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 **LEAVE TO FILE GRANTED ON MAY 2, 2007**

AMGEN INC.'S RESPONSE TO THE COURT'S QUESTIONS REGARDING PRECEDENTIAL EFFECT OF PRIOR CLAIM CONSTRUCTIONS AND DEFENDANTS' REPLY BRIEF REGARDING CLAIM CONSTRUCTION

TABLE OF CONTENTS

PAGE NO.

TABLE OF AUTHORITIES

PAGE NO.

I. INTRODUCTION

Amgen submits this brief in response to the Court's questions regarding the precedential effect of prior claim construction rulings as well as the arguments raised in Defendants' claim construction reply, filed by leave of Court on March 30, 2007.

In its March 30, 2007 Order, the Court asked the parties:

> What is the status of claim constructions made by this Court and affirmed by the Federal Circuit in the earlier case? Since these constructions are matters of law [citing *Markman*], do they have precedential force, binding Roche/Hoffman as well as Amgen in this subsequent case?[1]

Defendants' March 30 reply further frames the issue by asking this Court to adopt a claim construction of "purified from mammalian cells grown in culture" that differs from the claim construction previously adopted by this Court and affirmed by the Federal Circuit.

Because Defendants were not parties to the prior lawsuit between *Amgen and HMR/TKT*, the doctrine of issue preclusion (collateral estoppel) does not apply. However, insofar as the prior claim construction rulings have been reviewed and affirmed by the Federal Circuit, they are binding on this Court under principles of *stare decisis*.[2] Under existing Federal Circuit precedent, a claim construction ruling is treated purely as a question of law.[3] As such, the prior legal rulings of the Federal Circuit and this Court construing Amgen's claims bind this Court under *stare decisis*. Defendants are not precluded from challenging the prior rulings, but it is the Federal Circuit, not this Court, that has the authority to reverse or alter such binding legal precedent.

Even if the prior claim construction rulings were subject to independent review in this

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[1] 3/30/07 Order at 18.

[2] *See*, e.g., Wang Labs, Inc. v. Oki Elec. Indus. Co., 15 F. Supp. 2d 166, 175-76 (D. Mass. 1998).

[3] *See Cybor Corp. v. FAS Technologies, Inc.*, 138 F.3d 1448 (Fed. Cir. 1998).

proceeding, Defendants have failed to show that a different construction is appropriate. The term ***"purified from mammalian cells grown in culture"*** was properly construed by both this Court and the Federal Circuit without reference to any particular structure in the cells themselves, precisely because the claim need not recite a specific structure where it is the recited source from which the claimed product is obtained that imparts the novel structure. Defendants' proposed construction confuses and improperly conflates their burden to prove their invalidity defenses by clear and convincing evidence, with the separate and distinct analysis required for proper claim construction. As to the claim terms ***"diluent, adjuvant, or carrier,"*** Defendants' attempt to read in a requirement that the recited "diluent, adjuvant, or carrier" be "distinct and separate" from human EPO also finds no support in the intrinsic record. The claim language, specification, and prosecution history impose no such requirement. Defendants' attempt to construe the term ***"CHO cell"*** in a manner that would exclude the very CHO cells described in the patent specification's preferred embodiment should also be rejected. Finally, Defendants' attempt to construe the process claims of the '868 patent to require an additional step – transformation and transfection of host cells with DNA encoding EPO – is also flawed. The limitation ***"cells transformed or transfected with an isolated DNA sequence encoding human erythropoietin"*** defines a required characteristic of the cells used to perform the claimed '868 process for producing a glycosylated EPO polypeptide, not an additional step that must be performed to practice the claimed processes.

