EXHIBIT E

UNITED STATES DEPARTMENT OF COMMERCE
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SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
[illegible]	[illegible]	[illegible]	[illegible]

[illegible]

EXAMINER	
[illegible]	
ART UNIT	PAPER NUMBER
[illegible]	8

DATE MAILED: [illegible]

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

X 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. X Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. X 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. X Claims 1-72 are pending in the application.
   Of the above, claims 1-13, 16, 37-37 and 59-60 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. X Claims 14, 15, 17-36, 58 and 61-72 are rejected.
5. ☐ Claims _____ are objected to.
6. X Claims 1-72 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. ☐ Acknowledgement 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) EX: 197

Serial No. 675298

Art Unit 127

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-13, 16, 39-41, 47-54 and 59, drawn to polypeptide, classified in Class 260, subclass 112.

II. Claims 14, 15, 17-36, 58 and 61-72, drawn to DNA, classified in Class 536, subclass 27.

III. Claims 37-38, drawn to plasmid, classified in Class 435, subclass 317.

IV. Claims 42-46, drawn to cells, classified in Class 435, subclass 240.

V. Claims 55-57, drawn to pharmaceutical composition, classified in Class 435, subclass 177.

VI. Claim 60, drawn to assay, classified in Class 435, subclass 6.

Inventions I and II are related as process of making and product made.

The inventions are distinct if either (1) the process as claimed can be used to make another and materially different product, or (2) the product as claimed can be made by another and materially different process. MPEP 806.05(f).

In this case, the product as claimed may be made by a materially different product, such as isolation from a naturally occurring source.

Inventions II and III are related as product and process of use.

The inventions are distinct if either (1) the process for using the product as claimed can be practiced with another and materially different product, or (2) the product as claimed can be used in a materially different process of using the product. MPEP 806.05(h).

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In this case, the product as claimed may be made by a materially different product, such as isolation from urine.

Inventions I and V are related as subcombinations disclosed as useable together in a single combination. The subcombinations are distinct from each other if they are shown to be separately useable. In the instant case, invention I has separate utility such as use in an assay. See MPEP 806.05(d).

Inventions I and VI are related as subcombinations disclosed as useable together in a single combination. The subcombinations are distinct from each other if they are shown to be separately useable. In the instant case, invention I has separate utility such as use as a pharmaceutical. See MPEP 806.05(d).

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter restriction for examination purposes as indicated is proper.

In a preliminary amendment, filed April 24, 1986, Applicant elected group II, claims 14, 15, 17-36, 58 and 61-72 without traverse. The non-elected claims are withdrawn from further consideration.

Chingwin et al (Ref. C8) has not been considered because a complete copy of the article was not among the papers in applicants prior art statement.

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 provide an enabling disclosure. The invention depends on certain specific plasmids/microorganisms. As such, a deposit is required under 35 USC 112. Conditions surrounding the deposit which must be met are enumerated in MPEP 608.01(p)(C). The deposit papers supplied with the preliminary amendment have been considered. However, it is not clear that applicants promises to replace these cultures should this become necessary. Assurance of compliance may be in the form of an oath or declaration.

Claims 14, 15, 17-36, 58 and 61-72 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the above objection to the specification.

Claims 14, 15, 17-36, 58 and 61-72 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. Claims 14, 15, 62, 64, 66,

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68, and claims depending from them are unduly alternative in their recitation of "procaryotic or eucaryotic" host cell as these are not equivalent terms. Claims 14, 17, 34, 58, 69-72 and claims depending from them are indefinite in that the fragment size claimed is so vague as to read on single base pairs. Purported limitations as to "biological properties" without further characterizations are so indefinite as to be meaningless. Claims 14, 20, 23, 27, 30, 58 and those depending on them are indefinite in that they refer to a figure when they can be adequately expressed in words. Claim 14 has improper Markush language. Claim 69 omits the number of the claim it is dependent upon.

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 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. 582185.

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

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 1-48 of copending application Serial No. 655841.

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

Claims 14, 24, 34 and 36 are rejected under 35 U.S.C. 101 because the claimed invention is directed towards non-statutory subject matter. claims 14, 24, 34 and 36 all read on the naturally occurring erythropoietin gene and portions of it present in erythropoietin-producing cells. The purported limitation of "manufactured" in claim 24 does not distinguish over naturally occurring as it could read on DNA manufactured by the cell naturally. As products of nature, these DNA sequences are not subject to patent protection.

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-
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent.
>
> (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, 24, 34 and 36 are rejected under 35 U.S.C. 102 (b) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over Sugimoto et al. Sugimoto et al teach a cell line which produces erythropoietin. It appears that the DNA inherently present in

these cells is the same as the DNA claimed. Thus applicants DNA is the same as or obvious over that of Sugimoto et al.

Claims 14, 15, 17, 18, 20, 24, 25, 26, 27, 33, 34, 58, 61, 62, 63, 64, 65, 66, 69, 70, and 71 are rejected under 35 U.S.C. 102(a) as being anticipated by Lee-Huang et al. The DNA sequences specifically claimed appear to be the same as those made by Lee-Huang et al.

Claims 14, 15, 17-20, 24, 33, 34, 36, 58, 61, 62, 63, 64, 65, 66, 69, 70, 71 are rejected under 35 U.S.C. 102 (a) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over anticipated Lin et al. The sequences cloned by Lin et al appear to be the same as those of the instant case.

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) 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.

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Claims 14, 15, 17, 18, 20, 21, 22, 23, 24, 34, 35 36, 58 and 61-72 rejected under 35 U.S.C. 103 as being unpatentable over Sugimoto et al in view of Sugimoto et al in view of Paddock and Cohen et al. Sugimoto et al teach cells from which erythropoietin RNA can be isolated, as they have a high erythropoietin production. Paddock teaches making cDNA from RNA, and Cohen et al teach cloning of a desired strand of DNA. Further, Sugimoto et al suggest that the erythropoietin gene could be so cloned. Thus it would be obvious to one of ordinary skill in the art to isolate and clone the erythropoietin gene, as the techniques for doing so are well known in the art and the expected result is obtained.

Claim 19 is rejected under 35 U.S.C. 103 as being unpatentable over Sugimoto et al in view of Paddock and Cohen et al as applied to claims 14, 15, 17, 18, 20, 21, 22, 23, 24, 34, 35, 36, 58 and 61-72 above, and further in view of Farber et al. The process and production of human EPO DNA is obvious as explained supra. Farber et al teach a monkey source of RNA for erythropoietin, and its subsequent translation. Thus in the absence of unexpected results, it would be obvious to substitute one source of the mRNA for another known source.

Claims 25-30 are rejected under 35 U.S.C. 103 as being unpatentable over Sugimoto et al in view of Paddock and Cohen et al as applied to claims14, 15, 17,

18, 20, 21, 22, 23, 24, 25, 34, 35, 36 58 and 61-72 above, and further in view of Bennetzen et al or Gouy et al. The process and production of the DNA is obvious, as discussed supra. Using codons which are known to be preferred by Lewin. The process and production of the DNA is obvious, as discused supra. Lewin teaches radioactively labeled DNA, and its use. Thus in the absence of unexpected results, it would be obvious to be label applicants' DNA, as its use is the same.

Any inquiry concerning this communication should be directed to Joanne M. Giesser at telephone number 703-557-0296.

Giesser:st

6-16-86

THOMAS G. WISEMAN
SUPERVISORY PATENT EXAMINER
ART UNIT 127

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