

## **EXHIBIT H-13**





**UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office**

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SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
AM675,298	11/30/94	LIP	

MERRIAM, MARSHALL & BICHPPELL  
TWO FIRST NATL. PLAZA- STE 2100  
30 SOUTH CLARY ST.  
CHICAGO, IL 60603

EXAMINER	
TAMETHOLT	
ART UNIT	PAPER NUMBER
	13

DATE MAILED: 02/05/97

This is a communication from the examiner in charge of your application  
COMMISSIONER OF PATENTS AND TRADEMARKS

This application has been examined  Responsive to communication filed on 10/3/86  This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~from~~ 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 1-72 are pending in the application.  
Of the above, claims 1-13, 16, 37-57 and 59-60 are withdrawn from consideration.
- 2.  Claims \_\_\_\_\_ have been cancelled.
- 3.  Claims \_\_\_\_\_ are allowed.
- 4.  Claims 14, 15, 17-36, 58 and 61-72 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 which are acceptable for examination purposes until such time as allowable subject matter is indicated.
- 8.  Allowable subject matter having been indicated, formal drawings are required in response to this Office action.
- 9.  The corrected or substitute drawings have been received on \_\_\_\_\_. These drawings are  acceptable;  not acceptable (see explanation).
- 10.  The  proposed drawing correction and/or 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 \_\_\_\_\_, has been  approved,  disapproved (see explanation). However, the Patent and Trademark Office no longer makes drawing changes. It is now applicant's responsibility to ensure that the drawings are corrected. Corrections **MUST** be effected in accordance with the instructions set forth on the attached letter "INFORMATION ON HOW TO EFFECT DRAWING CHANGES", PTO-1474.
- 12.  Acknowledgment is made of the claim for priority under 35 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

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PTOL-326 (Rev. 7-82)

EXAMINER'S ACTION

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The disclosure is objected to because of the following informalities:

Tables V, VI, XIV and XXX have not been submitted as new drawing Figures 5-8 as applicant contends.

Appropriate correction of the disclosure is required.

Claims 20, 23, 27 and 30 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. Ordinarily claims should not refer to drawings particularly as here where the material referred to can be easily described without resort to drawings.

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 14, 15, 17-36, 58 and 61-72 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 13-24 and 27 of copending application Serial No. 582,185 and claims 1-48 of copending application Serial No. 655,841.

This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Contrary to applicant's contention 35 U.S.C. 101 does in fact bar the allowance of the same invention in more than one application.

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Claims 14-19, 21, 22, 24, 25, 28, 31-34, 36, 58, 61-66 and 69-71 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to the DNA sequence coding for erythropoietin. The recitation of "fragments thereof" the recitation of and/or "having at least a part of the primary structural conformation and one or more of the biological activities of naturally-occurring erythropoietin" permits the claims to read on proteins and peptides completely unrelated to erythropoietin. Note for example that those unrelated proteins could possess the common biological activity of being an antigen. See MPEP 706.03(n) and 706.03(z).

Claim 35 is 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. The use of brackets for indicating different species and strains of erythropoietin DNA sequence is improper since brackets in claims designates excluding the bracketed matter.

Claims 14, 15, 61, 62 and 69 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited the conditions of hybridization. As is clear from Walker et al and Kennell almost any mismatched pair of nucleotides can be

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hybridized to each other given the right set of conditions. See MPEP 706.03(n) and 706.03(z).

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 negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (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 14, 17, 18, 21-24, 26, 27, 31-36, 58 and 61-68 are rejected under 35 U.S.C. 103 as being unpatentable over Sue et al (PNAS 80) taken together with Boeslow et al or Woods et al. Sue disclose what they believed to be the 26 amino acid sequence of human erythropoietin amino terminal peptide and indicate that the sequence was known by Goldwasser et al in 1981. Breslow et al and Woods et al disclose screening a cDNA library derived from human adult liver for blood protein sequences with oligonucleotide probes deduced from known amino acid sequence of blood proteins.

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It would be obvious to isolate the human erythropoietin cDNA sequence by utilizing the Sue et al erythropoietin amino acid sequence data to devise oligonucleotide probes for use in screening a cDNA liver library in the manner taught by Breslow et al or Woods et al. The fact that the erythropoietin 26 amino acid terminal peptide sequence of Sue et al differs from that of erythropoietin by designating an Asn instead of a Cys at the seven position is patentably irrelevant since it would not interfere with the preparation of effective oligonucleotide probes.

