UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, v. F. HOFFMANN-LA ROCHE LTD, ROCHE DIAGNOSTICS GmbH, and HOFFMANN-LA ROCHE INC. Defendants.	CIVIL ACTION No.: 05-CV-12237WGY

APPENDIX D, EXHIBIT 2 TO DEFENDANTS' MEMORANDUM IN SUPPORT OF ITS MOTION TO COMPEL PRODUCTION OF DOCUMENTS IMPROPERLY WITHHELD ON GROUNDS OF PRIVILEGE

Dated: March 27, 2007
Boston, Massachusetts

Respectfully submitted,
F. HOFFMANN-LA ROCHE LTD,
ROCHE DIAGNOSTICS GMBH, and
HOFFMANN-LA ROCHE INC.

By their attorneys,
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EXHIBIT 2

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, vs. F. HOFFMANN-LA ROCHE LTD, ROCHE DIAGNOSTICS GmbH, and HOFFMANN-LA ROCHE INC. Defendants.	CIVIL ACTION No.: 05-CV-12237WGY

DEFENDANTS' MOTION FOR LEAVE TO AMEND THEIR ANSWER AND COUNTERCLAIMS

Defendants F. Hoffmann-La Roche Ltd, Roche Diagnostics GmbH, and Hoffmann-La Roche Inc. (collectively "Roche") respectfully move the Court pursuant to Rule 15(a) of the Federal Rules of Civil Procedure for leave to amend their Answer and Counterclaims to add a sham litigation counterclaim (Count 2) and an equitable estoppel affirmative defense (Affirmative Defense No. 12).

At the December 20, 2007 hearing, this Court (A) denied Amgen's motion to strike Roche's Affirmative Defenses Nos. 2, 7, 8, and 10[1]; (B) granted, *without prejudice*, Amgen's motion to strike Roche's affirmative Defense No. 12; (C) denied Amgen's motion to dismiss Counterclaim Counts 1 and 6; (D) took under advisement Amgen's motion to dismiss Counterclaim Counts 3, 4, 5, 7, 8, and 9; (E) granted, *without prejudice*, Amgen's motion to

[1] At the December 20, 2007 hearing, the Court stated that the "motion to strike affirmative defenses 1, 2 and 3 is denied." Amgen did not move to strike Roche's affirmative defenses 1 (failure to state a claim) and 3 (non-infringement). Based on the underlying motion and opposition papers, Roche understands that the Court was referring to the first 3 affirmative defenses that Amgen sought to strike, which were defenses Nos. 2 (patent misuse), 7 (inequitable conduct), and 8 (unclean hands), and seeks confirmation of this by the Court.

dismiss Counterclaim Count 2, and permitted Roche to move for leave to amend its pleading with respect to Counterclaim Count 2 and Affirmative Defense No. 12, within 30 days of the Order.

For the reasons set forth in Roche's accompanying Memorandum, Roche's motion for leave to amend to add Counterclaim Count 2 and Affirmative Defense No. 12 should be granted.

CERTIFICATE PURSUANT TO LOCAL RULE 7.1

I hereby certify that counsel for Roche conferred with counsel for Amgen Inc. in a good faith effort to resolve or narrow the issues presented by this motion and that no agreement could be reached.

Dated: January 19, 2007
Boston, Massachusetts

F. HOFFMANN-LA ROCHE LTD,
ROCHE DIAGNOSTICS GMBH, and
HOFFMANN-LA ROCHE INC.

By its Attorneys,

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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 (NEF) and, due to the federal holiday, paper copies will be sent to those indicated as non-registered participants on the above-referenced date.

/s/ Keith E. Toms
Keith E. Toms

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EXHIBIT B

Applicant's Amendment and Response Under 37 C.F.R. §§1.115 and 1.111 dated 1/3/94).

