IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, v. F. HOFFMANN-LA ROCHE LTD., ROCHE DIAGNOSTICS GmbH, HOFFMANN-LA ROCHE INC., Defendants.	))))))))))))	Civil Action No. 05-12237 WGY

AMGEN INC.'S L.R. 56.1 STATEMENT IN OPPOSITION TO ROCHE'S STATEMENT OF MATERIAL FACTS IN SUPPORT OF ITS MOTION FOR SUMMARY JUDGMENT THAT CLAIM 7 OF U.S. PAT. NO. 5,756,349 IS INVALID UNDER 35 U.S.C. § 112 AND IS NOT INFRINGED

Pursuant to Local Rule 56.1, Plaintiff Amgen Inc. ("Amgen") submits the following response to Roche's L.R. 56.1 statement of material facts ("Roche's SOF") submitted in support of its motion for summary judgment that Claim 7 of U.S. Pat. No. 5,756,349 is invalid and not infringed.

AMGEN'S RESPONSES TO ROCHE'S STATEMENTS OF MATERIAL FACT ("SOF")

1. Amgen does not contest Roche's SOF ¶ 1.

2. Amgen does not contest Roche's SOF ¶ 2.

3. Amgen does not contest Roche's SOF ¶ 3.

4. Amgen does not contest Roche's SOF ¶ 4.

5. Amgen does not contest Roche's SOF ¶ 5.

6. Amgen contests Roche's SOF ¶ 6 to the extent that Amgen has not limited its contention of Roche's infringement of Claim 7 to "cells according to Claims 1, 2 and 3 of the '349 patent." The page cited by Roche does not mention the '349 patent, much less support the contention found in Roche's SOF ¶ 6. Amgen contends that Roche infringes '349 claim 7 as it depends from each of '349 claims 1-6. *See* Exh. 1 (Plaintiff's Supplemental Response to Defendants' First Set of Interrogatories) at 21.[1] Further, Roche's SOF ¶ 6 does not accurately reflect the claim language. Exh. 2 ('349 patent) at Col. 38, lines 34–36. Roche infringes Claim 7 by practicing a process for producing erythropoietin

[1] All Exhibits cited in this Statement are attached to the Declaration of Cullen N. Pendleton in Support of Amgen Inc.'s Opposition To Roche's Motion For Summary Judgment That Claim 7 Of U.S. Pat. No. 5,756,349 Is Invalid Under 35 U.S.C. § 112 And Is Not Infringed.

comprising the step of culturing, under suitable nutrient conditions, vertebrate cells according to any of Claims 1-6.

7. Amgen does not contest Roche's SOF ¶ 7.

8. Amgen contests Roche's SOF ¶ 8 to the extent that it is misleading, inaccurate, and incomplete. While the term "units" ("U") can refer to the *in vivo* biological activity of erythropoietin ("EPO") measured in an *in vivo* bioassay, the term does not only refer to the results of such an assay; the term was also customarily used in the prior art (and in the '349 patent) to report the results of *in vitro* cellular assays and radioimmunoassays for EPO. As the prior-art scientific literature and the '349 patent itself make clear, to one of ordinary skill in 1983-84, "Units" of erythropoietin also "quantify" the immunological activity of a sample as measured in a radioimmunoassay. *See* Exh. 3 (Lin 3-28-07 Depo. Tr.) at 165:22–24; Exh. 4 (Goldwasser 5-31-07 Depo. Tr.) at 72:22 to 73:8; Exh. 5 (Rebuttal Expert Statement of Ronald W. McLawhon, M.D., Ph.D.) at ¶¶ 30–33, 48, 75; Exh. 6 (Rebuttal Expert Statement of Eugene Goldwasser, Ph.D.) at ¶¶ 119–21, 123–26, 157; Exh. 10 (Sherwood & Goldwasser (1979), *Blood* 54(4):885-893) at, *e.g.*, 891 (Tables 2 & 3); Exh. 24 (Garcia *et al.* (1979) *Blood Cells* 5:405–19 at, *e.g.*, 412 (Table I and accompanying text); Exh. 23 (Zaroulis *et al*. (1981) *Am. J. Hematology* 11:85–92) at, *e.g.*, 89 (Fig. 2; Tables I & II); Exh. 8 (Goldwasser and Sherwood (1981) *Brit. J. Haematology* 48:359–63) at, *e.g.*, 359; Exh. 28 (Rege *et al*. (1982) *J. Lab. Clin. Med*. 100(6):829–843) at, *e.g.*, 836 (Table IV); Exh. 30 (Koeffler & Goldwasser (1981), *Annals of Internal Medicine* 94:44–47) at, *e.g.*, 46 (Table I); Exh. 25 (Cotes *et al*. (1982), *Brit. J. Haematology* 50:427–38) at, *e.g.*, 430 (Table I); Exh. 31 (Thomas *et al*. (1983), *Brit. J. Obst. Gynec*. 90:795–800) at, *e.g.*, 798 (Table 3); Exh. 32 (Garcia (1974),

