgen a procedure to attempt to have Amgen agree on a process for trial exchanges of witnesses and demonstratives. Amgen would not agree to Roche's proposal, which Roche respectfully contends is more practical and reasonable, and Amgen imposed a counter-proposal

above that is not manageable given the fluid nature of the trial and the need for flexibility given the presentation to the jury. Since the parties did not agree, Roche believes that it is inappropriate to include the parties' respective positions in this Pretrial Memorandum, and the proper course was for Amgen to file a motion in limine, but Amgen refused to do so.

For example, Amgen takes the unreasonable position that it is entitled to know what witnesses Roche will call 3 days beforehand. While Roche will of course give Amgen reasonable notice, which has in many trials been the day before, but the nature of trial makes Amgen's proposal an unreasonable burden. Roche has proposed a 2-day period, which is much more practical. In addition, Amgen insists that Roche identify by exhibit number each document it will use with a witness 2 days before that witness is called, despite the fact that Roche will have already furnished Amgen with copies of all the marked trial exhibits and will provide an extra copy to Amgen's counsel at the time the exhibit is offered. Roche is willing to advise Amgen of the documents in intends to use with a witness the afternoon of the prior day, and that is quite reasonable and indeed generous given that there is no requirement that Roche do so at all.

Roche has proposed the following schedule:

Opening Statements

- By 5 PM on September 2, 2007, the parties will exchange their demonstratives for their openings on validity. On September 3, 2007, the parties will meet and confer in an attempt to resolve objections to each others' opening demonstratives.

- By 5 PM the day before the openings for the other infringement and inequitable conduct sections of the jury trial, the parties will exchange their demonstratives for their openings.

Witnesses Appearing Live at Trial

- If either party intends to call a fact witness of the opposing party in their case, the party will provide reasonable advance notice as practical of their intent to do so.

- Except as set forth above, by 5 PM two (2) days before a party intends to call a

witness live, the party will identify that witness by name to the opposing party.

- By 5 PM the day before a party intends to call a witness live[12], the party will provide to the opposing party the name of the witness who will testify, identify the exhibit number/letter of any exhibits to be used with that witness, provide copies of any demonstratives to be used with that witness, and exchange or make available for inspection physical exhibits and photographs to be used with that witness.

- The parties will exchange designations and counterdesignations sufficiently in advance, so that a completed transcript or video is available for the Court 24 hours in advance of being played to the jury.

This schedule has been used by numerous Courts in the past and is fair and reasonable as it applies equally to both sides. All of Amgen's protests of "on the fly" will do nothing more than create multiple satellite issues that will needlessly burden the Court will anticipatory objections and require possible unnecessary argument and Court attention.

2. Prior Findings

In order to aid in the efficient and speedy resolution of the issues in suit Roche provides the following list of findings and holdings from previous cases by this Court and the Federal Circuit to which Amgen was a party, and therefore to which Amgen is bound, and which involved some of the same issues in suit here.[13] Roche submits that these findings and holdings have a preclusive effect on Amgen and obviate the need to relitigate various issues. Amgen refuses to acknowledge that it is bound to these rulings and therefore refused to agree to have them included in the Undisputed Fact section where Roche submits they clearly are applicable.

[12] This excludes witnesses of the opposing party called as a hostile witness. As the Court has acknowledged, counsel may lead such witness as akin to a cross examination. Thus, it is not customary nor necessary to provide advance notice of the documents or demonstratives to be used with such a witness.

[13] Roche, of course, was not a party to any of these actions, and therefore the holdings or findings in these actions, as this Court has already found,cannot bind or be preclusive against Roche..

1. "[A] skilled artisan in 1984 would have understood that urinary erythropoietin samples obtained using different purification methods could have different glycosylation. As a result, the glycosylation of human urinary erythropoietin was in 1984, and continues to be, a moving target." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 129 (D. Mass. 2001).

2. "Although the patent specification [of the patents-in-suit] refers to different urinary EPO preparations and methods for purifying urinary EPO, including the methods of Miyake et al. and Yanagawa et al., in the portion of the patent specification describing glycosylation experiments with recombinant and urinary EPO products, no specific information is provided regarding how to select a urinary EPO preparation for purposes of comparison. Furthermore, the patent does not specify which urinary EPO preparation ought be used as a standard in determining whether a particular EPO sample has glycosylation which differs from that of human urinary EPO. Though a skilled worker might be able to guess, such an artisan reading the '933 patent would not know which urinary erythropoietin preparation should be used as a standard in making the comparison described in the patent and called for by the claims." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 128 (D. Mass. 2001) (internal citations to evidence omitted).

3. "[T]he heterogeneity of EPO glycosylation is manifested by differences in the number, type, and arrangement of the individual monosaccharides that make up the carbohydrate chains." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 26 F. Supp. 2d 69, 128 (D. Mass. 2001).

4. "In addition, the use of different methods of purifying erythropoietin results in different glycosylated erythropoietin populations." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 128 (D. Mass. 2001).

5. "Additional experiments conducted by Amgen scientists in 1984 showed that different urinary EPO preparations had different glycosylation." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 129 (D. Mass. 2001).

6. "Dr. Joan Egrie conducted a series of SDS-PAGE experiments comparing Lot 82 EPO with a uEPO received from Dr. Eugene Goldwasser. Dr. Egrie compared the preparations side-by-side on the same gel and concluded that the Lot 82 and Goldwasser uEPO samples migrated differently on SDS-PAGE, with the Lot 82 material having a higher molecular weight. After performing additional tests before and after treatment with enzymes effecting deglycosylation, she also concluded that this difference in migration was due to differences in glycosylation. In particular, the Lot 82 and Goldwasser uEPO migrated differently before enzymatic treatment, and the two preparations migrated the same after such treatment. These tests confirmed that the difference in apparent molecular weight between Lot 82 and Goldwasser uEPO was caused by differences in glycosylation. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 129 (D. Mass. 2001) (internal citations to evidence omitted).

7. "Dr. Egrie came to the same conclusion when she compared a commercially available urinary EPO from Alpha-Therapeutics to Goldwasser uEPO." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 129 (D. Mass. 2001) (internal citations to evidence omitted).

8. "Dr. Egrie's various SDS-PAGE experiments reveal that different uEPOs have varying glycosylation." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 129 (D. Mass. 2001) (internal citations to evidence omitted).

9. "[T]he molecular weights of uEPOs vary as well." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 130 (D. Mass. 2001).

10. "Dr. Lin's disclosure [in the patents-in-suit] fails adequately to describe an EPO glycoprotein whose glycosylation differs from that of human urinary erythropoietin." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 155 (D. Mass. 2001).

11. "[T]he glycosylation of human urinary erythropoietin is a standardless standard"... [because] (1) the glycosylation of urinary erythropoietin has 'enormous heterogeneity'; (2) different purification techniques, several of which were known by one skilled in the art in 1984, result in differing glycosylated erythropoietin populations; (3) despite referring to at least two purification methods, the patent does not identify which human urinary erythropoietin preparation ought be used as a standard, nor would a skilled person know which urinary EPO preparation should be used; and (4) different urinary erythropoietin samples have different glycosylation. As a result, making comparisons between the glycosylation of recombinant EPO and that of human urinary EPO is virtually impossible." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 155 (D. Mass. 2001).

12. Dr. Lin failed to disclose in the patents-in-suit which of the varying urinary EPO preparations should be used as a standard for the glycosylation of natural EPO. "[O]ne of ordinary skill in the art as of 1984 would not be able to guess the appropriate EPO preparation. As a result, the patent fails to convey to one of ordinary skill in the art as of 1984 that Dr. Lin invented an erythropoietin glycoprotein product having glycosylation which differs from that of human urinary erythropoietin." *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 155 (D. Mass. 2001).

