Exhibit 3

UNITED STATES DISTRICT COURT

DISTRICT OF MASSACHUSETTS

AMGEN INC.,	)	
	)	Civil Action
Plaintiff,	)	No. 97-10814-WGY
	)	
v.	)	
	)	
HOECHST MARION ROUSSEL, INC.	)	
and	)	
TRANSKARYOTIC THERAPIES, INC.,	)	
	)	
Defendants.	)	
	)	

AMGEN'S REPLY IN SUPPORT OF ITS MOTION FOR SUMMARY JUDGMENT OF NO INEQUITABLE CONDUCT

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I. INTRODUCTION

Given the opportunity to amend their Answer to plead with particularity their inequitable conduct defense, Defendants based their allegations on Amgen's alleged failure to disclose to the PTO: (1) certain SDS-PAGE analyses comparing rEPO and uEPO; (2) the incorrect monosaccharide composition data reported in Dr. Lin's specification; and (3) Dr. Goldwasser's three-patient study using uEPO. But as shown in Amgen's Opening Brief, since all of this information was in fact disclosed to the PTO, there can be no inequitable conduct.

Confronted with this plain record of disclosure, Defendants respond by arguing that the information was only disclosed to the PTO in the context of the interference with Genetics Institute ("G.I.") and that disclosure in an interference is not a proper disclosure to an examiner. Further, Defendants and their legal expert, Mr. Chisum, assert that Amgen did not disclose the interference decision and record to the Examiner and that even if the record were before the Examiner, he would not have reviewed it.

Defendants, however, are wrong on all these points. First, Amgen disclosed the allegedly withheld information both during the interference and during *ex parte* prosecution before the Examiner. Second, the written record shows that the interference record and the Board's decision were both reviewed by the Examiner over the course of two months. (Exhibit A hereto.) Third, Defendants fail to even address the impact of the interference decision in which the Board expressly found that the allegedly withheld information did not contradict the statements of Dr. Lin's specification that rEPO has a different glycosylation from uEPO.

Specifically, the Board acknowledged Amgen's admission that the monosaccharide composition data in the patent was incorrect and cited to the pages of Amgen's PLA which

reported the correct values. Further, in full view of all of the Amgen SDS-PAGE data allegedly withheld and with the same pin-point focus provided by G.I. as argued by Defendants here, the Board held that the data was "not sufficient to contradict the information disclosed on page 64 of the Lin application."[1] Since the Board is the entity within the PTO having the ultimate jurisdiction over all matters concerning patentability,[2] and given that the Examiner received and reviewed the Board's decision, there is no question that the SDS-PAGE and monosaccharide information was disclosed, considered, and held not to be inconsistent with a claim to a difference in glycosylation.

Similarly, Defendants mistakenly assert that the "results" of the Goldwasser study were not disclosed to the PTO. As shown in Amgen's Opening Brief, however, the only "results" of Dr. Goldwasser's use of uEPO to treat three anemic patients was that "the amount [of uEPO] was too small to extend the trial long enough to see any result."[3] Defendants do not contest that the Goldwasser study showed "no significant increase in the hematocrit" of the three anemic patients and that, as confirmed by Defendants' own witnesses, hematocrit is the critical measure of therapeutic efficacy in the treatment of anemia. Defendants' only argument is that the claim term "therapeutically effective amount" should be construed not in accordance with its ordinary meaning but more broadly to encompass any of the known biological effects of EPO, including e.g., the stimulation of reticulocyte response. Defendants' proposed claim construction is erroneous because it conflicts with the ordinary meaning of the claim term as admitted by Defendants' witnesses.

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[1] *Fritsch v. Lin*, 21 U.S.P.Q.2d 1739, 1742 (B.P.A.I. 1991). Page 64 of the Lin application corresponds to the SDS-PAGE data reported at Col. 28:33-50 of the '933 patent specification.

[2] *Woo v Wang*, 129 F.3d 1237, 1240 (Fed. Cir. 1997); *In re Van Gunns*, 946 F.2d 845, 846 *et seq.* (Fed. Cir. 1991); *see also* 35 U.S.C. § 7(b) (1984).

[3] Ex. A to Declaration of Richard M. Wong dated 3/21/00 ("Wong Decl. II"); Goldwasser ITC testimony, pp. 22-23, submitted to PTO.

Plainly, Defendants' arguments on claim construction do not convert a failed attempt to treat patients with uEPO into a showing of therapeutic effectiveness.

Finally, unable to support their pleaded allegations and in a desperate attempt to stave off the entry of summary judgment, Defendants move the target and proffer a hodgepodge of new allegations. For instance, Defendants now for the first time allege that Amgen failed to disclose to the PTO: (1) the present litigation; (2) Judge Saris' 1989 decision in *Amgen v. Chugai*; (3) other Amgen documents and publications; and (4) a Kirin IEF gel. These allegations should not be considered because Defendants failed to state them in their interrogatory response[4] and failed to plead them in their Amended Answer. Defendants cannot belatedly change the scope of their inequitable defense in order to defeat summary judgment, particularly since Defendants were given the opportunity to amend their Answer after full fact discovery to conform to the requirements of Rule 9 in pleading inequitable conduct. In any event, as shown below, the record incontrovertibly refutes every one of Defendants' new allegations as the information was indeed disclosed to the PTO.

II. LEGAL STANDARDS

Defendants assert that in deciding Amgen's motion "the Court must assume that the facts relied upon by TKT/HMR are true."[5] The law, however, does not permit Defendants to avoid summary judgment by relying upon a façade of facts shown to be false. As non-movant, Defendants may not rest upon the mere allegations or denials of their pleadings, but rather must set forth specific facts showing that there is a genuine issue for trial.[6] Given that

[4] By Order dated January 28, 2000, this Court sanctioned Defendants for their misconduct in discovery and limited the grounds for their defenses to those specified in their interrogatory responses of December 7, 1999, Ex. B to Wong Decl. II. None of these newly raised allegations were stated in the interrogatory response. Defendants filed their Amended Answer on January 10, 2000 also without making these allegations.

[5] TKT/HMR's Memorandum in Opposition to Amgen's Motion for Summary Judgment of No Inequitable Conduct ("Defendants' Opp.") at 10.

[6] *See Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248 (1985).

Defendants ultimately bear the burden of establishing their case by clear and convincing evidence at trial, the quantum of evidence required of Defendants is that much higher.[7] To avoid summary judgment, Defendants must proffer evidence of sufficient caliber and quantity to meet their burden at trial of clear and convincing evidence. Defendants have cited to no such evidence.

