Summary of Differences Between '008 Claims and '868 and '698 Claims*

*The following table summarizes the differences between each '008 claim asserted as an ODP reference by Roche and the later-issued '868 and '698 claims-in-suit. A more detailed discussion of the differences between these claims, and the significance of those differences, is provided in Amgen's Bench Memorandum and Offer of Proof Regarding No Obviousness-Type Double Patenting, at Part III.D, and the supporting Declaration of Harvey F. Lodish, Ph.D.

Summary of Differences Between '008 Claims and '868 and '698 Claims

'008 Claims	'868 and '698 Claims	Differences
'008 Claim 2: 2. A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin.	*'868 Asserted Claims:* 1. A process for the production of glycosylated erythropoietin polypeptide having the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells comprising the steps of: (a) growing, under suitable nutrient conditions, mammalian host cells transformed or transfected with an isolated DNA sequence encoding human erythropoietin; and (b) isolating said glycosylated erythropoietin polypeptide therefrom. 2. The process according to claim 1 wherein said host cells are CHO cells. *'698 Asserted Claims:* 6. A process for the production of a glycosylated erythropoietin polypeptide having the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells comprising the steps of: (a) growing, under suitable nutrient conditions, vertebrate cells comprising amplified DNA encoding the mature erythropoietin amino acid sequence of FIG. 6; and (b) isolating said glycosylated erythropoietin polypeptide expressed by said cells. 7. The process of claim 6 wherein said vertebrate cells further comprise amplified marker gene DNA. 8. The process of claim 7 wherein said amplified marker gene DNA is Dihydrofolate reductase (DHFR) gene DNA. 9. The process according to claims 2, 4 and 6 wherein said cells are mammalian cells.	*'008 Claim 2 vs. '868 Asserted Claims:* • '008 claim 2 is to a composition of matter, whereas the '868 claims require the specific recited combination of steps • The '868 claims require mammalian host cells, whereas '008 claim 2 does not require any host cell • The '868 claims require that the recited host cell be capable of producing isolatable quantities of EPO, whereas '008 claim 2 does not require the production of any amount of EPO • The '868 claims require production of a glycosylated polypeptide, whereas '008 claim 2 requires neither glycosylation nor a polypeptide • The '868 claims require that any EPO expressed have the stated *in vivo* biological function, whereas '008 claim 2 does not require either *in vitro* or *in vivo* biological function *'008 Claim 2 vs. '698 Asserted Claims:* • [All of the differences listed above] • The '698 claims require "amplified DNA," whereas '008 claim 2 does not • '698 claims 7 and 8 require "amplified marker gene DNA," whereas '008 claim 2 does not.

Summary of Differences Between '008 Claims and '868 and '698 Claims

'008 Claims	'868 and '698 Claims	Differences
'008 Claims 4 and 6: 4. A procaryotic or eucaryotic host cell transformed or transfected with a DNA sequence according to claim 1, 2 or 3 in a manner allowing the host cell to express erythropoietin. 6. A procaryotic or eucaryotic host cell stably transformed or transfected with a DNA vector according to claim 5. *[5. A biologically functional circular plasmid or viral DNA vector including a DNA sequence according to claim 1, 2 or 3.]* *[2. A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin.]*	*'868 Asserted Claims:* 1. A process for the production of glycosylated erythropoietin polypeptide having the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells comprising the steps of: (a) growing, under suitable nutrient conditions, mammalian host cells transformed or transfected with an isolated DNA sequence encoding human erythropoietin; and (b) isolating said glycosylated erythropoietin polypeptide therefrom. 2. The process according to claim 1 wherein said host cells are CHO cells. *'698 Asserted Claims:* 6. A process for the production of a glycosylated erythropoietin polypeptide having the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells comprising the steps of: (a) growing, under suitable nutrient conditions, vertebrate cells comprising amplified DNA encoding the mature erythropoietin amino acid sequence of FIG. 6; and (b) isolating said glycosylated erythropoietin polypeptide expressed by said cells. 7. The process of claim 6 wherein said vertebrate cells further comprise amplified marker gene DNA. 8. The process of claim 7 wherein said amplified marker gene DNA is Dihydrofolate reductase (DHFR) gene DNA. 9. The process according to claims 2, 4 and 6 wherein said cells are mammalian cells.	*'008 Claims 4 and 6 vs. '868 Asserted Claims:* • '008 claims 4 and 6 are to compositions of matter, whereas the '868 claims require the specific recited combination of steps • The '868 claims require mammalian host cells, whereas '008 claims 4 and 6 broadly cover any procaryotic and any eucaryotic host cells transformed or transfected with the recited DNA sequence • The '868 claims require that the recited host cell be capable of producing isolatable quantities of EPO, whereas '008 claims 4 and 6 do not require the production of any amount of EPO • The '868 claims require that any EPO expressed by the recited host cell be glycosylated, whereas '008 claims 4 and 6 require neither glycosylation nor a polypeptide • The '868 claims require that any EPO expressed have the stated *in vivo* biological function, whereas '008 claims 4 and 6 do not require either *in vitro* or *in vivo* biological function *'008 Claims 4 and 6 vs. '698 Asserted Claims:* • [All of the differences listed above] • The '698 claims require "amplified DNA," whereas '008 claims 4 and 6 do not • '698 claims 7 and 8 require "amplified marker gene DNA," whereas '008 claims 4 and 6 do not.