RADIOIMMUNOASSAY AND RELATED PROCEDURES IN MEDICINE Vol. I, Vienna IAEA-SM-177:275–287) at, *e.g.*, 280 (Table I); Exh. 35 (Lertora *et al*. (1975), *J. Lab. Clin. Med*. 86(1):140–151) at, *e.g.*, 146 (Table 4); Exh. 33 (Goldwasser *et al*. (1975), *Endocrinology* 97(2):315–323) at, *e.g.*, 322 (Table 6); Exh. 34 (Lange *et al*. (1980), *Human Immunology* 1:197–224) at, *e.g.*, 206–207 (Table 1).

9. Amgen contests Roche's SOF ¶ 9 to the extent that is misleading, inaccurate, and incomplete. The claim term "U of erythropoietin" cannot be interpreted in isolation; the complete claim limitation is "U of erythropoietin per 10^6 cells in 48 hours as determined by radioimmunoassay." This limitation is described in the '349 patent, and one of ordinary skill in 1983-84 already knew what the term "U of erythropoietin . . . as determined by radioimmunoassay" meant. *See* Exh. 2 ('349 patent) at, *e.g.*, Col. 26:43 to Col. 27:34–41; Exh. 3 (Lin 3-28-07 Depo. Tr.) at 165:22–24; Exh. 4 (Goldwasser 5-31-07 Depo. Tr.) at 72:22 to 73:8; Exh. 5 (Rebuttal Expert Statement of Ronald W. McLawhon, M.D., Ph.D.) at ¶¶ 30–33, 48, 75; Exh. 6 (Rebuttal Expert Statement of Eugene Goldwasser, Ph.D.) at ¶¶ 119–21, 123–26, 157; Exh. 10 (Sherwood & Goldwasser (1979), *Blood* 54(4):885-893) at, *e.g.*, 891 (Tables 2 & 3); Exh. 24 (Garcia *et al.* (1979) *Blood Cells* 5:405–19 at, *e.g.*, 412 (Table I and accompanying text); Exh. 23 (Zaroulis *et al*. (1981) *Am. J. Hematology* 11:85–92) at, *e.g.*, 89 (Fig. 2; Tables I & II); Exh. 8 (Goldwasser and Sherwood (1981) *Brit. J. Haematology* 48:359–63) at, *e.g.*, 359; Exh. 28 (Rege *et al*. (1982) *J. Lab. Clin. Med*. 100(6):829–843) at, *e.g.*, 836 (Table IV); Exh. 30 (Koeffler & Goldwasser (1981), *Annals of Internal Medicine* 94:44–47) at, *e.g.*, 46 (Table I); Exh. 25 (Cotes *et al*. (1982), *Brit. J. Haematology* 50:427–38) at, *e.g.*, 430 (Table I); Exh. 31 (Thomas *et al*. (1983), *Brit. J. Obst. Gynec*. 90:795–800) at, *e.g.*, 798

(Table 3); Exh. 32 (Garcia (1974), RADIOIMMUNOASSAY AND RELATED PROCEDURES IN MEDICINE Vol. I, Vienna IAEA-SM-177:275–287) at, *e.g.*, 280 (Table I); Exh. 35 (Lertora *et al*. (1975), *J. Lab. Clin. Med*. 86(1):140–151) at, *e.g.*, 146 (Table 4); Exh. 33 (Goldwasser *et al*. (1975), *Endocrinology* 97(2):315–323) at, *e.g.*, 322 (Table 6); Exh. 34 (Lange *et al*. (1980), *Human Immunology* 1:197–224) at, *e.g.*, 206–207 (Table 1)..

