UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, v. F. HOFFMANN-LAROCHE LTD., a Swiss Company, ROCHE DIAGNOSTICS GmbH, a German Company and HOFFMANN LAROCHE INC., a New Jersey Corporation, Defendants.	Civil Action No.: 05-12237 WGY

AMGEN INC.'S SEPARATE STATEMENT OF UNDISPUTED FACTS IN SUPPORT OF ITS MOTION FOR SUMMARY JUDGMENT OF NO INEQUITABLE CONDUCT

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Plaintiff Amgen Inc. ("Amgen") has moved for summary judgment on the three inequitable conduct claims asserted as the seventh affirmative defense by Defendants F. Hoffmann-LaRoche Ltd., Roche Diagnostics GmbH, and Hoffman LaRoche Inc. (collectively, "Roche") in Defendants' First Amended Answer and Counterclaims to Plaintiff's Complaint, dated March 30, 2007. The following facts are beyond genuine dispute and compel summary judgment in favor of Amgen as a matter of law.[1]

ROCHE'S FIRST CLAIM RELATING TO AMGEN'S ALLEGED OMISSIONS REGARDING SIMILARITIES BETWEEN R-EPO AND U-EPO

1. Lin *et al.*, *Cloning and Expression of the Human Erythropoietin Gene*, 82 Proc. Nat'l Acad. Sci., 7580, 7582 (1985)) ("Lin PNAS Publication") is listed on the face of the United States Patent No. 5,547,933 ("'933 Patent").

- Exh. 39 (Lin PNAS Publication);
- '933 Patent.

2. The Lin PNAS Publication reports, "The secreted Epo has an apparent *M*, of 34,000 when analyzed in an electrophoretic transfer blot."

- Exh. 39 (Lin PNAS Publication), at p. 7582;

3. During the 102,096 ("'096"), 102,097 ("'097), and 102,334 ("'334") interference proceedings, Egrie, *et al.*, 1986 Characterization and Biological Effects of Recombinant Human Erythropoietin, *Immunobiol.*, vol 172, pp. 213-224 (1986) ("Egrie 1986 Publication") was offered into evidence.

- Exh. 1 (Egrie 1986 Publication);
- Exh. 7 (Lin Notice, '096, '097, and '334 interferences), at p. 1 ("Lin hereby offers into evidence, pursuant to the provisions of 37 CFR 1.682(a), the following publications, copies of which are attached: (1) 'Characterization and

[1] All exhibits cited herein are attached to the Declaration of Craig H. Casebeer in Support of Amgen Inc.'s Memorandum in Support of Its Motion For Summary Judgment of No Inequitable Conduct.

Biological Effects of Recombinant Human Erythropoietin', Egrie et al, *Immunobiol*, Vol. 172, pages 213-224 (1986).").

4. The Egrie 1986 Publication contains the same SDS-PAGE gel that Amgen submitted to the FDA, describes the migration of rEPO and uEPO as "identical," and indicates that both are "glycosylated to the same extent."

- Exh. 4 (Product License Application) ("PLA"), at pp. 762 and 890;
- Exh. 1 (Egrie 1986 Publication), at pp. 214, 218-19 ("EPO was subjected to electrophoresis on a 12.5% sodium dodecyl sulfate (SDS), polyacrylamide according to the method of Laemmli (11).").

5. During the '096, '097, and '334 interference proceedings, the lab notebook of Dr. Joan Egrie (including the "Egrie Input file") was offered into evidence.

- Exh. 2 (Egrie Input file);
- Exh. 31 (Notice Pursuant to 37 C.F.R. § 1.682(a) and Offer of Official Record From Civil Action No. 87-2617-Y Regarding Testimony of Egrie and Attachments, '096, '097, and '0334 interferences), at p. 1, 4, and attachment ("Dr. Egrie's laboratory notebook (DX 319) says…");
- *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F.Supp.2d 69, 142 (D. Mass. 2001) ("First, the Egrie Input was disclosed and considered by the Patent Office. In particular, Mr. Borun testified that it had been disclosed during the *Fritsch v. Lin* Interferences and used as an exhibit in the *Amgen v. Chugai* litigation.").

6. The Egrie Input file describe COS-1 produced rEPO and uEPO as having "the same molecular weight," and that "the recombinant EPO is glycosylated to the same extent as the native protein."

- Exh. 2 (Egrie Input file), at p. 17;
- *Amgen*, 126 F.Supp.2d at 141 (quoting Egrie Input file).