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'008 Claims	'868 and '698 Claims	Differences
'008 Claim 7: 7. A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding a polypeptide having an amino acid sequence sufficiently duplicative of that of erythropoietin to allow possession of the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells, and to increase hemoglobin synthesis or iron uptake.	*'868 Asserted Claims:* 1. A process for the production of glycosylated erythropoietin polypeptide having the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells comprising the steps of: (a) growing, under suitable nutrient conditions, mammalian host cells transformed or transfected with an isolated DNA sequence encoding human erythropoietin; and (b) isolating said glycosylated erythropoietin polypeptide therefrom. 2. The process according to claim 1 wherein said host cells are CHO cells. *'698 Asserted Claims:* 6. A process for the production of a glycosylated erythropoietin polypeptide having the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells comprising the steps of: (a) growing, under suitable nutrient conditions, vertebrate cells comprising amplified DNA encoding the mature erythropoietin amino acid sequence of FIG. 6; and (b) isolating said glycosylated erythropoietin polypeptide expressed by said cells. 7. The process of claim 6 wherein said vertebrate cells further comprise amplified marker gene DNA. 8. The process of claim 7 wherein said amplified marker gene DNA is Dihydrofolate reductase (DHFR) gene DNA. 9. The process according to claims 2, 4 and 6 wherein said cells are mammalian cells.	*'008 Claim 7 vs. '868 Asserted Claims:* • '008 claim 7 is to composition of matter, whereas the '868 claims require the specific recited combination of steps • The '868 claims require mammalian host cells, whereas '008 claim 7 does not require any host cell • The '868 claims require that the recited host cell be capable of producing isolatable quantities of EPO, whereas '008 claim 7 does not require the production of any amount of EPO • The '868 claims require production of a glycosylated polypeptide, whereas '008 claim 7 requires neither glycosylation nor a polypeptide • The '868 claims require that any EPO expressed have the stated *in vivo* biological function, whereas '008 claim 7 does not require either *in vitro* or *in vivo* biological function • '008 claim 7 covers an enormous number of DNAs coding for EPO analogs ("all possible genetic sequences that [encode a polypeptide] hav[ing] EPO-like activity"[1]), whereas the '868 claims do not cover DNAs coding for EPO analogs • '008 claim 7 has been held invalid for lack of sufficient enablement, whereas it is undisputed that the '868 and '698 claims are sufficiently enabled *'008 Claim 7 vs. '698 Asserted Claims:* • [All of the differences listed above] • The '698 claims require "amplified DNA," whereas '008 claim 7 does not • '698 claims 7 and 8 require "amplified marker gene DNA," whereas '008 claim 7 does not

[1] *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F. 2d 1200, 1213 (Fed. Cir. 1991).

Summary of Differences Between '008 Claims and '868 and '698 Claims

'008 Claims	'868 and '698 Claims	Differences
'008 Claims 25 and 27: 25. A transformed or transfected mammalian host cell according to claim 24. 27. A transformed or transfected CHO cell according to claim 25. *[24. A transformed or transfected host cell according to claim 23 which host cell is capable of glycosylating said polypeptide.]* *[23. A procaryotic or eucaryotic host cell transformed or transfected with a DNA sequence according to claim 7, 8 or 11 in a manner allowing the host cell to express said polypeptide.]* *[7. A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding a polypeptide having an amino acid sequence sufficiently duplicative of that of erythropoietin to allow possession of the biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells, and to increase hemoglobin synthesis or iron uptake.]*	*'868 Asserted Claims:* 1. A process for the production of glycosylated erythropoietin polypeptide having the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells comprising the steps of: (a) growing, under suitable nutrient conditions, mammalian host cells transformed or transfected with an isolated DNA sequence encoding human erythropoietin; and (b) isolating said glycosylated erythropoietin polypeptide therefrom. 2. The process according to claim 1 wherein said host cells are CHO cells. *'698 Asserted Claims:* 6. A process for the production of a glycosylated erythropoietin polypeptide having the in vivo biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells comprising the steps of: (a) growing, under suitable nutrient conditions, vertebrate cells comprising amplified DNA encoding the mature erythropoietin amino acid sequence of FIG. 6; and (b) isolating said glycosylated erythropoietin polypeptide expressed by said cells. 7. The process of claim 6 wherein said vertebrate cells further comprise amplified marker gene DNA. 8. The process of claim 7 wherein said amplified marker gene DNA is Dihydrofolate reductase (DHFR) gene DNA. 9. The process according to claims 2, 4 and 6 wherein said cells are mammalian cells.	*'008 Claims 25 and 27 vs. '868 Asserted Claims:* • '008 claims 25 and 27 are to compositions of matter, whereas the '868 claims require the specific recited combination of steps • The '868 claims require that the recited host cell be capable of producing isolatable quantities of EPO, whereas '008 claims 25 and 27 do not require the production of any amount of EPO • The '868 claims require that any EPO expressed by the recited host cell be glycosylated, whereas '008 claims 25 and 27 require neither glycosylation nor a polypeptide • The '868 claims require that any EPO expressed have the stated *in vivo* biological function, whereas '008 claims 25 and 27 do not require either *in vitro* or *in vivo* biological function • '008 claims 25 and 27 cover host cells transformed or transfected with any of an enormous number of DNAs coding for EPO analogs ("all possible genetic sequences that [encode a polypeptide] hav[ing] EPO-like activity"), whereas the '868 claims do not cover DNAs coding for EPO analogs or host cells transformed or transfected with such DNAs • '008 claims 25 and 27 have been held invalid for lack of sufficient enablement, whereas it is undisputed that the '868 and '698 claims are sufficiently enabled *'008 Claims 25 and 27 vs. '698 Asserted Claims:* • [All of the differences listed above] • The '698 claims require "amplified DNA," whereas '008 claims 25 and 27 do not • '698 claims 7 and 8 require "amplified marker gene DNA," whereas '008 claims 25 and 27 do not.