II. PRIOR CLAIM CONSTRUCTION RULINGS OF THIS COURT AND THE FEDERAL CIRCUIT REGARDING THE PATENTS-IN-SUIT MUST BE FOLLOWED UNDER PRINCIPLES OF STARE DECISIS

In *Markman v. Westview Instruments, Inc.*,[4] the Supreme Court held that claim

[4] 517 U.S. 370, 372 (1996).

construction is exclusively for the court, in part due to the "importance of uniformity in treatment of a given patent."[5] By treating claim construction as a legal issue for the court, the Supreme Court explained that the application of *stare decisis* would promote (but not guarantee) intrajurisdictional certainty in the enforcement of patents through interjurisdiction "uniformity" under the authority of the Federal Circuit.

> But whereas issue preclusion could not be asserted against new and independent infringement defendants even within a given jurisdiction, treating interpretive issues as purely legal will promote (though it will not guarantee) intrajurisdictional certainty through the application of *stare decisis* on those questions not yet subject to interjurisdictional uniformity under the authority of the single appeals court.[6]

Subsequent decisions have followed *Markman* by declining to apply issue preclusion on issues of claim construction to non-parties,[7] but applying the Federal Circuit's prior claim constructions based on *stare decisis*, even against new and independent infringement defendants.[8]

In *Wang Labs, Inc. v. Oki Elec. Indus. Co.*, Judge Lindsay of this Court confronted a similar situation. In a prior lawsuit, the Federal Circuit had construed Wang's patents. The

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[5] *Id.* at 390.

[6] *Id.* at 391.

[7] *See, e.g., Texas Instruments, Inc. v. Linear Techs. Corp.*, 182 F. Supp. 2d 580, 586 (E.D. Tex. 2002); *see also Blonder-Tongue Labs., Inc. v. Univ. of Ill. Found.*, 402 U.S. 313 (1971).

[8] *Wang Labs, Inc. v. Oki Elec. Indus. Co.*, 15 F. Supp. 2d 166, 175-76 (D. Mass. 1998); *Hynix Semiconductor Inc. v. Rambus Inc.*, 2004 U.S. Dist. LEXIS 23230 at * 15-16 (N.D. Cal. 2004) ("Since the Federal Circuit has already construed certain claim terms, these constructions are done as a matter of law and are given *stare decisis* effect"); *Tate Access Floors, Inc. v. Architectural Resources, Inc.*, 185 F. Supp. 2d 588 **,** 595 n.4 (2002); *see also KX Indus., L.P. v. PUR Water Purification Prods., Inc.*, 108 F. Supp. 2d 380, 387 (D. Del. 2000). Decisions of sister court's generally have been applied if persuasive, but not treated as binding. *See Lamps Plus, Inc. v. Dolan*, 2003 U.S. Dist. LEXIS 19578 (N.D. Tex. 2003); *Wilson Sporting Goods Co. v. Hillerich & Bradsby Co.*, 2003 U.S. Dist. LEXIS 13900 (N.D. Ill. 2003) *see also Texas Instruments*, 182 F. Supp. 2d at 589 n.3 (concluding that "the question of deferring to prior claims construction is at its discretion").

defendant, Oki, pressed for a different claim construction, arguing that it could not be bound by the results of the prior decision since it was not a party and the issue had only been "superficially" briefed in the prior case. This Court, however, concluded that it was bound to follow the Federal Circuit's prior construction based on *stare decisis*, explaining: "*Stare decisis*, unlike the doctrines of res judicata and collateral estoppel, is not narrowly confined to parties and privies . . . . The doctrine is broad in its impact, reaching strangers to the earlier litigation."[9] According to Judge Lindsay, "Adopting the Federal Circuit's construction of the Wang patents comports with the purpose for which a special appeals court for patent cases was created."[10]

In accordance with the principles of *stare decisis*, this Court is bound to follow the prior constructions of Amgen's patents adopted or affirmed by the Federal Circuit in the prior *Amgen v. HMR/TKT* litigation. To the extent that Defendants disagree with any of the prior constructions, they must seek relief from the Federal Circuit, not this Court.

