

EXHIBIT 20



#13 6.2.97 80
TGray

PATENT APPLICATION
ATTORNEY DOCKET NO. 11009/32022

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:)	I hereby certify that this paper is
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Fu-Kuen Lin)	States Postal Service as first class
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Serial No: 08/468,369)	envelope addressed to:
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Filed: June 6, 1995)	Assistant Commissioner for Patents
)	Washington, DC 20231, on this
For: PRODUCTION OF)	date:
ERYTHROPOIETIN)	
)	Dated: May 13, 1997
Group Art Unit: 1804)	
)	
Examiner: James Martinell, Ph.D.)	
)	
)	Michael F. Borun
)	Reg. No. 25,447
)	Attorney for Applicant

RECEIVED
MAY 30 1997
GROUP 12

AMENDMENT AND RESPONSE UNDER 37 C.F.R. §1.111 AND §1.115

Assistant Commissioner for Patents
Washington, DC 20231

Sirs:

This is in response to the Office Action dated February 14, 1997 in the above-identified application wherein all pending claims (42-44, 46 and 61) were rejected under 35 U.S.C. §112, first paragraph and claim 61 was rejected under 35 U.S.C. §112, second paragraph. Reconsideration and allowance is respectfully requested in view of the following amendments and remarks.

AMENDMENT

Please cancel claims 42-44, 46 and 61 without prejudice. Please enter new claims 66 through 72.

~~66~~¹. Vertebrate cells which can be propagated *in vitro* and which are capable upon growth in culture of producing erythropoietin in the medium of their growth in excess of 100 U of erythropoietin per 10⁶ cells in 48 hours as determined by radioimmunoassay, said cells comprising non-human DNA sequences which control transcription of DNA encoding human erythropoietin.--

~~67~~². Vertebrate cells according to claim ~~66~~¹ capable of producing in excess of 500 U erythropoietin per 10⁶ cells in 48 hours.--

~~68~~³. Vertebrate cells according to claim ~~66~~¹ capable of producing in excess of 1000 U erythropoietin per 10⁶ cells in 48 hours.--

~~69~~⁴. Vertebrate cells which can be propagated *in vitro* which comprise transcription control DNA sequences, other than human erythropoietin transcription control sequences, for production of human erythropoietin, and which upon growth in culture are capable of producing in the medium of their growth in excess of 100 U of erythropoietin per 10⁶ cells in 48 hours as determined by radioimmunoassay.--

~~70~~⁵. Vertebrate cells according to claim ~~69~~⁴ capable of producing in excess of 500 U erythropoietin per 10⁶ cells in 48 hours.--

~~71~~⁶. Vertebrate cells according to claim ~~69~~⁴ capable of producing in excess of 1000 U erythropoietin per 10⁶ cells in 48 hours.--

~~72~~⁷. A process for producing erythropoietin comprising the step of culturing, under suitable nutrient conditions, vertebrate cells according to claim ~~66~~¹, ~~67~~², ~~68~~³, ~~69~~⁴, ~~70~~⁵ or ~~71~~⁶.--

REMARKS

Upon entry of the above amendment, claims 66 through 72 will be pending in the application.

The Applicant acknowledges with thanks the interview of May 6, 1997, kindly granted by Examiner Martinell to the undersigned and counsel for Applicant's assignee. As indicated in the Interview Summary (Paper No. 11), alternative forms of amendment for claim 42 were discussed and two forms of amendment were indicated by the Examiner to overcome the outstanding rejection under 35 U.S.C. §112, first paragraph, and to not present issues of Obviousness-Type Double Patenting *vis-a-vis* host cell claims of U.S. 4,703,008. Applicant also agreed to remedy informalities in prior claims 44 and 61.

In claims 66 through 72 submitted herewith, claim 66 represents the "B" version of amendment for claim 42 and claim 69 represents the "C" version of claim 42 amendment discussed at the interview. Claim 72 replaces prior claim 61 and includes a positive process step.