13. "Although the language [of the '933 patent] contemplates that a competitor concerned with infringing the '933 patent can empirically determine whether its product's glycosylation differs from the glycosylation of human urinary erythropoietin, a definitive comparison is

rendered impossible by the fact that human urinary erythropoietin itself varies significantly." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 156 (D. Mass. 2001).

14. "[B]ecause different urinary erythropoietin preparations vary in their glycosylation, and because neither the ['933] patent nor the prior art provides clear guidance as to which human urinary EPO standard ought be used, one of ordinary skill in the art would be unable to determine whether a particular erythropoietin has glycosylation which differs from that of human urinary erythropoietin. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*,126 F. Supp. 2d 69, 156 (D. Mass. 2001) (citations to evidence omitted).

15. "Dr. Lin's specification falters, ..., because it fails to enable one of ordinary skill in the art to compare the glycosylation of the recombinant EPO product with that of human urinary erythropoietin." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 165 (D. Mass. 2001).

16. "[T]wo uEPO [urinary EPO] preparations produced from the same batch of starting materials could nevertheless have different glycosylation patterns." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1340-41 (Fed. Cir. 2003).

17. "By definition, one must know what the glycosylation of uEPO is with certainty before one can determine whether the claimed glycoprotein has a glycosylation different from that of uEPO. In its discussion characterizing recombinant glycoprotein products, the specification of the '933 patent does not direct those of ordinary skill in the art to a standard by which the appropriate comparison can be made." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1341 (Fed. Cir. 2003)

18. The reference Miyake, et al., Purification of Human Erythropoietin, J. Bio. Chem. 252, 5558, 5562 (1977) provides a method of purification, but does not suggest uniformity of

glycosylation of the human uEPO studied. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1341(Fed. Cir. 2003).

19. "It is undisputed that [the '933 patent at column 33, lines 19-22] declares that Amgen's recombinant EPO is similar to natural EPO in that it shares some of the same in vivo activity." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 339 F.Supp.2d 202, 232-233 (D. Mass. 2004).

20. "In November of 1984, Mr. Michael F. Borun, Amgen's patent counsel, received a package of information from Dr. Joan Egrie that was later placed in a folder labeled 'Egrie Input.' The Egrie Input included an SDS-PAGE gel that compared COS-1 produced recombinant EPO and Goldwasser's human urinary EPO standard. Dr. Egrie reported that these EPOs 'have the same molecular weight' and 'that the recombinant EPO is glycosylated to the same extent as the native protein.' The Egrie Input also included SDS-PAGE gels comparing CHO cell produced recombinant EPO and Lot 82 human urinary EPO; she explained that these gels indicated that the differing EPOs had the same molecular weight." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 141-142 (D. Mass. 2001) (internal citations omitted).

21. "Mr. Borun received the [Egrie Input file] data from Dr. Lin or members of Dr. Lin's staff and after Mr. Borun drafted the patent application, Dr. Lin reviewed and approved it." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 141-142 (D. Mass. 2001) (internal citations omitted).

22. The source or process limitations "with respect to 'purified from mammalian cells grown in culture' and 'not isolated from human urine,' cannot alone confer a basis for patentability of the subject matter of the asserted claims of the patents-in-suit. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 339 F.Supp.2d 202, 335 fn.163(D. Mass. 2004); *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 n. 20 (Fed. Cir. 2003).

23. "Claim 1 of the '422 patent claims a product: a pharmaceutical composition." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 150 (D. Mass. 2001).

24. "After splicing, the [EPO] mRNA is translated into the 166-amino acid protein shown in Figure 6 of the common specification [of the patents-in-suit]." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1299 (Fed. Cir. 2006).

25. "Figure 6, [of the patents-in-suit] therefore, demonstrates the deduced amino acid sequence that is arrived by reading the codons of the DNA encoding the protein. Figure 6 numbers the amino acids from -27 to a final position of 166, which is labeled arginine." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 287 F.Supp.2d 126, 145-46 (D. Mass. 2003) (internal citations omitted).

26. "[O]n October 30, 1987, Amgen explained in its FDA product license application that the 166th arginine (depicted in Figure 6) cleaves off leaving 165 amino acids (instead of the originally believed 166)...." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 287 F.Supp.2d 126, 147-48 (D. Mass. 2003) (internal citations to evidence omitted).

27. "If, then, as the specification states, 'the primary structural conformation (amino acid sequence) of mature human EPO as including 166 specified amino acid residues,' it is simply illogical for Amgen to argue that that means anything other than, at a minimum, the 166 amino acids shown in Figure 6...." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1345 (Fed. Cir. 2003).

28. "Unknown to Dr. Lin at the time of the invention, arginine is cleaved off at some point during protein synthesis prior to secretion from the cell. Thus, the protein that is actually secreted from the cell contains only 165 amino acids. Figure 6, however, depicts the arginine." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F.Supp.2d 69, 86 (D. Mass. 2001).

29. "Key language in the patent specification describes what is depicted by Figure 6: 'FIG. 6 thus serves to identify the primary structural conformation (amino acid sequence) of mature human EPO as including 166 specified amino acid residues ... .' Id. at 21:3-5. This language equates the amino acid sequence of mature human EPO with the specifically enumerated 166 amino acid sequence that is disclosed in Figure 6." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 100 (D. Mass. 2001).

30. "[A]t the time the patent was written, it was not yet known that the arginine at the carboxyl terminus was cleaved off prior to secretion of the protein from the cell." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 101 (D. Mass. 2001).

31. "In addition, Figure 6 is described extensively in the specification and Figure 6 itself provides critical information regarding the sequence of erythropoietin amino acid residues necessary for the production of claimed EPO glycoproteins." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 151 (D. Mass. 2001).

32. The reference, Judith B. Sherwood & Daniel Shouval, Continuous Production of Erythropoietin by an Established Human Renal Carcinoma Cell Line: Development of the Cell Line, 83 Proc. Nat'l Acad. Sci. USA 165-69 (1986) reports that Sherwood and Shouval's "human carcinoma cell line had maintained its EPO-producing function continuously since 1981." *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 107 (D. Mass. 2001).

33. The Sherwood and Shouval 83 Proc. Nat'l Acad. Sci. USA 165-69 (1986) reference and the reference Tsunehiro Saito et al., Translation of Messenger RNA from a Renal Tumor into a Product with the Biological Properties of Erythropoietin, 13 Exp. Hematol. 23-28 (1985) evidence that the reported work performed by the authors was done in the United States prior to Dr. Lin's work on EPO in 1983 and 1984. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 107 (D. Mass. 2001).

34. The work underlying the Sherwood and Shouval 83 Proc. Nat'l Acad. Sci. USA 165-69 (1986) reference and the reference was performed in the United States. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 107 (D. Mass. 2001).

35. The work reported in the Saito et al., 13 Exp. Hematol. 23-28 (1985) reference was performed in the United States sometime prior to August of 1983. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 107 (D. Mass. 2001).

36. "[T]he EPO-producing tumor cell work described by the Sherwood and Shouval and Saito et al. references qualifies as 102(a) prior art." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 107 (D. Mass. 2001).

37. The three references U. Essers et al., Effect of Erythropoietin in Normal Men and in Patients with Renal Insufficiency, 11 European Dialysis & Transplant Ass'n Proc., Biomed W1 EU715, 398-402 (1975); U. Essers et al., Weitere Untersuchungen zur Wirksamkeit von Erythropoietin bei Patienten mit Niereninsuffizienz, 99 Deutsche Medizinische Wochenschrift, 1618-24 (1974); and U. Essers et al., Zur Wirkung von Erythropoietin bei Gesunden und bei Patienten mit chronischer Uramie, 51 Klinische Wochenschrif 1005-09 (1973) all report experiments performed by Dr. U. Essers "whereby a small group of both anemic and healthy patients received infusions of erythropoietin-rich plasma. Dr. Essers had to use raw human plasma because, at the time she performed her work, there was no erythropoietin available in the quantity and purity required for therapeutic use. Dr. Essers reported that many of the patients showed an increase in their reticulocyte counts." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 110 (D. Mass. 2001) (internal citations to evidence omitted).

