WHAT IS CLAIMED IS:

1. A fusion protein having a prolonged half-life *in vivo* in comparison to naturally occurring or recombinant native human erythropoietin comprising:

   (a) a naturally occurring human erythropoietin molecule having a cysteine residue proximate to a C terminal thereof; and

   (b) a human IgG Fc fragment having an N terminal linked to said C terminal of said erythropoietin molecule, said fragment comprising a hinge region having a non-naturally occurring amino acid sequence, said hinge region comprising a mutation replacing a cysteine residue of said hinge region located nearest said erythropoietin molecule with a non-cysteine residue, whereby the first cysteine residue of said hinge region located nearest said N terminal is spaced at least 17 amino acids apart from said cysteine residue of said erythropoietin molecule.

2. The protein as defined in claim 1, wherein the half-life of said protein is at least three fold higher than said native human erythropoietin.

3. The protein as defined in claim 2, wherein said half-life of said protein is at least four fold higher than said native human erythropoietin.

4. The fusion protein of claim 2, wherein said fusion protein has enhanced erythropoietic bioactivity in comparison to said native human erythropoietin.

5. The fusion protein as defined in claim 1, wherein said Fc fragment is an IgG1 fragment.

6. The fusion protein as defined in claim 5, wherein said Fc fragment comprises said hinge region and CH2 and CH3 domains.

7. The fusion protein as defined in claim 1, wherein said protein comprises the amino acid sequence present in SEQ ID NO: 2.

8. A fusion protein having a prolonged half-life *in vivo* in comparison to native human erythropoietin and an erythropoietic potency at least equal to said native human erythropoietin, wherein said protein comprises the amino acid sequence present in SEQ ID NO: 2 or a sequence having at least 98% sequence identity thereto, said protein comprising an erythropoietin molecule directly linked to an Fc fragment comprising a hinge region, said hinge region having a mutation whereby a cysteine amino acid of said hinge region proximate a N terminal thereof is replaced by a non-cysteine amino acid.

9. A dimeric protein comprising two fusion proteins as defined in claim 1.

10. A dimeric protein having an *in vivo* half-life and erythropoietic potency at least equal to native human erythropoietin, wherein said protein comprises comprising two polypeptides each comprising the amino acid sequence present in SEQ ID NO: 2 or a sequence having at least 98% sequence identity thereto and having a non-cysteine residue at a location corresponding to amino acid residue 172 of SEQ ID NO:2.

11. The protein as defined in claim 10, wherein said dimer comprises disulfide bonds between respective hinge domains of said polypeptides.

12. The protein as defined in claim 10, wherein each of said polypeptides has a molecular mass of about 75 kDa.

13. The protein as defined in claim 10 wherein said dimer has a molecular mass of about 180 kDa.

14. A pharmaceutical composition comprising a protein as defined in claim 1 together with a pharmaceutically acceptable carrier, adjuvant or diluent.

15. A nucleic acid sequence that encodes a polypeptide with at least 98% amino acid sequence identity to SEQ ID NO: 2, wherein said polypeptide has a prolonged half-life *in vivo* in comparison to native human erythropoietin and an erythropoietic potency at least equal to said native human erythropoietin, said polypeptide comprising a fragment of a human immunoglobulin molecule whose N terminal is directly linked to a C terminal of an erythropoietin molecule, and a hinge region of said immunoglobulin molecule having a mutation whereby a cysteine residue nearest said N terminal is replaced by a non-cysteine residue.

16. A recombinant DNA molecule comprising the nucleic acid sequence as defined in claim 15.

17. A cell line transfected with a recombinant DNA molecule as defined in claim 16.

18. The cell line as defined in claim 17, wherein said cell line is a CHO cell line.

19. A method of producing a protein as defined in claim 1, comprising culturing a cell line transfected with the DNA molecule as defined in claim 16 and purifying the polypeptide encoded thereby.

20. The fusion protein as defined in claim 8, wherein said non-cysteine residue is a neutral amino acid.

21. The fusion protein as defined in claim 20, wherein said non-cysteine residue is glycine.

22. The fusion protein as defined in claim 1, wherein the half-life of said protein when administered to a mammal is at least three fold higher than native human erythropoietin administered to said mammal by the same means.

23. The fusion protein as defined in claim 22, wherein the half-life of said protein when administered to a mammal is at least four fold higher than native human erythropoietin administered to said mammal by the same means.

24. The fusion protein as defined in claim 22, wherein said mammal is a human.

25. A dimer comprising first and second fusion proteins each as defined in claim 1, wherein said hinge region of said first fusion protein is bonded to said hinge region of said second fusion protein by disulphide bonds.