III. THE COURT SHOULD ENTER SUMMARY JUDGMENT OF NO INEQUITABLE CONDUCT

A. DEFENDANTS PROVIDE NO COMPETENT EVIDENCE OF THE WITHHOLDING OF ANY MATERIAL INFORMATION.

Defendants' response fails to raise any issues of fact that would preclude summary judgment. In the guise of an expert declaration, Defendants proffer the unfounded and speculative assertions of a lawyer, Mr. Chisum. Although an author of a legal treatise, Mr. Chisum is not a scientist, medical doctor, or even a patent attorney and readily confesses his incompetence to testify as to how a person of ordinary skill in the art would have viewed any of the information alleged to have been withheld.[8] For this reason alone, Chisum's declaration cannot raise genuine issues of fact and cannot discharge Defendants' burden of proof on inequitable conduct.[9]

Additionally, the substance of Defendants' position, as argued through Chisum, fails to establish the withholding of any material information. All of the information relied upon by Defendants, including the newly raised allegations, was disclosed to the PTO, in both the context of the interference and during *ex parte* prosecution with the Examiner. Even if it had not been disclosed, Defendants fail to present any evidence on the materiality of the

[7] *Schneider Inc. v. C.R. Bard, Inc.*, 18 U.S.P.Q.2d 1076, 1990 U.S. Dist. LEXIS 18962 at *16-17 (D. Mass. 1990) (denying patent challenger's motion for summary judgment of inequitable conduct); *see also*, *Anderson*, 477 U.S. at 256.

[8] Ex. C to Wong Decl. II; Chisum Depo., pp. 22:12-24:6, 27:3-29:9, 32:18-35:5 and 39:3-19.

information. None of the alleged information presents a "prima facie case of unpatentability" as required by 37 C.F.R. §1.56(b).[10]

Most of the information relied upon by Defendants relates to the issue of glycosylation differences between the EPO products claimed in the '933 and '080 patents and uEPO.[11] Yet, none of the information is prior art and thus cannot anticipate or render obvious the patent claims. Even if construed in a light most favorable to Defendants' position, at best, the information shows that some rEPOs have the same glycosylation as uEPO. But these products are expressly excluded from the claims by the phrase "having glycosylation which differs." The argument that some uEPO preparations may differ from other uEPO preparations is also not material because all uEPO preparations are excluded from the patent claims.[12] Thus, Defendants' evidence fails to show that any of the cited information on SDS-PAGE and other glycosylation data presents a prima facie case of unpatentability for any of the claims. Defendants' argument that the allegedly withheld SDS-PAGE data is inconsistent with the data presented in the patent is shown to be plainly wrong by the Board's conclusion after reviewing the same data that it "is not sufficient to contradict the information" disclosed in the patent.[13]

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[9] Because such "evidence" is not admissible, Amgen has recently filed a motion to exclude the trial testimony and to strike the declaration of Donald Chisum on this issue.

[10] 37 C.F.R. § 1.56 (b) defines "material" as "Under this section, information is material to patentability when it is not cumulative to information already of record or being made of record in the application, and (1) It establishes, by itself or in combination with other information, a prima facie case of unpatentability of a claim; or (2) It refutes, or is inconsistent with, a position the applicant takes in: (i) Opposing an argument of unpatentability relied on by the Office, (ii) Asserting an argument of patentability."

[11] The allegations of withholding the SDS-PAGE and monosaccharide data are only relevant to the '933 and '080 patent claims and do not affect the '349, '698, and '422 patent claims. The allegations of withholding the Goldwasser study can only relate to unasserted claim 2 of the '422 patent because all other claims expressly exclude uEPO.

[12] For example, in the '933 patent claims (and '080 claim 3), the term "non-naturally occurring" excludes all EPO products isolated from a natural source including all uEPO products. In fact, the Examiner did not allow these claims until after "non-naturally occurring" was added to ensure that uEPO was not included. *See* Ex. D to Wong Decl. II, Amendment received July 12, 1989.

[13] *Fritsch v Lin*, 21 U.S.P.Q.2d at 1742.

B. BECAUSE THE EXAMINER REVIEWED THE INTERFERENCE DECISION AND RECORD, THE INFORMATION SUBMITTED IN THE INTERFERENCE WAS DISCLOSED TO THE EXAMINER.

The prosecution history of the '933 and '080 patents evidences that the Examiner received and considered the interference decision and record over the course of two months in 1993. The Examiner's Search Notes (Exhibit A hereto) entered in the file after the completion of the Interference unambiguously state:

> **"Reviewed parent file 675,298**
> **Reviewed Interference file # 102,334**
> **Reviewed published Intf. Decision (*Fritsch v. Lin*)**
> **& *Amgen v. Chugai* (18 U.S.P.Q.2d @1016)**
>
> **Oct- Nov 1993**
> **Fitzgerald DF"**[14]

The docket of the '334 interference also reflects that the interference decision and record was sent to the PTO's Examining division, and that the Supervisory Examiner specifically acknowledged in writing, **"Decision noted."**[15] Thus, there can be no genuine issue of fact as to whether the Examiner received and considered the interference decision and record.

Failing to disclose the Examiner's Search Notes, Defendants instead proffer only Chisum's erroneous speculation. Although he purports to summarize for the Court's benefit the salient aspects of the prosecution history, Chisum ignores this dispositive evidence — evidence that is undeniably part of the prosecution history. Such omission is either the result of Chisum's lack of competence to testify as to PTO practices and procedures, as his

[14] Goolkasian Decl. ¶ 3, March 20, 2000. In his December 29, 1993 Office Action, the Examiner expressly notes that the '334 Interference was resolved in Amgen's favor. Ex. Y to Wong Decl. II; Of. Act. at 2, December 29, 1993, U.S. Patent No. 5,547,933.

[15] Goolkasian Decl. ¶ 5, March 20, 2000, filed herewith.

deposition testimony evidences,[16] or it is simply a misguided attempt to create an issue of fact. Unlike the Examiner, Chisum did not review the interference record.[17]

Chisum further speculates that even if the Examiner had access to the interference record, he would not have been expected or have had the time to review it.[18] But the record plainly shows that the Examiner reviewed both the decision and record over the course of two months.[19] While doing so, the Examiner had the benefit of having in hand the Board's decision which provides explicit citations to the interference record. Moreover, in order for the Examiner to know how to proceed with examination after the Board resolved the interference, the Examiner had to read and understand the Board's decision.[20] It was for this reason that the interference record and decision were sent to the PTO's Examining division and a record made that the decision had been noted.[21]

Thus, the very information upon which Defendants premise their inequitable conduct defense was disclosed to the Examiner by his review of the interference decision and record.[22] Contrary to Defendants' assertions, there was no need for Amgen to resubmit that information again to the Examiner. As the Federal Circuit has repeatedly held, a reference

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[16] Ex. C to Wong Decl. II; Chisum Depo., pp. 27:8-29:9.

[17] Ex. E to Wong Decl. II; Chisum Depo., pp. 88:3-89:8, 91:18-92:11.

[18] Both in his declaration and at his deposition, Mr. Chisum argues that because all business of the PTO must be conducted in writing, the state of mind of the Examiner can only be divined from the express statements of the prosecution history. Ex. E to Wong Decl. II; Chisum Depo., pp. 189:13-190:9, 88:3-89:8, 91:18-92:11; Chisum Decl. ¶ 36, March 8, 2000. He goes on to assert that based on his review of the prosecution history, it is his view that the Examiner did not review the interference record. Ex. F to Wong Decl. II; Chisum Decl. ¶ 45, March 8, 2000; Chisum Depo., pp. 125:4-19, 128:15-21, 129:1-17, 261:25-262:8. But by his own logic, because the prosecution history expressly states in writing that the Examiner reviewed the interference decision and record, and did so over a 2-month period, the Court must reject Chisum's unfounded assertion.

