EXHIBIT N-3

UNITED STATES DEPARTMENT OF COMMERCE
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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER
HODGES, R

18N2/0215

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

ART UNIT	PAPER NUMBER
1805	34

DATE MAILED: 02/15/94

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

Docketed: 5-17-94

☒ 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 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 70-75 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.
3. ☒ Claims 70 ~~are~~ is allowed.
4. ☒ Claims 71-75 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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EXAMINER'S ACTION

PTOL-326 (Rev. 9-89)

Newly submitted claims 70-75 have obviated all previous grounds of rejection under 35 U.S.C. §§ 101, 103 and 112 for essentially the reasons set forth by applicant in the Response filed 1/10/94.

Newly submitted claims 70-75 are also not rejectable over Lai et al. (Patent No. 4,667,016) because, as applicants note, this reference is not available as prior art.

In regard to the obviousness-type double patenting rejection, applicant's argument that the multistep purification process claimed in Lai et al. is not an obvious variation of the instant process is persuasive. And while the instantly claimed method *is* an obvious variation of the process of Lai et al., it is considered that applicant is not responsible for the delay in the prosecution of the instant application which resulted in the prior patenting of a later filed application to an invention derived from the instant invention (see Ex parte Nesbit 25 USPQ2d 1817 (1992)). Accordingly, the two-way test for obviousness double patenting has been applied (see In re Braat 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991)). In support of this conclusion the examiner notes that the instant application, and its immediate parent, 06/675,298, have been subjected to extensive interparty interference and court proceedings which have delayed prosecution.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to teach how to make and use the claimed invention, as failing to provide an adequate written description of the claimed invention and as failing to provide an enabling disclosure.

Applicants claim a process for preparing erythropoietin (EPO) by growing cells transformed with, inter alia, any DNA sequences which hybridize under stringent conditions to a specifically disclosed DNA sequence encoding human EPO. Applicants have placed no limits on the nature of the claimed hybridization (e.g. length of hybridized region, detection method) and so it is considered that applicants are claiming production of EPO using any DNA which has as little as a 10-15 nucleotide region identical to a region of the disclosed EPO-encoding sequence. The transformed DNA must encode an active EPO polypeptide because the process is specifically limited to "the preparation of an *in vivo* biologically active glycosylated erythropoietin polypeptide." However, only a few of the myriad DNA sequences which would hybridize to the disclosed EPO-encoding DNA would encode active EPO.

(1) Since there is no way to tell, a priori, 1) whether any given DNA sequence will hybridize to the disclosed EPO-encoding sequences, or 2) which of the hybridizing DNA sequences will support production of active EPO in the instant method, applicants have left an undue burden of experimentation on those of skill in the art wishing to practice the full scope of the claimed process. In this regard it is noted that it would require tremendous effort to obtain the starting material for the claimed process. Although applicants are claiming a process which makes use of a product, not the product itself, it is considered that the process cannot be fully described and enabled unless the starting material is itself described and enabled.

(2) It is also considered that a claim to the use of myriad DNA sequences, only a few of which will have the required activity, is not enabled by the instant disclosure. In other words, even allowing, arguendo, that the *set* of DNA sequences which will hybridize to the disclosed EPO-encoding sequences is adequately described and enabled, it is considered that that *subset* of DNA sequences that will yield operable embodiments of the instantly claimed process (i.e. hybridizing DNA sequences which encode active EPO) is not supported by the instant disclosure. In this regard it is noted that the Federal Circuit has held, in regard to a similar issue based on the instant specification, that a claim to myriad DNA sequences, only a few of which will have the required activity, is not enabled by applicant's disclosure (Amgen v. Chugai, 18 USPQ2d at 1026-1028 (Fed. Cir.)). Quoting in pertinent part:

> ...[applicant] has not enabled preparation of DNA sequences sufficient to support [his] all-encompassing claims.
>
> ****
>
> [The instant disclosure] represents inadequate support for [applicant's] desire to claim all EPO gene analogs. There may be many other genetic sequences that code for EPO-type products. [Applicant] has told how to make and use only a few of them and is therefore not entitled to claim all of them.
>
> ****
>
> Considering the structural complexity of the EPO gene, the manifold possibilities for change in its structure, with attendant uncertainty as to what utility will be possessed by these analogs, we consider that more is needed concerning identifying the various analogs that are within the scope of the claim, methods for making them, and *structural requirements for producing compounds with EPO-like activity*. It is not sufficient, having made the gene and a handful of analogs whose activity has not been clearly ascertained, to claim all possible genetic sequences that have EPO-like activity. [emphasis added]

In view of this, it is considered that applicant is not entitled to claim the use of all DNA sequences which both hybridize to the disclosed EPO-encoding DNA and encode active EPO.

(3) By claiming the use of any DNA sequence which hybridizes to a specific sequence, applicants are claiming the use of a product by merely reciting a method to obtain that product. In view of the complexity, in both number and structure, of the DNA sequences which would hybridize to the disclosed sequences, and in view of the limited number of embodiments disclosed, it is considered that applicants have not adequately described the recited DNA sequences. Accordingly, the instant disclosure does not support the broad scope of the invention as now claimed.

Claims 71-75 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

It is noted that the above rejection would be obviated if applicants deleted the third member of the Markush group of claim 71 which recites DNA sequences which hybridize under stringent conditions to the DNA sequences defined in (1) and (2).

Claim 70 is allowed.

This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

It is noted that although applicant intended to substitute figures in place of tables in the specification (see amendment filed 10/23/87, especially page 5, top), a substitution required in, and completed in, parent application no. 06/675,298, there are no copies of Figures 15 to 21 present in the instant application. Accordingly, applicant should submit copies of Figures 15-21.

As part of an Information Disclosure Statement, filed 1/10/94, applicant's list of references (Form 1449) includes three "U.S. Patent Documents" (A27, A28 & A29) which are inadequately identified. Specifically, the examiner could find no evidence of any U.S. Patents with the listed

numbers, dates or inventors. Since applicant did not submit copies, and because no copies were available in any of the parent applications, these references have not been considered. It is further noted that if the cited documents are, in fact, U.S. Applications, their citation in an IDS is improper because they are not considered to be published documents.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (October 19, 1988) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The CM1 Fax Center number is (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

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[redacted]

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Hodges whose telephone number is (703) 308-4229.

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.

Robert Hodges
February 10, 1994

RICHARD A. SCHWARTZ
SUPERVISORY PATENT EXAMINER
GROUP UNIT 185

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