EXHIBIT 1
(Part 1 of 4)

In The
United States Patent and
Trademark Office

Before the Board of Patent Appeals and Interferences

Interference No. 102,097

FRITSCH

v.

LIN

Examiner-in-Chief Marc L. Caroff

BRIEF FOR THE SENIOR PARTY LIN

PAUL N. KOKULIS
CUSHMAN, DARBY & CUSHMAN
1615 L Street, Suite 1100
Washington, D.C. 20036-5601
(202) 861-3000
Attorney for the Party Lin

Of Counsel:
WATSON T. SCOTT
MICHAEL F. BORUN
STEVEN M. ODRE

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STATUTES

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OTHERS

I. STATEMENT OF ISSUES PRESENTED FOR CONSIDERATION

(1) Should the interference be terminated in favor of Lin, and unfavorably to Fritsch, in view of the Federal Circuit decision which was favorable to Lin on the priority and patentability issues raised by Fritsch et al?

(2) Is Lin entitled to priority award in this interference?

(3) Has Lin satisfied best mode requirements?

(4) Are the Lin claims corresponding to the count patentable to Lin under 35 USC 103?

(5) Is Lin the inventor of the subject matter at issue?

(6) Should Fritsch et al be permitted to change their inventorship?

II. STATEMENT OF THE FACTS

(A) The Subject Matter

The invention involved in this interference relates to a process for producing in vivo biologically active recombinant erythropoietin ("EPO") by growing a mammalian host cell transformed or transfected with an isolated DNA sequence encoding EPO and isolating the EPO product.

(B) The Parties

This interference involves U.S. application Serial No. 693,258 filed on January 22, 1985 by Edward Fritsch, Rodney M. Hewick and Kenneth Jacobs ("Fritsch et al" or "Fritsch") and U.S. application Serial No. 113,179, filed October 23, 1987 by Fu-Kuen Lin. The Lin application is a division of U.S. Patent 4,703,008 (the '008 patent) which was filed on November 30, 1984.

The Fritsch et al application is assigned to Genetics Institute, Inc. ("GI"). The Lin application is assigned to Amgen Inc. ("Amgen").

Fritsch et al have been given the benefit of an earlier U.S. application Serial No. 688,622, filed January 3, 1985 while Lin has been given the benefit of his '008 patent filing date (November 30, 1984) and three earlier filings as follows:

U.S. Serial No. 561,024, filed December 13, 1983

U.S. Serial No. 582,185, filed February 21, 1984

U.S. Serial No. 655,841, filed September 28, 1984

Each of Lin's earlier applications is prior to the initial Fritsch et al filing and Lin is the senior party by virtue of these earlier filings.

(C) The Count

The interference involves a single count which is set forth in Appendix I. In essence, the count defines a process for the preparation of an in vivo biologically active glycosylated polypeptide (recombinant EPO) by growing a mammalian host cell which is transformed or transfected with an isolated DNA sequence encoding EPO and isolating the recombinant EPO product.

In the declaration of the interference, Fritsch et al claims 72 and 73 and Lin claims 65-69 were identified as corresponding to the count. Lin's claim 65 is identical to the count.

None of the Fritsch et al claims is identical to the count. The Fritsch et al claims 72 and 73 are more general in nature and read:

> *72. A method of producing human erythropoietin comprising culturing the cell line of claim 50 in a suitable culture medium and isolating erythropoietin from said medium.*
>
> *73. A method of producing human erythropoietin comprising culturing the cell line of claim 52 in a suitable culture medium and isolating erythropoietin from said medium.*

Fritsch et al claims 50 and 52, from which claims 72 and 73 depend, themselves refer back to claim 48 and then to claim 46. These claims (claims 50, 52, 48 and 46 read as follows:

> *50. A mammalian cell line transformed with the vector of claim 48.*

> *52. The mammalian cell line of claim 50 wherein said mammalian cells are CHO cells.*
>
> *48. A recombinant DNA vector comprising a heterologous promoter and the cDNA sequence of claim 46.*
>
> *46. A cDNA sequence comprising a DNA sequence encoding the amino acid sequence 1-166 as shown in Figure 3B.*

Fritsch et al claims 46, 48, 50 and 52, which are drawn to DNA sequence encoding EPO or host cells transformed therewith, are listed as corresponding to the count in Interference No. 102,096. Thus, in essence, Fritsch et al claims 72 and 73 call for producing human EPO by culturing a host cell transfected with DNA according to the count of Interference No. 102,096 and isolating the product.