10. Amgen contests Roche's SOF ¶ 10 to the extent that it is misleading, inaccurate, and incomplete. As stated in response to Roche's SOF ¶ 8, while the term "units" ("U") can refer to the *in vivo* biological activity of erythropoietin ("EPO") measured in an *in vivo* bioassay, the term was also customarily used in the prior art to report the results of *in vitro* cellular assays and radioimmunoassays for EPO. *See* Exh. 3 (Lin 3-28-07 Depo. Tr.) at 165:22–24; Exh. 4 (Goldwasser 5-31-07 Depo. Tr.) at 72:22 to 73:8; Exh. 5 (Rebuttal Expert Statement of Ronald W. McLawhon, M.D., Ph.D.) at ¶¶ 30–33, 48, 75; Exh. 6 (Rebuttal Expert Statement of Eugene Goldwasser, Ph.D.) at ¶¶ 119–20, 123–26, 157; Exh. 10 (Sherwood & Goldwasser (1979), *Blood* 54(4):885-893) at, *e.g.*, 891 (Tables 2 & 3); Exh. 24 (Garcia *et al.* (1979) *Blood Cells* 5:405–19 at, *e.g.*, 412 (Table I and accompanying text); Exh. 23 (Zaroulis *et al*. (1981) *Am. J. Hematology* 11:85–92) at, *e.g.*, 89 (Fig. 2; Tables I & II); Exh. 8 (Goldwasser and Sherwood (1981) *Brit. J. Haematology* 48:359–63) at, *e.g.*, 359; Exh. 28 (Rege *et al*. (1982) *J. Lab. Clin. Med.* 100(6):829–843) at, *e.g.*, 836 (Table IV); Exh. 30 (Koeffler & Goldwasser (1981), *Annals of Internal Medicine* 94:44–47) at, *e.g.*, 46 (Table I); Exh. 25 (Cotes *et al*. (1982), *Brit. J. Haematology* 50:427–38) at, *e.g.*, 430 (Table I); Exh. 31 (Thomas *et al*. (1983), *Brit. J. Obst. Gynec*. 90:795–800) at, *e.g.*, 798 (Table 3); Exh. 32 (Garcia (1974), RADIOIMMUNOASSAY AND RELATED PROCEDURES IN MEDICINE Vol. I, Vienna IAEA-SM-

177:275–287) at, *e.g.*, 280 (Table I); Exh. 35 (Lertora *et al*. (1975), *J. Lab. Clin. Med*. 86(1):140–151) at, *e.g.*, 146 (Table 4); Exh. 33 (Goldwasser *et al*. (1975), *Endocrinology* 97(2):315–323) at, *e.g.*, 322 (Table 6). Exh. 34 (Lange *et al*. (1980), *Human Immunology* 1:197–224) at, *e.g.*, 206–207 (Table 1).

11. Amgen contests Roche's SOF ¶ 11 to the extent that the term "specific portions of EPO" used therein is vague and ambiguous in the context of the statement. Roche cites ¶ 12 of Dr. McLawhon's Expert Report in support of SOF ¶ 11, but Dr. McLawhon did not use the term "specific portions of EPO" in his Rebuttal Expert Statement. Exh. 11 (Expert Rebuttal Statement of Ronald W. McLawhon, M.D., Ph.D.) at ¶ 12.

12. Amgen does not contest Roche's SOF ¶ 12.

13. Amgen does not contest Roche's SOF ¶ 13, but notes that the statement is immaterial to the validity or infringement of '349 claim 7.

14. Amgen contests Roche's SOF ¶ 14 to the extent that it is unclear, misleading, and unsubstantiated. On its face, Roche contends no more than that antibodies will recognize that to which they bind. This is a tautology that Amgen does not contest. However, to the extent Roche is contending that all antibodies that one of ordinary skill would have used in the radioimmunoassay called for by the '349 claims would recognize "EPO fragments" or that non-protein "molecules" can contain epitopes recognizable by antibodies, such conclusions are unsupported by the testimony cited by Roche or any other evidence of record. Roche cites Dr. McLawhon's deposition testimony in support of SOF ¶ 14, but Dr. McLawhon did not testify that antibodies used in an EPO RIA would recognize "protein fragments." Dr. McLawhon was not asked about non-protein molecules, and

when asked about antibody binding to "epitopes that are not necessarily EPO," he replied "it would be speculation." Exh. 7 (McLawhon 5-17-07 Depo. Tr.) at 152:9–15.

