EXHIBIT 16

IN THE

UNITED STATES PATENT and TRADEMARK OFFICE

Before the Board of Patent Appeals and Interferences

Interference No. 102,334

FRITSCH

v.

LIN

Examiner-in-Chief Marc L. Caroff

REPLY BRIEF FOR THE PARTY FRITSCH

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TABLE OF CONTENTS

TABLE OF CONTENTS (Cont.)

TABLE OF AUTHORITIES

Page

CASES

TABLE OF AUTHORITIES

TABLE OF AUTHORITIES

STATUTES AND RULES

OTHER AUTHORITIES

INTRODUCTION

Lin's case rests almost entirely on the alleged preclusive effect of the district court and Federal Circuit decisions in the Amgen v. Chugai litigation. Resurrecting arguments from its previously-filed Motion For Judgment, Lin urges that the district court's finding of "simultaneous conception and reduction to practice," which survived appellate review under the "clearly erroneous" standard, disposes of all priority issues here. Lin argues that those same decisions also dispose of the patentability issues raised in Fritsch's preliminary motions.

In effect, Lin argues that all of the evidence of record here is irrelevant, that the Board of Patent Appeals and Interferences is an impotent tribunal with no function but to rubber-stamp the courts' decisions, and that this entire interference proceeding is a nullity. Lin does not rebut the authorities cited by Fritsch which demonstrate that the Amgen decisions are not binding here, and it ignores the extensive evidence summarized in Fritsch's main brief which shows that both priority and patentability issues should be decided in Fritsch's favor.

As shown below: (1) the Amgen decisions are not binding on the Board; (2) the doctrine of simultaneous conception and reduction to practice is inapplicable to the facts here; (3) the evidence now before the Board -- including substantial new evidence not of record in the Amgen litigation -- shows that Fritsch is

entitled to judgment of priority against Lin; and (4) Fritsch also is entitled to judgment that Lin's claims are unpatentable to Lin.

ARGUMENT

I. THE AMGEN DECISIONS ARE NOT BINDING HERE

A. The Board Must Make An Independent Determination Of Priority

Fritsch's Opposition to Lin's Motion for Judgment, filed May 15, 1991, explains in detail why the prior decisions of the Boston district court and the Federal Circuit are not binding on the Board in this interference. Briefly stated, 35 U.S.C. § 135(a) vests in the Board of Patent Appeals and Interferences exclusive authority to determine who is entitled to a patent based on priority of invention as between:

1. a patentee and an applicant (as in Interference No. 102,096) and
2. two applicants (as in Interference Nos. 102,097 and 102,334).

This unique and mandatory authority stems from 35 U.S.C. § 135(a), which provides: "The Board...shall determine questions of priority of the inventions...." (emphasis added). Indeed, the Commissioner in related Interference No. 102,097 has noted:

> Inasmuch as Congress has determined [35 U.S.C. § 135(a)] that the Commissioner in the first instance should resolve interferences, a very good case exists for having Interference No. 102,097 proceed expeditiously in the PTO-not some other forum.

Lin v. Fritsch, 14 USPQ2d 1795, 1801-02 (Comm'r of Patents and Trademarks 1989).

It has long been recognized that proceedings before other tribunals do not bind the PTO in interferences and cannot discharge the PTO's duty to independently decide questions of priority of invention. Judge Learned Hand explained the merit of this rule in affirming the PTO's refusal to be bound by a prior decision that the U.S. Court of Appeals for the Seventh Circuit had earlier made in an infringement action between the same parties to an interference:

> It has, however, apparently for many years been the practice of the Patent Office to refuse to recognize such findings as conclusive upon the issue of priority between inventors in interference proceedings. The theory is that the statute charges the Office and the Office alone with the duty of deciding which of two applicants is in fact the prior inventor, and that no decision of a court can divest it of the responsibility.
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> * * * *
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> Suppose that the Patent Office, although rightly of opinion that Sinko was not the first inventor and Johnson was, was constrained by the finding to award a patent to Sinko....The grant of such a patent would be a fraud; it would not represent the conclusion of the Office that the patentee was in fact the first inventor.

Sinko Tool & Mfg. Co. v. Automatic Devices Corp., 136 F.2d 186, 189-90, 57 USPQ 356, 359-60 (2d Cir. 1943) (emphasis added).

The Sinko decision was followed in Piher, S.A. v. CTS Corp., No. S 78-174, slip op. at 14, (N.D. Ind. Sept. 27, 1979) [Exhibit 2 accompanying Fritsch's Opposition to Lin's Motion For Judgment]:

> In Sinko, there had been a previous infringement suit between the same parties in which it had been held that certain tests had been made establishing a "reduction to practice". The Court discusses the question of "estoppel" at some length, and specifically held that it has no applicability to an interference proceeding between the parties in the Patent Office, because of the public duty which rests upon the tribunals of the Patent Office, to make its own determination of the question of priority of invention to insure that a patent shall be granted only to the true first inventor.

And as stated in Childers Foods, Inc. v. Rockingham Poultry Co-Op, Inc., 203 F. Supp. 794, 796-97, 133 USPQ 648, 650 (W.D. Va. 1962), the district court

> has no control over the Interference Proceeding.... [T]he finding of this court on the question of who was the first inventor will have little, if any, influence upon the conclusion to be reached in the Interference Proceeding.
>
> The determination of priority of invention, would seem to be a matter peculiarly within the expertise of the Patent Office.

Although Lin tries unsuccessfully to distinguish these cases, it cites no authorities to the contrary. In re Katz, 467

F.2d 939, 167 USPQ 487 (CCPA 1970), cited for the proposition that the Amgen decision is "res judicata" as to the priority issue, has nothing to do with interferences. It merely holds that an applicant who loses in both the district court and court of appeals in a section 145 action to compel issuance of a patent cannot go back to the PTO and try to obtain allowance of the same claims all over again.

Henning v. Hunt, 223 F.2d 926, 106 USPQ 307 (CCPA 1955), quoted at length in Lin's brief, involved a district court decision which reversed the final rejection of certain claims by the Patent Office Board of Appeals. The CCPA held that the Board was bound by this decision in later proceedings involving those same claims. Unlike the situation in Sinko Tool and here, there it was the Board's own action that was reviewed in the prior judicial action. There was no attempt in Henning to preempt the Board from rendering its own judgment in an interference proceeding based on the results of a prior infringement action.

In re Pearne, wherein the Commissioner denied a request for reexamination under 35 U.S.C. § 303, is even less pertinent. That case merely illustrates the Commissioner's broad discretion to determine whether a given reference raises "a substantial new question of patentability" with regard to reexamination of an issued patent. Pearne shows that one of the factors the Commissioner may consider in the exercise of that discretion is the result of prior litigation in which the reference was asserted as

prior art against the patent. The decision is irrelevant to the PTO's statutorily-imposed duty to decide priority issues in interferences under 35 U.S.C. § 135.

Finally, Lin's contention that the Amgen decisions are "the law of the case," LB 5,[1] is utterly meritless. That doctrine requires decisions on "issues of law" to be followed "in successive stages of the same litigation." 1B J. Moore, J. Lucas & T. Currier, Moore's Federal Practice, ¶0.404[1], at 117 (2d ed. 1991) (emphasis added). But this interference pursuant to 35 U.S.C. § 135 is not the "same litigation" as the Amgen patent infringement action; nor are the court's findings relied upon by Lin "issues of law." Thus, those findings are not controlling here.