7. The Egrie Input file is not inconsistent with Dr. Lin's disclosure.

- *Fritsch v. Lin*, 21 U.S.P.Q.2d 1739, 1742 (BPAI 1991) ("In our view, the Egrie testimony which is cited in Fritsch's reply brief (FRB-36) is at best ambiguous and, thus, is not sufficient to contradict the information disclosed on page 64 of the Lin application."); and

- *Amgen*, 126 F.2d at 144 ("Contrary to TKT's contentions, then, data in the Egrie Input is actually consistent (or at least not inconsistent) with Amgen's representations in the patent specification.").

8. The Board of Patent Appeals and Interferences ("Interference Board") reviewed the Egrie Input file and the Product License Agreement during the '334 Interference.

- *Fritsch v. Lin*, 21 U.S.P.Q.2d 1739, 1741-42 (BPAI 1992).

9. During the prosecution of '933 Patent, Examiner Fitzgerald reviewed the record and opinion of the '334 interference proceedings.

- Exh. 15 ('933 Patent File History), at p. 715 ("Reviewed Interference file # 102,334; Reviewed published Intf. Decision (*Fritsch v. Lin*) and *Amgen v. Chugai* (18 U.S.P.Q.2d @ 1016); Oct-Nov 1993; Fitzgerald DL");

- *Amgen*, 126 F.Supp.2d at 139-140, 142 ("After resolution of the Interference proceedings, Examiner David L. Fitzgerald recorded on the file wrapper of the application that led to both the '933 and '080 patents, that he had received and, for a two-month period, reviewed the Interference record and decision.".

10. During the prosecution of United States Patent Application No. 202,874 ("'874 application"), parent to the '933 Patent, Browne, *et al.*, "Erythropoietin: Gene Cloning, Protein Structure, and Biological Properties," *Cold Spring Harbor Symposia on Quantitative Biology*, vol. L1, pp. 693-702 (1986) ("Browne 1986 Publication") was submitted as an attachment to a declaration submitted to the Patent Office.

- Exh. 3 (Browne 1986 Publication);

- Exh. 13 (2/16/1995 Amendment, '874 application), at p. 9;

- Exh. 14 (Declaration of Richard D. Cummings, dated January 6, 1994), at pp. 17-18;

- *Amgen*, 126 F.Supp.2d at 145.

11. During the '096, '097, and '334 interferences, the Browne 1986 Publication was offered into evidence.

- Exh. 7 (Lin Notice, '096, '097, and '334 interferences), at p. 1 ("Lin hereby offers into evidence, pursuant to the provisions of 37 CFR 1.682(a), the following publications, copies of which are attached: … (2) 'Erythropoietin: Gene Cloning, Protein Structure, and Biological Properties", Browne et al,

Cold Spring Harbor Symposia on Quantitative Biology, Vol. L1, pages 693-702 (1986)."

12. The Browne 1986 Publication reports that:

> The r-hEPO produced in COS-1 cells is indistinguishable from urinary EPO by Western blot analysis (Egrie et al. 1985).
>
> …
>
> Human urinary EPO and CHO-cell-derived r-hEPO migrate identically in SDS-polyacrylamide gels, indicating that both molecules are glycosylated to a similar extent. …Trace amounts of *N*-aceylgalactosamine were found in r-hEPO, indicating the presence of O-linked glycosylation.
>
> …
>
> ..Although the presence of *N*-acetylgalactosamine had not been detected previously (Dordal et al. 1985), these results demonstrate that urinary EPO, as well as r-hEPO, contains O-linked carbohydrate…In addition, direct carbohydrate analysis of endoglycosidase-F-treated r-hEPO yields galactose, sialic acid, and *N*-acetyl galactosamine, confirming the presence of O-linked carbohydrate (T.W. Strickland et al., in prep.). As shown in Figure 4, the proportion of EPO containing O-linked carbohydrate is comparable in urinary EPO and r-hEPO.

- Exh. 3 (Browne 1986 Publication), at p. 696 and 698.

13. Amgen notified the Patent Office of the *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, Civil Action No. 97-10814-WGY (D.Mass. filed Apr. 15, 1997) on April 16, 1997.

- Exh. 15 (4/16/1997 Peterson Letter) ("In the above-referenced matter, enclosed please find a copy of the completed report on the Filing or Determination of an Action Regarding a Patent or Trademark.");

- *Amgen*, 126 F.Supp.2d at 146 ("Amgen directly informed the Patent and Trademark Office of this lawsuit by letter the day after the complaint was filed.").

14. The Declaration of Thomas W. Strickland, dated Feb. 13, 1992 ("1992 Strickland Declaration") provides experimental data on the presence of O-linked glycosylation on and monosaccharide content of recombinant human EPO produced in CHO cells by Amgen in 1985, and does not compare rEPO with uEPO, from the standpoint of molecular weight, carbohydrate composition or otherwise.

