Exhibit C

EXHIBIT C

Claims and Groups Relating to Restriction Requirement

Restriction Group	Claim Language
Group I: **Polypeptide**	1. A purified and isolated polypeptide having part or all of the primary structural conformation and one or more of the biological properties of naturally-occurring erythropoietin and characterized by being the product of prokaryotic or eukaryotic expression of an exogenous DNA sequence. 2. A polypeptide according to claim 1 further characterized by being free of association with any mammalian protein. 3. A polypeptide according to claim 1 wherein the exogenous DNA sequence is a cDNA sequence. 4. A polypeptide according to claim 1 wherein the exogenous DNA sequence is a manufactured DNA sequence. 5. A polypeptide according to claim 1 wherein the exogenous DNA sequence is a genomic DNA sequence. 6. A polypeptide according to claim 1 wherein the exogenous DNA sequence is carried on an autonomous replicating circular DNA plasmid or viral vector. 7. A polypeptide according to claim 1 possessing part or all of the primary structural conformation of human erythropoietin as set forth in Table VI or any naturally occurring allelic variant thereof. 8. A polypeptide according to claim 1 possessing part or all of the primary structural conformation of monkey erythropoietin as set forth in Table V or any naturally occurring allelic variant thereof. 9. A polypeptide according to claim 1 which has the immunological properties of naturally-occurring erythropoietin. 10. A polypeptide according to claim 1 which has the *in vivo* biological activity of naturally-occurring erythropoietin. 11. A polypeptide according to claim 1 which has the *in vitro* biological activity of naturally-occurring erythropoietin. 12. A polypeptide according to claim 1 further characterized by

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	being covalently associated with a detectable label substance. 13. A polypeptide according to claim 12 wherein said detectable label is a radiolabel. 16. A polypeptide product of the expression of a DNA sequence of claim 14 in a prokaryotic or eukaryotic host. 39. A polypeptide product of the expression in a prokaryotic or eukaryotic host cell of a DNA sequence according to claims 17 or 34. 40. A glycoprotein product having a primary structural conformation sufficiently duplicative of that of a naturally-occurring erythropoietin to allow possession of one or more of the biological properties thereof and having an average carbohydrate composition which differs from that of naturally-occurring erythropoietin. 41. A glycoprotein product having a primary structural conformation sufficiently duplicative of that of a naturally-occurring human erythropoietin to allow possession of one or more of the biological properties thereof and having an average carbohydrate composition which differs from that of naturally-occurring human erythropoietin. 47. A synthetic polypeptide having part of all of the amino acid sequence as set forth in Table V and having one or more of the *in vivo* or *in vitro* biological activities of naturally-occurring monkey erythropoietin. 48. A synthetic polypeptide having part of all of the amino acid sequence as set forth in Table VI, other than a sequence of residues entirely within the sequence numbered 1 through 20, and having a biological property of naturally-occurring human erythropoietin. 49. A synthetic polypeptide having part of all of the secondary conformation of part or all of the amino acid sequence set forth in Table VI, other than a sequence of residues entirely within the sequence numbered 1 through 20, having a biological property of naturally-occurring human erythropoietin. 50. A process for the production of a polypeptide having part of all of the primary structural conformation and one or more of the biological properties of naturally-occurring erythropoietin, said process comprising: growing, under suitable nutrient conditions, prokaryotic or eukaryotic host cells transformed or transfected with a DNA vector according to claim 37, and isolating desired polypeptide products of the expression of DNA sequences in said vector.