26. A recombinant DNA molecule comprising the nucleic acid sequence present in SEQ ID NO: 1.

27. A dimer comprising a pair of polypeptides each having the amino acid sequence present in SEQ ID NO: 2.

28. A fusion protein having a prolonged half-life *in vivo* in comparison to naturally occurring or recombinant native human erythropoietin comprising:

(a) a erythropoietin peptide portion having a cysteine residue proximate to a C terminal thereof, wherein said peptide portion has erythropoietic activity; and

(b) a Fc fragment comprising a hinge region, wherein the N terminal of said Fc fragment is directly linked to said C terminal of said erythropoietin peptide portion and wherein said hinge region has a mutation at an amino acid position proximate to said N terminal replacing a cysteine residue with a non-cysteine residue, whereby the first cysteine residue of said hinge region located nearest

said N terminal is spaced at least 12 amino acids apart from said cysteine residue of said erythropoietin peptide portion.

29. The fusion protein as defined in claim 28, wherein said hinge region is at least 9 amino acids in length.

30. The fusion protein as defined in claim 29, wherein said hinge region is a human Fc fragment variant having a non-cysteine residue at amino acid 6 measured from the N terminal of said Fc fragment.

31. The fusion protein as defined in claim 30, wherein said protein has an erythropoietic potency at least equal to native human erythropoietin and wherein said hinge region has the amino acid sequence VEPKSGDKTSTCPPCP or a sequence having at least 90% sequence identity thereto and having a non-cysteine residue at amino acid 6 measured from the N terminal of said Fc fragment.

32. The fusion protein as defined in claim 28, wherein said protein comprises the amino acid sequence present in SEQ ID NO: 2 or a sequence having at least 98% sequence identity thereto having said mutation, said protein having an erythropoietic potency at least equal to native human erythropoietin.

33. The fusion protein as defined in claim 28, wherein said erythropoietin peptide portion is a complete human erythropoietin molecule.

34. The fusion protein as defined in claim 28, wherein said Fc fragment is a human IgG Fc fragment comprising said hinge region and CH2 and CH3 domains.

35. The fusion protein as defined in claim 34, wherein said IgG Fc fragment is a IgG1 fragment.

36. A fusion protein comprising:

(a) an erythropoietin peptide portion having a cysteine residue proximate to a C terminal thereof, wherein said peptide portion has erythropoietic activity; and

(b) a Fc fragment comprising a hinge region, wherein an N terminal of said Fc fragment is directly linked to said C terminal of said erythropoietin peptide portion and wherein said hinge region has a mutation whereby a cysteine residue located proximate said N terminal is replaced with a non-cysteine residue, wherein said protein comprises the amino acid sequence present in SEQ ID NO: 2 or a sequence having at least 90% sequence identity thereto and wherein said protein has an *in vivo* half-life and erythropoietic potency at least equal to native human erythropoietin.

37. An isolated fusion protein having a prolonged half-life *in vivo* in comparison to native human erythropoietin and an erythropoietic potency at least equal to said native human erythropoietin comprising:

(a) an erythropoietin peptide portion having a cysteine residue proximate to a C terminal thereof, wherein said peptide portion has erythropoietic activity ; and

(b) a Fc fragment comprising a hinge region, wherein an N terminal of said Fc fragment is directly linked to said C terminal of said erythropoietin peptide portion and wherein said hinge region has a mutation whereby a cysteine residue located proximate said N terminal is replaced with a non-cysteine residue, whereby the first cysteine residue of said hinge region located nearest said N terminal is spaced at least 12 amino acids apart from said cysteine residue of said erythropoietin peptide portion, wherein said protein comprises the amino acid sequence present in SEQ ID NO: 2 or a sequence having at least 98% sequence identity thereto.

38. An isolated homodimer protein having an *in vivo* half-life and erythropoietic potency at least equal to native human erythropoietin, said protein comprising a plurality of polypeptides each having the amino acid sequence present in SEQ ID

NO:2 or a sequence having at least 98% sequence identity thereto, said sequence having a non-cysteine amino acid residue at residue 172.

39. A fusion protein having an *in vivo* half-life and erythropoietic potency at least equal to native human erythropoietin comprising:

(a) an erythropoietin peptide portion having erythropoietic activity; and

(b) an immunoglobulin peptide portion linked to said erythropoietin peptide portion and comprising a hinge region having a non-naturally occurring amino acid sequence, wherein said hinge region comprises a mutation whereby a cysteine residue located nearest to the N-terminal of hinge region is replaced by a non-cysteine residue.

40. The fusion protein as defined in claim 39, wherein said mutation is at a location corresponding to amino acid residue 172 of SEQ ID NO: 2.

41. The fusion protein of claim 40, wherein said protein has an amino acid sequence at least 98% identical to SEQ ID NO:2 and includes said mutation.

42. The fusion protein as defined in claim 40, wherein said protein comprises the sequence set forth in SEQ ID NO: 2.

43. A pharmaceutical composition comprising a protein as defined in claim 28 together with a pharmaceutically acceptable carrier, adjuvant or diluent.