38. "If the claim term 'therapeutically effective' [of the patents-in-suit] encompasses the patient responses described in the specification [of the patents-in-suit], ... then [Dr. Eugene Goldwassers's EPO clinical study conducted at the University of Chicago in Illinois in 1979-

1980] may constitute invalidating prior art under §102(a) or §103 even if he did not achieve his intended result." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 (Fed. Cir. 2003).

39. "Because [documentary evidence shows that] Dr. Goldwasser began [his] clinical study in 1979-1980 at the University of Chicago in Illinois" it is prior art under 35 U.S.C. § §102(a) and 102 (g) to the patents-in-suit. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*,126 F. Supp. 2d 69, 111 (D. Mass. 2001).

40. "Amgen neither submitted the actual scientific data relating to the study to the Patent Office nor extensively described the [Goldwasser EPO clinical study conducted at the University of Chicago in Illinois in 1979-1980] in any of its submissions." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 140 (D. Mass. 2001).

41. In Dr. Goldwasser's EPO clinical study conducted at the University of Chicago in Illinois in 1979-1980, "Dr. Goldwasser observed a number of biologic effects in the patients. He reported an increase in reticulocyte count in all three patients, an increase in erythroid cells in the marrow and an increased plasma iron clearance rate in two patients, and an increase in red cell mass in one patient." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F.Supp.2d 69, 111 (D. Mass. 2001) (internal citations to evidence omitted).

42. "Instead of attempting to purify EPO from natural sources, [Dr.] Lin isolated and characterized monkey and human EPO genes, then used conventional recombinant DNA technology to produce large amounts of rEPO." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1321 (Fed. Cir. 2003).

43. "[B]y 1984, a variety of mammalian cells useful for protein expression had been adapted for growth in culture and were readily available to those of ordinary skill in the art from the American Type Culture Collection ("ATCC"). A number of cultured human cell lines were

available as well." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F.Supp.2d 69, 159 fn. 55 (D. Mass. 2001) (internal citations to evidence omitted).

44. "[P]lacement of the promoter further upstream and splicing out deleterious data was a technique known to skilled artisans in 1983-84." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 339 F.Supp.2d 202, 273-74 (D. Mass. 2004).

45. "[P]lacement of the promoter further upstream of the EPO coding region and splicing out deleterious ATGs was indeed a concept known and understood to those skilled in the art at the time Amgen filed its application (1983-84)." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 339 F.Supp.2d 202, 295-296 (D. Mass. 2004).

46. "[T]he technique of placing the promoter in close proximity to the gene intended to be expressed was believed, by those of ordinary skill in the art in 1984, to be the technique most likely to result in the proper transcription of that gene." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F.Supp.2d 69, 104 (D. Mass. 2001).

47. The EPO gene, containing about 4,000 nucleotides, is not a very large gene by most standards. This is one of the reasons it was a good candidate for cloning in 1981. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *7 (internal citations to evidence omitted).

48. In 1981 and 1982, there was general agreement in the scientific community that the genomic library prepared by Dr. Thomas Maniatis, one of the founders of Genetics Institute, was a good library. A scientist could predict that the gene of interest might be in the billions of sequences contained in that genomic library. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *8 (internal citations to evidence omitted).

49. Another kind of library is a complementary DNA ("cDNA") library, which is much smaller and less complex than the genomic library. cDNA is a DNA copy that has been made in

a test tube with an enzyme that reproduces the information in mRNA. It is made from the messenger RNA of a particular cell or tissue type. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *8 (internal citations to evidence omitted).

50. By going to the mRNA in a tissue source for a given gene, a scientist has significantly reduced the overall complexity of the cloning project because only a small portion of the human genome will actually be expressed as messenger RNA. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *8 (internal citations to evidence omitted).

51. Moreover, because the cDNA is made from mRNA, there are no introns in the cDNA and a scientist is not faced with the problem of probes which do not hybridize properly because they "span" an intron. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *8 (internal citations to evidence omitted).

52. An oligonucleotide probe, which is a probe involving a short sequence of nucleotides, can be used to screen a library and to isolate a gene. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *8 (internal citations to evidence omitted).

53. To design a probe where the gene has not yet been isolated, a scientist must know the amino acid sequence of the protein of interest, or a portion of that sequence. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *8 (internal citations to evidence omitted).

54. In 1981, scientists had a table which told them the codons that code for each amino acid. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *8 (internal citations to evidence omitted).

55. In developing a cell line to express rEPO, Amgen used as starting material a host cell called CHO DHFR-(DuXBll) for transfection. This host cell was from a cell line developed by Professor Lawrence Chasin at Columbia University who has no connection with Amgen.

Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., 1989 WL 169006 at *16 (internal citations to evidence omitted).

56. Example 10 describes expression systems employing CHO DHFR- cells. The CHO DHFR- cell, known by its clone name DuX-Bll, could be obtained from Dr. Chasin at Columbia University. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *49 (internal citations to evidence omitted).

57. Example 10 of the patents-in-suit discusses the standard procedures of transfection, MTX amplification and limited dilution cloning. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *10 (internal citations to evidence omitted).

58. Example 10 of the patents-in-suit also sets forth, as step 3 of the process, a gene amplification technique to amplify DHFR expression, and thereby EPO expression, by using MTX selections. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *50 (internal citations to evidence omitted).

59. By December, 1983, gene amplification utilizing MTX was commonly known and was a published procedure. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *11 (internal citations to evidence omitted).

60. The first step in the gene amplification process is that MTX kills all the cells which have not received the cloned gene, contained in the vector also carrying the DHFR. Then the concentration of MTX is increased, thereby reducing the growth of cells because it prevents them from making nucleic acid. The process of increasing the MTX concentration is called amplification. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *11 (internal citations to evidence omitted).

61. A procedure called “limited dilution cloning,” which was regularly used in 1983, is employed to separate each cell into a “cell well.” Every cell that grows up as a daughter cell

from that single cell is now a clone of the original parental cell. The cell which produces the most protein is isolated. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *11 (internal citations to evidence omitted).

62. "[T]he final step set forth in Example 10 [of the patents-in-suit] is the employment of '[s]tandard screening procedures ... in an attempt to isolate genetically homogeneous clones with the highest production capacity.' Dr. Lin testified that this last step meant the use of routine limited dilution cloning procedures." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *50 (internal citations to evidence omitted).

63. The purpose of gene amplification and limited dilution cloning is to obtain a clone, defined as a progeny of the cell which was transfected with the cloned gene, with a very high level of expression of recombinant protein, like erythropoietin. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *11 (internal citations to evidence omitted).

64. As of November 30, 1984, Amgen had made the decision that a clone from CHO cell strain Bll 3,.1 would be used to produce EPO, and Dr. Lin knew this. On December 3, 1984, Dr. D. Vapnek, research director at Amgen, wrote a memorandum to Amgen's general counsel, R. Weist, stating that the EPO-producing CHO cell line designated CHO Bll 3,.1 was available for transfer. The Lin patents do not identify by name any clones of CHO Bll 3,.1. *See Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *17 (internal citations to evidence omitted).

65. No mammalian host cell strain or line, including any CHO cell, was ever deposited with the ATCC by Dr. Lin or Amgen. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *17 (internal citations to evidence omitted).

66. Dr. Lin filed his first patent application relating to EPO on December 13, 1983. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *16 (internal citations to evidence omitted).

67. On February 21, 1984, Lin filed his second patent application relating to EPO. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *16 (internal citations to evidence omitted).

68. Lin filed his third application for a patent relating to EPO on September 28, 1984. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *17 (internal citations to evidence omitted).