B. The Board Must Make An Independent Determination Of Patentability

Similar considerations require the PTO to decide the issues of patentability raised by Fritsch's preliminary motions, several of which bear no relation to issues previously litigated.[2] Lin's brief unpersuasively attempts to distinguish Perkins v. Kwon,

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[1] "LB 5" refers to Lin's Brief at page 5. In addition, the following abbreviations are used throughout this Brief: "FB" (Fritsch's Main Brief in this interference); "FX" (Fritsch Exhibit); "LX" (Lin Exhibit); "FCX" (Fritsch Cross Exhibit); "LCX" (Lin Cross Exhibit); "FR" (Fritsch Record); "LR" (Lin Record). Citations to "Tr. Vol." refer to portions of the trial record in the Amgen district court litigation, submitted as part of Lin's record in this interference.

[2] E.g., motion I in the '334 interference (unpatentability under §102(b)); motion II in the '334 interference (no support under § 112 for subject matter described in count).

in which the Federal Circuit made it clear that because patentability issues concern not only the private rights of litigants, but also the rights of the public, the PTO must decide them as long as an appropriate record has been adduced:

> The legislative history [of the latest amendment to § 135(a)]...shows that Congress intended that if patentability is fairly placed at issue in the proceeding, it will be determined. ...[I]t would contradict the remedial purpose of the legislation if the Board could refuse to decide questions of patentability for which there had been adduced an appropriate record.
>
> * * * *
>
> The Board, by resolving both priority and patentability when these questions are fully presented, settles not only the rights between the parties but also rights of concern to the public. The public interest in the benefits of a patent system is best met by procedures that resolve administratively questions affecting patent validity that arise before the PTO. To do otherwise is contrary to the PTO's mission to grant presumptively valid patents, 35 U.S.C. § 282, and thus disserves the public interest.

Perkins v. Kwon, 886 F.2d 325, 328-29, 12 USPQ2d 1308, 1311 (Fed. Cir. 1989) (emphasis added).

Thus, the Board must render its own independent decision, based on the record now before it, as to priority of invention between the parties and the patentability of Lin's claims to Lin. Lin's arguments that the Board should abdicate its responsibility are plainly wrong and should be disregarded.

C. The Board Should Reach Different Conclusions From The Amgen Courts

The evidence presented herein, when evaluated in the context of the applicable law, mandates that the Board reach different conclusions than did the Amgen courts. The following factors distinguish this proceeding from the Amgen litigation:

- The Amgen district court made no findings on the critical issue of when Dr. Fritsch had sufficient information to distinguish the EPO gene from other materials, or when Dr. Fritsch's conception was sufficiently complete to enable a person to reduce the invention to practice with the exercise of no more than routine skill.
- The Amgen district court did not have before it all of the evidence from the present record showing that Dr. Fritsch's probing technique was fully operable prior to the isolation of the EPO gene.
- The Amgen district court explicitly "guaranteed" that it would not read or consider Fritsch's Rule 608(b) showing. Tr. Vol. 36, p. 6. Lin's argument that the Rule 608(b) evidence was "rejected" by the courts, LB 8, 35, is therefore meritless. This is additional important evidence which the courts did not consider and which is now available to the Board.
- Fritsch's assignee in the Amgen litigation had to prove prior invention by clear and convincing evidence; here,

properly so, the question is whether Fritsch's evidence meets the less stringent preponderance of the evidence standard. Reid v. Engelskirchen, 213 USPQ 59, 61 (Bd. Pat. Int. 1980); see also 18 C. Wright, A. Miller & E. Cooper, Federal Practice and Procedure, § 4422 at 209 (1981) ("well established principle that failure to carry a higher standard of proof does not preclude a subsequent attempt to satisfy a lower standard"); Restatement (Second) Of Judgments § 28(4) (1980).

- Lin's patent involved in the Amgen litigation was given a presumption of validity pursuant to of 35 U.S.C. § 282. No such presumption applies in this interference.

Moreover, the court of appeals reviews factual findings of both district courts and the Board under the "clearly erroneous" standard. Fed. R. Civ. P. 52(a); Lacotte v. Thomas, 758 F.2d 611, 613, 225 USPQ 633, 634 (Fed. Cir. 1985). The standard contemplates that different fact-finders can reach different conclusions based upon the same evidence, neither of which will be "clearly erroneous." Anderson v. City of Bessemer, 470 U.S. 564, 574 (1985) ("where there are two permissible views of the evidence, the fact-finder's choice between them cannot be clearly erroneous"). Further, it "does not entitle a reviewing court to reverse the finding of the trier of fact simply because it is convinced that it would have decided the case differently." 470 U.S. at 573. Thus,

where the record here is inconsistent with a finding by the district court, or where the different burdens of proof so warrant, the Board should not hesitate to make a contrary finding.

A prime example of such a finding is the district court's finding that conception occurred simultaneously with reduction to practice.

II. LIN HAS NOT REBUTTED THE SHOWING THAT FRITSCH IS THE PRIOR INVENTOR

A. Fritsch's Conception Did Not Occur Simultaneously With Reduction To Practice

Lin's case is built upon the proposition, argued redundantly throughout its brief, that the district court's finding of simultaneous conception and reduction to practice, affirmed by the Federal Circuit, compels judgment in favor of Lin on the issue of priority. LB 6-7, 24-25, 30, 32-38. As explained above, however, that finding does not bind the Board. Lin has not called the Board's attention to a single fact that would support a conclusion that Dr. Fritsch's conception was not complete and operative. And the evidence before the Board does not support such a finding here.

The "simultaneous conception" doctrine concerns arts where "extensive research characterized by perplexing intricate difficulties arising every step of the way" is "necessary before achieving minimum satisfactory performance" with the inventor's then-existing conception. Rey-Bellet v. Engelhardt, 493 F.2d 1380,

1386, 181 USPQ 453, 457 (CCPA 1974), citing Alpert v. Slatin, 305 F.2d 891, 894, 134 USPQ 296, 299 (CCPA 1962). It is limited to those "rare cases where the technology is so unpredictable that the inventor does not know the invention will work until actually reduced to practice." D'Silva v. Drabek, 214 USPQ 556, 562 (Bd. Pat. App. & Int. 1981).

Although Lin's conception occurred simultaneously with his reduction to practice, Fritsch's conception was earlier. There was no evidence in the district court and there is no evidence here that Dr. Fritsch engaged in the sort of unpredictable trial and error that is the hallmark of "those unusual cases" where conception cannot occur prior to reduction to practice. See Alpert v. Slatin, 305 F.2d at 894, 134 USPQ at 299. Rather, Dr. Fritsch formulated his conception of isolating the EPO gene from a genomic DNA library with two sets of fully degenerate probes from different regions of the EPO amino acid sequence, predicted its success using a mathematical formula, developed the technique for screening genomic DNA libraries with large numbers of fully degenerate oligonucleotide probes to apply that conception, and then consistently applied that conception until the EPO gene was isolated. The operability of Fritsch's conception throughout the period October 1982 to June 1983 has been independently corroborated by Dr. Shoemaker, FR 3494, and others, FR 3592 (Shaffer); FR 1068 (Neill).