INEQUITABLE CONDUCT RELATING TO MISREPRESENTATIONS REGARDING ALLEGED DIFFERENCES BETWEEN R-EPO AND U-EPO

Contradictory Statements of Amgen's Scientist

74. Amgen, and those acting on its behalf who were substantively involved in the prosecution of the patents-in-suit, knowingly misled the PTO through misstatements and omissions of material information with the intent to deceive and mislead the PTO to obtain the patents-in-suit, thereby tainting all patents sharing the common specification. Accordingly, the patents-in-suit should be held unenforceable for inequitable conduct before the PTO.

75. In order to obtain allowance for its protein claims, Amgen distinguished its recombinant EPO ("r-EPO") from natural urinary EPO ("u-EPO") by representing that the average carbohydrate composition, glycosylation, and molecular weight of its r-EPO were different from that of naturally occurring human EPO proteins. Amgen incorporated these alleged differences into claims of the '933 and '080 patents as elements of patentability and proceeded to argue to the PTO, even in the face of its own contradictory data, that these elements made these claims patentable over u-EPO.

76. Amgen and its representatives, in the course of foreign patent proceedings and before the FDA, relied on statements and information regarding the molecular weights and carbohydrate compositions of r-EPO and u-EPO that were inconsistent, and refuted the positions Amgen took during

prosecution of its patents before the PTO, and in the *Fritsch et al. v. Lin* patent interference No. 102,334.

77. Two declarations, which have *never been previously considered by this or any U.S. Court*, contain sworn statements by an Amgen scientist which utterly contradict positions that Amgen took in arguing patentability of its then pending EPO claims to the PTO.

78. Dr. Thomas W. Strickland became involved in Amgen's EPO project in August 1984 and worked on the purification of r-EPO. Dr. Strickland was also involved in the prosecution of Amgen's protein patents related to EPO. In December 1988, during the prosecution of the '178 application, Amgen submitted a declaration by Amgen's scientist, Dr. Strickland, stating that Amgen's recombinant EPO product was chemically distinct, and therefore novel and patentable over natural human EPO that was isolated and purified from urine ("the 1988 Strickland declaration"). Specifically, Strickland stated:

> recombinant erythropoietin as described by Serial No. 113,178 has a different carbohydrate composition than naturally occurring urinary erythropoietin.

('178 FH, Strickland Decl. dated 11/30/88, at 15).

79. The prosecution history for the '178 application shows that the assertions made in the 1988 Strickland declaration were crucial for the patentability of Amgen's product claim to EPO. The Examiner Interview Summary Record dated 1/26/89 makes it clear that the Examiner interpreted the declaration to relate to differences in carbohydrate content. As stated by the Examiner:

> [D]iscussed effect of declaration on 102 aspects of the original rejection. Discussed effect on 103-based arguments of the difference in glycosylation **(carbohydrate content)**.

('179 FH, Exam'r Interview Summary Record dated 1/26/89 (emphasis added)).

80. Amgen made this argument (both in 1988 in order to obtain the '933 patent, and then later in the Fritsch v. Lin interference proceeding) knowing it was false, and then continued to hide that fact from the patent office. The clear evidence for this is that the 1988 declaration by Strickland was directly contradicted by Dr. Strickland himself in two later declarations filed in connection with two opposition proceedings in Europe to Genetics Institute's erythropoietin patents EP 411 678 ("the '678 patent) and EP 209 539 ("the '539 patent").