69. At the end of December, 1980 or the beginning of 1981, Dr. Wallace and others published an article which was the "seminal paper" on using probes. In that experiment, Dr. Wallace used eight oligonucleotide probes, which were not fully redundant, to hybridize with cloned rabbit betaglobin DNA sequences. The article was useful because it showed that correct probes in a mixture of both correct and incorrect probes could distinguish the clone by hybridizing with it, whereas the incorrect probes would not. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *23 (internal citations to evidence omitted).

70. In November, 1981, a second article was published which had been submitted by Dr. Suggs and others in June of that year. That paper went "to the logical next step from what [Dr.] Wallace did, which [was] to use mixed oligonucleotide probes to screen an actual library." In the experiment, a cDNA library was used as well as two sets of probes. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *23 (internal citations to evidence omitted).

71. Next, in September, 1982, an article submitted in June, 1982 by Dr. Woods was published. Woods' article provided additional information because two fully degenerate sets of probes were used to screen a cDNA library. The first set of probes was 32-fold degenerate, and

the second was 48-fold degenerate. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *23 (internal citations to evidence omitted).

72. "The [Woods] experiment showed that one could isolate a cDNA clone from a complex cDNA library using two sets of fully redundant probes. Also, the quality of screening was 'considerably better' than before, with a much better signal-to-noise ratio so that the positive looks very positive and the negative looks very negative." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *23 (internal citations to evidence omitted).

73. The prior art references...did show that two fully degenerate sets of probes could be used to isolate a cDNA clone. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *45 (internal citations to evidence omitted).

74. "In 1982, an abstract by Reilly also was published in a journal called DNA. The abstract dealt with the cloning of a gene from a genomic library. Two probes of single redundancy were used to screen a genomic library of mouse DNA for the gene for transfer RNA. The probes were from separate regions of the tRNA sequence, one being 15 bases long and the other being 19 bases long. The abstract showed that what had been learned with respect to cDNA could be applied to genomic DNA." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *23 (internal citations to evidence omitted).

75. The prior art references...did show that...two probes of single redundancy from separate regions could successfully be used to screen a genomic mouse DNA library. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *45 (internal citations to evidence omitted).

76. "In April, 1982, another abstract by Seki, et al., was published. In that experiment, a genomic library was screened using two sets of fully degenerate probes. The first set of probes was a 16-mer probe of 48-fold redundancy, and the second was a 14-mer probe of 16-fold

redundancy. They were derived from different regions of the protein relatively close to one another." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *24 (internal citations to evidence omitted).

77. "In September, 1983, an article submitted by Whitehead and others in May, 1983 was published. That experiment involved the use of a very complex single 23-mer probe of 384-fold degeneracy to screen a human liver cDNA library for the C4 gamma gene. The set of probes used was fully degenerate." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *24 (internal citations to evidence omitted).

78. "Earlier, in April, 1983, Derek Woods, one of the authors of the article, presented this work at a meeting. He indicated at the meeting that 384 probes had been used, and that he had found the gene he was looking for." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *24 (internal citations to evidence omitted).

79. The prior art references... did show that ... that a single probe of extremely high degeneracy could successfully isolate a gene from a human cDNA library. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *45 (internal citations to evidence omitted).

80. "On October 28, 1983, Drs. Toole and Fritsch filed an application for a patent, which was eventually issued on July 12, 1988. The patent covered the screening of a genomic library with two probes to isolate the porcine Factor VIII gene. The first probe was not fully degenerate, but was a long probe or guessmer 45 nucleotides long of 4-fold redundancy. The second probe was a 15-mer fully degenerate probe of 16-fold redundancy." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *24 (internal citations to evidence omitted).

81. "The Toole/Fritsch patent set forth information in addition to the prior published literature on probing and cloning in that it described in great detail the use of redundant probes to

successfully isolate a genomic clone." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *24 (internal citations to evidence omitted).

82. The prior art references... did show that ...two probes, one fully degenerate and one not, could successfully be used to screen a porcine genomic library. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *45 (internal citations to evidence omitted).

83. "During the period from 1980 through 1983, the technology in the field of cloning advanced very quickly." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *23 (internal citations to evidence omitted).

84. Dr. Lin testified that the use of two sets of probes or the use of fully degenerate probes was not particularly innovative. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *43 (internal citations to evidence omitted).

85. Dr. Fritsch tried the use of two sets of probes or the use of fully degenerate probes as early as October, 1982 in his attempt to isolate the EPO gene at Genetics Institute. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *43 (internal citations to evidence omitted).

86. "[In] 1983 there was a probability of success in using mixed oligonucleotide probes to screen a DNA library." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *45 (internal citations to evidence omitted).

87. Clear and convincing evidence has shown that the probing and screening procedures used by Dr. Lin were "obvious to try." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *43.

88. It would have been "obvious to try" cloning the EPO gene if the EPO fragments that were available to Dr. Lin in 1983 had been made available to Biogen. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *43 (internal citations to evidence omitted).

89. "Details for preparing only a few EPO analog genes are disclosed" in the patents-in-suit. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1213-14 (Fed. Cir. 1991)

90. "There may be many other genetic sequences that code for EPO-type products. Amgen has told how to make and use only a few of them and is therefore not entitled to claim all of them." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1213-14 (Fed. Cir. 1991).

91. "Considering the structural complexity of the EPO gene, the manifold possibilities for change in its structure, with attendant uncertainty as to what utility will be possessed by these analogs, ... more is needed concerning identifying the various analogs that are within the scope of the claim, methods for making them, and structural requirements for producing compounds with EPO-like activity. It is not sufficient, having made the gene and a handful of analogs whose activity has not been clearly ascertained, to claim all possible genetic sequences that have EPO-like activity." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1214 (Fed. Cir. 1991).

92. Amgen has engaged in an EPO analog program headed by Dr. Steven Elliott, who has a PhD from the University of California at Irvine in molecular biology and biochemistry, and began work at Amgen in 1983. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *56.

93. "Over 3,600 different 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." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *56 (internal citations to evidence omitted).

94. Dr. Elliott said that Amgen had not measured all of the biological properties of the analogs he had made, and he did not know whether the analogs had 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. Dr. Elliott did not know if any of the plasmids described in the [patents-in-suit] had this biological property. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *56 (internal citations to evidence omitted).

95. "In April, 1989, Dr. Goldwasser testified concerning his work in an ongoing study funded by the National Institutes of Health to modify some of the amino acids in the intact EPO structure to see the result of those modifications on biological activity sites." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *57 (internal citations to evidence omitted).

96. By 1989 scientists had not yet sorted out which particular amino acid residue is required for biological activity in EPO, and the data was incomplete. By 1989 one would not know the effect of reagants on certain amino acid residues without empirical study because "[t]here is no theory that tells us what to look for." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *57 (internal citations to evidence omitted).

97. After five years of experimentation, as of 1989 Amgen was still unable to specify which EPO analogs have 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. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *57 (internal citations to evidence omitted).

98. "Prior to 1980, EPO was obtained by purifying the urine of patients suffering from aplastic anemia; that kind of urine was in short supply." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *25 (internal citations to evidence omitted).

99. "During the period from 1974 to 1976, Dr. Takaji Miyake, working with Dr. Goldwasser, developed a procedure for purifying this urinary EPO ("uEPO") in the laboratory of

Dr. Goldwasser at the University of Chicago. Miyake had begun working on the purification of EPO in about 1964. He believed that this procedure provided a homogeneous pure EPO product in the 1976 and 1977 time frame." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *25 (internal citations to evidence omitted).

100. "It is true that Amgen held an advantage over the other companies because it alone among the commercial biotechnical companies had access in usable amounts after 1981 to urinary source EPO, which was a 'rather rare commodity,' from Dr. Goldwasser, the primary person who had that material. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *35 (internal citations to evidence omitted).

101. "[T]he evidence is undisputed that Dr. Fritsch decided in August or September, 1982 to focus his efforts on cloning the EPO gene using currently available n-terminal sequence information from Dr. Hewick. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *38 (internal citations to evidence omitted).