[19] Exhibit A hereto.

[20] Ex. 22 to Wong Decl.; Goolkasian Decl. ¶¶ 7 –10, 18, February 16, 2000.

[21] Ex. 22 to Wong Decl.; Goolkasian Decl. ¶¶ 7-8, 13, 17, February 16, 2000; Goolkasian Decl. ¶¶ 4-6; March 20, 2000. *See E.I. Du Pont de Nemours & Co. v. Phillips Petroleum Co.*, 656 F. Supp. 1343, 1376 (D. Del. 1987), *rev'd on other grounds*, 849 F.2d 1430, 1439 (Fed. Cir. 1988).

that is "actually considered by the PTO" cannot be deemed to have been intentionally withheld even though the applicant did not disclose it.

Defendants' reliance on *A.B. Dick Co. v. Burroughs Corp.*,[23] is misplaced. In *A.B. Dick,* the prosecution history did not evidence that the Examiner had reviewed and considered the interference decision and record as the prosecution history indicates here. Also, in this case, disclosure was made not only during the interference but also during *ex parte* prosecution to the Examiner as well. [24]

C. THE EXAMINER KNEW OF THE ERRONEOUS MONOSACCHARIDE DATA.

Because Amgen's admission that the monosaccharide data was incorrect is stated in the Board's decision[25] and because the Examiner received and considered the decision, Defendants cannot persist in arguing that "there is no written record that Amgen ever disclosed to the Examiner the errors in the carbohydrate composition data."[26] In addition, after the interference decision, Amgen further informed the PTO that the Party Fritsch had

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[22] *Litton Sys., Inc. v. Honeywell, Inc.*, 87 F.3d 1559, 1571 (Fed. Cir. 1996) ("An applicant cannot intentionally withhold a reference actually considered by the PTO, even though the applicant may not have disclosed the art"); *see also Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565, 1582 (Fed. Cir. 1991)

[23] 617 F. Supp. 1382 (N.D. Ill. 1985).

[24] Likewise, Defendants' reliance on *General Electric Co. v. U.S.*, 206 U.S.P.Q. 260 (Ct. Cl. Trial Div. 1979) and *Mechanical Plastic Corp. v. Rawlplug Co.*, 14 U.S.P.Q.2d 1058 (S.D.N.Y. 1989) is also misplaced. Unlike this case, there is no evidence in *General Electric* that the examiner actually reviewed the interference record. Moreover, when *General Electric Co.* was decided, the Interference Board had no jurisdiction over the issue of patentability; the "on-sale" issue in *General Electric Co.* was, therefore, never addressed by the Board. (206 U.S.P.Q. at 279.) *Mechanical Plastic Corp. v. Rawlplug Co.*, is equally inapposite. In *Mechanical*, the applicant had taken a position during an interference that contradicted his subsequent position during prosecution that he was the sole inventor. Here, Amgen's positions in the interference and during the subsequent prosecution were not inconsistent whatsoever. Furthermore, in *Mechanical*, the Board did not reach the issue of inventorship. Here, the Board specifically decided the issues regarding molecular weight and the monosaccharide composition data. Thus, unlike *Mechanical*, the Board's decision as to these issues was binding on the Examiner. Finally, although the interference record was apparently before the Examiner in *Mechanical*, there is no evidence that the Examiner expressly recorded in the file history that he in fact had reviewed the record. Given the applicant's contradictory positions regarding inventorship and the Board's failure to decide inventorship, the court in *Mechanical* would not make the assumption that the Examiner had in fact reviewed the interference record. Here, no such assumption is required since the Examiner explicitly recorded that he reviewed the record.

[25] *See* Amgen Mem. at pp. 10-11.

[26] Defendants' Opp. at p. 9.

accused it of inequitable conduct in the appeal proceedings from the interference on the basis of the very arguments Defendants currently make.[27] Defendants have no bases for asserting that Amgen withheld the incorrect monosaccharide data.

D. THE PTO RECEIVED AND CONSIDERED ALL OF AMGEN'S SDS-PAGE INFORMATION REGARDING rEPO AND uEPO.

In their Amended Answer, Defendants only cite a document entitled "Egrie Input" as the information that was withheld from the PTO regarding the SDS-PAGE comparison of rEPO and uEPO. Since Defendants now admit that the Egrie Input document was submitted in the interference and that the pertinent pages were expressly argued by G.I. and considered by the Board in its decision,[28] Defendants scramble to point to other documents that were allegedly withheld. In this attempt, Defendants now assert that Amgen failed to disclose other Egrie documents and publications containing allegedly inconsistent SDS-PAGE data. But, as shown in Exhibit B hereto, all of the documents and publications that Defendants now assert were not disclosed were in fact disclosed to the PTO. All of Dr. Egrie's laboratory notebooks were exhibits in the interference as were her two publications. Defendants have not cited a single document that was withheld.

In addition to the information submitted during the interference, Amgen also disclosed information to the Examiner after the conclusion of the interference. In particular, Amgen submitted the declaration of Dr. Richard D. Cummings in support of the differences in glycosylation between uEPO and rEPO.[29] Attached to Cummings' declaration is the Amgen publication Browne et al. (1986) which Defendants allege was withheld.[30] Dr. Cummings

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[27] Ex. G at AM 17 017077-79 to Wong Decl. II.

[28] *See* TKT/HMR's Responses to Amgen's Statement of Undisputed Facts ("Defendants' Response") Nos. 11-14.

[29] Ex. H to Wong. Decl. II.

[30] The disclosed Browne et al. (1986) reference expressly states that "human urinary EPO and CHO-cell-derived r-hEPO migrate identically in SDS-polyacrylamide gels, indicating that both molecules are glycosylated

also addressed in detail the Storring et al. publication which discloses analyses of four rEPOs and two different uEPOs and concludes that there were differences in glycosylation between the two urinary EPOs and between both uEPOs and the rEPOs.[31]

Still trying to point to something that was not disclosed, Defendants further assert the withholding of: (1) Judge Saris' finding that Amgen had not proven that there were any differences between rEPO and uEPO, and (2) the Kirin IEF test results.[32] Since neither of these allegations appear in either Defendants' interrogatory responses or Amended Answer, Defendants cannot raise them now. The record, however, again disproves Defendants' ill-founded and late accusations as Judge Saris' opinion was disclosed to the Examiners on at least three separate occasions.[33]

The Kirin IEF data is both immaterial and duplicative of information disclosed to the Examiner. The cited document sent to Amgen's Dr. Egrie in 1990 states only that Kirin's own uEPO (purified by a new method) "showed similar pattern to recEPO on IEF at Kirin."[34] This statement is not inconsistent with a claim to differences in glycosylation because "similar" is not "identical." Nor is it inconsistent with any information submitted or relied upon by Amgen. The Kirin document refers to a collaborative study being conducted by the World Health Organization ("WHO") and its National Institute for Biological Standards and

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to a similar extent." Ex. H to Wong Decl. II; Browne et al. (1986) at AM 27 02 116-25 (p. 698) (attached to the Cummings Declaration, filed with the PTO on 2/16/95 during prosecution of '933 Patent and disclosed in Information Disclosure Statements in the '080, '349, '698 and '422 patents). The Browne et al. paper also cites to the two Egrie publications.

