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A 7211

The sequences on pages 38-40 designated as Table V; on pages 43-47 designated as Table VI; on page 50 as Table VII; on page 67 as Table IX; on page 69 as Table XI; on page 71 as Table XIII; on page 72 as Table XIV; on page 77 as Table XVI; on page 79 as Table XVIII; on page 81 as Table XX and on page 82 as Table XXI are not in fact Tables but drawings. As such they should be presented as official drawings and applicant is so required. In this regard it should be noted that Tables V VI submitted as part of an Exhibit are not official drawings since an exhibit is an improper way of presenting drawings. They should be submitted separately. Moreover, the designation on drawings that they are also Tables is improper and inaccurate. Note that in conforming to this requirement applicant should renumber the remaining Tables.

The previously approved citation of Documents A13, A15 and A16 has been withdrawn since those documents have not been submitted.

Claims 73-102 are rejected under 35 U.S.C. 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The recitation of markush member (c) in claim 73

is indefinite and unduly broad. It is not clear what is meant by the recitation "but for the degeneracy of the genetic code." Also the language "would hybridize ..." is permissive and thus not an absolute limitation. Further the Markush member (c), and the sequence of claim 77 and 96 appear to embrace substantially all known DNA sequences since the isolated DNA sequence is not designated as encoding for erythropoietin. One that encodes for a protein having "a" therapeutic activity of erythropoietin is not the same thing. In order to embrace the subject matter of that Markush member (c) a separate claim drawn to an isolated DNA sequence encoding an erythropoietin selected from the group consisting of human and monkey erythropoeitin would be acceptable. The embodiments of claims 77 and 96 could properly be expressed as for example an isolated DNA sequence consisting of a DNA sequence encoding a polypeptide having the structure sufficiently duplicative of that of a naturally-occurring erythropoietin to allow possession of the biological properties of being able to cause bone marrow cells to increase hemoglobin synthesis and iron uptake and stimulate reticulocyte response. Claim 74 appears to read on naturally occurring erythropoeitin producing cells. Claims 84, 86, 87, 89, 90 and 99 are redundant of claim 77 or claim 96 since the DNA sequence has no memory of its creation.

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Claim 100 absent the designation "isolated" reads on naturally occurring mutant erythropoietin sequences.

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.

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 73-79, 81, 84, 85, 88 and 91-99 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 Talmadge et al who disclose the expression of a mammalian protein using recombinant DNA transformed microorganisms. In view of the rejections under 35 USC 112 supra, the claims are deemed to embrace the recombinant materials disclosed by Talmadge et al.

Claims 73-103 are rejected under 35 U.S.C. 103 as being unpatentable over any of Goldwasser et al (US 4,558,005) of record, Weiss et al (PNAS Vol. 79) of record and Egrie (US 4,558,006) taken in view of either Young et al or Broome et al and in further view of Ullrich et al or Martial et al. Goldwasser, Weiss et al and Egrie teach the preparation of a monoclonal antibody to human erythropoietin. Young et al and Broome et al teach a process of isolating genes using antibody probes. More specifically, Young et al teach isolating unknown foreign antigenic proteins encoded by antigen producing clones of a lambda gt11 recombinant cDNA library by using antibody probes. The foreign gene is inserted into the galactosidase gene of the lamba phage so as to result in a fused protein. Ullrich et al and Martial teach a basic process for isolating mRNA and converting it into a cDNA library for use in cloning and expressing mammalian genes. It would be obvious to prepare erythropoietin as a fused peptide by extracting

the messenger RNA for erythropoietin from kidney cells known to be rich therein and converting that mRNA to a cDNA library in the manner taught by Ullrich et al or Martial. If desired, substituting the lambda gt 11 phage library vector of Young et al for its advantages would be an obvious choice. It would further be obvious to use the Young et al or Broome et al gene isolating technique together with erythropoietin antibody of the primary references as a probe for isolating a clone producing erythropoietin. At best only routine genetic engineering techniques would be involved.

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