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

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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[3]. Likewise, the Fritsch et al allegations of best mode violation in this interference and in Interference No. 102,096 are identical.

[3]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)[5] 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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[5] The references FR, FB, LR are used to refer to the Fritsch et al record, Fritsch et al brief and Lin record, respectively.