- Exh. 5 (1992 Strickland Declaration).

15. The Declaration of Thomas W. Strickland, dated May 19, 1994 ("1994 Strickland Declaration") does not compare rEPO with uEPO, from the standpoint of molecular weight, carbohydrate composition or otherwise, or even mention uEPO.

- Exh. 6 (1994 Strickland Declaration).

16. Takeuchi, *et al.*, *Comparative Study of the Asparagine-linked Sugar Chains of Human Erythropoietins Purified from Urine and the Culture Medium of Recombinant Chinese Hamster Ovary Cells*, J. Biol. Chem. 263(8) (1988) ("Takeuchi *et al.*") was disclosed to the Interference Board during the '096, 097, and '334 interferences, and is referenced on the face of the '933 patent, evidencing that it was disclosed to and considered by the examiner..

- Exh 34 (Takeuchi *et al.*);
- Exh. 36 (Fritsch's Proposed Findings of Fact and Law, '096, '097, and '334 interferences), at p. 225 (discussion of Takeuchi *et al.*);
- Exh. 37 (4/5/1990 Declaration of Thomas A. Strickland, '334 interference), at p. 6 (discussion of Takeuchi *et al.*);
- Exh. 38 (Lin's Brief, '334 interference), at p. 46 (discussion of Takeuchi *et al.*).

17. Takeuchi *et al.* reported in part:

> "Analysis of the monosaccharide composition of HuEPO performed in our laboratory confirmed the occurrence of one N-acetylgalactosamine residue, indicating that one O-linked sugar chain is included in recombinant Hu-EPO."

- Exh. 34 (Takeuchi *et al.*), at p. 3657.

18. Sasaki, *et al.*, *Carbohydrate Structure of Erythropoietin Expressed in Chinese Hamster Ovary Cells by a Human Erythropoietin cDNA*, J. Biol. Chem. 262, 12059-76 (1987) ("Sasaki *et al.*") was disclosed to the Interference Board during the '096, 097, and '334 interferences, and is referenced on the face of the '933 patent, evidencing that it was disclosed to and considered by the examiner.

- Exh 40 (Sasaki *et al.*), see Table 1 (carbohydrate composition of erythropoietin), p. 12061, and discussion of O-linked oligosaccharides, pp. 12060-61;

- Exh. 36 (Fritsch's Proposed Findings of Fact and Law, '096, '097, and '334 interferences), at p. 224 (discussion of Sasaki *et al.*);

- Exh. 38 (Lin's Brief, '334 interference), at p. 46 (discussion of Sasaki *et al.*).

19. Examiner Martinell discussed Takeuchi *et al.* in an office action in the prosecution of the '933 Patent.

- Exh. 33 (8/16/1994 Office Action, '933 Patent), at p. 4.

20. Examiner Martinell had before him Takeuchi *et al.* and Sasaki *et al.*

- *Amgen*, 126 F.Supp.2d at 144-145 ("In addition, the Examiner also had before him the correct carbohydrate data for CHO-cell produced human EPO and uEPO provided in the Takeuchi and Sasaki references.");

- Exh. 32 (Search Notes, '178 File History);

- MPEP § 704.01 (8th ed. Rev. 5 Aug. 2006) ("When an examiner is assigned to act on an application which has received one or more actions by some other examiner, full faith and credit should be given to the search and action of the previous examiner unless there is a clear error in the previous action or knowledge of other prior art. In general the second examiner should not take an entirely new approach to the application or attempt to reorient the point of view of the previous examiner, or make a new search in the mere hope of finding something.").

21. Both this Court and the Federal Circuit ruled that Amgen had no intention of deceiving the Patent Office by withholding information regarding the difference between rEPO and uEPO.

- *Amgen*, 126 F.2d at 141-145, 146-147 ("Nonetheless, even if Amgen had withheld [data regarding glycosylation differences] from the Patent Office, such withholding would not give rise to a charge of inequitable conduct because TKT has failed to prove by clear and convincing evidence that this data was material or that it was withheld with the intent to deceive. … Although the directness of Amgen's disclosures varies depending on the particular piece of disputed information, one truth remains the same throughout: Amgen's representatives never intended to deceive the Patent Office.");

- *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1357-58 (Fed. Cir. 2003) ("The district court found that TKT had not proven inequitable

conduct by clear and convincing evidence, and we have not been persuaded on appeal that a contrary result is compelled. In reaching this conclusion, we need look no further than the district court's determination that TKT's case was doomed because it was bereft of evidence of intentional deception…").