III. DEFENDANTS' PROPOSED CONSTRUCTIONS ARE INCONSISTENT WITH THE INTRINSIC RECORD AND IGNORE THE *STARE DECISIS* EFFECT OF PRIOR RULINGS

While Defendants originally informed Amgen that they believed that more than 40 claim terms required construction, Defendants chose to brief and seek constructions for eight claim terms only. Amgen submitted its proposed claim constructions for all of the limitations of all the asserted claims as Appendix A to its opening claim construction brief. Amgen had previously provided this complete set of claim constructions in discovery to Defendants in January 2007. Except for the 11 claim terms disputed by Defendants, they have not challenged the constructions proposed by Amgen. Accordingly, Amgen respectfully requests the Court to adopt

[9] *Wang Labs.*, 15 F. Supp. 2d at 176 (quoting *E.E.O.C. v. Trabucco*, 791 F.2d 1, 2 (1st Cir. 1986)).

the uncontested portions of Amgen's proposed claim construction (Appendix A) as law of the case.

The eleven claim terms disputed by Defendants are:

1. "human erythropoietin"
2. "purified from mammalian cells grown in culture"
3. "a non-naturally occurring erythropoietin glycoprotein"
4. "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"
5. "a pharmaceutical composition comprising… and a pharmaceutically acceptable diluent, adjuvant or carrier"
6. "a process for the production of a glycosylated erythropoietin polypeptide… comprising the steps of"
7. "CHO cells"
8. "cells transformed or transfected with an isolated DNA sequence encoding human erythropoietin"
9. "isolating said glycosylated erythropoietin polypeptide expressed [therefrom] [by said cells]"
10. "a process for producing erythropoietin comprising the step of"
11. "effective amount [of] a glycoprotein product effective for erythropoietin therapy"

Defendants' reply raises new arguments regarding the construction of four of the eleven disputed claim terms ("purified from mammalian cells grown in culture;" "adjuvant, diluent, or carrier;" "CHO cell;" and "transformed and transfected with an isolated DNA sequence encoding human erythropoietin.") A chart contrasting the differing constructions advanced by Amgen and by Defendants is attached hereto as Appendix A.

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[10] *Id.* at 175.

A. THE COURT SHOULD APPLY THE CONSTRUCTION OF "PURIFIED FROM MAMMALIAN CELLS GROWN IN CULTURE" PREVIOUSLY ADOPTED BY THIS COURT AND AFFIRMED BY THE FEDERAL CIRCUIT.

The limitation ***"purified from mammalian cells grown in culture"*** in claim 1 of the '422 patent was previously construed by this Court in the first *Amgen v. HMR/TKT* trial.[11] That legal ruling was reviewed and affirmed by the Federal Circuit.[12] In Defendants' latest reply brief, they ask the Court to rule, as a matter of claim construction, that the limitation "cannot define the structure of the claimed product."

"purified from mammalian cells grown in culture" ('422 claim 1)	
Amgen's Proposed Construction	*Defendants' Proposed Construction*
wherein the protein is obtained in substantially homogeneous form from mammalian cells grown in culture, such that it originates in mammalian cells, but need not be taken directly out of the interior of the cells	obtained in substantially homogeneous form from mammalian cells, using the word "from" in the sense that it originates in 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 *This limitation cannot define the structure of the claimed product*.

According to Defendants, the Court should rule, as a matter of law, that the "limitation cannot define the structure of the claimed product" because Amgen has not shown that the

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[11] *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 88-89 (D. Mass. 2001) ("'purified from mammalian cells grown in culture' means '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").

[12] *Amgen, Inc. v. Hoechst Marion Roussel, Inc* , 314 F.3d 1313, 1349 (Fed. Cir. 2003) ("We agree with the district court that this disclosure--the undisputed preferred embodiment of the invention--contemplates purification of erythropoietin from the culture media."); *id*. at 1329-30 ("As to the '422 patent, the limitation "purified from mammalian cells grown in culture" in claim 1 clearly limits the source of the EPO used in the claimed "pharmaceutical composition." The limitation only speaks to the source of the EPO and does not limit the process by which the EPO

specification specifically identifies the structure imparted by this limitation, nor has it shown "such structure was novel as compared to the prior art."[13] Defendants' argument, however, misapprehends the law, the intrinsic record, and the prior ruling of this Court and the Federal Circuit, and in so doing confuses their burden to prove their invalidity defenses with the Court's role in construing the claim's meaning.