The culturing and isolating steps recited in Fritsch et al claims 72 and 73 are the counterparts of steps (a) and (b) of the count. Step (a) is inherent in the culturing step of the Fritsch et al claims. Step (b) is accomplished when the expressed product is separated as media from the cells themselves, for example, for assay to determine in vivo biological activity.

(D) Related Interferences

There are two other closely related interferences involving the same parties. These interferences are Interference No. 102,096, which has already been referred to and which was declared concurrently with the present interference, and Interference No. 102,334. As indicated, Interference No. 102,096 is directed to a purified and isolated DNA

sequence encoding human EPO which is used in the process which is the subject of the present interference. The count of Interference No. 102,334 is directed to an in vivo biologically active human EPO product. A single Rule 608(b) showing by Fritsch et al is the basis for the declaration of all three interferences.

Papers common to all three proceedings have been filed and the evidentiary presentation has been consolidated.

The close relationship of the three interferences has been acknowledged by Fritsch et al in preliminary motions and in their Briefs at Final Hearing in this interference and in Interference No. 102,334. Thus, Fritsch et al in earlier motions urging the combination of Interference Nos. 102,096 and the present interference characterized these two interferences as "different manifestations of the same invention"[1]. Additionally, in their briefs at final hearing in this interference and Interference No. 102,334, Fritsch et al state:

> *Accordingly, as in the '096 interference, priority turns upon the first conception of the purified and isolated gene.*[2]

Fritsch et al thus admit that the priority issue is identical in all three interferences. Moreover, the prior art references relied on in support of the Fritsch et al obviousness arguments in the present interference (including Toole et al U.S. Patent No. 4,757,006) are the same references relied upon in the Fritsch et al brief arguing

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[1] See Fritsch et al Motion G in Interference No. 102,096 at page 86 and Motion Q in Interference No. 102,097 at page 159.

[2] See Fritsch et al brief page 24 in this interference and page 23 of their brief in Interference No. 102,334.

obviousness of Lin's claims to the purified and isolated DNA sequence in Interference No. 102,096[1]. Likewise, the Fritsch et al allegations of best mode violation in this interference and in Interference No. 102,096 are identical.

[1]Compare Fritsch et al brief pages 48-50 in the present interference with pages 40-43 of the Fritsch et al brief in Interference No. 102,096.

(E) **Related Litigation**

Lin's assignee (Amgen) and the Fritsch et al assignee (GI) and the latter's licensee (Chugai Pharmaceutical Co. Ltd.) have been involved in extensive litigation regarding erythropoietin. See the decision of the United States Court of Appeals for the Federal Circuit in Amgen Inc. v. Chugai Pharmaceutical Co. Ltd. and Genetics Institute, Inc., 927 F.2d 1200, 18 USPQ2d 1016 (1991) (hereinafter referred to as the "Federal Circuit decision"). This decision affirmed in relevant part a decision of the United States District Court for the District of Massachusetts, No. 87-2617-Y, Amgen Inc. v. Chugai Pharmaceutical Co. Ltd. and Genetics Institute, Inc., 13 USPQ2d 1737 (hereinafter the "District Court decision").

The Federal Circuit decision is thought to be dispositive of any basis for this interference as noted later.

