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-CV-12237-WGY** **AMENDED COMPLAINT FOR DECLARATORY JUDGMENT OF INFRINGEMENT OF U.S. PATENT NOS. 5,441,868, 5,547,933, 5,618,698, 5,621,080, 5,756,349 AND 5,955,422**

THE PARTIES

1. Plaintiff Amgen Inc. ("Amgen") is a corporation existing under the laws of the State of Delaware with its principal place of business in Thousand Oaks, California. Amgen discovers, develops, manufactures and sells innovative therapeutic products based on advances in molecular biology, recombinant DNA technology and chemistry.

2. On information and belief, defendant F. Hoffmann-LaRoche Ltd. ("HLR Ltd.") is a foreign corporation existing under the laws of Switzerland with its principal place of business in Basel, Switzerland.

3. On information and belief, defendant Roche Diagnostics GmbH ("Roche GmbH") is a foreign corporation existing under the laws of Germany with its principal places of business in Penzberg, Germany and Mannheim, Germany.

4. On information and belief, Defendant Hoffmann LaRoche Inc. ("HLR Inc.") is a corporation existing under the laws of the State of New Jersey with its principal place of business in Nutley, New Jersey.

5. On information and belief, HLR Ltd., Roche GmbH and HLR Inc., transact business within the District of Massachusetts and/or are otherwise subject to the jurisdiction of this Court.

6. Defendants HLR Ltd., Roche GmbH, and HLR Inc., are hereinafter referred to individually and collectively as "Roche."

JURISDICTION AND VENUE

7. This action arises under the patent laws of the United States, Title 35 of the United States Code. This Court has subject-matter jurisdiction pursuant to 28 U.S.C. §§ 1338(a), 2201 and 2202.

8. Venue is proper in this Court pursuant to 28 U.S.C. §§ 1391(b), (c), and (d), and 1400(b).

DR. LIN'S PIONEERING INVENTIONS

9. This dispute involves the current and impending infringement by the Roche defendants of six United States patents assigned to Amgen. The patents at issue describe and claim the pioneering inventions of an Amgen scientist, Dr. Fu-Kuen Lin, relating to erythropoietin ("EPO").

10. EPO is a protein naturally produced by animals (including humans) that stimulates the production of red blood cells. Naturally occurring human EPO is present in the blood or urine in vanishingly small amounts, making it virtually impossible to isolate from natural sources, even today.

11. For many years prior to Dr. Lin's path-breaking inventions, there was a long-standing, unmet need for a therapeutically effective product to treat anemia and related blood disorders. Early attempts to recover a therapeutically effective EPO product from urine or blood

proved unsuccessful, yielding only very small quantities of highly unstable and/or impure proteins that were not therapeutically effective for treating anemic patients. Attempts to purify human EPO from cultured cells that were said to produce EPO also proved futile, either because those cells were not available or because reports of their ability to produce EPO were overstated. Attempts by many scientists to use conventional scientific techniques to identify the amino acid sequence of human EPO and/or the DNA that encodes human EPO likewise proved unsuccessful.

12. Thus, before Dr. Lin's inventions, the world not only could not obtain therapeutically effective human EPO, it also did not even know whether isolated human EPO could be therapeutically effective for the treatment of anemic patients. Dr. Lin solved these problems through a succession of inventions that yielded the first—and to date only—therapeutically effective human EPO products. Dr. Lin's inventions demonstrated for the first time that human EPO could be an effective treatment for anemia and other blood disorders. Today, thanks to Lin's inventions, millions of patients worldwide have been freed from the debilitating effects of chronic anemia and the health hazards of repeated blood transfusions.

13. Dr. Lin opened the door to the therapeutic use of EPO products by a succession of pioneering inventions. Not only did he isolate and characterize the DNA that encodes human EPO, but he also identified the amino acid sequence of human EPO, invented vertebrate and other cells capable of producing human and other EPOs in abundance when grown in culture, invented methods for producing glycosylated EPO polypeptides, and invented the first therapeutically effective human EPO products, including pharmaceutical compositions effective for the therapeutic treatment of severely anemic patients.