While an ***old product*** previously known to the art cannot be patented merely by reciting a new process or source for its production, a ***new product*** — one whose structure is different from that of any prior product — may be claimed by reference to the process or source from which it is produced.[14] That is especially true where, as here, the source limitation imparts structural elements to the recited product that necessarily differ from all previously known products.[15]

The Lin patent specification discloses urinary EPO ("uEPO") isolated from aplastic anemia patients in Example 1 and human EPO produced by mammalian cells grown in culture in Examples 6 and 10. During prosecution of the patents-in-suit, the Examiner first challenged, then accepted, that Lin disclosed a novel EPO product whose structure differed from any prior art uEPO, based upon experiments comparing the structures of Lin's recombinant EPO and Goldwasser's uEPO, as well as publications characterizing those structural differences.[16] In the April 28, 1999 Amendment in which Amgen added the claim that eventually became '422 claim

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is expressed.)

[13] Defendants' Reply Br. at 2.

[14] *In re Luck*, 476 F.2d 650, 653 (C.C.P.A. 1973); *In re Moeller*, 117 F.2d 565, 568 (C.C.P.A. 1941).

[15] *Ex Parte Painter*, 57 O.G. 999, 1000 (Comm'r of Pats. 1891) ("When … an article of manufacture is a new thing … and that article cannot be properly defined and discriminated from the prior art otherwise than by reference to the process of producing it," it may be claimed as such).

[16] *See* Amgen's Brief, Exhibit 9 at AM-ITC-00899180 (U.S. Appln. 100,197 File History, 3/2/95 Amendment (Paper 25) at 2).

1, Amgen explained that it believed the new claims were "novel and non-obvious over the prior art."[17] Amgen described the "purified from mammalian cells grown in culture" limitation as a "source" limitation and stated, "The application further discloses that the glycosylation of human erythropoietin may differ depending on the host cell used for production."[18]

Neither this Court nor the Federal Circuit adopted Defendants' proposed construction in the prior lawsuit. To the contrary, the Federal Circuit affirmed this Court's prior construction, which did not have the additional broadening language that Defendants now propose. The Federal Circuit stated,

> The limitation only speaks to the source of the EPO and does not limit the process by which the EPO is expressed. Rather, the claim is broadly drawn to a "pharmaceutical composition" having certain elements, one of those being EPO "purified from mammalian cells in culture." This reading is in line with the district court's construction."[19]

On remand before this Court, Amgen introduced substantial evidence that prior art EPO preparations, including Goldwasser's urinary EPO preparation, did not satisfy this limitation because human EPO "purified from mammalian cells grown in culture" was structurally distinct from Goldwasser's uEPO preparation.[20] Amgen's evidence, relied, in part, on the fact that Goldwasser's uEPO was subjected to the degrading effects of urinary proteases and sialydases,

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[17] Exhibit 8 at AM-ITC-00899474 (U.S. Appln. 100,197 File History, 4/28/99 Amendment (Paper 33) at 5).

[18] *Id.*

[19] 314 F.3d at 1329-30.

[20] *See, e.g., Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 339 F. Supp. 2d at 333-334; Exhibit 4 to Amgen's Claims Construction Brief at AM-ITC 01008871 (providing that shortly after uEPO injected into patients, 25% of uEPO molecules degraded into fragments half the size of fully active human EPO); Exhibit 5 to Amgen's Claims Construction Brief at AM-ITC 00952087)(same); Exhibit 6 to Amgen's Claims Construction Brief at AM-ITC 00991063 (Goldwasser observed fragments having a molecular weight of 14 kD while native EPO weighs 34 kD)

whereas EPO purified from mammalian cells grown in culture is not.[21] This Court, however, concluded it did not need to reach the issue given its finding that Goldwasser's uEPO was not "therapeutically effective."[22]