102. "Dr. Fritsch had abandoned the approach of obtaining additional erythropoietin for further sequence information in August or September, 1982 because the terms that Dr. Miyake was asking for in exchange for supplying EPO to GI were 'well beyond what GI at the time could afford.'" *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *38 (internal citations to evidence omitted).

103. It is true that Dr. Fritsch used two sets of fully degenerate probes to screen a genomic library in October, 1982, before Dr. Lin. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *36.

104. By April or May, 1983, Dr. Fritsch had concluded that there was a problem with the available EPO sequence information. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *38.

105. "Dr. Sherwood also gave GI some partially purified uEPO but there was not enough for sequencing." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *38 (internal citations to evidence omitted).

106. "In early 1984, GI sought EPO from Dr. Miyake to obtain additional sequence information to construct probes. Dr. Hewick received four shipments of EPO from Dr. Miyake in April, May, July and November, 1984." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *26 (internal citations to evidence omitted).

107. "When Hewick received the first sample from Dr. Miyake on April 23, 1984, he subjected it to SDS-PAGE analysis. SDS-PAGE electrophoresis is another technique to isolate and purify proteins according to molecular weight." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *27 (internal citations to evidence omitted).

108. "When he examined the SDS-PAGE gel from the first Miyake shipment, Dr. Hewick saw that there were bands other than those he thought to be EPO. He then ran the sample on the RP-HPLC, and saw a series of peaks on the chromatogram." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *27 (internal citations to evidence omitted).

109. "Altogether, Hewick conducted five runs, and all the chromatographs revealed a small peak appearing at 17 to 18 minutes, a large plateau, and a larger peak appearing at 36 to 38 minutes. He sequenced the fractions from the fifth run on the gas phase sequenator. The sequences indicated that only the fraction corresponding to the large peak appearing at 36 to 38 minutes was EPO." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *28 (internal citations to evidence omitted).

110. "Hewick subjected the EPO fraction from run 5 to tryptic digestion, and then separated the fragments on RP-HPLC. The fragments produced a good tryptic map, indicating

areas of high 280 absorbance where the tryptic fragments contained the amino acids tyrosine and tryptophan, which facilitates the designing of probes. Hewick chose two of these fragments, T-30 and T-35, for sequencing and delivery to Dr. Fritsch for construction of probes." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *28 (internal citations to evidence omitted).

111. "The second shipment of Miyake material [to Dr. Hewick] arrived on May 30, 1984. Dr. Miyake and his colleague, Dr. Shimizu, sent a note stating that this was a problematic sample and unreliable. Dr. Hewick confirmed this and did not rely on shipment two in formulating his conclusions." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *28 (internal citations to evidence omitted).

112. "The third shipment from Dr. Miyake [to Dr. Hewick] arrived on July 22, 1984. Hewick received two samples in shipment number 3, which were designated as fractions two and three." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *28 (internal citations to evidence omitted).

113. "Hewick ran differing amounts of fraction two material on RP-HPLC seven times, and determined that the chromatographs were essentially the same as those from shipment one. He took the material under the large peak, subjected it to tryptic digestion and sequencing, and determined that the material corresponding to the large peak was EPO." *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 1989 WL 169006 at *28 (internal citations to evidence omitted).

3. Admissions in Amgen's Patents

Amgen also made various statements in the specification of the patents-in-suit regarding the state of the prior art. These statements constitute factual admissions by Amgen. *See PharmaStem Therapeutics, Inc. v. Viacell, Inc.*, --- F.3d ---, 2007 WL 1964863 at *17 (Fed. Cir.

2007). As such, these facts are binding on Amgen and need not be re-litigated here.[14]

1. The prior art to the patents-in-suit is "rich in patent and literature publications relating to 'recombinant DNA' methodologies for the isolation, synthesis, purification and amplification of genetic materials for use in transformation of selected host organisms." Col. 2, lns. 39-59.

2. "Manufacture of DNA sequences is frequently the method of choice when the entire sequence of amino acid residues of the desired polypeptide product is known." Col. 3, lns. 22-24.

3. An approach to microbiological processing known in the prior art to the patents-in-suit is "a gene that specifies the structure of a desired polypeptide product is either isolated from a 'donor organism' or chemically synthesized and then stably introduced into another organism which is preferably a self-replicating unicellular organism such as bacteria, yeast or mammalian cells in culture. Once this is done, the existing machinery for gene expression in the 'transformed' or 'transfected' microbial host cells operates to construct the desired product, using the exogenous DNA as a template for transcription of mRNA which is then translated into a continuous sequence of amino acid residues." Col. 2, lns. 27-38.

4. DNA manufacturing procedures taught in the prior art to the patents-in-suit "provide a superior means for accomplishing such highly desirable results as:" ease in assembly of expression vectors capable of providing high levels of microbial expression. Col. 3, lns 22-47.

5. DNA manufacturing procedures of the prior art to the patents-in-suit, "provide a superior means for accomplishing such highly desirable results as: … providing for ready insertion of the DNA in convenient expression vectors in association with desired promoter/regulator and terminator sequences.…" Col. 3, lns 22-47.

6. "Among the more significant recent advances in hybridization procedures [in the prior art to the patents-in-suit] for the screening of recombinant clones is the use of labeled mixed synthetic oligonucleotide probes, each of which is potentially the complete complement of a specific DNA sequence in the hybridization sample including a heterogenous mixture of single stranded DNAs or RNAs. These procedures are acknowledged to be especially useful in the detection of cDNA clones derived from sources which provide extremely low amounts of mRNA sequences for the polypeptide of interest." Col. 4, lns. 22-32.

7. "In general, the mixed probe procedures [of the prior art to the patents-in-suit], have been expanded upon by various workers to the point where reliable results have reportedly been obtained in a cDNA clone isolation using a 32 member mixed "pool" of 16-base-long (16-mer) oligonucleotide probes of uniformly, varying DNA sequences together with a single 11-mer to effect a two-site 'positive' confirmation of the presence of cDNA

[14] All specifications cited refer to U.S. Patent No. 5,441,868.

of interest." Col. 4, lns. 44-54.

8. "[R]eliable procedures exist for developing phage-borne libraries of genomic DNA of human and other mammalian species origins" are described in the prior art to the patents-in-suit. Col. 4, lns 61-64.

9. "[Prior art to the patents-in-suit] report the successful isolation of a gene coding for the alpha subunit of the human pituitary glycoprotein hormones from the Maniatis Library through use of a "full length" probe including a complete 621 base pair fragment of a previously-isolated cDNA sequence for the alpha subunit." Col. 5, lns 7-14.

10. "[Prior art to the patents-in-suit] report isolation of human genomic clones for human HLA-DR using a 175 base pair synthetic oligonucleotide." Col. 5, lns. 14-17.

11. "[Prior art to the patents-in-suit] report the isolation of genomic clone for bovine pancreatic trypsin inhibitor (BPTI) using a single probe 86 base pairs in length and constructed according to the known amino acid sequence of BPTI." Col. 5, lns. 17-22.

12. The prior art to the patents-in-suit taught "[e]rythropoiesis, the production of red blood cells, occurs continuously throughout the human life span to offset cell destruction. Erythropoiesis is a very precisely controlled physiological mechanism enabling sufficient numbers of red blood cells to be available in the blood for proper tissue oxygenation, but not so many that the cells would impede circulation. The formation of red blood cells occurs in the bone marrow and is under the control of the hormone, erythropoietin." Col. 5, lns. 58-66.

13. The prior art to the patents-in-suit taught "[e]rythropoietin, an acidic glycoprotein of approximately 34,000 dalton molecular weight, may occur in three forms: α, β and asialo. The α and β forms differ slightly in carbohydrate components have the same potency, biological activity and molecular weight. The asialo form is an α or α form with the terminal carbohydrate (sialic acid) removed. Erythropoietin is present in very low concentrations in plasma when the body is in a healthy state wherein tissues receive sufficient oxygenation from the existing number of erythrocytes. This normal low concentration is enough to stimulate replacement of red blood cells which are lost normally through aging." Cols. 5-6, lns. 67-11.