Proceedings prior to the District Court decision are briefly summarized under the heading "III Procedural History" beginning at page 1739 of the District Court decision.[4] This has included action before the International Trade Commission (ITC) wherein the validity of Lin's '008 patent was put at issue. The District Court and Federal Circuit decisions addressed priority and patentability issues directed towards Lin's '008 patent claims. These proceedings have involved many depositions and documents and extensive trial testimony. The District Court trial itself extended through 38 trial days. In both the ITC proceedings and the District Court action, invalidity and unenforceability

[4] All page references herein to the District Court and Federal Circuit decisions are based on the 13 USPQ2d and 18 USPQ2d reports, respectively.

defenses were raised against Lin's '008 patent. These defenses variously included alleged prior invention by Fritsch under 35 USC 102(g), obviousness over the prior art including Toole et al U.S. Patent 4,757,006 under 35 USC 103, failure to satisfy best mode requirements (35 USC 112) and inequitable conduct. Except for an issue of enablement with respect to Lin's claim 7, which is not relevant here, all invalidity and enforceability defenses against the '008 patent were rejected by the ITC, the District Court and most recently, the Federal Circuit. The Federal Circuit has denied rehearing and its mandate has issued.

The Federal Circuit decision stands as the law of the case insofar as issues decided by the Court are concerned. The Examiner-in-Chief, apparently referring to M.P.E.P. § 706.03(w), has noted this on the record (FR 1029-1030)[3] as follows:

> *... and we are bound by any decision of the Federal Circuit so that any issues here that might be identical as to ones that are decided by the Court of Appeals in the Federal Circuit would bind us as far as those issues go.*

The Federal Circuit decision is discussed in detail later in this brief. However, it is useful at this stage to note that the Federal Circuit specifically affirmed the District Court's ruling, in view of the state of the art concerning EPO, that a conception of the purified and isolated DNA sequence encoding EPO and host cells transfected therewith (at issue in Interference No. 102,096, and used in the process of the present count) required reduction to practice of the sequence. In other words, based on the

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[3] The references FR, FB, LR are used to refer to the Fritsch et al record, Fritsch et al brief and Lin record, respectively.

same record before the PTO in this interference, the District Court and Federal Circuit found that Lin's conception of the invention claimed, namely "a purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin" occurred simultaneously with reduction to practice so that there could be no conception of the DNA sequence until it was reduced to practice. This is the controlling law on the issue of priority in this interference and, by Fritsch et al's own admissions, the related interferences.

The District Court decision, which was affirmed by the Federal Circuit[6], includes a very helpful background discussion regarding EPO (Section V, pages 1741-1745) and in Section VI (pages 1745-1754) sets out the facts relevant to the efforts by Lin (Amgen), Fritsch[7] (Genetics Institute) and others to clone and express EPO. The prior art including the Toole et al U.S. patent is also discussed at pages 1753-1754. The facts as set out in the District Court decision, including the activities of Lin and Fritsch to clone and express EPO, have not been challenged and, therefore, stand established as the factual background for this interference.

The District Court decision considered in detail the following issues which Fritsch refers to in his brief:

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[6] Except for the District Court's ruling as to validity of GI's Hewick et al U.S. Patent No. 4,677,195, which is not here involved.

[7] As discussed infra with respect to the deferred Fritsch et al motion to change inventorship, at trial in the District Court, Edward Fritsch's co-inventors herein (Rodney Hewick and Kenneth Jacobs) were not identified as participants in the alleged prior conception by Fritsch (which the Courts found inadequate). One (Jacobs) did not even begin working for GI until July, 1983.

(1) Priority of invention as between Lin and Edward Fritsch with the holding of simultaneous conception and reduction to practice favorable to Lin (pages 1759-1764). The District Court also considered essentially the same question of prior conception as proposed by Fritsch et al in this interference, that is, the assumption that conception could occur prior to reduction to practice, and held against Fritsch based on the same facts now before the PTO (pages 1762-1763). The Court further considered the question of Fritsch's diligence (assuming prior conception) and again found against Fritsch (pages 1763-1764).

(2) Obviousness of the subject matter under Section 103 with the finding of unobviousness over the prior art (pages 1764-1769); and

(3) Best mode, with a finding favorable to Lin (pages 1769-1774).

The Federal Circuit affirmed the District Court on each of items (1), (2) and (3). See pages 1020 to 1022, 1022 to 1023 and 1023 to 1026, respectively, of the Federal Circuit decision.