[31] *Id* at pp. 7-11. Defendants assert that Amgen never told the Examiner that the glycosylation of some uEPOs differed from other uEPOs. Dr. Cummings' discussion of the Storring paper directly addresses this issue.

[32] Defendants' Opp. at 18.

[33] Ex. G at p. 2 to Wong Decl. II, Petition Under 37 CFR § 1.182 (AM 17 017068-085); July 23, 1993 Protest in '933 Patent File History at p. 3, Ex. I to Wong Decl. II, and April 8, 1994 Supplemental Information Disclosure Statement at 2, Ex. I to Wong Decl. II. The relevancy of Judge Saris' decision to these issues is unclear because the issue of differences between uEPO and rEPO in that litigation arose in the context of the enablement of the G.I.'195 patent and not to Amgen's pending claims to a product having glycosylation different from urinary EPO.

[34] *See* Ex. 32 at AM 47 014340 to Freeman Decl. (emphasis added).

Control ("NIBSC") for which some analyses were conducted at Kirin. The results of the NIBSC study were published in 1992 in the Storring et al. paper discussed in Dr. Cummings' declaration.[35] Using IEF, among other techniques, Storring et al. compared two uEPO preparations and four rEPO preparations, including Amgen's rEPO, and found that one of the uEPO preparations had a "similar" IEF pattern to the rEPOs but that "there were also differences . . . in the proportions and/or types of EPO isoforms present." Thus, the information from Kirin duplicated that disclosed to the Examiner by submission of the Storring et al. publication.

E. THE RESULTS OF THE GOLDWASSER STUDY WERE DISCLOSED TO THE PTO.

1. The ITC decision and Dr. Goldwasser's testimony discloses Goldwasser's study and its results.

Defendants admit that Amgen disclosed the ITC decision to the PTO.[36] This admission forces Defendants to assert that the ITC decision is insufficient to disclose Goldwasser's study and its results.[37] But the record, as shown in Exhibit C hereto, proves the contrary.

During prosecution, Amgen pointed the Examiner to the pages of the ITC decision relevant to the patentability and long-felt need for a therapeutically effective EPO product.[38] Indeed, the prosecution history shows that the Examiner specifically received and considered the ITC decision: ". . .the evidence of secondary considerations presented as the findings of

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[35] *See* Ex. H to Wong Decl. II.

[36] Defendants' Response at 2 ("TKT/HMR admit that Amgen submitted an amendment dated June 2, 1989 in the prosecution of USSN 113,179 that refers to the initial determination of Judge Harris in the Investigation No. 337-TA-281"); Defendants' Response at 4 ("TKT/HMR further admit that Amgen submitted the decision in the *Fritsch v. Lin* interference proceedings."); Defendants' Response at 5 ("TKT/HMR further admit that a paper filed with the patent office dated May 1, 1989 in USSN 133,170 indicates that the decision was submitted to the patent office.")

[37] *See* Defendants' Opp. at 14.

[38] *See* Exs. 2, 7 to Wong Decl. Amgen specifically pointed out to the Examiner pages 50-52 of Judge Harris' decision, whose pin-point citations directed the Examiner to Dr. Goldwasser's relevant testimony. *See* Ex. 2 at 6 to Wong Decl.

fact of the ITC decision submitted warrant removal of rejections over prior art which teach isolation of EPO from urine."[39] In those sections, Judge Harris found that the amounts necessary to study the therapeutic effectiveness of purified EPO in clinical trials were unavailable, and therefore, studies were limited to investigative research:

> "... [P]rior to the invention of recombinant EPO there was simply not enough EPO available to perform any sort of clinical study into this question [whether inhibitors would blunt the effect of EPO therapy]. Goldwasser, Tr. 22; FF 97,98."[40] ...
>
> "Efforts were made to obtain purified EPO from natural sources such as the urine of patients with aplastic anemia. FF 87-89. However, the result of these efforts yielded a small amount, barely enough for investigative research and far too little for clinical research into its effectiveness as a treatment for anemia. Goldwasser, Tr. 22."[41] ...
>
> "In sum, prior to 1983, therapeutic amounts of human EPO were not available to conduct clinical trials. (Goldwasser, TR. 23)"[42]

Notably, Judge Harris explicitly directs the reader to Dr. Goldwasser's testimony at "**Tr. 22**" and "**Tr. 23.**" At these pages, Dr. Goldwasser discusses the study that Defendants currently claim was not disclosed and describes it as "abortive" and its results as statistically insignificant and unable to show the "potential therapeutic effect" of EPO.[43] Thus, contrary to Defendants' assertion, the ITC decision discloses Goldwasser's study and its results.

Unable to undermine Judge Harris' findings, Defendants attack Dr. Goldwasser's testimony as being inconsistent with other statements of his and his colleague, Dr. Baron. However, the acknowledgement that some biological responses were observed during the

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[39] Ex. Q to Wong Decl. II, Office Action, June 20, 1989, at 7, U.S. Patent No. 5,547,933 and, as shown above, that the Examiner received and considered the interference record which contains both the ITC decision and Goldwasser's testimony.

[40] *See* Ex. 1 at p. 50 to Wong Decl.

[41] *See* Ex. 1 at pp. 51-52 to Wong Decl.

[42] *See* Ex. 1 at p. 92 to Wong Decl.

[43] Exhibit 5 to Decl. of R. Wong, pp. 22-23. Furthermore, Dr. Goldwasser in the 10 years since this testimony has not changed interpretation of these tests but rather reaffirmed them. *See* Ex. 6 to Wong Decl. No contrary view exists in the scientific community as the study's results were never deemed worthy of publishing.

study is not inconsistent with Dr. Goldwasser's testimony that the study failed to show that uEPO was therapeutically effective for treating the anemia of chronic renal failure. In fact, Defendants omit that the Goldwasser/Baron progress report stated that "there was no significant increase in the hematocrit observed" and that larger "amounts of purified hormone" and "more prolonged therapy" were needed "to adequately assess the potential role of erythropoietin administration in the therapy of anemia of chronic renal disease."[44]

Significantly, while attacking Dr. Goldwasser's personal knowledge and skilled opinion regarding the results of his study, Defendants provide no competent, much less contemporaneous, evidence of their own. Rather, Defendants proffer only the declaration of Mr. Chisum who admits he is not a medical doctor, clinician, scientist, or one of any skill in the art and that he is incompetent to determine whether a clinical trial with therapeutically effective amounts of EPO had been conducted.[45] Where an "expert" has no background in the art, and is merely acting as an advocate by giving his interpretation of claims, such testimony should not be considered.[46] Dr. Goldwasser's testimony that his abortive study failed to "see any result" therefore remains uncontroverted.[47]

In fact, Defendants fail to disclose that their own clinical expert, Dr. Means, agreed with Dr. Goldwasser's conclusions:

> "Q. Do you think that they used an appropriate amount in the sense that the therapeutic efficacy is used in the business -- in the profession?
>
> A. I would say -- they did not use an amount that was large enough to increase the hemoglobin and hematocrit.