Although no prior art rejections were lodged against prior claims 42-44, 46 and 61, Applicant notes that the vertebrate cell subject matter of Sugimoto *et al.*, U.S. 4,377,512 (Reference A11) was at one time cited as relevant to claims prosecuted in Serial No. 08/487,974 (which recently issued as U.S. 5,547,933). A number of grounds were advanced by Applicant to distinguish the claimed subject matter from the disclosures of the Sugimoto *et al.* patent including the observation that no repeatable means was presented in the reference for producing the (human tumor/human lymphoblastoid hybridomas cells which are alleged to generate a product with erythropoietin activity. Applicant further noted that the proprietors of the Sugimoto *et al.* reference had been contacted and had refused to provide either hybridoma cells described in the reference or any of the product assertedly produced by the cells. Copies of the relevant correspondence items (Exhibits A and B to the December 20, 1995 submission in Serial No. 08/487,774) are attached hereto as Exhibits A and B to simply make them of record in this application. In any event, Applicant submits that the present claims are patentable over the disclosures of Sugimoto *et al.*

Consistent with the Examiner's preference, Applicant refrains from submitting herein information including foreign decisions relating to foreign patent applications and patents based on the present specification.

Transmitted herewith is a replacement for Figure 13 which was submitted herein on December 24, 1996 as a replacement for Table XVIII appearing on page 79 of the Specification. The version of Figure 13 submitted as been found to contain a typographical error in designating a proper base pair complement. More specifically, the C/G base pair immediately below the "5" fragment designation in Table XVIII was mistranscribed as C/C immediately to the left of "5" in Figure 13 as originally presented. The replacement submitted wherewith corrects that error and introduces no new matter.

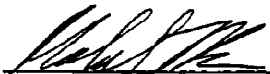
CONCLUSION

The foregoing amendments and remarks are believed to establish that claims 66 through 72 are in condition for allowance and an early notice thereof is solicited.

Respectfully submitted,

MARSHALL, O'TOOLE, GERSTEIN,
MURRAY & BORUN

BY:


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233 S. Wacker Drive
Chicago, IL 60606-6402
(312) 474-6300

Chicago, Illinois
May 13, 1997

Exhibit A

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DANIEL VAPNEK, Ph.D.
Senior Vice President
Research

Via Facsimile
Confirmation via Federal Express

December 4, 1985

Mr. Ken Hayashibara
Hayashibara Seibutsu Kagaku
2-3, 1-chome, Shimotsu
Okayama-shi
Okayama, Japan 700

Re: Erythropoietin producing cell line

Dear Mr. Hayashibara:

I am writing to you concerning U.S. patent No. 4,377,513 which lists Sugimoto, K. and Hayashibara, Y. as inventors and yourself and Shin Ashida as the assignees.

Amgen is interested in obtaining a sample of the erythropoietin producing cell line referenced in this patent as well as a sample of any erythropoietin produced by such a cell line. Also, I would request any information that might be available concerning analysis of such erythropoietin.

Would you please let me know whether samples of the cell line and the erythropoietin product are available. I look forward to hearing from you at your earliest convenience.

Very truly yours,

A handwritten signature in black ink, appearing to read "D. Vapnek".

Daniel Vapnek, Ph.D.
Senior Vice President, Research

DV/SLW/cs

Amgen Inc., 1840 DeHavilland Drive, Thousand Oaks, California 91320-1789
Telephone 805 447-4008 • TTT Telex 84984440 • Fax 805 499-9318

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Exhibit B

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DOCUMENT DISPATCH MESSAGE

Dispatch Date & Time: December 8, 1995

FROM: T. Miyake
Hayashibara Biochemical Labs., Inc.
Total pages 2 (including this cover)

TO: Dr. Daniel Vrsnak
Senior Vice President, Research
Amgen Inc.
1840 Dehavilland Drive
Thousand Oak, CA 91320
U.S.A.
Fax number 001-1-805-499-8011

Notice:

This message is for the exclusive use of the individual or entity to which it is addressed and is confidential. If you have received this message in error, please notify us immediately by telephone to arrange for its return.



Dr. Schwabert / CHIRI
Genetics, 700 West
Pacifi : 0800764-5111
FAX : 0800221-8405
0800221-8624

December 8, 1995

Dr. Daniel Vassak
Senior Vice President, Research
Amgen Inc.
1840 DeHavilland Drive
Thousand Oak, CA 91320
U.S.A.

Dear Dr. Vassak:

We received your letter of December 4, 1995 inquiring our U.S. patent No. 4,377,513 pertaining to erythropoietin producing cell line.

Your interest to the cell line as stated in said patent is gratifying encouragement to us. However, presently we are not in a position to provide such a cell line with any party having nothing to do with our research activities regarding erythropoietin.

Please feel free contact the undersigned if you have any question on this matter.

Sincerely yours,

Toshio Miyake
Toshio Miyake
Corporate Director

TMI/s

F: Our Fax No. (0)86-227-5285 and Phone No. (0)86-222-7776