44. A pharmaceutical composition comprising a protein as defined in claim 39 together with a pharmaceutically acceptable carrier, adjuvant or diluent.

45. A fusion protein having a prolonged half-life *in vivo* in comparison to naturally occurring or recombinant native human erythropoietin comprising:

(a) a naturally occurring human erythropoietin molecule; and

(b) a human IgG Fc fragment comprising a hinge region, wherein an N terminal of said Fc fragment is coupled to said C terminal of said erythropoietin molecule without the interposition of a peptide linker and wherein said hinge region comprises a mutation whereby a cysteine residue of said hinge region located nearest said N terminal is replaced with a non-cysteine residue.

46. The fusion protein as defined in claim 45, wherein said protein has the amino acid sequence present in SEQ ID NO. 2 or a sequence having 98% sequence identity thereto and including said mutation.

47. A pharmaceutical composition comprising a protein as defined in claim 45 together with a pharmaceutically acceptable carrier, adjuvant or diluent.

48. A fusion protein having a prolonged half-life *in vivo* in comparison to naturally occurring or recombinant native human erythropoietin comprising:

(a) a erythropoietin peptide portion; and

(b) a fragment of a human immunoglobulin molecule whose N terminal is linked to a C terminal of said erythropoietin peptide portion, said fragment comprising a hinge region having a mutation whereby a cysteine amino acid of said hinge region nearest to said N terminal is replaced by a non-cysteine amino acid, wherein said mutation is located at a position corresponding to residue 172 of SEQ ID NO:2.

49. The fusion protein as defined in claim 48, wherein said erythropoietin peptide portion is a naturally occurring human erythropoietin molecule.

50. The fusion protein as defined in claim 48, wherein said fragment of a human immunoglobulin molecule comprises the amino acid sequence set forth in residues 167-399 of SEQ ID NO:2

51. An isolated fusion protein comprising:

(a) an erythropoietin peptide portion having a cysteine residue proximate to a C terminal thereof; and

(b) a Fc fragment comprising a hinge region, wherein an N terminal of said Fc fragment is joined to said C terminal of said erythropoietin peptide portion without the interposition of a peptide linker and wherein said hinge region has a mutation whereby a cysteine residue located proximate said N terminal is replaced with a non-cysteine residue, wherein said protein comprises the amino acid sequence present in SEQ ID NO:2 or a sequence having at least 90% sequence identity thereto and having said mutation, wherein said protein has an *in vivo* half-life and erythropoietic potency at least equal to native human erythropoietin.

52. An isolated fusion protein comprising:

(a) an erythropoietin peptide portion having a cysteine residue proximate to a C terminal thereof; and

(b) a Fc fragment comprising a hinge region, wherein an N terminal of said Fc fragment is joined to said C terminal of said erythropoietin peptide portion without the interposition of a peptide linker and wherein said hinge region has a mutation whereby a cysteine residue located proximate said N terminal is replaced with a non-cysteine residue, whereby the first cysteine residue of said hinge region located nearest said N terminal is spaced at least 12 amino acids apart from said cysteine residue of said erythropoietin peptide portion, wherein said protein comprises the amino acid sequence present in SEQ ID NO:2 or a sequence having at least 90% sequence identity thereto and having said mutation wherein said protein has an *in vivo* half-life and erythropoietic potency at least equal to native human erythropoietin.

53. A fusion protein having a prolonged half-life *in vivo* in comparison to naturally occurring or recombinant native human erythropoietin comprising:

(a) a naturally occurring human erythropoietin molecule having a cysteine residue proximate to a C terminal thereof; and

(b) a human IgG1 Fc fragment comprising a hinge region, and CH2 and CH3 domains, wherein an N terminal of the Fc fragment is joined to said C terminal of said erythropoietin molecule without the interposition of a peptide linker and wherein said Fc fragment has a single amino acid replacement replacing the cysteine residue located nearest said erythropoietin molecule with a non-cysteine residue, whereby the first cysteine residue of said hinge region located nearest said N terminal is spaced at least 12 amino acids apart from said cysteine residue of said erythropoietin molecule.

54. A fusion protein having a prolonged half-life *in vivo* in comparison to naturally occurring or recombinant native human erythropoietin comprising:

(a) an erythropoietin peptide portion having a cysteine residue proximate the C terminal thereof, wherein said peptide portion is joined without the interposition of a peptide linker to

(b) a human IgG1 Fc fragment comprising a hinge region and CH2 and CH3 domains, wherein said hinge region has

(i) the amino acid sequence VEPKSGDKTSTCPPCP or

(ii) a sequence having at least 90% sequence identity thereto and having a non-cysteine residue at amino acid 6 measured from the N terminal of said hinge region,

whereby the cysteine residue of said hinge region located nearest said erythropoietin peptide portion is spaced at least 12 amino acids apart from said cysteine residue of said erythropoietin peptide portion.