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[44] *See* Ex. 8 at 2-3 to Freeman Decl.

[45] Ex. J to Wong Decl. II; Chisum Depo., pp. 22:12-24:6, 39:3-19, 270:1-18; 273:23-275:23.

[46] *See General Battery Corp. v. Gould*, 545 F. Supp. 731, 750 (D. Del. 1982).

[47] Where there is expert testimony, an Examiner cannot refute the significance of scientific investigations. *See In re Zeidler*, 682 F.2d 961, 966 (CCPA 1982); *see also In re Alton*, 76 F.3d 1168, 1174-75 (Fed. Cir. 1996). Thus, even if Amgen had been in a position to submit the raw data or underlying documents relating to Goldwasser's study, the Examiner would not have been permitted to second-guess Dr. Goldwasser's testimony.

Q. And you realize that that was a conclusion that they reached, too?

A. Yes. And, yeah, that was -- they were right about that.

. . .

Q. So would you agree then that the Goldwasser test did not produce an efficacious response in that sense?

A. In the sense of producing a therapeutic in the business -- in the routine clinical sense, yes, I would say it was not."[48]

Defendants other clinical expert, Dr. Erslev, agreed that Goldwasser's study was "very limited" and "abortive," and that if EPO's therapeutic effect were ever to be proven larger amounts of EPO would have been required.[49] Thus, it is hardly surprising that Defendants restricted their evidentiary showing to Chisum who readily professes his incompetence to testify about the technical aspects of Goldwasser's study.

2. Defendants' claim construction of "therapeutically effective amount" is flawed.

Given Dr. Goldwasser's incontrovertible testimony, Defendants and their experts are forced to attempt to redefine the claim term "therapeutically effective amount" in order to contrive a basis for asserting that Goldwasser's study results were material.[50] The plain and ordinary meaning of this term is "an amount sufficient to provide treatment or therapy to a patient." In arguing for a broader construction that includes an amount sufficient to achieve any biological effect of EPO, Defendants misquote and misread the specification and prosecution history.

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[48] Ex. K to Wong Decl. II; Means Depo. pp.116:11-21, 121:6-11, February 10, 2000. Dr. Means drew a distinction between the ordinary use of the term "therapeutically effective" as used in the clinical treatment of anemic patients and his view on how the term is used in the Amgen patents.

[49] Ex. L to Wong Decl. II, Erslev Depo., pp. 104:4-18, 110:9-14 and 20-22, 114:21-115:7.

[50] It should be apparent that the Goldwasser study is not material to any of the claims of the '933, '080, '698 or '349 patents because these patents do not claim ***urinary*** EPO. Similarly, claim 1 of the '422 patent excludes uEPO by the phrase "purified from mammalian cells grown in culture." Unasserted claim 2 of the '422 patent

Consistent with its ordinary meaning, the patent specification makes plain that "therapeutically effective" is directed to treatment of disease states and not to a mere biological response such as an increase in reticulocytes:

> 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 which allow for provision of erythropoietin therapy, especially in the treatment of anemic disease states and most especially such anemic states as attend chronic renal failure.

Col. 12:1-7 of the '933 patent specification.

Indeed, the specification expressly states that "effective" dosages are to be determined relative to the disease condition being treated.[51] The relevant disease condition for purposes of evaluating the significance of Goldwasser's study, according to Defendants' own expert is the anemia of chronic renal failure.[52] As Defendants' experts all agree, effective treatment of the anemia associated with chronic renal failure requires an increase in hematocrit.[53] Because Defendants admit that Goldwasser's study failed to demonstrate an increase in hematocrit,[54] Goldwasser's results therefore could not have been deemed material.[55]

(like the other composition claims) distinguishes uEPO by the phrases "therapeutically effective amount" and "pharmaceutically-acceptable preparation."

[51] The '933 specification states: "Effective dosages are expected to vary substantially depending upon the condition treated but therapeutic doses are presently expected to be in the range of 0.1 (~7U) to 100 (~7000 U) g/kg body weight of the active material." Col. 33: 57-61.

[52] Ex. M to Wong Decl. II; Erslev Depo., p. 26:10-25, February 4, 2000. Dr. Erslev also admitted that it would be impossible to tell if a patient's anemia was corrected with only the knowledge of an increase in reticulocytes. Erslev Depo., pp. 128:23-129:7.

[53] Ex. N to Wong Decl. II; *see* Means Depo., pp. 21:21-22:8, February 10, 2000; Erslev Depo., pp. 114:21-115:11, February 4, 2000. *See also* Amgen's Reply to Defendants' Claim Construction Submission on the '349 and '422 Patents at 14-15, Docket No. 199.

[54] Defendants' Response at 12; *see also* Ex. R to Wong Decl. II, Means Depo., pp. 115:20-116:21, 118:21-119:18, February 10, 2000, Erslev's Depo., pp. 114:21-115:11, February 4, 2000,.

[55] As set forth in 37 C.F.R. § 1.56(b) the standard for "materiality" is a "prima facie case of unpatentability." Absent a "therapeutically effective amount" or being a "pharmaceutically-acceptable preparation,"

Defendants' reliance on the sentence at Col. 33, lines 20-30 to construe the term "therapeutically effective amount" as including any biological response is misplaced because the term does not appear in that sentence.[56] Moreover, the sentence simply states that products of the invention "are conspicuously suitable for use in erythropoietin therapy procedures . . . to develop any or all of the effects herefore attributed in vivo to EPO." The use of any amount of EPO would "develop" its biological effects because that is what EPO does, but that does not mean it is an "effective" amount to treat anemia. To construe the term "therapeutically effective amount" to include an amount to "develop" any of the biological activities of EPO would render the term meaningless.[57]

The fact that "therapeutically effective amount" as used in the claims is distinct from the biological activity of increasing production of reticulocytes is made plain by a comparison of the dependent pharmaceutical composition claims of the '080 and '933 patents with the independent product claims. The product claims recite the biological activity of increasing production of reticulocytes while the dependent pharmaceutical composition claims add the further limitation of a "therapeutically effective amount" of the product.[58] Thus, "therapeutically effective amount must mean something different from simply increasing production of reticulocytes as argued by Defendants.

Goldwasser's uEPO does not provide a basis for a prima facie case of unpatentability of any claim of the Amgen patents.

[56] Amgen told the Examiner that "[i]t is believed that these sentences from the specification and others provide a clear and definite description of the uses for which the claimed erythropoietin compositions would be therapeutically effective." *See* Ex. 3 at 2 to Freeman Decl. (emphasis added). Amgen then pointed out that "the claim language 'therapeutically effective amount' is commonly used in this type of case where the product is useable to treat various conditions. Accordingly, the term is defined and meaningful to one of skill in the art. . . ." *Id.* Therefore, Amgen clarified that therapeutically effective was to be defined by "one of skill in the art" in terms of the uses of rEPO for disease states and not simply its biological effects.