ROCHE'S SECOND CLAIM RELATING TO AMGEN'S ALLEGED MISREPRESENTATIONS AND OMISSIONS IN ITS ARGUMENTS REGARDING DOUBLE PATENTING

22. The host cell claims in United States Patent No. 4,703,008 do not cover the process claims of the '179 application.

- *Amgen, Inc. v. U.S. Int'l Trade Comm'n*, 902 F.2d 1532, 1538 (Fed. Cir. 1990) (A host cell claim does not 'cover intracellular processes any more or less than a claim to a machine 'covers' the process performed by that machine.").

23. During the prosecution of the '179 application, Amgen provided the Federal Circuit's decision in *Amgen*, 902 F.2d 1532 (Fed. Cir. 1990) to the Patent Office.

- *Amgen*, 902 F.2d 1532;
- Exh. 18 (10/7/1994 Amendment), at p. 7.

24. Amgen argued during the '097 Interference that the two separate counts corresponding to the claims of the '178 and '179 applications respectively were not the same invention.

- Exh. 22 (Lin Opposition G, '096 and '097 interferences), at p. 81 ("Suffice it to say that Lin contends that the two counts are not the 'same invention.'").

25. Amgen argued during the '097 Interference that the process Count was not obvious.

- Exh. 21 (Lin '097 Interference Brief), at p.56 ("Furthermore, it was not obvious that in vivo biologically active recombinant human EPO could be made by the claimed process. Until Lin obtained the sequence, Browne used it in expression and Egrie with Dukes found the product had in vivo biological activity, the process at best was only a wish.").

ROCHE'S THIRD CLAIM RELATING TO AMGEN'S ALLEGED FAILURE TO DISCLOSE REJECTIONS BETWEEN THE '179 AND '178 APPLICATIONS

26. Examiner Martinell issued all the patents-in-suit, as noted by the face of each patent.

- Exh. 41 (collection of the front page of each patent-in-suit).

27. The inventions in the '178 and '179 applications have been found to be patentably distinct.

- Exh. 20 (2/9/90 Office Action, '178 application), at p. 2-3 ("While the subject matter of the three interferences is deemed to be patentably distinct, that subject matter is nevertheless related.");
- Exh. 23 (6/16/86 Office Action, '298 application) (restriction requirement);
- 37 C.F.R. 1.601(f) (1988 and 1990) ("A 'count' defines the interfering subject matter between (1) two or more applications or (2) one or more applications and one or more patents. When there is more than one count, each count shall define a separate patentable invention.").

28. Examiner Martinell, examiner to both the '178 and '179 application lines, had before him the prosecution history, including the rejections, of both lines of application.

- Exh. 25 (9/7/1994 Interview Summary, '178 application) (signed by Examiner Martinell);
- Exh. 26 (9/7/1994 Interview Summary, '179 application) (signed by Examiner Martinell);
- MPEP § 704.01 (8th ed. Rev. 5 Aug. 2006) ("When an examiner is assigned to act on an application which has received one or more actions by some other examiner, full faith and credit should be given to the search and action of the previous examiner unless there is a clear error in the previous action or knowledge of other prior art. In general the second examiner should not take an entirely new approach to the application or attempt to reorient the point of view of the previous examiner, or make a new search in the mere hope of finding something.");
- MPEP §§ 609.02 and 904 (8th ed. Rev. 5, Aug. 2006) ("Information which has been considered by the Office in the parent application of a continued prosecution application (CPA) filed uner 37 CFR 1.53 (d) will be part of the file before the examiner and need not be resubmitted in the continuing application to have the information considered and listed on the patent.");

- Exh. 27 (International Search Report, '298 application) (signed by Examiner Martinell).

29. On September 7, 1994, Examiner Martinell conducted a personal interview with representatives of Amgen regarding the '178 and '179 application lines, during which rejections from both applications were discussed.

- Exh. 25 (9/7/1994 Interview Summary, '178 application) (discussing rejection based upon Sugimoto reference);

- Exh. 26 (9/7/1994 Interview Summary, '179 application) (discussing rejection based upon Lin and Yokota references).

30. The references upon which rejections in the '179 and '178 applications were based are listed in Information Disclosure Statements ("IDS") submitted to the Patent Office in both the '179 and '178 applications' prosecution.

- Exh. 28 (4/8/1994 IDS, '874 application) (submitting "[r]eferences of record in U.S. Pat. Appln. No. 07/113,179");

- Exh. 29 (1/3/1994 IDS, '179 application) (submitting "[r]eferences of record in U.S. Pat. Appln. No. 07/113,178, including those listed on Form PTO-1449").

June 22, 2007

Respectfully Submitted,
AMGEN INC.,
By its attorneys,

/s/ Michael R. Gottfried

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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