Thus, contrary to Lin's argument, LB 37, the evidence here establishes that Dr. Fritsch's conception was neither "mere speculation" nor only a "generalized approach." As in Ernsthausen v. Nakayama, 1 USPQ2d 1539, 1551 (Bd. Pat. App. & Int. 1986), it was reasonable for him to expect and predict that his conception would succeed. Findings II-16 - II-26.[3]

There was only one reason why Dr. Fritsch did not isolate the EPO gene prior to October 1983: the non-availability of EPO protein from which correct sequence information could be obtained. FR 1900-1901 (Fritsch).[4] And the evidence stands unchallenged that (i) the EPO protein, (ii) the obtaining of additional protein sequence, and (iii) the design and preparation of correct probes based thereon were each within the routine skill in the art prior to Lin's date of invention. See pp. 16-17, 18-19, infra. This being so, Dr. Fritsch's conception was complete prior to Lin's earliest alleged conception date in September/October 1983. Radio Corp. of Am. v. Philco Corp., 275 F. Supp. 172, 189, 154 USPQ 570, 582 (D.N.J. 1967) (conception complete when one skilled in the art would know what needed to be done to reduce the invention to practice); Bell Tel. Laboratories, Inc. v. Hughes Aircraft Co., 422 F. Supp. 372, 379, 191 USPQ 23, 29 (D. Del. 1976) (lengthy process

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[3] All references to "Findings" herein are to the Proposed Findings of Fact and Conclusions of Law for the party Fritsch, which are annotated to the record.

[4] See also, Ginos v. Nedelec, 220 USPQ 831, 835 (Bd. Pat. Int. 1983) (need to enable suggested species of chemical molecules and conduct tests of efficiency does not negate conception).

to reduce invention to practice and need to solve problem does not negate an earlier date of conception), aff'd, 564 F.2d 654, 195 USPQ 695 (3d Cir. 1977), cert. denied, 435 U.S. 924 (1978).

In this respect, the present record contains important evidence regarding the operability of Dr. Fritsch's probing technique and the completeness of his conception which was not before the district court, e.g.,

- Corroborating testimony of Dr. Shoemaker that the genes that were isolated and sequenced in 1982 and 1983 (before Dr. Fritsch obtained new amino acid sequences) matched the expected sequence very closely so, as he explained, "we knew the technology was working...." Finding II-21.
- Testimony by Dr. Fritsch and his co-workers and others that the available amino acid sequence of the EPO protein, although containing an incorrect designation at one position within the probe sequence Dr. Fritsch was then using, was sufficient to enable the EPO gene to be identified from among clones isolated by the probing method conceived by Dr. Fritsch. Findings II-17 and II-18.
- Extensive testimony by Dr. Fritsch regarding the successful use of his probing strategy on model systems from May 1982 to September 1982, showing the operability of his probing technique during 1982. FR 1407-10, 1481-

82, 1487-90, 1529-30, 1559-65, 1580-84, 1587, 1592-94, 1596-1602, 1608-09, 1611-12 (Fritsch).

- Original autoradiograms (See, e.g., FX 136 and FX 137 relating to the E screen) which both corroborate and illustrate beyond question that prior to Lin's conception in October 1983, Fritsch's conception was fully operative in late 1982 and early 1983 to identify limited numbers of putative positive DNA clones without any technical obstacles to be overcome.
- Extensive corroborating testimony by Dr. Fritsch's laboratory personnel (e.g., Shaffer, Neill, Jacobs) demonstrating the operability and completeness of his probing technique. FR 3592 (Shaffer); FR 758, 860 (Neill); FR 5112-5113 (Jacobs).

This new evidence, together with the unrebutted evidence that it was only the lack of additional amino acid sequence data, readily obtainable through the exercise of routine skill, that delayed Dr. Fritsch's successful cloning of the EPO gene, confirms that the simultaneous conception doctrine has no applicability in this interference.

And it is of no moment whether others (or even Dr. Fritsch) reasonably expected or were "assured" that the EPO gene would be isolated by screening the genomic library with two sets of fully degenerate probes:

> Rey-Bellet seems to underscore that the ... doctrine is one of fact, not one of doctrine

> at all. If a person speculates that X can be combined with Y or that W will accomplish Z, such may be a complete conception if the nature of the testing or experimentation required to determine whether X or W will do so is routine and within the grasp of a person of ordinary skill in the art. This of course is the general Merganthaler[5] standard for completeness of a conception.

3 D. Chisum, Patents, §10.04[5] at 10-75 (1991); Applegate v. Scherer, 332 F.2d 571, 573-74, 141 USPQ 796, 799 (CCPA 1964) (it is not the law that conception requires an inventor to know his invention will work).

B. Lin Has Not Rebutted Fritsch's Showing That Fritsch Conceived First

1. The Prior Art Sequence Data Was Sufficient To Distinguish The EPO Gene From Other Materials

In attempting to use the Amgen litigation to foreclose the Board's independent determination of priority, Lin loses sight of the test that the Federal Circuit has iterated: conception of a purified and isolated gene occurs when the inventor has (1) sufficient information to envision the detailed constitution of the gene so as to distinguish it from other materials, and (2) a method for obtaining it. Amgen Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).

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[5] Mergenthaler v. Scudder, 11 App. D.C. 264, 1897 C.D. 724, 731 (D.C. Cir. 1897).

Knowledge of the complete DNA sequence of the gene is not required by this test, nor could it be required by the Board here: it is not set forth in the Count, which recites the DNA sequence functionally -- an "isolated ... DNA sequence encoding human erythropoietin." Clearly, the invention resides in the isolation of that DNA sequence, whatever its detailed structure might be. There is no requirement to conceive of its chemical structure because neither Lin nor Fritsch created that structure. It preexisted in nature.

Lin has not disputed that the prior art N-terminal amino acid sequence obtained from Dr. Hewick provided Fritsch with enough information to envision the detailed constitution of the EPO gene so as to distinguish it from other materials.[6] Nor has Lin rebutted the evidence - much of which was not considered by the district court - that demonstrates this fact.

The prior art N-terminal sequence data enabled Fritsch to construct probes for screening genomic libraries and to determine which putative positive clones encoded EPO and which did not. FR 1709 (Fritsch); FR 3034, 3099 (Orr); FR 3498 (Shoemaker); FR 3703 (Shaffer). Indeed, the N-terminal sequence allowed Fritsch in June 1983 to design two sets of fully degenerate probes which were correct and which would in fact have isolated the EPO gene. Findings II-98 - II-101. For this additional reason, the N-

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[6] Indeed, having the amino acid sequence allowed the prediction of all possible DNA sequences coding for those amino acids. FR 7210-11, 7372 (Wall).

terminal sequence information satisfied the requirement of enabling Fritsch to distinguish the EPO gene from other materials.