[57] HMR's 30(b)(6) witness, Dr. Hahner, stated that it would be "meaningless to the patient" to have an increase in reticulocytes without an increase in hematocrit. Hahner Dep. 421-422, 466-467. Wong Decl. II Ex. Z.

[58] Compare, e.g., '080 dependent claim 4 with claims 1-3.

Defendants further assert that the Miyake publication proves that there was enough uEPO to treat many more patients for a much longer period than in Goldwasser's study.[59] Defendants' assertion, however, contradicts the Goldwasser testimony that they rely upon[60] and the findings of various judicial and administrative bodies that before the advent of Dr. Lin's inventions there was a long felt need for sufficient amounts of EPO.[61] In any event, Defendants can hardly assert inequitable conduct on this basis given that Defendants admit that Amgen repeatedly disclosed to the Examiner the Mikaye et al. reference.[62]

Finally, Defendants do not contest the prior findings of this Court that Goldwasser's uEPO preparation was impure.[63] As this Court found in the *Chugai* litigation, in order for an EPO preparation to be a pharmaceutical composition, the EPO must be homogeneous,[64] and since the Goldwasser uEPO was held not to be homogeneous, it cannot be considered a "pharmaceutically-acceptable preparation" as recited in claim 2 of the '422 patent.[65]

3. Defendants present no evidence of an intent to deceive the PTO.

Significantly, Defendants present no evidence that would directly indicate or serve as the basis for a proper inference of an intent to deceive. Regarding Goldwasser's study, Defendants assert that Dr. Lin had knowledge of the study but, neglect to tell the Court that Dr. Lin testified that Dr. Goldwasser told him that the study results showed that the uEPO

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[59] Defendants' Opp. at 13.

[60] Freeman Decl. Ex. 5; Goldwasser Depo. 186:5-13, October 13, 1999.

[61] *See* Ex. 1 at pp. 50-52 to Wong Decl.; *see also* discussion and citations, Amgen Mem. pp. 15-16.

[62] Defendants' Response at 10.

[63] *See* discussion and citations, Amgen Mem. pp. 15-16.

[64] Ex. 17 to Wong Decl.

[65] Additionally, it should be noted that Defendants' fail to prove Goldwasser's study even qualifies as prior art under 35 U.S.C. § 102. Nor can they, as even Dr. Goldwasser described his study as an "abortive trial"—an experiment that he ultimately abandoned. *Fishburne Equip. Co. v. Lee Mach -Hydraulic, Inc.*, 203 U.S.P.Q. 601, 608 (W.D.N.C. 1978).

given was "not effective" and that the patients had "no response to the treatment."[66] Defendants also seek to rely on a 1990 memorandum which only provided attached hand-written (and nearly illegible) raw patient data showing no increase in hematocrit over the course of treatment.[67] Defendants also cite to a 1984 memorandum discussing dosing for Amgen's rEPO product in which a single sentence refers to Goldwasser's study along with Dr. Eschbach's sheep EPO study as "suggest[ing] a dose of ~1000 U/70kg **may** be efficacious."[68] Bereft of any probative value, it is hardly surprising that Defendants notably failed to allege in their Amended Answer that the 1984 memorandum constitutes a basis for inequitable conduct.

Given Dr. Goldwasser's testimony of his "abortive" study and its lack of results and the findings of the ITC and this Court regarding the long-felt need for therapeutically effective EPO, no grounds exist for a finding or an inference of intent.

F. AMGEN DID NOT WITHHOLD FROM THE PTO ANY MATERIAL INFORMATION REGARDING THIS LITIGATION.

Although not pled in their Amended Answer or included in their interrogatory responses, Defendants now seek to charge Amgen with inequitable conduct for failing to disclose the present litigation to the PTO. This allegation should not be considered because it was not pleaded, but in any event, the allegation is meritless.

As set forth in 37 C.F.R. §1.56 a patent applicant only has a duty to disclose "material" information which is defined as information that establishes a prima facie case of

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[66] Ex. O to Wong Decl. II; Lin Depo., pp. 60:17-61:4, October 4, 1999.

[67] Ex. P to Wong Decl. II; Ex. 7 to Freeman Decl.; *see also* Expert Report of Dr. Joseph Eschbach ¶ 50, January 20, 2000.

[68] Ex. 10 at AM 47 022967 to Freeman Decl. (emphasis added). But if Goldwasser's study with human patients had proven that a "therapeutically effective" amount of EPO had been successfully administered, as Defendants contend, the 1984 memorandum would not have used such speculative language and there would have been no need to take guidance from a sheep EPO study.

unpatentability.[69] With the filing of the lawsuit in 1997, Amgen disclosed to the PTO the existence of the present litigation, informing the PTO that the '933, '698 and '080 patents were in suit and therefore could not disclose any of the information relied upon by Defendants.[70] Moreover, as is clear from its claim construction submissions, Amgen relies upon the plain meaning of the claim terms of the '933, '080, and '698 patents. Accordingly, before the issuance of the '349 and '422 patents, Amgen did not take any positions in the litigation that were in any way inconsistent with its prosecution of the applications leading to the '349 and '422 patents. Furthermore, as evidenced by Amgen's motions for discovery sanctions and for failure to plead inequitable conduct with particularity, Amgen did not receive Defendants' factual allegations of invalidity or inequitable conduct until after the '349 and '422 patents had issued.[71] Thus, before the issuance of these patents, there was no material information from this litigation to disclose.[72]

IV. CONCLUSION

For the foregoing reasons, Amgen submits that summary judgment should be entered and Defendants' inequitable conduct defense be dismissed.

Dated: March 21, 2000

For the Plaintiff AMGEN INC.

By: 

D. Dennis Allegretti (BBO #545511)
DUANE, MORRIS & HECKSCHER LLP
One International Place
Boston, MA 02110-2600
(617) 598-3100

[69] 37 C.F.R. § 1.56.

[70] Goolkasian Decl. at ¶ 10, March 20, 2000; Ex. AA to Wong Decl. II.

[71] *See* Defendants' Opp. to Amgen's Motion to Strike Defendants' Twelfth Affirmative Defense, November 23, 1999, Docket No. 230.

[72] Defendants' arguments raised in response to Amgen's 1997 summary judgment motion only addressed Defendants' non-infringement positions including the clinical trial exemption issue. Defendants arguments that they do not infringe the '933, '080 or '698 patents could not possibly be material to the patentability of Amgen's '349 or '422 patent claims.

Lloyd R. Day, Jr.
DAY CASEBEER
MADRID & BATCHELDER LLP
20400 Stevens Creek Blvd., Suite 750
Cupertino, CA 95014
(408) 255-3255

Edward M. O'Toole
MARSHALL, O'TOOLE, GERSTEIN,
MURRAY & BORUN
6300 Sears Tower
233 S. Wacker Drive
Chicago, IL 60606-6402
(312) 474-6300

CERTIFICATE OF SERVICE

I hereby certify that a true copy of the above document was served upon the attorney of record for each other party by hand on March 21, 2000.