15. Amgen contests Roche's SOF ¶ 15 to the extent that it is unclear, misleading, and unsubstantiated. There is no dispute that the radioimmunoassay called for by the claims of the 349 patent will detect erythropoietin when present in a sample. To the extent Roche is contending that the radioimmunoassay called for by the '349 claims could recognize "EPO fragments," such a conclusion is unsupported by the testimony cited by Roche in SOF ¶ 15. When asked whether "it could be a fragment" reacting with the antibody, Dr. McLawhon responded "that's speculation." Dr. McLawhon did not testify that anti-EPO antibodies can bind to EPO "fragments." Exh. 7 (McLawhon 5-17-07 Depo. Tr.) at 220:4–7.

16. Amgen contests Roche's SOF ¶ 16 to the extent that it is unclear, misleading, and unsubstantiated. On its face, Roche contends in part no more than that antibodies will recognize that to which they bind. This is a tautology that Amgen does not contest. However, Amgen disputes any contention by Roche that seeks to generally extend this tautology to some undefined set of "EPO fragments." To the extent Roche is contending that antibodies in the radioimmunoassay that one of ordinary skill would have used in practicing '349 claim 7 could recognize "EPO fragments," such a conclusion is unsupported by the testimony cited by Roche. When asked whether "the antibody recognizes epitopes that are not necessarily EPO," Dr. McLawhon testified "[t]hat's speculation." Dr. McLawhon did not testify that anti-EPO antibodies can bind to EPO "fragments." Exh. 7 (McLawhon 5-17-07 Depo. Tr.) at 220:4–7.

17. Amgen contests Roche's SOF ¶ 17. Roche has not pointed to any evidence in this case that "EPO fragments" produced by cells in culture would be recognized by the radioimmunoassay that one of ordinary skill would have used in practicing '349 claim 7. When asked about the "fragments" issue, Dr. Goldwasser did not testify that an RIA cannot distinguish between EPO and EPO "fragments." Dr. Goldwasser testified that "if you put in something of small molecular size, the RIA would tell you that there was an immunologically reactive material that was not called epo." Exh. E to Suh Decl. (Docket No. 542) at 49:14-20. That an experiment could be contrived to add material to a sample, as opposed to detecting material produced by the cells recited in the '349 claims using radioimmunoassay, is not material to the validity of '349 claim 7.

18. Amgen contests Roche's SOF ¶ 18 to the extent that it is unclear, misleading, and unsubstantiated. The evidence in this case, including the documents cited in SOF ¶ 18, does not support Roche's contentions in this statement. The first document cited presents only a hypothesis that was retracted in a later publication by the same authors because the original observations that led to the hypothesis were based on inaccurate, artifactual data. Nor is there any evidence to support any contention that any such "EPO fragments," if they ever existed, could be generated by the cells recited in the '349 claims. The second document cited by Roche does not even mention the word "fragments." Exh. 8 (Goldwasser & Sherwood (1981) *Brit. J. Haematology* 48:359–63) at 360; Exh. 9 (Sherwood *et al*. (1991), *Endocrinology* 128(1):440); Exh. 10 (Sherwood & Goldwasser (1979), *Blood* 54(4):885-893) at 892–93.

19. Amgen does not contest Roche's SOF ¶ 19.

20. Amgen contests Roche's SOF ¶ 20 to the extent that it mischaracterizes the cited portion of the '349 patent. The cited portion of the '349 patent actually refers to "monoclonal and polyclonal antibodies generated by standard means which are immunoreactive with such polypeptides and, ***preferably***, ***also*** immunoreactive with naturally-occurring erythropoietin." Exh. 2 at Col. 10:58-62 (emphasis added).

21. Amgen does not contest Roche's SOF ¶ 21.

22. Amgen contests Roche's SOF ¶ 22 to the extent that its recitation of the term "unmodified erythropoietin" renders the statement unintelligible, and to the extent that it might be possible to develop a radioimmunoassay that could distinguish between *in vivo* biologically active human erythropoietin and desialylated human erythropoietin, but notes that in any event the statement is immaterial to the validity or infringement of '349 claim 7.

