UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

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

**ROCHE'S OPPOSITION TO AMGEN INC.'S MOTION *IN LIMINE* NO. 11: EXCLUDE THE 1986 LAI ET AL. PAPER [ROCHE TRIAL EXH. 501] BECAUSE IT IS NOT PRIOR ART**

Defendants F. Hoffmann-La Roche Ltd, Roche Diagnostics GmbH, and Hoffmann-La Roche Inc. (collectively "Roche") oppose Amgen Inc.'s Motion *In Limine* No. 11 to Exclude the 1986 Lai et al. Paper [Roche Trial Exh. 501]. The Lai paper was prepared by Por Lai, an Amgen employee with first hand knowledge about the technology of the patents in suit. Moreover the Lai paper is an ancient document within the meaning of FRE 803(16) and is admissible evidence that will assist the Court and the jury in their work in adjudicating the claims and defenses in this action, including written description, the state of the art, infringement and inequitable conduct. Amgen's motion mischaracterizes the purposes for which Roche offers this probative evidence and raises unsubstantiated claims of prejudice. In moving to exclude this probative evidence Amgen improperly seeks to invade the province of the jury with respect to analyzing and weighing evidence and making the ultimate factual determinations. Amgen's motion should be denied.

## I. THE LAI PAPER IS RELEVANT EVIDENCE THAT WILL ASSIST THE JURY AND THE COURT IN ADJUDICATING THIS ACTION

Roche's proposed Trial Exhibit 501, the paper entitled "Structural Characterization of Human Erythropoietin," (the "Lai Paper") should be admitted into evidence at trial because it is relevant to the claims and defenses in this action.[1]

### A. The Lai Paper is Relevant to Roche's Defense of Invalidity

The Lai Paper is relevant to Roche's claims regarding lack of written description, derivation and obviousness. In this case, Roche asserts that the patents-in-suit are invalid for inadequate written description because, among other reasons, a person of ordinary skill in the art, reading the patents-in-suit, would not have recognized that Dr. Lin was in possession of "human erythropoietin" as defined by the 165 amino acid sequence required by this Court's claim construction. *See* Exhibit B to Joint Pretrial Memorandum, D.I. 807-3, pp. 3-5; *see also* Memorandum and Order, D.I. 613, at 15.[2] The Lai Paper is probative evidence that as late as 1986, those of ordinary skill of the art, including Amgen, had no knowledge of human erythropoietin having a 165 amino acid sequence. *See* Lai Paper, D.I. 853-2 ("The amino acid sequence of human EPO, shown in Fig. 1, contains 166 residues and has a calculated $M_r$ = 18,398 for the protein moiety."). Such evidence demonstrates that Dr. Lin was not in possession

[1] Relevant evidence is that which has "any tendency to make the existence of any fact that is of consequence to the determination of the action more probable or less probable than it would be without the evidence." Fed. R. Evid. 401. As the United States Supreme Court has noted, this is a "liberal" standard. *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 587 (1993); *see e.g., U.S. v. O'Shea*, 426 F.3d 475, 484 (1st Cir. 2005) (evidence of a robbery was properly admitted over protests of prejudice as relevant to whether or not defendant possessed a firearm); *Shanklin Corp. v. Springfield Photo Mount Co.*, 521 F.2d 609, 618-19 (1st Cir. 1975) (non-prior art evidence was properly admitted and probative of level of ordinary skill in the art).

[2] Indeed, Amgen represented to this Court that a 165 amino acid human erythropoietin would have constituted impermissible new matter. Amgen Inc.'s Post-Hearing Memorandum In Support Of Its Fed. R. Civ. P. 52(c) Motion that '080 Claims 2-4 Are Infringed Under the Doctrine of Equivalents, dated August 18, 2003, at 1, *Amgen Inc. v. Hoechst Marion Roussel, Inc.,* Civ. Action No. 97-10814-WGY. AM-ITC 00852559-80 (D.I. 485-5-8).

of human erythropoietin having a 165 amino acid sequence, such as that derived from human urine, at the time that the Lin patent application was filed.

In addition, Roche asserts that the asserted claims are invalid because of subject matter derived from Dr. Goldwasser. Published in 1986, the Lai Paper details experiments performed by Dr. Por-Hsiung Lai and his research team at Amgen, in collaboration with Dr. Goldwasser, in 1983 and 1984 concerning the amino acid sequence for human erythropoietin. In describing the work of its authors in cloning the erythropoietin gene, the Lai Paper demonstrates that the sequences used by one of the authors of the Lai Paper, Dr. Goldwasser, were the same used by Amgen and disclosed by Dr. Lin. Accordingly, the Lai Paper is additionally relevant to whether the invention is derived from Dr. Goldwasser and invalid per 35 U.S.C. § 102(f).

