 Exhibit 4

19/J
B. White
1-29-90

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner
1-30-90
MM

In re application of

FU-KUEN LIN

RECEIVED GROUP 180
JAN 1 1990

Serial No. 07/113,178 Group Art Unit: 186

Filed: October 23, 1987 Examiner: J. Kushan

PRODUCTION OF ERYTHROPOIETIN

Entered
MM
2-7-90
B. White
2-9-90

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AMENDMENT UNDER RULE 116

The Honorable Commissioner
of Patents and Trademarks
Washington, D.C. 20036

Sir:

Responsive to the Final Official Action dated September 18, 1989, kindly amend the above-identified application as follows:

IN THE CLAIMS:

Please cancel claims 67-75.

Please add the following new claims:

--76. A non-naturally occurring glycoprotein product of the expression in a non-human ~~eucaryotic host cell~~ of an exogenous DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin said product possessing the in vivo biological property of causing human bone marrow cells to increase production of reticulocytes and red blood cells and having an average carbohydrate composition which differs from that of naturally occurring human erythropoietin.

Should the Examiner maintain the double patenting rejection, the Applicant's Assignee, in view of its immediate need for patent protection, is prepared to file the requested terminal disclaimer if the subject application would then be in condition for immediate allowance and issuance of a patent.

Claims 67-75 also stand rejected under 35 U.S.C. 112 first and second paragraphs. The Applicant has cancelled claims 67-75 without prejudice. These claims will be the subject of a continuation application.

The Applicant has added new claims 76-83, which are similar to cancelled claims 67-75, but which specify that the DNA sequences encode human erythropoietin. These new claims parallel claim 2 of U.S. Patent No. 4,703,008 (Lin '008 patent), the parent of the instant application[2]. The Examiners have indicated during the interview of December 20, 1989, that these new claims would be entered and be allowable.

* * *

During the interview of December 20, 1989, it was indicated that the Examiner would be checking with Examiner-in-Chief Caroff regarding possible suspension of this application pending resolution of Interference Nos. 102,096 (involving the Lin '008 patent) and 102,097 (involving the Lin process application). The Applicant submits that any suspension of prosecution or declaration of an interference would be improper in view of the entire record now before the Patent Office, in particular the new evidence, including the priority determination, in the decision rendered by the United States District Court for the District of Massachusetts in Amgen Inc. v. Chugai Pharmaceutical Co., Ltd., and Genetics Institute, Inc., Civil Action No. 87-2617-Y, on December 11, 1989. A copy of that decision is attached hereto. In deciding to declare the above-identified interferences, the Patent Office relied principally upon a Rule 608(b) showing by Fritsch et al. The Court's decision rejected a 102(g) anticipation attack based on Dr. Fritsch's work at Genetics Institute

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2 Claim 2 was held valid in the District Court decision referred to herein.

(including the evidence presented in the Rule 608(b) showing by Fritsch et al.), and upheld claims of the Lin '008 patent including the following:

> 2. A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin.
>
> 4. A procaryotic or eucaryotic host cell transformed or transfected with a DNA sequence according to claim 1, 2 or 3 in a manner allowing the host cell to express erythropoietin.

In determining that claims 2 and 4 of the Lin '008 patent are valid, the Court recognized that Lin is the first inventor of the DNA sequence encoding human erythropoietin and of the use thereof in a host cell to make recombinant erythropoietin. The discussion on pages 67-84 of the decision evaluates all of the priority evidence which was developed by the parties after extensive discovery and 38 days of trial (including the Rule 608(b) submission by Fritsch et al.). See, for example, the first full paragraph of the decision, pages 67-80, where the Court finds that Lin conceived of the invention before Fritsch et al., as well as pages 80-84 where the Court discusses Fritsch et al.'s lack of diligence.

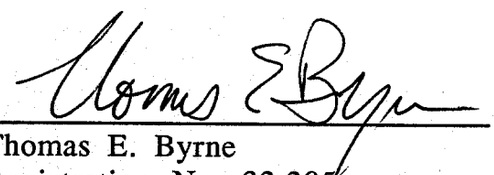
The decision is thought to be fully dispositive of not only the priority of invention issues in both interferences, and any priority issue in the subject application. Therefore, it is submitted that if Lin was the first to invent the DNA encoding erythropoietin, and the use of that DNA in a host cell to produce recombinant erythropoietin, then clearly he was the first to invent a recombinant erythropoietin product produced using such a host cell.

Even if the Examiner believes a priority issue remains in the subject application, the application should still issue as a patent under MPEP 2303. Section 2303 of the MPEP states:

Should any matters remain outstanding, the Examiner is encouraged to telephone Applicant's undersigned attorney collect at (805) 499-5725, so that same can be resolved without the necessity of an additional action and response thereto.

Respectfully submitted,

January 10, 1990

By 

Thomas E. Byrne
Registration No. 32,205
Amgen Inc.
1840 Dehavilland Drive
Thousand Oaks, CA 91320-1789