23. Amgen does not contest Roche's SOF ¶ 23.

24. Amgen contests Roche's SOF ¶ 24 to the extent that it is misleading, inaccurate, and incomplete. As stated in response to Roche's SOF ¶¶ 8 and 10, while the term "units" ("U") can refer to the *in vivo* biological activity of erythropoietin ("EPO") measured in an *in vivo* bioassay, the term was also customarily used in the prior art to report the results of *in vitro* cellular assays and radioimmunoassays for EPO. *See* Exh. 3 (Lin 3-28-07 Depo. Tr.) at 165:22–24; Exh. 4 (Goldwasser 5-31-07 Depo. Tr.) at 72:22 to 73:8; Exh. 5 (Rebuttal Expert Statement of Ronald W. McLawhon, M.D., Ph.D.) at ¶¶ 30–33, 48, 75; Exh. 6 (Rebuttal Expert Statement of Eugene Goldwasser, Ph.D.) at ¶¶ 119–20, 123–26, 157); Exh. 10 (Sherwood & Goldwasser (1979), *Blood* 54(4):885-893) at, *e.g.*, 891

(Tables 2 & 3); Exh. 24 (Garcia *et al.* (1979) *Blood Cells* 5:405–19 at, *e.g.*, 412 (Table I and accompanying text); Exh. 23 (Zaroulis *et al*. (1981) *Am. J. Hematology* 11:85–92) at, *e.g.*, 89 (Fig. 2; Tables I & II); Exh. 8 (Goldwasser and Sherwood (1981) *Brit. J. Haematology* 48:359–63) at, *e.g.*, 359; Exh. 28 (Rege *et al*. (1982) *J. Lab. Clin. Med*. 100(6):829–843) at, *e.g.*, 836 (Table IV); Exh. 30 (Koeffler & Goldwasser (1981), *Annals of Internal Medicine* 94:44–47) at, *e.g.*, 46 (Table I); Exh. 25 (Cotes *et al*. (1982), *Brit. J. Haematology* 50:427–38) at, *e.g.*, 430 (Table I); Exh. 31 (Thomas *et al*. (1983), *Brit. J. Obst. Gynec*. 90:795–800) at, *e.g.*, 798 (Table 3); Exh. 32 (Garcia (1974), RADIOIMMUNOASSAY AND RELATED PROCEDURES IN MEDICINE Vol. I, Vienna IAEA-SM-177:275–287) at, *e.g.*, 280 (Table I); Exh. 35 (Lertora *et al*. (1975), *J. Lab. Clin. Med*. 86(1):140–151) at, *e.g.*, 146 (Table 4); Exh. 33 (Goldwasser *et al*. (1975), *Endocrinology* 97(2):315–323) at, *e.g.*, 322 (Table 6). Exh. 34 (Lange *et al*. (1980), *Human Immunology* 1:197–224) at, *e.g.*, 206–207 (Table 1).

25. Amgen contests Roche's SOF ¶ 25 to the extent that it is misleading, inaccurate, and unsubstantiated. The cited passage from the Expert Report of Ronald W. McLawhon, M.D., Ph.D., does not mention "converting" a "measured amount of protein" to "U of erythropoietin," nor does the radioimmunoassay called for in the '349 claims require this; to the contrary, the cited passage reports "milliunits of EPO per milliliter of cell culture medium" as determined by radioimmunoassay and uses these numbers to calculate a production rate of "U of erythropoietin per 10^6 cells in 48 hours." *See* Exh. 11 (Expert Report of Ronald W. McLawhon, M.D., Ph.D.) at ¶¶ 12–15, 32.

26. Amgen does not contest Roche's SOF ¶ 26, but notes that the statement is immaterial to the validity or infringement of '349 claim 7, because any properly calibrated standard

used in the radioimmunoassay called for in the ‘349 claims would produce similar results for the same sample. *See* Exh. 5 (Rebuttal Expert Statement of Ronald W. McLawhon, M.D., Ph.D.) at ¶¶ 60, 83, 88, 94, 100; Exh. 6 (Rebuttal Expert Statement of Eugene Goldwasser, Ph.D.) at ¶¶ 128, 140, 144–50, 168, 174, 177–78, 183.