On appeal, the Federal Circuit acknowledged Amgen had argued that Dr. Goldwasser's uEPO preparation did not anticipate claim 1 of Lin's '422 patent because the claimed recombinant EPO "differed in structure and function from the uEPO utilized in Dr. Goldwasser's study."[23] The Federal Circuit did not suggest that such evidence was irrelevant under its claim construction as Defendants would now contend. Rather, the Federal Circuit instructed that "[i]f, on remand, the district court finds that the Goldwasser reference contains the "therapeutically effective" limitation, it must then determine whether the uEPO meets the other limitations of claim 1 of the '422 patent."[24]

The extensive prior history surrounding '422 claim 1 makes two points clear. First, this Court and the Federal Circuit have already construed the limitation "purified from mammalian cells grown in culture." The prior construction did not include the additional broadening language that Defendants now propose. Under principles of *stare decisis*, the prior construction must be followed. Second, whether or not this source limitation imposes a structural limitation that distinguishes prior art preparations like Goldwasser's uEPO from '422 claim 1 is properly an invalidity issue for the trier of fact, not a claim construction issue for the Court. Defendants will have the opportunity to prove, and Amgen the opportunity to contest, whether or not particular prior art references satisfy the limitation "purified from mammalian cells grown in culture." To

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[21] *Id.*

[22] *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 339 F. Supp. 2d 202, 345 n. 148 (D. Mass. 2004).

[23] *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293, 1304 (Fed. Cir. 2006).

resolve that issue under the guise of claim construction would be improper. .

B. THERE IS NO SUPPORT IN THE INTRINSIC RECORD FOR REQUIRING THE "DILUENT, ADJUVANT, OR CARRIER" TO BE "DISTINCT AND SEPARATE" FROM THE ACTIVE INGREDIENT.

Because the word "***and***" precedes the recited ***"diluent, adjuvant or carrier"*** in '422 claim 1, Defendants ask the Court to read a requirement for a "distinct and separate" diluent, adjuvant, or carrier into the claim.[25] But nowhere does a "distinct and separate" requirement appear in the claims, the specification, or the prosecution history.

"a pharmaceutical composition comprising… and a pharmaceutically acceptable diluent, adjuvant or carrier" ('422 claim 1, '933 claims 9 and 12)	
Amgen's Proposed Construction	*Defendants' Proposed Construction*
a composition suitable for administration to humans containing at least a diluent, adjuvant or carrier	a mixture having in addition to the active ingredient (as defined in the claim), an additional distinct and separate ingredient that acts as a diluent, an adjuvant or a carrier

Consistent with this Court's prior construction, the claimed pharmaceutical composition must satisfy at least two requirements: (a) "a therapeutically effective amount of erythropoietin" and (b) "a pharmaceutically acceptable diluent, adjuvant or carrier." Nothing in the claim language requires that these elements be separate from each other. Nor does the word "and" necessarily require a "separate and distinct" diluent, adjuvant or carrier. In fact, the specification teaches that these recited elements need not be separate and distinct, but rather can be "together" or "in combination with each other:"

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[24] *Id.* at 1305 n.8.

[25] Defendants make the same argument with respect to '933 claims 9 and 12. While the claims are worded differently than '422 claim 1, the same arguments apply.

- "Also comprehended by the invention are pharmaceutical compositions comprising ***effective amounts of polypeptide products of the invention together with*** suitable diluents, adjuvants and/or carriers."[26]
- ". . . the compositions administered would ordinarily include ***therapeutically effective amounts of product in combination with*** acceptable diluents, carriers and/or adjuvants"[27]

As Dr. Torchilin's declaration made clear, a person of ordinary skill in the art in 1983 reading the specification would have understood that some standard diluents, adjuvants, and carriers identified in the specification could form a variety of bonds with drugs, while others did not.[28] Defendants criticize Dr. Tochilin because he "makes no distinction among various forces, i.e., whether they are strong or weak, and makes no distinction between transient complexes and situations where the two entities combine to form a separate molecular entity."[29] But the specification makes none of these distinctions either. Defendants' attempt to treat certain "weak" bonds as falling within the scope of the claim, but disallowing certain "stronger" bonds, demonstrates the fallacy of Defendants' proposed construction.