81. In February 1992, Amgen submitted the first declaration by Dr. Strickland in support of Amgen's European opposition proceedings against the Genetics Institute '678 patent ("the 1992 Strickland declaration"). (Strickland European Decl. dated 2/13/92). The '678 patent contained claims drawn to a method for producing glycosylated recombinant EPO, which Amgen opposed by arguing, in part, that r-EPO and u-EPO were the same. Strikingly, the '678 patent reported its r-EPO as being analytically identical to human EPO purified from urine (u-EPO). The 1992 Strickland declaration argued that the '678 patent claims produced a protein that is indistinguishable in terms of carbohydrate composition from a protein that was produced by Amgen in 1985 using the procedures set forth in Example 10 of Amgen's European patent EP 148 605 ("the '605 patent"), which is the European counterpart to the '933 patent. Based on experiments discussed in the 1992 Strickland declaration, Strickland concluded that the carbohydrate

composition of the 1985 EPO prepared in accordance with Example 10 of Amgen's '605 patent was the same, within the range of experimental and analytical error, as the EPO of the Genetics Institute '678 patent which in turn, according to that '678 patent was chemically identical to u-EPO. The 1992 Strickland declaration was not disclosed to the PTO.

82. In May 1994, Amgen submitted another declaration by Dr. Strickland in support of Amgen's European opposition proceedings against Genetic Institute's '539 patent ("the 1994 Strickland declaration"). The Genetics Institute patent had claims directed to a recombinant EPO product, which Amgen again opposed by arguing, in part, that r-EPO and u-EPO were the same. In this declaration, Dr. Strickland stated:

> In order to demonstrate the viability of the specific disclosure of Example 10 of EP 148605 [counterpart U.S. patent], reverse phase HPLC was used to purify rEPO directly from cell culture media in which the rEPO had been expressed from CHO cells as described in Example 10. The results show that by following the disclosure of example 10 homogeneous erythropoietin is obtained that meets all the requirements of claim 2 of EP 209539, *i.e.*, ...(b) a molecular weight of about 34,000 daltons on SDS-PAGE ...

(Strickland European Decl. dated 5/14/94, at 2 (emphasis added)). According to this declaration, r-EPO prepared in accordance with Example 10 had a molecular weight of 34,000 daltons, the same as that of u-EPO as reported at Col. 5, line 48 of the '933 patent, and not higher, as reported in Example 10.

83. Significantly, Amgen submitted an IDS for the U.S. Application Ser. No. 202874 which listed dozens of references that were part of the

European proceedings involving EPO. However, the 1992 and 1994 Strickland declarations were not disclosed to the PTO. Amgen's knowing and intentional failure to disclose material information from Amgen's European opposition proceedings is evidenced at least by the direct involvement of Amgen attorneys Steven Odre and Stuart Watt in those proceedings, which included personally attending oral proceedings in Europe. (EP 411 678, EPO Opposition Proceedings , Record of Public Oral Proceedings Before the Opposition Division, dated 12/16/94). Additionally, the claims of the later issued '698, '080, '349 and '422 patents from the same family as the '933 patent, are sufficiently interrelated with the '933 claims and have a substantial relationship with the inequitable acts such that these patents should also be deemed unenforceable under the doctrine of "infectious unenforceability."

Additional Contradictory Statements

84. In addition to the contradictory statements made by Amgen in the 1992 and 1994 Strickland declarations, Amgen and its employees, including even the named inventor of the Amgen EPO Patents, have made numerous statements, in publications and to the FDA, that directly contradict positions Amgen has taken before the PTO during the prosecution of the patents in suit. These additional contradictory statements further evidence Amgen's intent to deceive the PTO. *See Digital Control Inc. v. Charles Mach. Works*, 437 F.3d 1309, 1319 (Fed. Cir. 2006) ("Intent . . . may be inferred from the totality of the evidence."). Tellingly, Amgen's conduct throughout prosecution reveals a consistent pattern of purposely failing to disclose material information to the

examiners. During the prosecution of the '349 and '422 patents, Amgen made no effort to inform the PTO of the then pending litigation against TKT (Civil Act. No. 97-10814-WGY).