While the process of the present count was not expressly at issue in the litigation, it is clear that the issues of priority and patentability of the process were directly addressed. Central to the process is the use of the DNA sequence encoding human EPO and host cells transfected therewith at issue in the litigation, to express in vivo biologically active human EPO. Fritsch et al have acknowledged this in admitting that priority with respect to the present count turns on conception of the purified and isolated gene (FB

24). The Section 112 issue raised here is identical to that raiased at trial. The obviousness issue raised here, as reflected by the Fritsch et al briefs, is not substantively different. Hence, the Federal Circuit decision is directly applicable to the issues in the present case.

(F) The Interference History

This interference was declared on May 9, 1989, prior to the District Court decision (December 11, 1989), concurrently with the declaration of Interference No. 102,096. As noted earlier, the interferences were declared on the basis of a showing under 37 CFR 1.608(b) ("Rule 608") by Fritsch et al purporting to establish prior conception, based on knowledge of a probing technique, with diligence up to reduction to practice. The 608(b) evidence was, for all intents and purposes, the same as that relied on by the defendants in the District Court action and rejected by both the District Court and Federal Circuit. The Federal Circuit decision regarding priority is final. Fritsch et al are now presenting the same arguments, for a third time, at final hearing.

Both parties filed preliminary statements and Fritsch et al filed ten preliminary motions generally on the lines of those filed in Interference No. 102,096. The Fritsch et al preliminary motions* included:

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* The motions are identified by the letters used by the Examiner-in-Chief in his decision on motions (Paper No. 35).

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(H) for judgment of unpatentability of Lin's claims corresponding to the count under 35 USC 102(e) and/or 103 based on the Toole et al U.S. Patent 4,757,006;

(I) for judgment of alleged failure to meet written description, enablement and/or best mode requirements of 35 USC 112, first paragraph;

(J) to deny benefit accorded to Lin as to earlier filings on written description or enablement grounds;

(K) to deny benefit accorded to Lin as to earlier filings on best mode grounds;

(L) for judgment of unpatentability to Lin under Section 102(g);

(M) for judgment of unpatentability to Lin under Section 102(f);

(N) to substitute or add a later-filed continuation-in-part application based on a probing technique described in the Toole et al patent which did not relate to EPO;

(O) to substitute a proposed method count directed towards the probing technique referred to in the later-filed continuation-in-part mentioned in (N);

(P) to be accorded the benefit of earlier Toole et al applications; and

(Q) as in motion (G) in Interference No. 102,096, to combine the two interferences because the two interferences represent "different manifestations of the same invention."

Subsequent to the filing of these motions, and Lin's oppositions thereto, the District Court issued its decision as reported at 13 USPQ2d 1737. As a consequence, Lin filed a motion to terminate (Paper No. 33) these proceedings.[1]

In his decision on motions (Paper No. 35), the Examiner-in-Chief ("EIC") dismissed the Lin motion to terminate. He also dismissed Fritsch et al motions (L), (O), (N) and (Q); deferred action on Fritsch et al motions (H) (Section 102/103 patentability), (I) (best mode only), (K) (Lin's priority benefit) and (M) (Section 102(f) patentability) and denied motions (P) (Fritsch et al priority benefit), and (I) and (J), as directed to "description" and "enablement".

Fritsch et al requested reconsideration of the motions decision with respect to motion (J) but this was denied, the Examiner-in-Chief (E-I-C) noting that Fritsch et al had taken no issue with Lin's assertion that a correlation between glycosylation and in vivo biological activity of EPO was art-recognized (Paper No. 44, sentence bridging pages 2-3).

Both parties have since presented their priority evidence in the form of deposition and declaration testimony and 37 CFR 1.682 submissions. Additionally, during the Fritsch et al testimony time, Fritsch et al filed a motion to amend the inventorship of their application here involved Serial No. 693,258 to list Fritsch as sole inventor, i.e. to delete Hewick and Jacobs as joint inventors. A companion motion to correct their

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[1] Lin also filed a contingent motion (Paper No. 34 1/2) proposing a substitute count in view of the District Court's position regarding claim 7 of Lin's '008 patent but this motion was dismissed (Paper No. 41).