But even if Dr. Fritsch had not had correct probes prior to Dr. Lin, this would be of no moment. It is uncontroverted that both Dr. Fritsch and Dr. Lin used routine skill in selecting the least degenerate regions of the amino acid sequence upon which to base their probes, a task that would take only a few hours, and all of these probes worked correctly to isolate the gene. FR 5624-25, 5631-32 (Davies); FR 7315-16, 7368-69, 7371-72, 7375-79, 7382 (Wall). Thus, it is beyond question that Dr. Fritsch's concept would have isolated the EPO gene with the additional amino acid sequences obtainable from the EPO protein.

The district court made no findings whether the available N-terminal sequence was sufficient to distinguish the EPO gene from other materials. Here, the Board is free to find, on this record, that the prior art sequence data was itself sufficient to envision enough of the EPO gene's constitution so as to distinguish it from other materials. Thus, from the beginning of Fritsch's involvement in GI's EPO project, the first element of a complete conception was in place.

2. Fritsch Had An Operative Method For Obtaining The EPO Gene

As to the second element of a complete conception, a method for obtaining the EPO gene, Lin does not and cannot dispute that Fritsch had perfected his technique of screening genomic

libraries with large numbers of fully degenerate oligonucleotide probes long before Lin ever attempted to do so. The evidence here is that Fritsch was the first to make and use different sets of 128 or more fully degenerate oligonucleotide probes corresponding to different regions of the EPO amino acid sequence to screen genomic libraries (Findings II-59, II-63) -- the very technique that Lin argued to the PTO was new and rendered the cloning of EPO patentable. FX 372 at 26143-44, 26151; Findings III-7 and III-8.

The record further shows that Fritsch's probing technique was fully operable. Findings II-21, II-63 - II-86. As noted above, much of the evidence demonstrating this operability was not before the district court.

The operability of Fritsch's method for obtaining the EPO gene is confirmed by his immediate success upon the receipt of additional amino acid sequence data in 1984. FR 1970-72, 1974-76, 1982, 1984-88, 2001, 2006-07, 2023, 2034-43 (Fritsch). There could hardly be any clearer proof that his conception -- the "method for obtaining" the EPO gene -- was complete. Nor could there be any clearer corroboration of Dr. Fritsch's testimony that lack of natural EPO from which sequence data could be obtained was the single obstacle that delayed his isolation of the EPO gene. FR 1899-1901 (Fritsch).

Since obtaining correct additional amino acid sequence information and designing probes based on the best regions for screening were routine tasks which persons of ordinary skill would

easily carry out prior to Lin's conception date, Tr. Vol. 3, 125-26, 128, 132 (Wall), lack of this additional sequence information and the specific probes based upon it does not preclude a finding of conception. Vanderkooi v. Hoeschele, 7 USPQ2d 1253, 1255 (Bd. Pat. App. & Int. 1987) ("determination of a suitable range of values for a suggested result-effective variable or agent is considered to be prima facie within the realm of ordinary skill"); Philco Corp. v. Radio Corp. of Am., 276 F. Supp. 24, 32-33, 155 USPQ 372, 378-80 (D. Del. 1967).

3. Fritsch's Conception Was Prior to Lin's

The record here establishes the following key dates in GI's EPO project showing that Fritsch's conception was prior to Lin's.

Date	Activity
December 1981	Disclosure of Fritsch's probing strategy to Dr. Maniatis, i.e., use of two sets of fully degenerate probes to screen a genomic library for the EPO gene. FR 6546-47 (Maniatis); FR 1407 (Fritsch).
early 1982	Fritsch obtains prior art N-terminal EPO amino acid sequence from Dr. Hewick. FR 1405-06 (Fritsch).
August 1982	Fritsch prepares written description of EPO cloning strategy proposing use of two sets of fully degenerate probes to screen a genomic DNA library. FX 113; FR 1566-71 (Fritsch).

September/ October 1982	The "E Screen." Fritsch's first use of his cloning strategy. Uses one fully degenerate probe of 256 fold degeneracy; second fully degenerate probe of 48 fold degeneracy from different region of the amino acid sequence. FR 1677-78, 1681 (Fritsch); FX 247 (summary chart).
December 1982	"G Screen." Fritsch uses his cloning technique again. First fully degenerate probe of 256 fold degeneracy; second fully degenerate probe of 48 fold degeneracy from different region of the amino acid sequence; third fully degenerate probe of 32 fold degeneracy. FR 1777-81 (Fritsch); FX 248 (summary chart).
February 1983	"H Screen." Another use of Fritsch's cloning technique. First fully degenerate probe of 256 fold degeneracy; second fully degenerate probe of 48 fold degeneracy from a different region of the amino acid sequence; third fully degenerate probe of 32 fold degeneracy. FR 1866-67 (Fritsch); FX 249 (summary chart).
May 1983	"A Screen." First fully degenerate probe of 256 fold degeneracy; second fully degenerate probe of 48 fold degeneracy from a different region of the amino acid sequence. FR 1893; FX 250 (summary chart).
Spring 1983	Fritsch concludes that his cloning technology is working well, but that additional amino acid sequence data is needed. FR 1899-1901 (Fritsch); see also FR 3494 (Shoemaker). Fritsch resumes efforts to obtain more natural EPO for sequencing. FR 1901, 1908 (Fritsch).
May 1983	Dr. Fritsch contacts Dr. Arthur Sytkowski, an investigator at Children's Hospital in Boston. Dr. Sytkowski has information regarding the N-terminal EPO sequence, some natural EPO, and an antibody to the N-terminal peptide of EPO. Contacts made with Dr. Sytkowski throughout the summer. By the fall of 1983, GI and Dr. Sytkowski fail to come to an agreement and GI is never supplied with crude EPO from Sytkowski. FR 1901-1907 (Fritsch); FX 180 (May 31, 1983 letter to Dr. Sytkowski).

June 1983	Fritsch designs two probe subsets based on a different, 576 fold degenerate, region of the sequence data that was available in 1981. First subset used in Jacobs A, U, T, V screens with second fully degenerate probe, which was correct. The second probe subset was constructed by March 1984. This probe subset was correct and would have succeeded in isolating the EPO gene. FR 2277-78, 2274, 2280-84 (Fritsch).
July 1983	Dr. Fritsch writes Dr. Judith Sherwood at Albert Einstein College of Medicine stating his interest in acquiring a kidney carcinoma cell line believed to be a good potential source of natural EPO for sequencing. Fritsch informs Sherwood that cell line must be assayed for level of EPO production before agreement on use of cell can be reached. FR 1901, 1908 (Fritsch); FR 3779, 3782 (Sherwood); FX 326 (July 19, 1983 letter from Dr. Fritsch to Dr. Sherwood). Culture was prepared in the period between July 13-29, 1983 to prepare samples for analysis. FR 3790-93 (Sherwood).
August 1983	At Fritsch's request, on August 3, 1983 Sherwood sends samples of supernatant from kidney carcinoma cell line to Dr. David Golde at UCLA for in vitro bioassay. Results were received about August 15, 1983. FR 3794-3797. Beginning on August 18, 1983, Dr. Sherwood prepared more samples to be sent to Dr. Golde. The samples were completed on September 6, 1983. FR 3801-3806 (Sherwood); FX 327, 328 (notes, Federal Express airbills re material sent to Golde).
September 1983	On September 6, 1983, Dr Sherwood sent the cell media samples to Dr. Golde. FR 3806 (Sherwood). Dr. Golde's assay results were reported back about the second week in September. FR 3807-9 (Sherwood). In the meantime, from September 6 through 21, 1983 Dr. Fritsch's laboratory technician Marilee Shaffer continued to do work on putative positive EPO clone 27e from the E screen. FR 3714-15 (Shaffer).