85. Lin, the inventor of the patents in suit, reported in a publication that "[r-EPO] has an apparent [molecular weight] of 34,000 when analyzed in an electrophoretic transfer blot." Lin et al, *Cloning and Expression of the Human Erythropoietin Gene*, 82 Proc. Nat'l Acad. Sci., 7580, 7582 (1985). The specification for the '933 patent states that the molecular weight of natural EPO was also "approximately 34,000 dalton." ('933 patent, Col. 5, lines 48-50). Lin, therefore, knew as of 1985 that the molecular weights of r-EPO and u-EPO were the same, yet, as shown in Example 10 of the '933 patent which issued from an application that was filed in 1995, continued to state that the molecular weight of r-EPO was higher than that of u-EPO.

86. In addition, two Amgen scientists, Dr. Joan Egrie, and Dr. Thomas Strickland, reported in a publication that "Both the purified natural and recombinant EPO preparations were characterized . . . by Western analysis. . . . By Western analysis, the recombinant and human urinary EPO migrate identically." Egrie et al *Characterization and Biological Effects of Recombinant Human Erythropoietin*, 172 Immunobiology 213 (1986). If r-EPO and u-EPO "migrate identically" that means that the two products have the same apparent molecular weight. Therefore, the finding that r-EPO and u-EPO "migrate identically" contradicts Dr. Egrie's data reported in Example 10 in the '933 patent. This publication, however, was withheld from the Examiner of the '933 patent.

87. Additional internal documents from Dr. Egrie provide evidence regarding glycosylation inconsistent with the positions that Amgen took during prosecution of its patents. (*See* AM-ITC 00828987-88). This information was never disclosed to the examiner.

88. Another Amgen scientist, Jeff Browne, corroborated the published findings of Egrie and Strickland, stating in a publication that human u-EPO and CHO-cell derived r-EPO migrate identically in SDS-polyacrylamide gels. Browne et al, *Erythropoietin: Gene Cloning, Protein Structure, and Biological Properties*, 51 Cold Spring Harbor Symposia on Quantitative Biology 693-702, 698 (1986). This publication also was not disclosed to the Examiner. Additionally, in order to receive approval for its r-EPO drug, Amgen made statements to the FDA that directly contradict the positions Amgen took in arguing patentability of its EPO claims to the PTO. Significantly, these statements were not submitted to the Examiner of the '933 patent. (*See* Amgen PLA, Vol. 4, pg 762 and Figure 9.C-1 (June 1989)).

EIGHTH DEFENSE - UNCLEAN HANDS

89. The asserted patents are unenforceable due to Amgen's unclean hands.

NINTH DEFENSE - PUBLIC HEALTH AND WELFARE

90. Amgen's request for an injunction precluding Roche from importing into, making, using, or selling CERA in the U.S. is contrary to the public health and welfare.

TENTH DEFENSE - AMGEN IS ESTOPPED FROM SEEKING DAMAGES

91. Amgen has taken the position that it is not seeking damages against Roche related to the accused product in this action.

92. Amgen contends that it is only seeking declaratory and injunctive relief against Roche's alleged acts of infringement.

93. Amgen has alleged that there are current acts of infringement in the United States in connection with the accused product.

94. Based on its decision to forgo damages, Amgen has argued to the Court that Roche is not entitled to a jury trial on Amgen's claims.

95. At the conclusion of the litigation, in the event that Amgen is successful in its claims against Roche and the asserted claims are found to be infringed, valid and enforceable, the Court must undertake an analysis mandated by the United States Supreme Court's decision in *eBay, Inc. v. MercExchange, L.L.C.*, 126 S. Ct. 1837 (2006), to determine if a permanent injunction would be appropriate.

96. Based on Amgen's decision to waive any damages, compensatory or otherwise, as a tactic to deprive Roche of its constitutional right to a jury trial on Amgen's claims (even though Roche contends that they are entitled to a trial by jury), Amgen is estopped and precluded from seeking, asserting or maintaining a claim for damages, compensatory or otherwise, for any damages, whether past, current or future, in the event that Amgen is successful on its claims and the Court determines that a permanent injunction is not warranted in this case.