14. The prior art to the patents-in-suit taught that "[b]ecause erythropoietin is essential in the process of red blood cell formation, the hormone has potential useful application in both the diagnosis and the treatment of blood disorders characterized by low or defective red blood cell production." Col. 6, lns. 42-46.

15. "[Prior art to the patents-in-suit described] a therapeutic regimen for uremic sheep based on in vivo response to erythropoietin-rich plasma infusions and proposing a dosage of 10 U EPO/kg per day for 15-40 days as corrective of anemia of the type associated with chronic renal failure." Col. 6, lns. 46-57.

16. "[Prior art to the patents-in-suit] describes a method for partially purifying erythropoietin from sheep blood plasma which provides low yields of a crude solid extract containing erythropoietin." Col. 7, lns. 23-25.

17. Prior art to the patents-in-suit taught a method of purifying human erythropoietin from urine of patients with aplastic anemia is described in Miyake, et al., J. Biol.Chem., Vol. 252, No. 15 Aug. 10, 1977), pp. 5558-5564. "This seven-step procedure includes ion exchange chromatography, ethanol precipitation, gel filtration, and adsorption chromatography, and yields a pure erythropoietin preparation with a potency of 70,400 units/mg of protein in 21% yield." Col. 7, lns. 35-42.

18. "[Prior art to the patents-in-suit] describes a process for the production of hybrid human lymphoblastoid cells, reporting production levels ranging from 3 to 420 Units of erythropoietin per ml of suspension of cells (distributed into the cultures after mammalian host propagation containing) up to 10^7 cells per ml. At the highest production levels asserted to have been obtained, the rate of erythropoietin production could be calculated to be from 40 to about 4,000 units/10^6 cells/48 hours in in vitro culture following transfer of cells from in vivo propagation systems." Col. 7, lns. 49-60.

19. A detailed description of the preparation and use of a monoclonal, anti-erythropoietin antibody appears in the prior art to the patents-in-suit. Col. 8, lns. 22-44.

20. "[In the prior art to the patents-in-suit, the] polypeptide sequence [of the] first twenty amino acid residues of mature human erythropoietin isolated according to the method of Miyake, et al., J.Biol.Chem., 252, 5558-5564 (1977) and upon which amino acid analysis was performed by the gas phase sequencer (Applied Biosystems, Inc.) according to the procedure of Hewick, M., et al., J.Biol.Chem., 256, 7990-7997 (1981)." Col. 9, lns. 17-25.

21. "[The prior art to the patents-in-suit described] expression systems employing Chinese hamster ovary (CHO) DHFR cells and the selectable marker, DHFR." Col. 26, lns. 59-65.

22. "CHO DHFR cells (DuX-B11) CHO K1 cells, … lack the enzyme dihydrofolate reductase (DHFR) due to mutations in the structural genes and therefore require the presence of glycine, hypoxanthine, and thymidine in the culture media" were described in the prior art to the patents-in-suit. Cols. 26-27, lns. 66-3.

23. Experimentally determined carbohydrate constitution values (expressed as molar ratios of carbohydrate in the product) for the urinary isolate and corresponding values for the recombinant product (derived from CHO pDSVL-gHuEPO 3-day culture media at 100 nM MTX) as reported in the patent-in-suit are incorrect. Col. 30, lns. 25-37.

24. The prior art to the patents-in-suit "reported the in vitro translation of human kidney mRNA by frog oocytes. The resultant translation product mixture was estimated to include on the order of 220 mU of a translation product having the activity of erythropoietin per microgram of injected mRNA. While such levels of in vitro translation of exogenous mRNA coding for erythropoietin were acknowledged to be quite low

(compared even to the prior reported levels of baboon mRNA translation into the sought-for product) it was held that the results confirm the human kidney as a site of erythropoietin expression, allowing for the construction of an enriched human kidney cDNA library from which the desired gene might be isolated. Col. 10, lns. 18-31.

25. With respect to the prior art to the patents-in-suit "[w]hile polyclonal and monoclonal antibodies as described above provide highly useful materials for use in immunoassays for detection and quantification of erythropoietin and can be useful in the affinity purification of erythropoietin, it appears unlikely that these materials can readily provide for large scale isolation of quantities of erythropoietin from mammalian sources sufficient for further analysis...." Col. 9, lns. 31-38.

IX. PROBABLE LENGTH OF TRIAL;

A. Length of trial

The Court has ordered that a jury trial will commence on September 4, 2007. The jury trial will continue until no later than October 17, 2007. The Court will not sit on September 13, September 17 – 21, and October 5 – 12.

B. Amgen's Position

1. Amgen's request for a bench trial

Amgen respectfully objects to the Court's July 17, 2007 decision that the patent case shall be tried to a jury. *See* Docket No. 762. For the reasons set forth in Amgen's Memorandum for the July 17, 2007 Case Management Conference, Amgen maintains its position that there is no right to a jury trial on the patent case. *See* Docket No. 687.

2. Inequitable conduct should be tried to the bench

Should the patent case be tried to a jury, Amgen respectfully requests that the inequitable conduct portion of the patent case be tried to the bench. "The defense of inequitable conduct, being entirely equitable in nature, is not an issue for a jury to decide." *Paragon Podiatry Lab., Inc. v. KLM Lab., Inc*., 984 F.2d 1182, 1190 (Fed. Cir. 1993), *see also Gardco Mfg., Inc. v. Herst*

Lighting Co., 820 F.2d 1209, 1211-13 (Fed. Cir. 1987).[15]

Roche's weak inequitable conduct claims are designed to confuse and bias the jury, and should be tried to the bench to avoid the substantial risk of unfair prejudice to Amgen. "A patent case is complex and confusing enough for a jury without infusing evidence which has no relevance to the issues to be decided by that jury. . . . Evidence tending to show fraud on the part of the inventor is so likely to prejudice the jury on other issues that the fraud issue should be tried separately." *THK America, Inc. v. NSK Corp.*, 1996 U.S. Dist. LEXIS 226 at *4-*5 (N.D. Ill. Jan 9., 1996).

The trial is already structured to facilitate this division. In the Pretrial Conference on July 17, 2007, the Court ruled that the trial would be structured in three parts, with validity first, infringement second, and inequitable conduct last. Thus, the Court has already ordered separation and separate presentation of the evidence that relates purely to inequitable conduct. Any common issues will be presented in the validity and infringement portions of the trial, and thus it would not be inefficient or unfairly prejudicial to Roche to try the inequitable conduct portion of the case to the bench while the jury deliberates on the validity and infringement portions of the case.[16]

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[15] In this case, a bench trial on the inequitable conduct issues is particularly appropriate because several of Roche's theories of inequitable conduct are predicated upon whether or not Amgen misled the PTO by characterizing various legal doctrines and rulings. *See, e.g.*, First Amended Answer ¶ 45 ("…Amgen misrepresented the court's decision in *Amgen, Inc. v. U.S. Int'l Trade Comm'n*, 902 F.2d 1532 (Fed. Cir. 1990). . . ."); ¶ 50 ("Amgen also asserted that it was inappropriate for the Examiner to consider prior art (the Yokota 4,695,542 patent) in conjunction with the claims of the '008 patent to show that the pending claims were obvious … [Amgen] misstated the law …."). To the extent those theories could provide a basis for a viable claim for inequitable conduct at all, the Court, not the jury, is uniquely equipped to evaluate and resolve those claims.

[16] Nor does trying inequitable conduct to the bench violate Roche's Seventh Amendment right to a jury trial, for the reasons set forth in Amgen's Memorandum for July 17, 2007 Case Management Conference, Docket No. 687, at 14-15.