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	51. An antibody substance characterized by immunoreactivity with erythropoietin and with a synthetic polypeptide having a primary structural conformation substantially duplicative of a continuous sequence of amino acid residues extant in naturally-occurring erythropoietin except for any polypeptide comprising a sequence of amino acid residues entirely comprehended within sequence, A-P-P-R-L-I-C-D-S-R-V-L-E-R-Y-L-L-E-A-K. 52. An antibody according to claim 51, which is a monoclonal antibody. 53. An antibody according to claim 51, which is a polyclonal antibody. 54. An antibody according to claim 51, which is immunoreactive with erythropoietin and a synthetic polypeptide having eh sequence selected from the sequences: V-P-D-T-K-V-N-F-Y-A-W-K-R-M-E-V-G; K-E-A-I-S-P-P-D-A-A-S-A-A; V-Y-S-N-F-L-R-G-K-L-K-L-Y-T-G-E-A-C-R-T-G-D-R. 59. A polypeptide product of the expression of a DNA sequence according to claim 58 in a prokaryotic or eukaryotic host cell.
Group II: DNA	14. A DNA sequence for use in securing expression in a prokaryotic or eukaryotic host cell of a polypeptide product having at least a part of the primary structural conformation and one or more of the biological properties of naturally-occurring erythropoietin, said DNA sequence selected from among: (a) the DNA sequence set out in Tables V and VI or their complementary strands; (b) DNA sequences which hybridize to the DNA sequences defined in (a) or fragments thereof; and (c) DNA sequences which, but for the degeneracy of the genetic code, would hybridize to the DNA sequences defined in (a) or (b). 15. A prokaryotic or eukaryotic host cell transformed or transfected with a DNA sequence according to claim 14 in a manner allowing the host cell to express said polypeptide product. 17. A purified and isolated DNA sequence coding for prokaryotic or eukaryotic host expression of a polypeptide having part or all of the primary structural conformation and one or more of the biological activities of erythropoietin.

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	18. A cDNA sequence according to claim 17. 19. A monkey species erythropoietin coding DNA sequence according to claim 18. 20. A DNA sequence according to claim 19 and including the protein coding region set forth in Figure 5. 21. A genomic DNA sequence according to claim 17. 22. A human species erythropoietin coding DNA sequence according to claim 21. 23. A DNA sequence according to claim 22 and including the protein coding region set forth in Figure 6. 24. A manufactured DNA sequence according to claim 17. 25. A manufactured DNA sequence according to claim 24 and including one or more codons preferred for expression in *E. coli* cells. 26. A manufactured DNA sequence according to claim 25, coding for expression of human species erythropoietin. 27. A manufactured DNA sequence according to claim 26 including the protein coding region set forth in Figure 7. 28. A manufactured DNA sequence according to claim 24 and including one or more codons preferred for expression in yeast cells. 29. A manufactured DNA sequence according to claim 28, coding for expression of human species erythropoietin. 30. A manufactured DNA sequence according to claim 29 including the protein coding region set forth in Figure 8. 31. A DNA sequence according to claim 17 covalently associated with a detectable label substance. 32. A DNA sequence according to claim 31 wherein the detectable label is a radiolabel. 33. A single-strand DNA sequence according to claim 31. 34. A purified and isolated DNA sequence coding for a

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	polypeptide fragment or polypeptide analog of naturally-occurring erythropoietin. 35. A DNA sequence coding for $[Phe^{15}]_{hEPO}$, $[Phe^{49}]_{hEPO}$, $[Phe^{145}]_{hEPO}$, $[His^{7}]_{hEPO}$, [Asn^2 des- Pro^2 through Ile^6]$_{hEPO}$, [des-Thr^{163} through Arg^{166}]$_{hEPO}$, or $[\Delta 27\text{-}55]_{hEPO}$. 36. A DNA sequence according to claim 34 which is a manufactured sequence. 58. A purified and isolated DNA sequence as set out in Figure 5 or 6 or a fragment thereof or the complementary strand of such a sequence or fragment. 61. A biologically functional circular plasmid or viral DNA vector including a DNA sequence according to claim 14. 62. A prokaryotic or eukaryotic host cell stably transformed or transfected with a DNA vector according to claim 61. 63. A biologically functional circular plasmid or viral DNA vector including a DNA sequence according to claim 17. 64. A prokaryotic or eukaryotic host cell stably transformed or transfected with a DNA vector according to claim 63. 65. A biologically functional circular plasmid or viral DNA vector including a DNA sequence according to claim 34. 66. A prokaryotic or eukaryotic host cell stably transformed or transfected with a DNA vector according to claim 65. 67. A biologically functional circular plasmid or viral DNA vector including a DNA sequence according to claim 35. 68. A prokaryotic or eukaryotic host cell stably transformed or transfected with a DNA vector according to claim 67. 69. A process for the production of a polypeptide having part or all of the primary structural conformation and one or more of the biological activities of naturally-occurring erythropoietin, said process comprising: growing, under suitable nutrient conditions, prokaryotic or eukaryotic host cells transformed or transfected with a DNA vector according to claim 62, and isolating desired polypeptide products of the expression of DNA sequences in said vector.