Exhibit A

SEARCHED

Class	Sub.	Date	Exmr.
530	350	5/89	[illegible]
	397		
514	8		
424	99		
435	69.2		
	172		
updated search		1/89	[illegible]
Updated		5/89	
435	69.1, 69.4, 69.6, 240.2, 320.1, 172.3		
530	350, 380, 387, 834, 835	5/7/92	[illegible]
514	8		
424	27		
935	13		
To date		11/11/93	[illegible]

33. [illegible] 11/24/93
34. NO PATENT 12/27
35. Key 3 more 12/29
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SEARCH NOTES

	Date	Exmr.
Biosis, CAS, CAS	5/88	[illegible]
APS (updated)	5/7/92	[illegible]
(APS/file. Reviewed parent file 675,298. Reviewed interference file #102,334. Reviewed published interf. decisions (Fritsch v. Lin) & Amgen v. Chugai (18 USPQ2d 1016)) Oct-Nov 1993 Fitzgerald: [illegible]		

INTERFERENCE SEARCHED

Class	Sub.	Date	Exmr.
530	397	11/22/93	[illegible]
	399		
514	8		


Exhibit B

EXHIBIT B

ASSERTED NONDISCLOSURE	DISCLOSURE IN FACT
Freeman Ex. 13: **Egrie, et al., October 1984 Abstract entitled "Characterization of Recombinant Human and Monkey Erythropoietin."** *See*, Defs. Opp. at 5, 8, 16-17; Defs. Resp. To Stmt. Nos. 9, 14.	**Disclosed** at Interference Exhibit 218 (Ex. S to Wong Decl. II: Full publication of Egrie, et al., October 1984 Abstract: **Egrie et al., "Characterization of Recombinant Monkey and Human erythropoietin" in Exp. App. For the Study of Hemoglobin Switching, pp. 339-350 (1985).**
Freeman Exs. 14 and 53: Correspondence reflecting that the **carbohydrate data included in Amgen's patents is erroneous.** *See*, Defs. Opp. at 8, 9; Defs. Resp. To Stmt. Nos. 9, 16.	**Disclosed** at *Fritsch v. Lin*, 21 U.S.P.Q.2d 1739 at 1741: Disclosing that the **hexose values (carbohydrate data) contained in Amgen's patents are incorrect** (Ex. 11 to Wong. Decl.). **Disclosed again** as Exhibits (Sasaki et al., and Takeuchi et al.) to Cummings Declaration, filed 2/16/95 during prosecution of the '933 Patent (Ex. H to Wong Dec. II: Disclosing **correct hexose values**. **Disclosed** at Interference Exhibit 399 (excerpts from Amgen's PLA) (Ex. 15 at Wong Decl): Disclosing **correct carbohydrate data.**

EXHIBIT B (continued)

ASSERTED NONDISCLOSURE	DISCLOSURE IN FACT
Freeman Ex. 15: **Browne et al., Cold Springs Harbor Symposia on Quantitative Biology 51: 693-702 (1986).** *See*, Defs. Opp. at 8, 16-17; Defs. Resp. To Stmt. Nos. 9, 14, 18.	**Disclosed** as Exhibit to Cummings Declaration, filed 2/16/95 during prosecution of the '933 Patent (Ex. H to Wong Decl. II); **Disclosed** in Information Disclosure Statements to the '080, '698, '349 and '422 Patents (Ex. T to Wong Decl. II); and **Disclosed** in Interference Exhibit 396 (Ex. U to Wong Decl. II): Each of which disclose **Browne et al., Cold Springs Harbor Symposia on Quantitative Biology 51: 693-702 (1986).**
Freeman Ex. 17 (A 95578, A 95587-98, A 95582, 85-86): **"Egrie Input" File.** *See*, Defs. Opp. at 6, 8, 9, 16-18; Defs. Resp. To Stmt. Nos. 9, 14.	**Disclosed** as Lin Interference Exhibit 115 and DX 316 in prior Boston Litigation (submitted to the PTO with testimony from Dr. Egrie by the Party Fritsch) (Ex. 10 to Wong Decl.): Each of which discloses the **"Egrie Input" File** and/or data contained therein. *See also*, Defendants "admit that the party Fritsch submitted the 'Egrie Input' document in the interference proceedings . . ." [Defs. Resp. To Stmt. No. 12].

EXHIBIT B (continued)

ASSERTED NONDISCLOSURE	DISCLOSURE IN FACT
Freeman Ex. 19 (AM 47 028391): **Egrie et al., Exp. App. For the Study of Hemoglobin Switching, pp. 339-350 (1985).** *See*, Defs Opp. at 5, 8, 16-17; Defs. Resp. To Stmt. Nos. 9, 14.	**Disclosed** as Interference Exhibit 218 (Ex. S to Wong Decl. II): **Egrie et al., Exp. App. For the Study of Hemoglobin Switching, pp. 339-350 (1985).**
Freeman Ex. 21. (p. 69): Excerpts from the **laboratory notebook of Joan C. Egrie** reflecting comparative rEPO and uEPO studies:	**Disclosed** in Interference Ex. 114, 116-119 (Ex. V to Wong Decl. II); Ex. 115 (Ex. 9 to Wong Decl.): Excerpts from the **laboratory notebook of Joan C. Egrie** reflecting comparative rEPO and uEPO studies: *See also,* Defendants admit that excerpts of the laboratory notebooks of Dr. Egrie and Amgen scientist Geri Lane as Lin Exhibits 114-119 in the interference proceeding. (p. 20) Included in these notebooks submissions were SDS-PAGE gels showing a comparison between COS or CHO produced EPO and urinary EPO. [Defs. Resp. To Stmt. No. 11] *See also,* Defendants admit that "in her [interference] declaration, Dr. Egrie admitted that Amgen's COS rEPO had the same molecular weight as uEPO." [Defs. Resp. To Stmt. No. 9]. *See also,* Defendants admit that Fritsch's Reply Brief in the Interference Proceeding argues: ". . . the primary examiner was not informed of an SDS-PAGE gel prepared by Dr. Egrie in September 1984, two months before Lin's involved application was filed, in which two

EXHIBIT B (continued)

ASSERTED NONDISCLOSURE	DISCLOSURE IN FACT
	uEPO samples were compared with Lin's rEPO. The rEPO sample migrated identically with the uEPO samples on the gel, clearly contradicting the import of the [patent's disclosure] of an apparent difference in molecular weight between rEPO and uEPO." [Defs. Resp. To Stmt. No. 13] *See also,* Defendants admit that, in the Interference Proceeding, Fritsch argued: "an entry in Dr. Egrie's own notebook No. 633 dated 9/19-9/21/84 states that Amgen's rEPO appeared to be the same size as uEPO sample obtained from Alpha Therapeutics and a uEPO sample designated as "Lot 82." Dr. Egrie has acknowledged that the uEPO and rEPO samples migrated identically on the SDS-polyacrylamide gel . . ." [Defs. Resp. To Stmt. No. 13]
See, Defs. Opp. at 5, 8, 9, 16-18; Defs. Resp. To Stmt. Nos. 9, 14.	
Freeman Ex. 22 (p. 218): **Egrie et al., Immunobiol. 172:213-224 (1986).** *See*, Defs. Opp. at 8, 16-17; Defs. Resp. To Stmt. Nos. 9, 14.	**Disclosed** as "Publication 1" attached to Lin's Notice IV (AM 17 028197-208) (Ex. W to Wong Decl. II): **Egrie et al., Immunobiol. 172:213-224 (1986).**