There is ample precedent for trying inequitable conduct to the bench outside the presence of the jury. In fact, this Court has previously separated inequitable conduct to be tried to the bench in several different jury trials. For example, in *Avco Corp. v. PPG Indus., Inc.*, 867 F. Supp. 84 (D. Mass. 1994), validity and infringement were tried to a jury, but inequitable conduct defenses were tried to the bench. In *Ethos Tech. v. Realnetworks, Inc.*, inequitable conduct was tried to the bench after evidence of validity, infringement, and damages was tried to a jury. *See* 1:02-cv-11324-WGY, 2/22/06 Electronic Clerk's Notes of proceedings. Amgen respectfully requests that inequitable conduct be tried to the bench.

3. Obviousness-type double patenting should be tried to the bench[17]

The issue of obviousness-type double patenting ("ODP") should be decided by the Court, not by a jury.[18] ODP is a matter of claim interpretation, an issue of law exclusively reserved for resolution by the Court. In this case, the ODP analysis will require construction of the claims of the '008 patent and the '016 patent, both of which Roche has alleged invalidate all of the patents-in-suit under obviousness-type double patenting. As the Federal Circuit has stated, "double patenting is a matter of what is claimed, and therefore is treated like claim construction upon appellate review." *Georgia-Pacific Corp. v. U.S. Gypsum Co.*, 195 F.3d 1322, 1326 (Fed. Cir. 1999). *See also General Foods Corp. v. Studeingesellschaft Kohle mbH*, 972 F.2d 1272, 1277 (Fed. Cir. 1992) ("[d]ouble patenting is altogether a matter of what is claimed."). It is hornbook law that patent claims are interpreted by the Court as a matter of law. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370 (1996).

[17] As noted herein, Amgen has moved for summary judgment regarding certain of Roche's ODP allegations.

[18] ODP is an equitable defense, not a legal one, and therefore there is no right to a jury trial with respect to ODP defenses. This principle was recognized in *Refac Intern. Ltd. v. Matsushita Elec. Corp. of America*, 1990 WL 269885 at *7 (D.N.J. Nov. 14, 1990).

The Federal Circuit has explicitly stated that the ODP analysis should be performed by the Court. In *Eli Lilly and Co. v. Barr Labs, Inc.*, 251 F.3d 955, 968 (Fed. Cir. 2001), the Federal Circuit stated that there are two steps in ODP analysis: "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." *Eli Lilly and Co. v. Barr Labs, Inc.*, 251 F.3d 955, 968 (Fed. Cir. 2001) (citations omitted) (emphases added). In the Federal Circuit's formulation, both steps of the analysis are performed by the Court. Accordingly, the issue of ODP should be decided by this Court, not a jury.

C. Roche's Position

The Court has ordered that the jury trial on the patent issues will begin on September 4, 2007. The jury trial will continue no later than Oct. 17, 2007, and Court will not be in session on 9/13/07, 9/17/07-9/21/07, 10/5-10/12/07. The trial will begin with Roche presenting its invalidity case, and there will be three separate sets of opening remarks, one each for invalidity, infringement and inequitable conduct. Each side has 10 days to present its evidence.

Roche notes that this Court ordered that this trial would proceed by jury on July 17, 2007, and Roche has been operating under that Order. The right to a jury trial is fundamental to our system of justice and Roche contends that a jury can properly handle the issues in this case.

1. The Court Correctly Held All Patent and Antitrust Issues in This Case Will be Tried to a Jury.

Although this Court has twice before ruled that this case will be tried to a jury, including inequitable conduct and obviousness-type double patenting issues, Amgen has insisted upon placing argument regarding the jury trial in the Pretrial Memorandum (although there is no such section called for in the local rule describing the pretrial memorandum). Roche does not agree that this is a proper forum for Amgen to reargue points that this Court has previously decided.

This Court has correctly determined that all of the patent and antitrust claims are to be tried to a jury, and reiterated its prior correct ruling at the hearing and final pretrial conference held on July 17, 2007. The Court ruled that this case would be tried to a jury, and that it will proceed in stages, including Roche's counterclaims of unenforceability based upon inequitable conduct and invalidity based upon obviousness-type double-patenting. The jury will deliberate on all patent issues at the end of the presentation of the evidence in October 2007. (Docket Item 762) As it has repeatedly done throughout this case, Amgen now attempts to reargue points on which this Court has already ruled. Roche relies on its Memorandum for July 17, 2007 Case Management Conference for a full discussion of Roche's jury trial rights. (Docket Item 739). Requiring the inequitable conduct defense and obviousness-type double patenting invalidity defense to be tried to the Court would deprive Roche of its right to a jury trial, particularly since there are so many overlapping factual and legal issues between these defenses and the other issues being tried to the jury, as is further set forth below. Moreover, in ordering a jury trial in this case, the Court correctly acknowledged that, "in a case with both equitable (non-jury) and legal (jury) issues, the jury determination may govern the equitable decree." Order dated March 30, 2007, Docket Item 342, at 17 (citing *Dairy Queen, Inc. v. Wood*, 369 U.S. 469, 479 (1962). The Court's decision was correct and need not be disturbed.

2. The Court Correctly Ruled That The Patent Jury Should Hear and Decide Inequitable Conduct

Amgen's argument that the inequitable conduct portion of this case should be heard by the Court and not the jury completely ignores this Court's ruling that Roche has a jury trial right on both its patent and its antitrust and state law counterclaims and that there are substantial common issues between Roche's inequitable conduct allegations and both its invalidity claims and antitrust claims. Roche's claims of inequitable conduct by Amgen include allegations of failing to disclose material prior art and mischaracterizing material prior art to the PTO. A

central question in the determination of whether inequitable conduct has been committed is the materiality of the prior art, a question that depends on the same evidence and requires the same determinations necessary to decide whether the prior art renders Amgen's patents invalid as anticipated under 35 U.S.C § 102 or obvious under 35 U.S.C § 103. For example, Roche contends that Amgen's product claims read on prior art substances, or that prior art substances make the claims obvious. Amgen had scientific information (that it intentionally withheld from the PTO) which shows that the claimed products are indistinguishable over the prior art. The jury should decide whether the withheld information invalidates the claim and whether a reasonable examiner would have wanted to have such information before allowing the claims of the patents-in-suit to issue. Where common issues exist between claims of inequitable conduct and invalidity claims, the jury must decide the inequitable conduct issues. *C.R. Bard, Inc. v. M3 Sys., Inc.*, 1994 WL 258880, at *2 (N.D. Ill. June 9, 1994) (requiring trial to jury of inequitable conduct defense because it would resolve "factual questions that must also be determined" by jury for invalidity). The jury in this case will be required to consider many of the facts relevant to Amgen's inequitable conduct in making its determinations on the issues of anticipation and obviousness. Anticipation and obviousness are questions to be decided by the jury. See, e.g., *In re Graves*, 69 F.3d 1147, 1151 (Fed. Cir. 1995), *cert. denied*, 116 S. Ct. 1362 (1996). In order to determine whether Amgen's patents have been anticipated or rendered obvious by the prior art, the jury will have to consider facts relating to whether the elements of the claimed invention are found in the prior art, as viewed by a person of ordinary skill in the art. See *In re Paulsen*, 30 F.3d 1475, 1478-79 (Fed. Cir. 1994). These same considerations need be decided to determine the materiality of Amgen's omissions and misrepresentations of the prior art to the PTO in determining inequitable conduct. Given this significant overlap of issues and evidence between the invalidity claims and the inequitable conduct claims, the patent jury should hear and decide

the inequitable conduct claims.

