Exhibit 10

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/113,179	10/23/87	LIN	F D-8272

HODGES, R EXAMINER

18N2/0901

MARSHALL, O'TOOLE ET AL.
TWO FIRST NATIONAL PLAZA, SUITE 2100
CHICAGO, IL 60603

ART UNIT	PAPER NUMBER
1805	29

DATE MAILED: 09/01/93

...from the examiner in charge of your application
...PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~_____ 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 65-69 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 65-69 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

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well known principles (i.e. selecting a fragment because its encoding probe would be less degenerate). In fact, Protestor indicates (Exhibit O, Explanation of Item 10) that fragments T-35 and T-38 were merely the first fragments chosen (at random?) for sequencing. In addition, Protestor indicates (Exhibit O, Explanation of Item 13) that fragment T-38, like T-35, was chosen for the presence of tryptophan. Choosing such an amino acid sequence for the derivation of degenerate cloning probes on this basis was well known at the time (see Suggs et al., page 6614, first paragraph of Results).

Protestor's history of his dispute with Amgen over inventorship (Protest, page 5, bottom) and the correspondence from Protestor's representative to Amgen is not evidence of Protestor's alleged co-inventorship but merely evidence of a dispute.

The examiner finds that all of the submitted evidence remains consistent with the inventorship as originally presented by Dr. Lin. Accordingly, Protestor has failed to provide clear and convincing evidence that Dr. Lin did not himself invent the instantly claimed subject matter.

New Grounds of Rejection

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 therefore, subject to the conditions and requirements of this title".

Claims 65-69 are rejected under 35 U.S.C. § 101 because the claimed invention is inoperable and therefore lacks patentable utility.

Claim 65 recites "a process for the preparation of...[a] biologically active glycosylated polypeptide" but then limits the transformed gene to one encoding human EPO. It is not seen how a process involving only DNA encoding human EPO can lead to the preparation of any

desired polypeptide. Accordingly, the instantly claimed process is inoperable and therefore lacks patentable utility. It is noted that the instant rejection could be overcome by amending the claim to recite "a process for the preparation of biologically active glycosylated human erythropoietin."

Claims 65-69 are directed to an invention not patentably distinct from claim 9 of commonly assigned Patent No. 4,667,016 (Lai et al.).

Claim 9 of Lai et al. recites a process of preparing EPO from a cell culture fluid. The claimed process implicitly involves the basic steps of 1) production of EPO containing cell culture fluid and 2) isolation of EPO from the fluid. While claim 9 of Lai et al. recites details of step 2 and the instant claims recite details of step 1, both claim 9 and the instant claims read on both steps. In this regard it should be noted that Lai et al. refers (paragraph bridging columns 2 and 3 and column 4, lines 34-48) explicitly to the instantly claimed method of producing recombinant EPO containing fluid. The referenced applications are ancestors of the instant application and Example 10 therein describes the exact subject matter of the instant claims.

Commonly assigned Patent No. 4,667,016, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. § 103 if the commonly assigned case qualifies as prior art under 35 U.S.C. § 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 C.F.R. § 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application. A showing that the inventions were commonly owned at the time the invention in this application was made will

Applicant also claims "glycosylation...in a pattern directed by the amino acid sequence of said...polypeptide and sufficiently duplicative of the pattern of glycosylation of naturally occurring human erythropoietin." Firstly, there is no basis in the specification for glycosylation directed by the amino acid sequence of the expressed polypeptide. It is also not clear what limitation applicant is claiming with the recitation "glycosylation...in a pattern directed by the amino acid sequence of said...polypeptide.

Secondly, applicant has provided no guidance for, and no working examples of, "sufficiently duplicative" glycosylation. Applicant has not described what constitutes sufficiency. Applicant has provided no guidance for or means of determining the similarity of any glycosylation pattern. The evidence applicant has provided that the glycosylation pattern between recombinant EPO and urinary EPO are different indicates that EPO made by the instantly claimed method is not "duplicative" of natural glycosylation. It is noted that this objection may be overcome by deleting the recitations of "glycosylation...in a pattern directed by the amino acid sequence of said...polypeptide" and "sufficiently duplicative of the pattern of glycosylation of naturally occurring human erythropoietin."

Claims 65-69 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 65-69 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to preparation of human EPO. See M.P.E.P. §§ 706.03(n) and 706.03(z).

Applicant claims a process for the preparation of a biologically active glycosylated polypeptide. However, the specification provides guidance for and a working example of only

the production of EPO. Considering the primitive state of the art of heterologous gene expression at the time the invention was made, it is questioned whether the instantly claimed method could have been practiced by one of ordinary skill in the art to produce any other biologically active glycosylated polypeptide. For example, at the time the invention was made, it was highly unpredictable that a heterologous protein would be produced in a biologically active glycosylated form. In addition, at the time the invention was made, most of the genes encoding the instantly claimed polypeptides were unknown. The instantly claimed invention is critically dependent on an isolated clone encoding a polypeptide of interest. At the time the invention was made, it would have required extensive and unpredictable experimentation to obtain such a clone for most of the myriad claimed polypeptides because gene isolation methods at the time depended on unavailable and unpredictable sequence information. Accordingly, it would have required undue experimentation by one of ordinary skill in the art to practice the instantly claimed invention to produce most of the claimed polypeptides. It is noted that the instant rejection may be overcome by amending the claim to recite "a process for the preparation of biologically active glycosylated human erythropoietin."

It is noted that enablement of the above mentioned scope is provisional pending the resolution of the objection to the specification presented supra.

Claims 65-69 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 65 is vague and indefinite because it claims a process for the production of any polypeptide but recites only DNA encoding human EPO. It is not clear if applicant intends to

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.

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Robert Hodges
September 1, 1993

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SUPERVISORY PATENT EXAMINER
ART UNIT 185