EXHIBIT 24

UNITED STATES DEPARTMENT OF COMMERCE
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08/100,197 08/02/93 LIN F 202986D155C1

STANTON, B EXAMINER

18M2/0601

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1100 NEW YORK AVENUE, N.W.
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1804 20

DATE MAILED: 06/01/94

☑ This application has been examined ☑ Responsive to communication filed on 1/10/94 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire THREE (3) month(s), 0 days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 61-63 ROMAN are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 61-63 STANDARD are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☑ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 9-89)

A 42411

250-B

This Application is a Continuation of Application No. 07/957,073, filed 10/6/92, now abandoned, which is a Continuation of Application No. 07/609,741, filed 11/6/90, now abandoned, which is a Divisional of Application No. 07/113,179, filed 10/23/87, now pending, which is a Continuation of Application No. 06/675,298, filed 11/30/84, now U.S. Patent No. 4,703,008, which was a Continuation-in-Part of Application No. 06/561,024, filed 12/13/83, now abandoned, and a Continuation-in-Part of Application No. 06/582,185, filed 2/21/84, now abandoned, and a Continuation-in-Part of Application No 06/655,841, filed 9/28/84, now abandoned.

The amendment after final filed 1/10/94 (Paper No. 18) has been entered. Claims 61-63 remain pending in the instant Application.

Applicant is hereby informed that the FINALITY of the previous Office Action mailed 10/5/93 (Paper No. 16) is WITHDRAWN. Prosecution on the merits of the instantly claimed invention is herein reopened and the following new grounds of rejection are advanced.

Claims 62 and 63 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 62 is vague and indefinite because it is unclear what the claimed composition is required to be "effective" for.

Claim 63 is vague and indefinite because it is unclear as to how the recitation that the claimed erythropoietin is "recombinant" modifies the physical erythropoietin composition. It is noted that in the body of the paragraph bridging pages 18 and 19, the specification indicates that a "recombinant" erythropoietin molecule may be prepared in eukaryotic cells and be fully glycosylated. Therefore, while the claimed erythropoietin may be prepared using recombinant techniques, the product would not necessarily distinguish over that found in nature.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 61-63 are rejected under 35 U.S.C. § 103 as being unpatentable over any one of Miyake et al., 1977 (R), Takezawa et al., 1981 (B) or Takezawa et al., 1982 (C) in view of either applicant's admission on page 87, lines 29-31 or Bock et al., 1982 (D).

The claims under instant consideration are drawn towards pharmaceutical compositions comprising erythropoietin in combination with human serum albumin.

Miyake et al. disclose the purification of human erythropoietin derived from human urine (see e.g. Abstract, section entitled "Experimental Procedures" and Table V). Miyake et al. further disclose that "(e)rythropoietin is the substance that is responsible, in large part for the regulation of normal red blood cell differentiation. Because of this function and because it may have role in replacement therapy of some kinds of anemia, it is important to have pure erythropoietin in an amount sufficient for chemical characterization" (page 5558, first column, first paragraph, lines 7-10).

Each of Takezawa et al. (B and C), disclose methods of purifying erythropoietin (see e.g. Claims of each U.S. Patent and Example 3 of reference C). Note that Takezawa et al. (B) specifically state that "erythropoietin...is a promising medicine for curing anemia" (Abstract at lines 2 and 3) and Takezawa et al. (C) states in column 1 at lines 21-23 that "erythropoietin is a promising therapeutic medicine in the clinic (sic) treatment of anemia or, in particular, renal anemia".

None of Miyake et al. or Takezawa et al. (B or C) disclose a composition of erythropoietin comprising human serum albumin.

Applicant admits on page 87 at lines 29-31 that "(s)tandard diluents such as human serum albumin" may be used in the claimed pharmaceutical compositions and therefore tacitly acknowledge that human serum albumin was a known and accepted pharmaceutical excipient.

Bock et al., 1982 (D) teach that human serum albumin (HSA) was a known and recognized pharmaceutical carrier and that the carrier use of HSA was established as early as 1975 (see e.g. column 11 at lines 56-66).

Since erythropoietin was a known compound with accepted therapeutic use, one of ordinary skill in the art at the time of the instant invention, would have been motivated to prepare pharmaceutical compositions comprising erythropoietin. Further, since HSA was a known and accepted pharmaceutically excipient, one would have used HSA in preparing any pharmaceutical composition. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have prepared the claimed pharmaceutical compositions comprising erythropoietin and HSA.

It should be noted that the instant specification in general and claim 63 in particular is addressed towards the use of erythropoietin that is prepared using recombinant DNA technology. Within the paragraph bridging pages 18 and 19 of the specification, applicant states that.

> The present invention provides...isolated polypeptide products having part or all of the primary structural conformation...and one or more of the biological properties (e.g. immunological properties and in vivo and in vitro biological activity) of naturally occurring erythropoietin...These polypeptides are also uniquely characterized by being the product of procaryotic or eucaryotic host expression...of exogenous DNA sequences obtained by genomic or cDNA cloning or by gene synthesis...Depending upon the host employed, polypeptides of the invention may be glycosylated with mammalian or other eucaryotic carbohydrates or may be non-glycosylated

From this quotation, it is apparent that the claimed erythropoietin (EPO) compositions read on any erythropoietin molecule regardless of its source. In particular, the specification indicates that glycosylated erythropoietin that exhibits the characteristic amino acid sequence and biological properties of naturally occurring erythropoietin is envisioned. Therefore, the EPO recited in the claims reads directly upon natural isolates and the basis of the instant rejection as explained above properly establishes that the claimed invention would have been *prima facie* obvious

This Application contains claims which conflict with the claims of U.S. Patent No. 4,806,524 Although the instant Application has an effective U.S. filing date earlier than that of the conflicting patent, the instant Application may not issue if it would result in two patents being directed toward the same patentable invention. (see MPEP 2308.03).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian R. Stanton telephone number is (703) 308-2801.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C Weiman

ELIZABETH C. WEIMAR
SUPERVISORY PATENT EXAMINER
ART UNIT 184

Brian R. Stanton, Ph.D.
May 26, 1994

A 42414

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A 42415

...ATE, HOLD TOP AND BOTTOM EDGES, SNAP-APART AND ...SCARD CARBON

...S. DEPARTMENT OF COMMERCE
...TENT AND TRADEMARK OFFICE

SERIAL NO.	GROUP ART UNIT	ATTACHMENT TO PAPER NUMBER	
08/00,197	404		20

NOTICE OF REFERENCES CITED

APPLICANT(S)
LIN

U.S. PATENT DOCUMENTS

		DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE
	A	4,303,655	12/1/81	TAKEZAWA ET AL	424	177	
	B	4,397,840	8/9/83	TAKEZAWA ET AL	424	99	
	D	4,517,294	5/14/85	BOCK ET AL.	435	70	7/30/82
	C						
	E						
	F						
	G						
	H						
	I						
	J						
	K						

FOREIGN PATENT DOCUMENTS

		DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUB-CLASS	PERTINENT SHTS DWG	PERTINENT PP SPEC
	L								
	M								
	N								
	O								
	P								
	Q								

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

R MIYAKE ET AL. 1977. J. ORGANIC BIOL. CHEM. 252(15): 5558-5564

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EXAMINER	DATE	
[signature]	5/26/91	1/9/11

* A copy of this reference is not being furnished with this office action.
(See Manual of Patent Examining Procedure, section 707.05 (a).)

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A 42416