September/ October 1983	Following Dr. Fritsch's instructions, Dr. Fritsch's technician Suzanne Neill performed the V screen (June 1983) and Dr. Jacobs carried out the A screen (July 1983) and the T and U screens (August 1983), FR 2272-80 (Fritsch); FR 5115-16 (Jacobs), which implemented Dr. Fritsch's conception. Throughout September and October 1983 Dr. Jacobs and Ms. Neill performed a number of routine experiments directed toward the eventual reduction to practice of Fritsch's conception. FR 5118-5128 (Jacobs); FR 865-834, 843-844 (Neill).
October 1983	Dr. Sherwood sends EPO antibodies to Dr. Fritsch on October 1, 1983 to be used in GI's EPO purification efforts. FR 3813-15. On October 6, 1983 Sherwood wrote to GI to confirm her collaboration in the EPO project. During October 19-25, 1983, Dr. Sherwood prepared further cell media for Dr. Fritsch. FR 3818-21 (Sherwood) Dr. Golde reports to Fritsch on bioassays conducted on Sherwood's cell line. One assay indicates significant EPO production. FR 1951-53 (Fritsch).
October 1983	GI and Dr. Sherwood come to an agreement regarding a collaboration on using Sherwood's cell line as a source of natural EPO. FR 1912-1913 (Fritsch); FR 3821-3827 (Sherwood); FX 181 (Agreement).
early November 1983	Pursuant to GI/Sherwood agreement, GI sends funds to Sherwood for purchase of equipment to be used in culturing the EPO producing cells in order to maximize EPO production. FR 3833-34 (Sherwood); FX 336 (memo re receipt of funds from GI).
late November 1983	Sherwood sends EPO-producing cell lines to Fritsch. FR 3835-36 (Sherwood); FX 337 (Federal Express receipt); through remainder of year, GI attempts to obtain EPO from Sherwood's cell line. FR 38404-41 (Sherwood); as per agreement, Sherwood continues efforts to improve EPO production in her cell line. FR 3837 (Sherwood).

December 1983/ January 1984	Assays done to quantify the amount of EPO protein Sherwood's cell line is producing. FR 1940, 1943-1944 (Fritsch); 3567-3573 (Rudersdorf); FX 182 (Rudersdorf Laboratory Notebook).
January 1984	Dr. Fritsch receives partially purified EPO from Dr. Sherwood. FR 1918, 1955 (Fritsch). Material purified. FR 1918-1919, 1955 (Fritsch). Assays show no EPO in sample. FR 1960 (Fritsch), 3573-3576 (Rudersdorf); FX 182.
January/ February 1984	GI contacts Dr. Miyake to make arrangements for Miyake to purify and supply natural EPO for sequencing. FR 1961 (Fritsch); FX 185-186 (letters between Miyake and GI, February 1984).
April 1984	GI receives first sample of natural EPO from Dr. Miyake. FR 1965 (Fritsch). Dr. Hewick derives amino acid sequences from tryptic fragments of first Miyake EPO sample. FR 6274-6285 (Hewick); FR 1966-1967 (Fritsch).
May 1984	Beginning of work on "K screen" using fully degenerate probes based on new sequence data derived from Miyake's EPO. FR 1975-78 (Fritsch); FX 255 (summary chart).
June/July 1984	Confirmation that genomic EPO clone had been isolated in K screen. FR 2042-43 (Fritsch)

As the foregoing summary shows, Dr. Fritsch actually used the technique of screening a genomic library with two sets of fully degenerate oligonucleotide probes containing more than 128 probes and corresponding to different regions of the EPO amino acid sequence - the very technique that Lin argued to the PTO rendered the cloned EPO gene patentable (FX 372 at 26143-44, 26151) - not later than October 1982. It is undisputed that Lin never designed,

ordered, and used two sets of fully degenerate probes to screen a genomic library for the EPO gene until September 1983. LB 38.

Moreover, there was nothing speculative or unpredictable about Fritsch's technology. It worked as it was expected to work, and the only factor preventing earlier isolation of the EPO gene was lack of additional natural EPO from which sequence data could be derived. See supra p. 18. Therefore, each of the above dates establishes Fritsch's conception, and each is prior to Lin's earliest date of September 1983, e.g., early 1982, when Fritsch first obtained the N terminal amino acid sequence; August 1982, when he prepared a written description of his cloning strategy; September/October 1982, when he first used his cloning strategy; or June 1983, when he designed, ordered, and received the first of a set of probes which would have succeeded in isolating the EPO gene. No matter which date is considered, nothing more than routine skill was required to isolate the EPO gene.

4. Lin's Evidence Is Inadequate To Establish An Earlier Conception

Lin's alternative position is reliance on a district court finding of an October 1981 conception of the same cloning strategy used by Fritsch. LB 30-31. This argument must be rejected for at least two reasons. First, independent and corroborated proof is necessary to establish a conception prior to the '008 patent's effective filing date, and Lin has proffered no

such evidence. Second, the evidence showed that Lin was unable to put that strategy to practice until September/October 1983.

The district court's finding was based upon testimony concerning a 1981 conversation between Dr. Lin and Martin Cline, a member of Amgen's scientific advisory board, and certain handwritten notes allegedly taken by Dr. Cline during that conversation. This testimony, however, fails to corroborate a conception by Lin prior to September 1983. Findings II-304 - II-312. Indeed, Dr. Cline's testimony does not mention any conversations with Dr. Lin at all. Nor is there competent testimony in the record that Dr. Cline's notes were based on conversations with Dr. Lin.

Neither the notes nor Dr. Cline's testimony, alone or in combination, describes in full an operative method for obtaining the EPO gene. Indeed, the evidence is that whatever strategy Lin intended to use, it did not enable him to employ probes of more than 16 or 32-fold degeneracy, far fewer than the 128-probe sets required for Lin's reduction to practice. Findings II-314 - II-318, II-321 - II-324. Nor did it enable Lin to screen the library with two fully degenerate sets of probes, for the first time Lin put this method to practice was in September/October 1983. Finding II-312. In short, the only evidence of a conception by Dr. Lin in 1981 other than the vague and virtually meaningless Cline

notes is Lin's own testimony. This is insufficient to satisfy the corroboration requirement. Ganguly v. Sunagawa, 5 USPQ2d 1970, 1973 (Bd. Pat. App. & Int. 1987).

C. Lin Has Not Rebutted Fritsch's Showing Of Diligence

Extensive and detailed evidence shows that Dr. Fritsch diligently attempted to reduce his invention to practice from a time before any conception date provable by Lin. Indeed, with the exception of honoring pre-existing commitments to teach cloning techniques, Fritsch's professional work was continuously devoted to GI's EPO project from the time he first conceived of the invention until its reduction to practice. Findings II-1 - II-15, II-27 - II-147. The record also contains extensive evidence of diligence on the part of the GI employees working under Dr. Fritsch's direction. Findings II-154 - II-301.