27. Amgen does not contest Roche’s SOF ¶ 27 but notes that the statement is immaterial to the validity or infringement of ’349 claim 7.

28. Amgen does not contest Roche’s SOF ¶ 28, but notes that the statement is immaterial to the validity or infringement of ’349 claim 7, because multiple suitable standards were available for use in the radioimmunoassay called for in the ‘349 claims which would produce similar results for the same sample. *See* Exh. 5 (Rebuttal Expert Statement of Ronald W. McLawhon, M.D., Ph.D.) at ¶¶ 60, 83, 88, 94, 100; Exh. 6 (Rebuttal Expert Statement of Eugene Goldwasser, Ph.D.) at ¶¶ 128, 140, 144–50, 168, 174, 177–78, 183.

29. Amgen does not contest Roche’s SOF ¶ 29.

30. Amgen contests Roche’s SOF ¶ 30. The 2nd international reference preparation for human erythropoietin (“2nd IRP”) was not established by the National Institute for Biological Standards and Control (NIBSAC) in 1972, but rather was established by the World Health Organization Expert Committee on Biological Standardization in 1971, following an international collaborative study organized by the Division of Biological Standards, National Institute for Medical Research, London. *See* Exh. 12 (Annable *et al*. (1972), *Bull. World Health Org.* 47:99–112) at 99.

31. Amgen contests Roche's SOF ¶ 31 because the phrase "strong heterogeneity" is not defined, thus rendering the statement vague and ambiguous, and as unsubstantiated, because the cited documents do not support the contention in the statement. The "data" referred to in the cited document (and the subjects of the statements in the two cited documents themselves) was not generated by radioimmunoassay but rather by *in vivo* bioassay. The second document cited by Roche contradicts ¶ 31 insofar as it asserts heterogeneity among "assay methodologies" because it also states that "the results of the present study did not show statistically significant differences between estimates using these methods; indeed, the study was not defined to investigate this point." The final cited document does not even mention the "data which determined the second international reference preparation for human erythropoietin" and so does not support the contention in the statement. The statement is also not material with regard to either validity or infringement of Claim 7 because *in vivo* bioassay data, not RIA data, was used to determine the unitage of the 2nd IRP. *See* Exh. 12 (Annable *et al*. (1972), *Bull. World Health Org.* 47:99–112)) at 100–101; Exh. 13 (AM-ITC 00558662); Exh. 14 (UCH000005950-51).

32. Amgen contests Roche's SOF ¶ 32 to the extent that it is misleading and/or immaterial to the validity or infringement of '349 claim 7. While it is true that the document Roche cites (Exh. T to Roche's Rule 56.1 Statement, at AM-ITC 0000550542) does not indicate whether the "CAT-1" standard used at Amgen was directly calibrated against the 1st IRP, that same document states that "CAT-1" was calibrated against "both highly purified human urinary EPO and in-house sheep EPO standards whose potencies were determined in *in vivo* bioassays using either WHO IRP #1 or standard A (Sheep EPO standard which

preceded WHO IRP # 1)." Thus, although CAT-1 may not have been specifically calibrated against the 2nd IRP, it was calibrated against two secondary standards, which had in turn been calibrated against two international reference preparations of EPO, including the 1st IRP. The 2nd IRP was itself calibrated against the 1st IRP, and it was customary practice in the prior art to produce and calibrate secondary standards against primary standards. Exh. 15 at AM-ITC 00550541–42; Exh. 12 (Annable *et al*. (1972), *Bull. World Health Org.* 47:99–112) at 99–100; Exh. 6 (Rebuttal Expert Statement of Eugene Goldwasser, Ph.D.) at ¶¶ 148, 163.

33. Amgen does not contest Roche's SOF ¶ 33, but notes that the identity of the EPO preparation used as a standard for the radioimmunoassays conducted at Amgen and reported in the '349 patent is immaterial to the issue of how one of ordinary skill in 1983-84 would have interpreted the validity or infringement of '349 claim 7, because any properly calibrated standard would have given essentially the same results for the same sample in a radioimmunoassay. Exh. 5 (Rebuttal Expert Statement of Ronald W. McLawhon, M.D., Ph.D.) at ¶¶ 60, 83, 88, 94, 100; Exh. 6 (Rebuttal Expert Statement of Eugene Goldwasser, Ph.D.) at ¶¶ 128, 140, 144–50, 168, 174, 177–78, 183; Exh. 23 (Zaroulis *et al.* (1981), *Am. J. Hematology*, 11:85-92) at 91; Exh. 25 (Cotes (1982) *Brit. J. Haematology* 50:427–38) at 436; Exh. 26 (Egrie *et al.* (1987), *J. Immunological Methods* 99:235:241) at 235, 240.