14. Many of Dr. Lin's inventions are described and claimed in seven United States

patents assigned to Amgen, six of which are at issue here:

a. U.S. Patent No. 5,441,868 (the "'868 patent"), issued on August 15, 1995, claims a process for the production of glycosylated EPO polypeptides having specified *in vivo* biological properties by growing certain mammalian host cells transformed or transfected with an isolated DNA sequence encoding human EPO. A true and correct copy of the '868 patent is attached to the original Complaint as Exhibit 1.

b. U.S. Patent No. 5,547,933 (the "'933 patent"), issued on August 20, 1996, claims non-naturally occurring human EPO glycoproteins having specified biological activities that are produced by the process of growing mammalian host cells transformed or transfected with an isolated DNA sequence encoding human EPO, pharmaceutical compositions containing said human EPO glycoproteins, and methods for using such pharmaceutical composition. A true and correct copy of the '933 patent is attached to the original Complaint as Exhibit 2.

c. U.S. Patent No. 5,618,698 (the "'698 patent"), issued on April 8, 1997, claims processes for the production of glycosylated EPO polypeptides having specified *in vivo* biological properties by growing certain mammalian host cells transformed or transfected with non-EPO promoter DNA that is operatively linked to DNA encoding EPO DNA or cells having amplified EPO DNA. A true and correct copy of the '698 patent is attached to the original Complaint as Exhibit 3.

d. U.S. Patent No. 5,621,080 (the "'080 patent"), issued on April 15, 1997, claims non-naturally occurring EPO glycoproteins having certain *in vivo* biological activity and a specified amino acid sequence, and pharmaceutical compositions containing such EPO glycoproteins. A true and correct copy of the '080 patent is attached to the original Complaint as Exhibit 4.

e. U.S. Patent No. 5,756,349 (the "'349 patent"), issued on May 26, 1998, claims certain vertebrate cells capable of growth in culture that have been engineered to produce human EPO as well as processes for producing human EPO comprising the step of culturing said cells under suitable nutrient conditions. A true and correct copy of the '349 patent is attached to the original Complaint as Exhibit 5.

f. U.S. Patent No. 5,955,422 (the "'422 patent"), issued on September 21, 1999, claims pharmaceutical compositions comprising a therapeutically effective amount of human EPO purified from mammalian cells grown in culture. A true and correct copy of the '422 patent is attached to the original Complaint as Exhibit 6.

15. The pioneering nature of the inventions claimed in Dr. Lin's patents has been widely heralded by the scientific community, the United States Food and Drug Administration, the President of the United States and a succession of courts.

16. In this Court, Amgen successfully enforced and defended the validity of an earlier patent issued to Dr. Lin (claiming isolated purified EPO DNA and cells containing such DNA) against Genetics Institute, Inc. (under whose license the current Roche defendants manufacture in Europe their recombinant human EPO product (referred to by regulatory agencies as epoetin beta)) and Chugai Pharmaceutical Co. Ltd. (now a Roche subsidiary). More recently in this Court, Amgen successfully enforced and defended the validity of claims in Dr. Lin's '698, '080, '349 and '422 patents against Hoechst Marion Roussel, Inc. (now Aventis Pharmaceuticals Inc.) and Transkaryotic Therapies, Inc. This Court also held '933 claims 1 and 2, which are not asserted by Amgen in this action, to be invalid.

17. Amgen manufactures and sells recombinant human EPO (referred to by regulatory agencies as "epoetin alfa") in the United States under its EPOGEN® brand. A

subsidiary of Johnson & Johnson, licensed by Amgen under Dr. Lin's patents, also sells the same recombinant human EPO under the PROCRIT® brand. Beginning with its introduction in 1989, Amgen's recombinant human EPO has been approved to treat patients suffering from the anemias associated with kidney failure (1989), acute lymphocytic leukemia in HIV-infected patients (1990), AZT treatment of HIV infection (1990), and cancer chemotherapy (1993). It also has been approved to reduce the need for blood transfusions in patients undergoing elective, non-cardiac, non-vascular surgery (1996) and for pediatric use (1999).

ROCHE'S INFRINGING PROCESS AND PRODUCT

18. On information and belief, the Roche defendants are currently importing into the United States a pharmaceutical composition containing a recombinant human EPO product that Roche calls "Ro50-3821." Roche also calls this product "R744" or "Continuous Erythropoiesis Receptor Activator," hereinafter referred to as "PEG-EPO."

19. On information and belief, PEG-EPO contains EPO as claimed in Lin's '933, '080 and '422 patents.

20. On information and belief, PEG-EPO contains glycosylated human EPO, to which Roche has attached a polyethylene glycol ("PEG") polymer.