Lin's response to this showing of diligence is yet another attempt to hide behind the Amgen decisions. All of Fritsch's evidence on diligence is irrelevant, we are told, because diligence is of no consequence until there is a conception, which did not occur here until Fritsch reduced to practice. LB 33. Lin further alludes to a period of non-diligence found by the district court. Id.

Lin does not address the detailed showing of diligence made by Fritsch and at least 36 GI scientists, summarized at FB 23-26. This showing -- most of which was not before the district

court -- therefore stands unchallenged. The district court's finding of non-diligence between June 1983 and January 1984, moreover, was not reviewed by the Federal Circuit and is manifestly wrong in any event.

The sole basis for the district court's finding was that, between June 1983 and January 1984, GI tried to obtain EPO from sources other than Dr. Miyake which, in hindsight, proved unsatisfactory. Its analysis therefore wrongly substituted for the requirement of reasonable diligence a requirement that an inventor use what (with hindsight) constitutes the most expeditious method of reducing an invention to practice. Justus v. Appenzeller, 177 USPQ 332, 340 (Bd. Pat. Int. 1971) ("it is immaterial that the inventor may not have taken the most expeditious course").

It is particularly egregious that Lin should assert lack of diligence in obtaining EPO for sequencing. It was, after all, Lin's assignee Amgen (the real party in interest here) which did everything within its power to deny competitors, including Dr. Fritsch, access to EPO. Knowing that Dr. Goldwasser at the University of Chicago had the only source in the world of purified EPO, paid for by public NIH funds, Amgen entered into a consulting agreement with Dr. Goldwasser which prevented him from disclosing amino acid sequences to anyone else and from supplying EPO to Amgen's competitors who might use it to isolate the EPO gene before Amgen. Findings II-330 - II-333. Amgen's improper conduct should not be rewarded. Amgen should be estopped from contending that any

competitor, Dr. Fritsch included, lacked diligence in obtaining purified EPO for sequencing.

The evidence now before the Board in any event shows that Fritsch was diligent. He attempted to obtain EPO during this six month period from two logical sources in the United States, Drs. Judith Sherwood and Arthur Sytkowski. Indeed, materials believed to contain EPO were obtained and characterized but found to be either deficient or inadequate for sequencing. Findings II-87 - II-96. The evidence is overwhelming that Fritsch exercised reasonably continuous diligence over the critical time period commencing well prior to Lin's "simultaneous conception and reduction to practice" in October 1983 and continuing to Fritsch's reduction to practice, with no long unexplained gaps in activity. See summary at pp. 21-23, supra. The Board should therefore find that Fritsch satisfies the "reasonable diligence" requirement of 35 U.S.C. § 102(g).

III. LIN SETS FORTH NO FACTS SHOWING CHANGE OF INVENTORSHIP IS IMPROPER

Fritsch has submitted evidence which details the error in naming Hewick and Jacobs as joint inventors, how the error arose and when the error was discovered. FB 27-29. Lin offers no evidence contradicting these statements, merely attorney's argument.

In an apparent effort to show that Dr. Fritsch was not diligent in seeking to correct inventorship, Lin argues that during

the district court litigation "[i]nventorship was discussed with trial counsel[7] in a context from which it is clear that at least Dr. Fritsch considered himself the sole inventor." LB 55. This is a misrepresentation of the record. Indeed, Lin's argument is contradicted by the very Fritsch testimony upon which Lin relies:

> Well, the response was that yes, I had the concept by myself in 1981, that Dr. Hewick and Dr. Jacobs were co-inventors on the patent because of what had been my understanding at the time and standards for deciding inventorship....

FR 2790, lines 13-18.

> I told him that neither of them [Hewick and Jacobs] contributed to that part of the invention [1981 conception] and that they were co-inventors because of their contributions in the reduction to practice of it.

FR 2793, lines 21-24.

Accordingly, Dr. Fritsch believed at the time of the trial that Hewick and Jacobs were co-inventors of the involved applications. Moreover, Lin cites no evidence which casts any doubt that Dr. Fritsch's mistaken understanding about the standards for naming co-inventors was an honest error which was never appreciated earlier.

Lin also argues that Fritsch's attorney was not diligent in correcting the error in inventorship. LB 56. This argument is based entirely on suppositions about what the attorney knew when preparing the Rule 608(b) showing, LB 56, and lacks any record

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[7] GI's trial counsel, Mr. William Lee, is not a patent lawyer by training. FR 2863.

support. Fritsch's attorney has testified that in preparing the Rule 608(b) showing, he principally relied on Dr. Fritsch to explain the technology and the role of each scientist at GI who participated in the EPO project. FR 4206. Drs. Fritsch, Hewick and Jacobs each testified that they believed they were joint inventors at the time the Rule 608(b) showing was prepared. Findings VII-4, VII-5.

The evidence in this interference is clear. Until September 1990, Drs. Fritsch, Hewick and Jacobs each believed they were joint inventors of the claims of the involved applications based on an erroneous standard of inventorship each used, i.e. whether a person should be named as a co-author on a scientific publication. Findings VII-6 - VII-11.

Lin argues that no newly discovered facts have been presented to form the basis of a determination that an error had been made. That is not true. Interference counsel asked Dr. Fritsch to consider the question of inventorship with Drs. Hewick and Jacobs, and explained to him the correct standard for determining inventorship. Findings VII-6, VII-7. After careful examination of the applications and the individual contributions of each to the claimed invention, an error in naming Hewick and Jacobs as co-inventors with Fritsch was discovered on September 10, 1990. Finding VII-11. Correction of this error was promptly sought on October 6, 1990. Findings VII-13, VII-14.

Lin's argument that interference counsel "could have" and "should have" discovered the error, even if accepted, is irrelevant. The question is whether and when the error was in fact discovered. That occurred on September 10, 1990. Moreover, Lin's suggestion that a stated 1981 conception date (for Dr. Fritsch) in the Rule 608(b) showing and preliminary statement should have made Fritsch aware of the error in inventorship at the time these papers were prepared is simply hindsight. Co-inventors need not work at the same time and need not make the same type or amount of contribution to the invention. 35 U.S.C. §116. Thus, Dr. Fritsch's early conception would not have stimulated an immediate realization that one or more co-inventors were erroneously included.

Fritsch has satisfied the statutory criteria for correcting the inventorship of the application involved in this interference. Lin has failed to contradict the stated facts with evidence and has relied solely on unfounded attorney's arguments. Fritsch's motion to correct the inventorship of the involved Fritsch application and to amend Fritsch's preliminary statement to correct inventorship accordingly should be granted.

IV. LIN'S CLAIMS CORRESPONDING TO THE COUNT ARE UNPATENTABLE UNDER 35 U.S.C. §§102(b) and 112 (MOTIONS I & II)

The following facts must now be taken as established:

- The term "average carbohydrate composition" in the Lin claims refers to the average relative proportions of monosaccharide components in the EPO protein. Finding VI-3.
- The average relative proportions of the monosaccharide components in human recombinant EPO ("rEPO") are the same as those in the prior art human urinary-source EPO ("uEPO"). Finding VI-13.
- The only direct evidence in the Lin patent application to support the alleged difference in average carbohydrate composition, namely, the Yu composition data is unreliable and incorrect. Lin now concedes, as indeed it must, that the Yu carbohydrate composition data set forth in its patent application is invalid. LB 45, ¶6.