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	70. A process for the production of a polypeptide having part or all of the primary structural conformation and one or more of the biological activities of naturally-occurring erythropoietin, said process comprising: growing, under suitable nutrient conditions, prokaryotic or eukaryotic host cells transformed or transfected with a DNA vector according to claim 63, and isolating desired polypeptide products of the expression of DNA sequences in said vector. 71. A process for the production of a polypeptide having part or all of the primary structural conformation and one or more of the biological activities of naturally-occurring erythropoietin, said process comprising: growing, under suitable nutrient conditions, prokaryotic or eukaryotic host cells transformed or transfected with a DNA vector according to claim 65, and isolating desired polypeptide products of the expression of DNA sequences in said vector. 72. A process for the production of a polypeptide having part or all of the primary structural conformation and one or more of the biological activities of naturally-occurring erythropoietin, said process comprising: growing, under suitable nutrient conditions, prokaryotic or eukaryotic host cells transformed or transfected with a DNA vector according to claim 67, and isolating desired polypeptide products of the expression of DNA sequences in said vector.
Group III: Plasmid	37. A biologically functional circular plasmid or viral DNA vector including a DNA sequence according to either of claims 14, 17, 34 or 35. 38. A prokaryotic or eukaryotic host cell stably transformed or transfected with a DNA vector according to claim 37.
Group IV: Cells	42. Vertebrate cells which can be propagated *in vitro* continuously and which upon growth in culture are capable of producing in the medium of their growth in excess of 100 U of erythropoietin per 10^6 cells in 48 hours as determined by radioimmunoassay. 43. Vertebrate cells according to claim 42 capable of producing in excess of 500 U erythropoietin per 10^6 cells in 48 hours. 44. Vertebrate cells according to claim 42 capable of producing in excess of 1,000 U erythropoietin per 10^6 cells in 48 hours. 45. Vertebrate cells according to claim 42 which are mammalian

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	or avian cells. 46. Vertebrate cells according to claim 45 which are COS-1 cells or CHO cells.
Group V: Pharmaceutical Composition	55. A pharmaceutical composition comprising an effective amount of a polypeptide according to claims 1, 16, 39, 40 or 41 and a pharmaceutically acceptable diluent, adjuvant or carrier. 56. A method for providing erythropoietin therapy to a mammal comprising administering an effective amount of a polypeptide according to claims 1,16, 39, 40 or 41. 57. A method according to claim 56 wherein the therapy comprises enhancing hematocrit levels.
Group VI: Assay	60. An improvement in the method for detection of a specific single stranded polynucleotide of unknown sequence in a heterogeneous cellular or viral sample including multiple single-stranded polynucleotides wherein: (a) a mixture of labeled single-stranded polynucleotide probes is prepared having uniformly varying sequences of bases, each of said probes being potentially specifically complementary to a sequence of bases which is putatively unique to the polynucleotide to be detected; (b) the sample is fixed to a solid substrate; (c) the substrate having the sample fixed thereto is treated to diminish further binding of polynucleotides thereto except by way of hybridization to polynucleotides in said sample; (d) the treated substrate having the sample fixed thereto is transitorily contacted with said mixture of labeled probes under conditions facilitative of hybridization only between totally complementary polynucleotides; and (e) the specific polynucleotide is detected by monitoring for the presence of a hybridization reaction between it and a totally complementary probe within said mixture of labeled probes, as evidenced by the presence of a higher density of labeled material on the substrate at the locus of the specific polynucleotide in comparison to a background density of labeled material resulting from non-specific binding of labeled probes to the substrate, said improvement comprising using in excess of 32 mixed probes and

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	performance of one or more of the following: (1) employing a nylon-based paper as said solid substrate; (2) treating with a protease in step (c); (3) employing individual labeled probe concentrations of approximately 0.025 picomoles; and (4) employing as one of the hybridization conditions in step (d) stringent temperatures approaching to with 4°C away from the lowest calculated Td of any of the probes employed.