21. On information and belief, Roche produces the glycosylated human EPO contained in PEG-EPO by means of one or more processes claimed in Lin's '868, '698 and '349 patents.

22. On information and belief, Roche produces the glycosylated human EPO contained in PEG-EPO by culturing cells as claimed in Lin's '349 patent. Roche isolates the glycosylated human EPO produced by those cells, attaches PEG to the EPO, formulates the resulting combination as a pharmaceutical composition, and uses the infringing composition in

the United States.

23. The addition of PEG to glycosylated human EPO does not materially change the glycosylated human EPO contained in PEG-EPO.

24. But for the glycosylated human EPO contained in PEG-EPO, PEG-EPO would not stimulate the production of red blood cells when administered to human patients.

FIRST CAUSE OF ACTION
(DECLARATORY JUDGMENT OF INFRINGEMENT)

25. Amgen re-alleges and incorporates by reference the allegations in paragraphs 1 through 24 above.

26. On information and belief, Roche's importation and/or use of PEG-EPO in the United States currently infringes or will imminently infringe the claims of Amgen's '868, '933, '698, '080, '349 and '422 patents.

27. On April 19, 2006, Roche submitted its Biologic License Application ("BLA") with the United States FDA to sell pharmaceutical compositions containing PEG-EPO for the treatment of anemia associated with chronic kidney disease. On information and belief, Roche has completed all Phase III clinical trials it believes necessary to support its application for approval in the United States.

28. Roche announced that it expects to obtain regulatory approval to market and sell PEG-EPO in the United States within the next 12-14 months.

29. In anticipation of FDA approval to market and sell PEG-EPO in the United States, Amgen is informed and believes that, in addition to filing its BLA, Roche has been and is making meaningful preparations to market and sell PEG-EPO in the United States, including:

a. Hiring key management, support, and sales personnel, including actively recruiting Amgen marketing and medical personnel involved in the sale and use of recombinant

human EPO, to market and sell PEG-EPO upon receipt of regulatory approval to market and sell PEG-EPO in the United States;

b. Retaining outside consultants and vendors to assist in its marketing and sale of PEG-EPO in the United States;

c. Contacting potential customers, including large dialysis organizations ("LDOs"), to solicit interest in purchasing PEG-EPO from Roche upon regulatory approval in the United States; and

d. Completing construction and commencing operations of a new facility in Penzberg Germany to manufacture the recombinant human EPO in PEG-EPO for export to the United States, at a reported cost of 182 million Euros.

30. Upon receipt of regulatory approval to market and sell products containing PEG-EPO in the United States, Roche's manufacture, importation, use, sale, and/or offer to sell PEG-EPO in the United States will infringe, either literally or under the doctrine of equivalents, one or more claims of Amgen's '868, '933, '698, '080, '349 and '422 patents.

31. Despite actions by Amgen demonstrating its intent to enforce its patents against Roche's marketing and sale of PEG-EPO in the United States, Amgen is informed and believes that Roche has demonstrated a refusal to desist from continued and impending infringement of Amgen's '868, '933, '698, '080, '349 and '422 patents, such that a definite and concrete controversy now exists between Amgen and Roche regarding Roche's continued and impending infringement of one or more claims of the '868, '933, '698, '080, '349 and '422 patents.

32. Amgen seeks a judicial determination and declaration that Roche is currently infringing or, upon FDA approval will infringe one or more claims of Amgen's '898, '933, '698, '080, '349 and/or '422 patents by making, importing, using, selling, and/or offering for sale products containing recombinant human EPO, including PEG-EPO. Such a determination and declaration is necessary and appropriate at this time in order that the parties may ascertain their respective rights and duties.

PRAYER FOR RELIEF

Wherefore, Amgen requests that the Court enter judgment in its favor and against Roche as follows:

a. Declaring that the '868, '933, '698, '080, '349 and /or '422 patents are currently infringed or will be infringed by Roche's importation, use, offer for sale, and/or sale in the United States of products containing recombinant human EPO, including PEG-EPO;

b. Enjoining Roche from making, importing, using, selling or offering to sell products containing recombinant human EPO, including PEG-EPO, in the United States;

c. Awarding Amgen its costs and expenses of suit;

d. Granting Amgen such other and further relief as the Court deems proper.

Respectfully Submitted,

AMGEN INC.,
By its attorneys,

/s/ Michael R. Gottfried

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April 25, 2006

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 on April 25, 2006.

/s/ Michael R. Gottfried