Although Lin adheres to the Strickland declaration, Lin has neither overcome the proven deficiencies which require that the Strickland declaration be disregarded nor answered the affirmative evidence that Lin's claimed rEPO is anticipated by the uEPO of the prior art.

A. The Average Carbohydrate Composition Of Lin's rEPO Is Identical To That Of The Prior Art uEPO

Lin's first contention is that Fritsch's arguments are not supported "by way of an actual test" showing that Lin's Example 10 product is identical to the prior art natural product. LB 43-44. However, Fritsch has shown through the statements and conclusions of Amgen's own scientists, through scientific data in publications which Lin himself relies upon, through data in the Amgen PLA, and through the declarations of Dr. Cumming (whose qualifications are not challenged by Lin) that the average carbohydrate compositions of recombinant EPO and uEPO are the same.[8]

Contrary to Lin's bald assertion that Fritsch has "not presented any evidence" on the issue and has merely speculated "as to the basis for Lin's determination that his product had a different average carbohydrate composition," LB 52, Fritsch has provided direct evidence that no such difference exists. Specifically:

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[8] Lin's assertion that the missing fact in Fritsch's proofs is that Lin's rEPO product has the same average carbohydrate composition as the prior art uEPO, LB 44, is a semantic play on words. Lin's claims are directed to an rEPO product whose average carbohydrate composition "differs from that of naturally occurring erythropoietin." Thus, to show anticipation Fritsch need only prove that the average carbohydrate composition of Lin's rEPO is not different, i.e., is anticipated by urinary source EPO which is prior art to Lin.

- Lin's assignee, Amgen, in its PLA submission to the FDA reports that "physical tests performed on both r-HuEPO and u-huEPO show these proteins to be indistinguishable ..." FX 399 at 789 (emphasis added), and that "the differences between r-HuEPO and u-HuEPO oligosaccharide populations are not significant." Id. at 800.
- Lin's own involved patent application proves that the relative proportions of n-acetylglucosamine and n-acetylneuraminic acid (sialic acid) in uEPO and Lin's recombinant product are identical within the limits of analytical error. Finding VI-5.
- Sasaki et al. (1987), FX 626 at 12061, cited by Lin himself, indicates that the sialic acid content of human rEPO is identical to that of human uEPO.
- Lin now concedes that the hexose monosaccharide data in the Lin application is erroneous and does not deny that the hexose content of human uEPO and human rEPO is the same. LB 45, ¶6. Fritsch has shown that the experimental data in published literature establish that the hexose content of Lin's human rEPO is identical to that of human uEPO. See Findings VI-13 - VI-16. Lin has submitted no evidence showing that the hexose content of these materials differs.
- Lin has not challenged that human rEPO and uEPO contain the same monosaccharides in the same general proportions.

Finding VI-13. Indeed, Lin acknowledges that "when various data on the carbohydrate composition of rEPO and uEPO are averaged there is no statistical difference between them" and that the "hexose content ... for rEPO produced according to Lin's Example 10 is identical to the value published for uEPO." FB 36, ¶9 and LB 46, ¶9 (emphasis added).

B. Lin's Reliance On The Primary Examiner's Determination of Allowability Is Misplaced

Confronted with reliable scientific evidence of the identity of the average carbohydrate composition of uEPO and rEPO, Lin resorts to arguing that the primary examiner reached a contrary conclusion based upon the same evidence. LB 47-48. This is not true. Not only was the primary examiner's determination based upon a record far less complete than the one before the Board, but Lin concealed from the examiner evidence now before the Board which would have discredited the arguments he was making to secure allowance of the claims now at issue.

Specifically, Lin concealed the data in Amgen's PLA which revealed that the hexose content data in its application was wholly inaccurate, and which reported physical tests that led Amgen scientists to conclude that human rEPO and human uEPO were "indistinguishable." FX 399 at 782; Findings VI-13 - VI-16.

Second, Lin concealed the silver-stained gel resulting from the experiments reported in the Strickland declaration upon which the primary examiner relied. LR '334, 667-74 (Strickland); FCX 10; FX 617. This silver-stained gel is material, since it undermines the entire basis for Dr. Strickland's conclusion that observed differences in isoforms of rEPO and uEPO were attributable to differences in carbohydrate composition. See '178 File History, Amendment dated December 1, 1988 at pp. 11-12; Findings VI-35 to VI-37.

Third, the primary examiner was not informed of an SDS PAGE gel prepared by Amgen's Dr. Egrie in September 1984, two months before Lin's involved application was filed, in which two different 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 disclosure at p. 64, line 20 to p. 65, line 3 of the Lin application of an apparent difference in molecular weight between rEPO and uEPO. See Finding VI-17.

Lastly, Lin overlooks that the Board is not bound by the determination of the primary examiner during ex parte prosecution of the Lin application. The Board has a duty to "reweigh the entire merits of the application and consider all of the evidence of record anew." Ex parte Meyer, 6 USPQ2d 1966, 1968 (Bd. Pat. App. & Int. 1988); Okada v. Hitotsumachi, 16 USPQ2d 1789, 1790-91 (Comm'r Pat. & Tmks. 1990). That is especially important here

because new evidence material to the issue of patentability has been adduced.

C. Lin Has Provided No Evidence Of A Difference In The Average Carbohydrate Compositions Of Human rEPO And uEPO

Notwithstanding Lin's admission of the identity in the average values of the proportions of monosaccharides in rEPO and uEPO, LB 49, ¶9, Lin cites the papers of Takeuchi et al., LX 214 (pp. L01364-70) and Sasaki et al., FX 626, as evidence of alleged differences in average carbohydrate composition. LB 49. However, Lin has presented no expert testimony explaining how either of these two papers supports Lin's assertions, and Sasaki et al. directly contradicts Lin's position.

Table I of Sasaki et al. reports the carbohydrate composition values of several batches of human rEPO and one uEPO sample. The values for the uEPO samples fall squarely within the batch-to-batch range of values for the rEPO samples. With respect to the Takeuchi et al. paper, suffice it to say that the most significant conclusion reached by the authors is that "the most important evidence is that all the oligosaccharides found in rHuEPO were included in urinary HuEPO." LX 214 at L01367.

Lin apparently is now seeking to have the Board alter the definition of the "average carbohydrate composition" to refer to a minute difference in the way sialic acid is attached to the sugar chains in a minority of the molecules present in uEPO. Takeuchi et

al. reports the presence of an alpha 2-6 linkage in some molecules of uEPO which is not present in rEPO. However, the same paper also reports that rEPO contains no oligosaccharide structures which are not also present in the uEPO of the prior art. In short, there is nothing novel about the sialic acid linkage upon which Lin seems now to rely. Accordingly, to the extent Lin seeks to interpret his claims as directed to a new molecular structure in rEPO, the claims are anticipated by the identical molecular structure in uEPO.