Defendants' reliance on cases like *Exxon Chem. Patents, Inc. v. Lubrizol Corp*., 64 F.3d 1553 (Fed. Cir. 1995), is misplaced. The claim in *Exxon* involved a product with a very different kind of claim. One of the components of the claimed product was "ashless dispersant" which the Federal Circuit described as "(i.e. one that neither contains nor is complexed with metal)."[30] The crux of the dispute was that when one of the other claimed ingredients (copper) was mixed with another (ZDDP), zinc was released which would bind with the "ashless dispersant" rendering it

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[26] '933 patent at Col. 12:1-4

[27] '933 patent at Col. 33:52-55.

[28] Torchilin Decl., ¶¶ 33, 35.

[29] Defendants' Reply Br. at 6.

[30] *Id.* at 1556.

"non-ashless," since it would then be bound to a metal. The key in *Exxon* was that one component "ashless dispersant" was specifically defined based on the absence of metal. Obviously, by binding metal to the formerly "ashless dispersant," it lost its defining characteristic.

Here, by contrast, human EPO is not defined in the specification to exclude any interaction with or binding to a "diluent, adjuvant or carrier." EPO is defined by its amino acid sequence. The specification teaches that EPO could be used "together with" or in "combination with" diluents, adjuvants, or carriers.[31] Defendants' attempt to re-write this limitation should therefore be rejected.

C. "CHO CELLS" SHOULD NOT BE CONSTRUED TO EXCLUDE CELL LINES DERIVED FROM THE OVARY OF A CHINESE HAMSTER.

Defendants' apparently ask the Court to construe the term "***CHO cells***" in a manner calculated to exclude Chinese Hamster Ovary cells that have been altered, adapted or modified from naturally occurring Chinese Hamster Ovary cells.

"wherein said cells are CHO cells" ('868 Claim 2, '933 claim 8)	
Amgen's Proposed Construction	*Defendants' Proposed Construction*
A cell derived from the ovary of a Chinese hamster.	A cell from the ovary of a Chinese hamster.

Defendants criticize Amgen's proposed construction of "CHO cells" – "a cell derived from the ovary of a Chinese hamster" – as inconsistent with this Court's prior construction of "mammalian cells" and "vertebrate cells." It is not.

[31] Defendants' attempt to construe this limitation to be limited to allow for "one and only one" of "a diluent, adjuvant or carrier" is inconsistent with the well-established meaning of "comprising" as an open-ended term which may include additional elements. *See, e.g., Amgen*, 314 F.3d at 1344-45; *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1572 (Fed. Cir. 1997).

Amgen would not object to Defendants' proposed construction of CHO cells – "a cell from the ovary of a Chinese hamster" – if the term were understood, like the terms "mammalian cells" and "vertebrate cells," to include cells from a Chinese hamster, mammal, or vertebrate that have been further selected, altered or adapted for growth in culture or other desirable traits. Despite the opportunity to clarify their position in their reply brief and disavow a construction that would exclude the preferred embodiment, Defendants position remains somewhat obscured.

Lin's patent specification describes the use of CHO host cells. The CHO cells are identified as "CHO DHFR$^-$ cells (DuX-B11) CHO K1 cells."[32] Dr. Lin did not directly remove the cells from the ovary of a Chinese Hamster (CHO). He used an established cell line that was developed by others, described in a 1980 publication, and made available to scientists around the world.[33] Even after the CHO cells were further altered by the insertion of human DNA, the specification still described the cells as CHO cells.[34] The "CHO cells" described in the patent were immortalized cells adapted for growth in culture, genetically engineered and many generations removed from the cells originally taken from the Chinese hamster. Indeed, such unaltered cells would likely not be capable of sustained growth in culture. Amgen believes its proposed construction better captures Dr. Lin's express teaching and claimed inventions. To the extent Defendants are seeking a construction that would exclude the preferred embodiment described in the specification, it should be rejected.