Additionally, as discussed in detail in Roche's Memorandum for July 17, 2007 Case Management Conference (Docket Item 739), there are common issues between Roche's inequitable conduct and invalidity claims and Roche's antitrust and state law counterclaims which require that all patent issues, including inequitable conduct, be tried to a jury to secure Roche's Seventh Amendment right to a jury trial on both the antitrust and patent issues. See, *Beacon Theatres, Inc. v. Westover*, 359 U.S. 500 (1959) (where legal and equitable claims have common issues, Seventh Amendment jury trial right requires that jury decide common issues). Amgen in its own Case Management Memorandum filed before the July 17, 2007 Conference admits that there are common issues between the patent issues, including inequitable conduct, and the antitrust claims, but it tried unsuccessfully to argue these were "factual" issues, not "legal issues." Amgen's Memorandum for July 17, 2007 Case Management Conference, Docket Item 687, at 8-9. This Court correctly rejected this argument when it held that all patent issues would be tried to a jury, and Amgen has not pointed to anything to indicate this Court was incorrect. Common Seventh Amendment issues include not only ultimate legal issues, but also "factual issues." *C.R. Bard*, 1994 WL 258880, at *2. These common issues require that the inequitable conduct claim be tried to a jury to preserve the seventh amendment right on the antitrust claims. See, e.g., *Cabinet Vision v. Cabinetware*, 129 F.3d 595, 600 (Fed. Cir. 1997) (explaining that "[w]e have long recognized that a Walker Process counterclaim and an affirmative defense of inequitable conduct share common factual elements" for Seventh Amendment purposes); *Therma-Tru Corp. v. Peachtree Doors, Inc.*, 44 F.3d 988, 994-95 (Fed. Cir. 1995) (citing numerous cases from numerous circuits and recognizing that *Beacon Theatres*, applies when "equitable claims are joined with legal claims and have factual questions in common."). As with Roche's claims of invalidity based on anticipation and obviousness, the

inequitable conduct claims share many common issues with Roche's antitrust claims, requiring inequitable conduct to be tried to the jury. *See In re Innotron Diagnostics*, 800 F.2d 1077, 1085-86 (Fed. Cir. 1986) (Seventh Amendment satisfied because juries would hear both antitrust claims and patent claims, where "most of the facts and issues are "overwhelmingly intertwined with and overlapping with those in [the] antitrust counterclaims," and where the antitrust claims turned on prevailing on patent defenses); *Implant Innovations, Inc. v. Nobelpharma AB*, 1996 WL 568791, at *3 (N.D. Ill. Oct. 2, 1996) (holding that "in order to preserve [the] Seventh Amendment jury trial guarantee the Court finds that the inequitable conduct issue must be tried by a jury" because that issue "overlaps with the antitrust claim" (citing both *Innotron* and *United States Gypsum Co. v. Nat'l Gypsum Co.* 1994 WL 74989 (N.D. Ill. Mar. 10, 1994), both cited by Amgen)); *C.R. Bard*, 1994 WL 258889, at *2 (*Beacon Theaters* required jury trial of inequitable conduct defense because that phase would resolve "factual questions that must also be determined" by jury for validity); *see also Cabinet Vision*, 129 F.3d at 599-600.

3. The Court Correctly Ruled That Roche's Claim of Invalidity Based on Obviousness-Type Double-Patenting Will Be Tried To The Jury

Just as there are substantial common issues between Roche's claims of invalidity based on anticipation/obviousness and inequitable conduct, there are substantial common issues between anticipation/obviousness and Roche's claim of invalidity based on obviousness-type double patenting which require that the double patenting claim be tried to the jury.

Roche contends that the claims of patents-in-suit are invalid for obviousness in view of the prior art. The jury will have to decide whether such prior art would give a person of skill in the art a reasonable expectation of success to make or use the products and processes claimed in the patent-in-suit. Amgen's responsive arguments on obviousness are intertwined with its arguments on double-patenting. By way of one example, Amgen argues that it would not have been obvious for an expressed recombinant EPO to be biologically active even if obtaining the

gene and producing the polypeptide was obvious. This position of Amgen's is identical for both Section 103 obviousness and obviousness-type double patenting. Having two different fact finders decide the same issue is not only inefficient but also could lead to an irreconcilable contradictory result. The prudent procedure is to have the jury decide both obviousness and obviousness-type double patenting. Clearly, as with inequitable conduct, the jury can efficiently and effectively decide obviousness-type double patenting. See, *Slade Gorton & Co., Inc. v. Millis*, 62 F.3d 1433, 1995 WL 471106, 39 U.S.P.Q.2d 1939 (Fed. Cir.) (affirming jury verdicts of invalidity for obviousness-type double patenting and unenforceability for inequitable conduct). The case cited by Amgen for the proposition that obviousness-type double patenting must be decided by the court, *Eli Lilly and Co. v. Barr Labs, Inc.*, 251 F.3d 955, 968 (Fed. Cir. 2001), in fact does not support this proposition at all. In Lilly, the Federal Circuit reversed denial of a motion for summary judgment that the patent was invalid for obviousness-type double patenting, finding there were no genuine issues of material fact and that the patent was invalid as a matter of law. *Id*. The language quoted by Amgen was the court explaining the law on double patenting, not making any statement about whether at trial obviousness-type double patenting should be decided by the jury or the court, and is disingenuously cited by Amgen.

To preserve Roche's right to a jury on both the patent issues and antitrust and state law issues in this case, both inequitable conduct and obviousness-type double patenting must be tried to the jury in this case. However, even if the Court believed that it was not necessary to try these issues to the jury, the prudent course is to allow the jury to hear and decide these issues because "striking the jury demand and proceeding with a protracted non-jury trial runs the considerable risk that if the right to a jury trial is sustained on appeal, the whole case would have to be retried. On the other hand, if it were determined that a right to a jury trial does not exist, all that would need to be done is for the Court, on the basis of the trial record which was presented to the jury,

to make findings of fact and conclusions of law. The case would not need to be retried." *Zeneca Ltd. v. Pharmachemie B.V.*, 1998 WL 1013126, at *1 (D. Mass. Oct. 8, 1998) (Collings, M.J.).

Additionally, even if the Court does not believe the jury should make the ultimate determinations of invalidity based on double patenting and unenforceability based on inequitable conduct, the Court has the power to submit these issues to the jury and to treat the jury's determination as advisory under Fed. R. Civ. P. 39(c). Rule 39(c) provides that "[I]n all actions not triable of right by a jury the court upon motion or of its own initiative may try any issue with an advisory jury." Rule 39(c) (emphasis added). Use of an advisory jury is thus also clearly within this Court's discretion. *Gentex Corp. v. Donnelly Corp.*, 1993 WL 207619, 26 U.S.P.Q.2d 1558 (W.D. Mich.) (having advisory jury hear and decide inequitable conduct claim is the most expedient and fair way to conduct trial); *Williams v. Collier*, 32 F. Supp. 321, 325 (E.D. Pa. 1940) ("the court, in its discretion, may always try any issue with an advisory jury"). Once jury renders its verdict, this Court may then adopt the jury's advisory verdict by making findings of fact and conclusions of law in accordance with the jury's verdict. *Reliance Life Ins. Co. v. Everglades Discount Co.*, 204 F.2d 937 (5th Cir. 1953).

Accordingly, this Court was correct when it ruled that all patent and antitrust issues, including inequitable conduct and obviousness-type double patenting would be tried to a jury and Amgen has not presented any grounds to suggest this Court should reverse its ruling on these issues.

X. NAMES, ADDRESSES AND TELEPHONE NUMBERS OF POTENTIAL WITNESSES (INCLUDING EXPERTS)

A. Amgen's List of Potential Witnesses

Amgen's list of witnesses is attached as Exhibit E.

B. Roche's List of Potential Witnesses

Roche's list of potential witnesses is attached as Exhibit F.

XI. LIST OF PROPOSED EXHIBITS

As a result of ongoing disputes that require resolution, the parties have agreed to postpone the submission of exhibit lists to the Court. The parties will submit a list of exhibits identified in accordance with the Court's Order in advance of trial.

Respectfully Submitted,

AMGEN INC.,
By its attorneys,

August 10, 2007

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CERTIFICATE OF SERVICE

I hereby certify that this document filed through the Electronic Case Filing (ECF) system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF) and paper copies will be sent to those indicated as non registered participants on the above date.

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