Claims 15 and 69-72 are rejected under 35 U.S.C. 103 as being unpatentable over Sue et al taken together with Breslow et al or Woods et al as applied to claims 14, 17, 18, 21-24, 26, 27, 31-36, 58 and 61-68 above, and further in view of Talmadge et al who disclose expressing mammalian proteins using recombinant expression plasmids. It would be obvious to express the erythropoietin gene sequence by using that sequence in expression plasmids of Talmadge et al.

Claims 19 and 20 are rejected under 35 U.S.C. 103 as being unpatentable over Sue et al taken together with Breslow et al or Woods et al as applied to claims 14, 17, 18, 21-24, 26, 27, 31-36, 58 and 61-69 above, and further in view of Farber et al who teach a monkey source for erythropoietin. It would be obvious to use

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a cDNA liver library from monkey in place of that from human or use the isolated erythropoietin cDNA sequence for isolating the monkey m RNA for ultimate conversion to monkey cDNA.

Claims 25 and 28-30 are rejected under 35 U.S.C. 103 as being unpatentable over Sue et al taken together with Breslow et al or Woods et al as applied to claims 14, 17, 18, 21-24, 26, 27, 31-36, 58 and 61-68 above, and further in view of Goury et al or Bennetzen et al who disclose the preferred codons for E. coli and yeast, respectively. It would be obvious to select those codons where the ultimate expression is in E. coli or yeast.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless-

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 14, 15, 17-19, 21, 22, 24, 25, 28, 31-34, 36, 58 and 61-72 are rejected under 35 U.S.C. 102(b) as being anticipated by Talmadge et al who disclose the expression of a mammalian protein using recombinant DNA transformed microorganisms. In view of the recitation of "fragments thereof" and the recitation of "having at least... activities" (see the 35 U.S.C. 112 rejection

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supra) the claims are deemed to embrace the DNA sequences and protein expression method of Talmadge et al.

Claims 69-72 are rejected under 35 U.S.C. 103 as being unpatentable over Talmadge et al and who disclose the basic process of recombinantly expressing and isolating polypeptides as claimed herein. Even <sup>where</sup> it is considered that one or more of the starting materials is novel, the application of an old process to such materials to produce the expected result would still be obvious within the meaning of 35 U.S.C. 103; In re Durden, supra; In re Larsen, 141 U.S.P.Q. 730 (1964). Whether or not a product produced by the claimed process possesses any unique or unexpected properties is not material to the question of whether or not the process itself would have been obvious.

A.E.Tanenholtz/pww

A/C 703

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2/4/87

*Alvin E. Tanenholtz*  
ALVIN E. TANENHOLTZ  
PRIMARY EXAMINER  
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TO SEPARATE, HOLD TOP AND BOTTOM EDGES, SNAP-APART AND REMOVE CARBON

FORM PTO-892 (REV. 3-78)	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	SERIAL NO. <b>675 298</b>	GROUP UNIT <b>127</b>	ATTACHMENT TO PAPER NUMBER <b>13</b>
NOTICE OF REFERENCES CITED		APPLICANT(S) <i>Lin</i>		

U.S. PATENT DOCUMENTS							
	DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE	
A							
B							
C							
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FOREIGN PATENT DOCUMENTS								
	DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUB-CLASS	PERTINENT SHTS. PP. DWG. SPEC.	
L								
M								
N								
O								
P								
Q								

OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)	
R	Walker et al, <i>Techniques In Molecular Biology</i> , Macmillan Pub. Co. New York pp 280 (1983)
S	Kennell, <i>Prog. Nucl. Acid. Res. Mol. Biol.</i> , 11, 259-301, page 293 (1971)
T	Breslow et al, <i>PNAS USA</i> 79 pp 6861-6865 Nov. 1982
U	Woods et al, <i>PNAS USA</i> 79 pp 5661-5665 Sep. 1982

EXAMINER <i>Trenton</i>	DATE <i>1/23/87</i>
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\* A copy of this reference is not being furnished with this office action.  
(See Manual of Patent Examining Procedure, section 707.05 (a).)