[32] '933 patent at Col. 25:46.

[33] '933 patent at Col. 25:39-51.

[34] '933 patent at Col. 27:8-27.

D. THE LIMITATION "CELLS TRANSFORMED OR TRANSFECTED WITH AN ISOLATED DNA SEQUENCE ENCODING HUMAN ERYTHROPOIETIN" IS A CHARACTERISTIC OF THE RECITED CELLS, NOT A CLAIMED STEP OF THE '868 PROCESS CLAIMS.

Defendants' proposed construction for the limitation ***"transformed or transfected with an isolated DNA sequence encoding human erythropoietin"*** seeks to turn an inherited characteristic of the cells used in the claimed process into a step of the process itself.

"cells transformed or transfected with an isolated DNA sequence encoding human erythropoietin" '868 claims 1 and 2	
Amgen's Proposed Construction	*Defendants' Proposed Construction*
cells receiving purified genetic instructions for human erythropoietin	introduction purified exogenous DNA molecules encoding the genetic instructions for human erythropoietin into a host cell

The asserted claims of the '868 patent require only two steps: (1) growing cells with certain recited characteristics under suitable nutrient conditions and (2) isolating glycosylated EPO polypeptide from the cells. "Transformed or transfected" is a past-tense characteristic of the cells. It is not a step of the claimed process.

The specification describes "transformed or transfected" as a previously engineered characteristic of the cells used in the recited process. For example, the specification states:

> "[A] gene that specifies the structure of a desired polypeptide product is . . . 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 . . . ."[35]

After "transformation or transfection" of a single cell, the cell "self-replicates" in culture to produce daughter cells that possess the engineered characteristic. The subsequent generations of host cells are nevertheless described as "transformed or transfected," even though the

[35] '933 patent at Col. 2:22-31.

transformation step may have been performed in the distant past with an ancestral cell. Thus, "transformed or transfected" is not a step in the claimed process, it is an inherited characteristic of the claimed cells. Under Defendants' construction, a newly transformed or transfected cell would have to be prepared each time EPO was produced. Clearly, Lin's method imposes no such requirement.

Defendants note that their use of the phrase "introduction" of DNA is not very different from Amgen's use of the phrase "cells receiving purified genetic instructions for human erythropoietin" and criticize Amgen for retreating from its original use of the word "receiving" – an active present verb suggesting a present action.[36] Upon further reflection, briefing on this limitation has exposed a significant ambiguity or imprecision in both Amgen's proposed construction and Defendants' proposed construction. Since the claim term is "transformed or transfected," not "transforming or transfecting," Amgen proposes the following modification to its prior proposed construction: "cells transformed or transfected with an isolated DNA sequence encoding human erythropoietin" should be construed as "cells that have received an isolated DNA sequence human erythropoietin." As shown above, this proposed construction more accurately tracks the language of the claim and the teaching of the specification than Defendants' proposed construction.

IV. CONCLUSION

Based on the foregoing, Amgen requests that the Court adopt Amgen's proposed claim constructions as detailed in Appendix A of Amgen's opening brief, subject to the modification of the proposed construction for the limitation "cells transformed or transfected with an isolated DNA sequence encoding human erythropoietin" as discussed above.

[36] Defendants' Reply Br. at 11.

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Respectfully submitted,

AMGEN INC.,
By its attorneys,

/s/ Michael R/ Gottfried

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

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

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

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

Of Counsel:

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

CERTIFICATE OF SERVICE

I hereby certify that this document, filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of electronic filing and paper copies will be sent to those indicated as non-registered participants on May 2, 2007.

/s/ Michael R/ Gottfried
Michael R. Gottfried