Lastly, the Lai Paper provides valuable information about the level of ordinary skill in the art during this time – a factual issue which must be resolved as part of the obviousness analysis. It is well-established that there are several factual determinations which rest squarely with the jury, which in turn is entitled to a complete record in order to make its decision. *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17 (1966) ("basic factual inquiries" include the "scope and content of the prior art," "differences between the prior art and claims at issue," and "the level of the ordinary skill in the pertinent art"). The Lai Paper, regardless of its publication date,[3] is appropriate evidence of ordinary skill in the art; there is no requirement that evidence of this level of skill must qualify as prior art. *See Orthopedic Equipment Co., Inc. v. U.S.*, 702 F.2d 1005, 1011-12 (Fed. Cir. 1983) ("The evidence in support of the § 102 defenses…can be probative on the issue of the level of skill in the pertinent art even if it be considered inadequate to establish the existence of a § 102 defense…."); *Thomas & Betts Corp. v. Litton Sys., Inc.*, 720

[3] Although the Lai Paper was published in the March 5, 1986 issue of the *Journal of Biological Chemistry*, it was received for publication on August 26, 1985. Lai Paper at p. 3116.

F.2d 1572, 1580-81 (Fed. Cir. 1983) (materials that weren't "technically prior art, were, in effect, properly used as indicators of the level of ordinary skill in the art to which the invention pertained.").

**B. The Lai Paper is Relevant to Roche's Defense of Noninfringement**

The Lai Paper is relevant to the jury's evaluation of Amgen's contentions and Roche's defenses concerning infringement. Amgen asserts claims that cover "human erythropoietin," which this Court has construed to mean a "protein having the amino acid sequence of human EPO, such as the amino acid sequence of EPO isolated from human urine." Memorandum and Order dated July 3, 2007 at 15 (D.I. 613). Therefore, what one of skill in the art reading Lin's application at the time it was filed understood to be the amino acid sequence of human EPO is relevant to understanding the scope of asserted claims. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) The Lai paper demonstrates that not only at the time that Amgen filed its application in 1984, but also after that time through 1985 and 1986, Amgen and those of ordinary skill in the art would have understood human erythropoietin to consist of 166 amino acids, not 165.

**C. The Lai Paper is Relevant to Amgen's Inequitable Conduct**

Roche has asserted that Amgen's patents are unenforceable for inequitable conduct because, among other reasons, Amgen made misrepresentations to the USPTO as it attempted to expand its patent rights beyond its stated disclosure. The Lai Paper, in demonstrating what Amgen (and others in the field) knew during the prosecution of its original patent application, shows that Amgen's later statements to the USPTO concerning the scope of its invention were materially misleading. For example, during the prosecution of the '422 patent, Amgen knew that scientists outside of Amgen had discovered and published the correct amino acid sequence. *See*

Recny, M.A., at al (1987) Structural Characterization of Natural Human Urinary and Recombinant DNA-derived Erythropoietin, *J. Biol. Chem.*, 262, 17156-63 (D.I. 485-9). Yet Amgen, in an attempt to avoid a rejection based on 35 U.S.C. § 112, represented to the USPTO that its original Figure 6 disclosed human erythropoietin. As the Lai Paper shows, during and after the time that Figure 6 was created, Amgen still did not have the information regarding the length of the amino acid chain in human erythropoietin.

## II. AMGEN WILL SUFFER NO PREJUDICE FROM THE INTRODUCTION OF THE LAI PAPER

Amgen's cries of unfair prejudice are baseless. Amgen has long been aware of the relevance of Dr. Lai's experiments and his contribution to the state of the art. Amgen's entire argument concerning prejudice is premised on an underestimation of the jury's ability to understand relevant evidence and apply it to factual questions. The Lai Paper provides much-needed background to several key issues in the case, including evidence of what Amgen knew about human erythropoietin at critical times during the prosecution of its patents. The jury will receive a great deal of information on the importance of gene sequencing and the landscape of the art and will be well-instructed in how to evaluate the different types of information. There is simply no basis for assuming that the jury would be unable to apply the Court's instructions to this particular piece of evidence.

## CONCLUSION

Amgen's requested relief will have the effect of denying the jury the ability to consider relevant evidence in determining the infringement, validity and inequitable conduct. For the foregoing reasons, Roche respectfully requests that the Court deny Amgen's Motion *In Limine* No. 11.

Dated: August 31, 2007
Boston, Massachusetts

Respectfully submitted,

F. Hoffmann-La Roche Ltd, Roche Diagnostics GmbH, and Hoffmann-La Roche Inc.

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