The allegedly "unrebutted testimony" by Lin witnesses Egrie and Browne, LB 49, provides no evidence to the contrary. The Browne testimony refers to a publication for the proposition that CHO cells are incapable of forming an alpha 2-6 linkage, whereas normal humans cells have such a capability. Even if this were true, as stated above, it does not establish that Lin's rEPO molecules are novel, since they are not different from the molecules contained in uEPO, as Takeuchi et al. concluded.[9]

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[9] Indeed, if Lin's claims are construed as claiming a structural difference between the glycosylated molecules in uEPO and rEPO, they would likely be invalid for lack of both written description and enablement under §112. At the time that Lin filed his application, little was known of the structure of uEPO and rEPO, as acknowledged by Lin during prosecution of the involved Lin application. See '178 File History, paper No. 6 at p. 9. Lin's application gives no clue that Lin had discovered or intended to claim any such structural difference; and there was no way anyone could determine, for purposes of infringement, whether and in what manner the structure of the rEPO protein differed (if at all) from the structure of the uEPO protein. No tests, methods or assays are disclosed or even suggested in the Lin application by which anyone could make such a determination.

D. The Strickland Experiments Are Invalid And Do Not Prove The Claimed Difference In Average Carbohydrate Composition

Lin's last piece of evidence of the claimed difference in average carbohydrate composition is Dr. Strickland's declaration. However, the Strickland experiments submitted to the primary examiner to support the alleged difference in average carbohydrate composition are defective and of no probative value. FB 45-49. In a nutshell, Dr. Strickland's conclusion that certain additional isoforms in uEPO are attributable to differences in carbohydrate was critically and crucially dependent upon an identity of uEPO and rEPO isoforms following treatment of the samples with N-glycanase and sialidase, and the simple fact of the matter is that they were not the same. FR 4106 (Cumming). Lin has no explanation for this fact; nor does Lin explain why the highly material silver-stained gel, revealing this non-identity following enzyme treatment, was withheld from the primary examiner.

Finally, Fritsch has shown that isoelectric focusing gel experiments of the type performed by Dr. Strickland are, as a scientific fact, incapable of revealing differences in the relative proportions of the monosaccharide components of proteins. This was made clear by Dr. Cumming in his declarations filed in support of the motion, and he was cross-examined by Lin without effect for two days concerning the basis for his opinions.

Lin's only response to this testimony, which Lin was unable to dent by cross-examination, is to characterize it as "rank

speculation" and to argue that no direct evidence was presented that the samples used by Dr. Strickland were "deamidated, sulfated or otherwise altered in chemical composition." LB 51. This argument is irrelevant. That isoelectric focusing is incapable of indicating differences in average carbohydrate composition has nothing to do with deamidation, sulfation or other alterations, as Lin well knows. See FR 3980-82, 4045-4047, 5272-76 (Cumming). Further, as Dr. Cumming made plain, Dr. Strickland eschewed the use of available controls which were essential to making any valid conclusions about the causes for the observation of some additional isoforms in the uEPO sample. See Findings VI-36 - VI-39.

Fritsch's motions for judgment of unpatentability pursuant to §§102(b) and 112 should be granted.

V. LIN IS NOT ENTITLED TO THE BENEFIT OF THE FILING DATES OF HIS EARLIER FILED APPLICATIONS (MOTION IV)

Fritsch has shown above that the involved Lin application does not satisfy 35 U.S.C. §112. It follows with even greater force that the same conclusion must be reached in regard to Lin's earlier benefit applications. Accordingly, Fritsch Motion IV to deny Lin the benefit of the filing dates of those prior applications should be granted.

VI. FRITSCH CLAIMS 13, 17 AND 28-31 SHOULD NOT BE DESIGNATED AS CORRESPONDING TO THE COUNT

Lin's motion to designate Fritsch claims 13, 17 and 28-31 as corresponding to the count was correctly denied by the EIC. In denying Lin's motion, the EIC noted that these claims depend from a canceled claim (3, 4 or 15) and that the claims are of indeterminate scope. That continues to be true.

Lin asserts, but does not support, that there is no patentable difference between claims 13, 17 and 28-31 and Fritsch claim 8. That is not true. Claims 28-31, for example, are directed to a high purity product having a specific activity of greater than about 200,000 units/mg (claim 28) or greater than about 275,000 units/mg (claims 29, 30). Claim 8, on the other hand, contains no such limitations. Clearly, this is a patentable distinction between the subject matter of the count, directed to the carbohydrate composition of the EPO product, and the highly purified rEPO product of would-be claims 28-31. Indeed, Lin's assignee Amgen received U.S. Patent 4,667,016 (FX 377) directed to a later-developed process which was able to achieve such high purity.

Similarly, claims 13 and 17 cannot be amended sua sponte to claim an invention that Lin thinks should be claimed. Claim 17 depended originally from canceled claims 14 and 15, directed to the expression product of a specific mammalian cell line transfected with a vector containing a genomic DNA clone of a specific sequence. Lin fails to establish that such a product would not be

patentably distinct from the count or the other Fritsch claims corresponding thereto. Similarly, claim 13 depended from each of canceled claims 9, 10 and 11 and was directed to a product expressed from cells transfected with a vector containing a specific cDNA clone, lambda-HEPOFL13. Once again, Lin does not show that the expression product of the cells containing such a clone construction would not be patentably different. Lin's assertion, unsupported by any evidence, is not sufficient.

In any event, the examiner was correct in refusing to designate claims which, in effect, are so incomplete that their ultimate form cannot be ascertained. Lin's motion to designate Fritsch claims 13, 17 and 28-31 as corresponding to the count should be denied.

CONCLUSION

For the foregoing reasons, and for the reasons set forth in Fritsch's Main Brief and Proposed Findings of Fact and Conclusions of Law, the Board should enter judgment:

1. That Dr. Edward Fritsch is the prior inventor of the subject matter corresponding to the count of this interference;

2. That Dr. Fritsch is the sole inventor of the subject matter claimed in the Fritsch application involved in this interference;

3. That Lin's claims corresponding to the count are unpatentable to Lin under 35 U.S.C. § 102(b);

4. That Lin's claims corresponding to the count are unpatentable to Lin under 35 U.S.C. § 112 for for failure to enable the claimed subject matter;

5. That Lin is not entitled to the benefit of the filing dates of his prior applications because those applications do not satisfy the requirements of 35 U.S.C. § 112; and

6. That Lin's motion to designate Fritsch claims 13, 17 and 28-31 as corresponding to the count is denied.

Respectfully submitted,

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Dated: August 12, 1991

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CERTIFICATE OF SERVICE
AND FILING BY EXPRESS MAIL

It is hereby certified that on August 12, 1991 the original and three copies of the foregoing REPLY BRIEF FOR THE PARTY FRITSCH have been deposited with the United States Postal cService in an envelope as "Express Mail Post Office to Addressee" mail label number B33337730Y, in an envelope addressed to Box Interference, Hon. Commissioner of Patents and Trademarks, Washington, D.C. 20231, and that copies thereof have been served upon counsel for Lin by first class mail, postage-prepaid, and by overnight courier, addressed as follows:

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