EXHIBIT B (continued)

ASSERTED NONDISCLOSURE	DISCLOSURE IN FACT
Freeman Ex. 32 (AM 47 014340) Kirin data allegedly reflecting that **uEPO and rEPO possess "similar patterns" on IEF.** *See,* Defs. Opp. at 8, 9; Defs. Resp. To Stmt. Nos. 9, 14	**Disclosed** at Storring et al., attached as an exhibit to the declaration of Richard Cummings, and submitted to the Patent Office during prosecution of the '933 Patent on 2/16/95 (Ex. H to Wong. Decl. II). Publication of a World Health Organization study comparing the IEF patterns of two uEPO preparations and four rEPO preparations, including a sample of Amgen's rEPO, and providing that **one of the uEPO preparations and the four rEPO preparations had "similar" IEF points.**
Freeman Ex. 46 (p.24347): **Vapnek et al., Banbury Report 29 (1992).** *See,* Defs. Opp. at 8, 16-17; Defs. Resp. To Stmt. Nos. 9, 14.	**Disclosed** as "Publication 16," attached to Lin's Notice IV (AM 17 024642-657) (Ex. X to Wong Decl. II): **Vapnek et al., Banbury Report 29 (1992).**
Freeman Ex. 49 (pp. 118-126): Describing **Dr. Strickland's work with uEPO and rEPO.** *See,* Defs. Opp. at 6, 8, 9, 16-18; Defs. Resp. To Stmt. Nos. 9, 14.	**Disclosed** in Interference Exhibit 399 (Ex. 15 to Wong Decl.) and as "Publication 1" attached to Lin's Notice IV (AM 17 028197-208) (Ex. W to Wong Decl. II): Excerpts from Amgen's PLA and an Amgen publication disclosing **Dr. Strickland's work with uEPO and rEPO.**

EXHIBIT B (continued)

ASSERTED NONDISCLOSURE	DISCLOSURE IN FACT
Freeman Ex. 50: Testimony describing **the submission of Dr. Strickland's work with uEPO and rEPO to FDA.** *See*, Defs. Resp. To Stmt. Nos. 9, 18.	**Disclosed** in Interference Exhibit 399 (Ex. 15 to Wong Decl.): **The submission of Dr. Strickland's work regarding uEPO and rEPO to FDA:** *See also*, Defendants "admit that excerpts from Amgen's PLA was submitted in the interference proceeding . . ." [Defs. Resp. To Stmt. No. 18]
Judge Saris' decision in ***Amgen Inc. v. Chugai Pharmaceuticals Co., Ltd.*, 13 U.S.P.Q.2d 1737 (D. Mass. 1989)** *See*, Defs. Opp. at 8, 9, 17; Defs. Resp. To Stmt. Nos. 9, 14.	**Disclosed** at 3/6/92 Petition Under 37 C.F.R. § 1.182 (Ex. G to Wong. Decl. II); **Disclosed again** at 7/23/93 Protest, Exhibit B (Ex. I to Wong. Decl. II); and **Disclosed again** at 4/8/94 Supplemental Information Disclosure Statement (Ex. I to Wong. Decl. II): Each of which discloses Judge Saris' decision in ***Amgen Inc. v. Chugai Pharmaceuticals Co., Ltd.*, 13 U.S.P.Q.2d 1737 (D. Mass. 1989).**

EXHIBIT C (continued)

ASSERTED NONDISCLOSURE	DISCLOSURE IN FACT
	b. The trial was "an abortive trial" (ITC Goldwasser Depo pp. 22-23.) (Ex. A to Wong Decl. II) **c. It "is absolutely correct" that therapeutic amounts of EPO were not available. (ITC Goldwasser Depo pp. 22-23.) (Ex. A to Wong Decl. II)** **d. "If [EPO's] potential therapeutic effect were ever to be found out, it needed to have large enough amounts to use relatively large doses in the patient and to use enough patients to get statistically significant results." (ITC Goldwasser Depo pp. 22-23.) (Ex. A to Wong Decl. II)**
See, Defs. Resp. To Stmt. Nos. 2, 4, 6-7, 11; Defs. Opp. at 14.	
Defendants assert that "Amgen never submitted Dr. Baron's letter to the PTO nor did Amgen at any time tell the PTO the results of the Goldwasser clinical trial that demonstrated that urinary EPO is therapeutically effective." *See* Defs. Resp. To Stmt. No.12; Freeman Ex. 9.	**Defendants' have presented no evidence to show that anyone at Amgen involved in the prosecution of the patents in suit was aware of Dr. Baron's letter and was in a position to disclose it.** **As shown above, Amgen accurately disclosed its knowledge of the Goldwasser's study to the PTO. (See ITC Goldwasser Depo. pp. 22-23.) (Exs. 2, 3, 25 to Wong Decl.)**

EXHIBIT C (continued)

ASSERTED NONDISCLOSURE	DISCLOSURE IN FACT
Defendants assert that Dr. Lin testified that he knew before the filing of the '298 application in 1984, that Dr. Goldwasser had conducted a clinical study and failed to disclose it. *See* Defs. Opp. at 12; Freeman Decl. Ex 6; Def. Opp. to Amgen's Motion to Strike.	**Dr. Lin's testimony actually stated that Dr. Goldwasser had told him that the study results showed the uEPO given was "not effective" and that the patients had had "no response to the treatment." Lin Depo. pp. 60:17-61:4. (Ex. O Wong Decl. II)**
Defendants assert that Amgen's counsel, Steve Odre, knew about both Goldwasser sheep EPO work and "clinical study" but disclosed only the sheep work to the PTO. *See* Defs. Opp. at 13, Freeman Decl. Ex. 7, Freeman Decl. Ex. 11.	**As shown above, Amgen disclosed Goldwasser's study to the PTO. (See ITC Goldwasser Depo. pp. 22-23.) (Exs. 2, 3, 25 to Wong Decl.)**
Defendants assert that Amgen failed to disclose to the Examiner that "Miyake published that they obtained 720,000 units of uEPO in a single purification." *See* Defs. Opp. at 13, Freeman Ex. 6.	**Miyake et al. was repeatedly disclosed to the PTO and is cited in the patent specification at Col. 7, lines 10-17, U.S. Patent No. 5,547,933. (See also IDS 12/24/96, Paper No. 7, U.S. Patent No. 5,621,080; IDS 1/3/96, Paper No. 9, U.S. Patent No. 5,756,349; IDS 1/3/96, Paper No. 10, U.S. Patent No. 5,618,698.)**