34. Amgen does not contest Roche's SOF ¶ 34, but notes that it is not a material fact with regard to either validity or infringement of Claim 7 since multiple suitable standards were available which after calibration against a known standard would produce essentially the same results for the same sample in a radioimmunoassay. Exh. 5 (Rebuttal Expert

Statement of Ronald W. McLawhon, M.D., Ph.D.) at ¶¶ 60, 83, 88, 94, 100; Exh. 6 (Rebuttal Expert Statement of Eugene Goldwasser, Ph.D.) at ¶¶ 128, 140, 144–50, 168, 174, 177–78, 183; Exh. 23 (Zaroulis *et al.* (1981), *Am. J. Hematology*, 11:85-92) at 91; Exh. 25 (Cotes (1982) *Brit. J. Haematology* 50:427–38) at 436; Exh. 26 (Egrie *et al.* (1987), *J. Immunological Methods* 99:235:241) at 235, 240.

35. Amgen contests Roche's SOF ¶ 35, because it is inaccurate, misleading and immaterial to the validity or infringement of claim 7. There is no evidence in the document that Roche cites that shows that Amgen ***ever*** reported specific activity ***as determined by radioimmunoassay*** in "arbitrary (Amgen) units rather than in International Units." Contrary to Roche's statement, the document it cites in support of SOF ¶ 35 does not establish that Amgen was reporting "arbitrary" units for any assay either before or after March 15, 1990. And one need only read the actual statements in the document Roche cites to see that the document was discussing only *in vivo* bioassays, not radioimmunoassays. Indeed, the title of the document itself is "Erythropoietin ***biological activity***," and it ***never*** mentions anything about the measurement of EPO by radioimmunoassay. *See* Exh. T to Roche's Rule 56.1 Statement at AM-ITC 00558618. *See also id*. at Exh. 16 (AM-ITC 00558619) ("Ideally, we should know to what degree any known variable can affect ***the mouse response*** (ex-hypoxic or other) and which of these effects might affect the red cell conversion from different sources of EPO or from cobalt.") (emphasis added). When Dr. Egrie, who was indicated to be a recipient of the document, was asked about this at her deposition, she also indicated that the discussion in the document related to *in vivo* bioassays. ("Q. And was that because there had not yet been established an excellent correlation between Amgen units and international units?

[Objection] THE WITNESS: In the in vivo bioassay performed by Dr. Dukes, there was a lack of parallelism with [IRP] number 2."). Exh. 16 at AM-ITC 00558618–19; Exh. 17 (Egrie 3-27-07 Depo Tr.) at 193:2–9.

36. Amgen does not contest Roche's SOF ¶ 36, but notes that it is not material to either validity or infringement of Claim 7.

37. Amgen contests Roche's SOF ¶ 37 to the extent that it states "Amgen cancelled a pending claim that the **Patent Office it** [sic] considered . . ." and so is unintelligible. To the extent the statement is intelligible, it is immaterial to the validity or infringement of '349 claim 7. The documents that Roche cites in support of this statement (Exh. X and Y to the Suh Declaration) do not establish anything more than that the Patent Office rejected claims 65-69 in U.S. Patent Appl. No. 07/113,179 "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" (Exh. X at AM-ITC 00953598), that claim 65 was specifically rejected as "vague and indefinite because it claims a process for the production of any polypeptide but recites only DNA encoding human EPO," *id*., and that Amgen subsequently cancelled claims 65-69 "without prejudice to Applicant's right to present claims of the same or similar scope in a duly-filed continuing application" (Exh. Y at AM-ITC 00953638).

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Respectfully Submitted,

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CERTIFICATE OF SERVICE

I hereby certify that this document, filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of electronic filing and paper copies will be sent to those indicated as non-registered participants.

/s/ Michael R. Gottfried
Michael R. Gottfried