UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

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

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

I. INTRODUCTION

Roche has indicated that it will rely at trial on a 1986 publication, Lai *et al*., "Structural Characterization of Human Erythropoietin," *J. Biol. Chem*. (1986) 261(7):3116-21 ("the 1986 Lai *et al*. paper"), that shows the amino acid sequence of human urinary erythropoietin. Apparently, Roche intends to rely on the 1986 Lai *et al*. paper as evidence in support of its invalidity arguments that address whether a person of ordinary skill in the art years earlier could have obtained the accurate amino acid sequence of human urinary erythropoietin (from which one, according to Roche's arguments, would have made a DNA sequence encoding erythropoietin). Roche should be precluded from making arguments and otherwise relying on the 1986 Lai *et al*. paper since it does not qualify as prior art under 35 U.S.C. §§ 102 or 103 and is not probative of what a person of ordinary skill in the art in 1983-84 would have reasonably expected to accomplish at the time of the Lin inventions. Indeed, Lai *et al*. acknowledged in their paper that they relied upon the DNA sequence of erythropoietin, which Dr. Lin had published in 1985, as well as at least one post-1984 technology. Dr. Lin's DNA sequence and that technology were simply not available to persons of ordinary skill in the art in 1983 or 1984. Consequently, the 1986 Lai *et al*. paper is irrelevant to Roche's invalidity defenses, is likely to mislead the jury as to the applicable state of the art, and it should therefore be excluded from evidence.

II. THE 1986 LAI ET AL. PAPER DOES NOT QUALIFY AS PRIOR ART

No matter which effective filing date each of Amgen's asserted patent claims is entitled to, the 1986 Lai *et al*. paper does not qualify as prior art under 35 U.S.C. §§ 102 or 103. The authors submitted it for publication ***over one and one-half years after*** (and it was published ***over two years after***) Dr. Lin filed his first patent application on December 13, 1983. Even if one of Amgen's asserted patent claims were given the latest possible effective filing date (November 30, 1984, the date Amgen filed the last of its continuation-in-part applications), the 1986 Lai *et*

al. paper was submitted for publication ***almost one year after*** (and was published ***about one and one-half years after***) that latest possible effective filing date.[1]

III. THE 1986 LAI *ET AL.* PAPER USES DR. LIN'S DNA SEQUENCE AND LATER-DEVELOPED TECHNOLOGY

While in some circumstances a later-dated reference may be evidence of the level of ordinary skill in the art at the time of an earlier-filed patent application, that is not the case here. The 1986 Lai *et al*. paper is clearly later-developed technology, and on its face demonstrates that the authors employed their knowledge of Dr. Lin's DNA sequence for human erythropoietin and at least one technology that was not available to or within the competencies of persons of ordinary skill in the art until 1984. When a party fails to show that a later-dated reference such as the 1986 Lai *et al.* paper is probative of the state of the art at the pertinent time, courts generally exclude such references from evidence.[2]

The DNA sequence of erythropoietin allowed the authors to identify or confirm the identity of several amino acids that they would have been unable to identify or be certain of in 1983 or 1984. For example, Lai *et al*. acknowledged "***Analysis of the DNA sequence*** indicated

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[1] *See* Exhibit 1 (the 1986 Lai *et al*. paper) to the attached Declaration of Matthew C. Nielsen ("Nielsen Decl."), at page 3116 ("Received for publication, August 26, 1985," and indicating a publication date of March 5, 1986).

[2] *See Stewart-Warner Corp. v. City of Pontiac*, 767 F.2d 1563, 1570 (Fed. Cir. 1985) (reversing judgment of invalidity where district court considered activities that did not qualify as prior art, and stating that while "[t]he district court did not state its degree of reliance on subsequent events or on its measure of the level of skill in the art," "[***t***]***he impropriety of such evidence of later developments is magnified in the context of rapidly evolving technology***") (emphasis added); *In re Omeprazole Patent Litigation*, Nos. 03-1101 *et seq*., 84 Fed. Appx. 76, 81 (Fed. Cir. Dec. 11, 2003) (*reh'g and reh'g en banc denied*) (non-precedential) ("the district court did not clearly err in declining to consider [a later-dated document] as reflecting the level of skill in the art" when the party seeking to rely on the document failed to offer "additional support in the form of testimony about the state of art at the time of the publication"); *Graco Children's Products, Inc. v. Century Products Company, Inc*., No. CIV. A. 93-6710, 1996 WL 421966 at * 15-16 (E.D. Pa. July 23, 1996) (excluding seven exhibits offered as evidence of the level of skill in the art, stating "[t]his evidence is not indicative of the level of technical sophistication in the [pertinent art] at the time of the invention of the [patent-in-suit].").

that a serine is present at position 126."[3] They also acknowledged that for certain amino acids, "[o]ur data for these positions are ***confirmed by the DNA sequence*** of the human gene."[4] They further acknowledged that "Determination of the C-terminal residue was based on sequence analysis and alignment of peptide T2 and ***confirmed by DNA sequencing***."[5] Other examples are evident from the sparse data provided by the authors. In 1983-84, a person of ordinary skill would simply not have had Lai *et al*.'s luxury of consulting the DNA sequence for erythropoietin, and the Lai *et al*. paper consequently does not reflect what such a person would have reasonably expected to accomplish in 1983 or 1984.

The authors also relied on a then-unpublished technique of amino acid compositional analysis, *e.g.*, "Compositional analysis of peptide hydrolysates . . . were performed according to ***the improved method*** of a published procedure."[6]

IV. THERE IS NO DISPUTE THAT THE 1986 LAI *ET AL.* PAPER EMPLOYED DR. LIN'S DNA SEQUENCE AND LATER-DEVELOPED TECHNOLOGY

Roche's experts (none of whom are experts in protein sequencing, which is the subject Amgen's Motion *in limine* No. 9 (Docket Nos. 803 & 804)) do not dispute that (i) Dr. Lin's DNA sequence and the "improved method" of "compositional analysis" were unavailable to persons of ordinary skill in the art in 1983 and 1984, and (ii) the authors of the 1986 Lai *et al*. paper employed both to accomplish their reported results. For example, while Roche's expert Michael Fromm first raised this particular Roche argument of invalidity in his April 6, 2007 expert report, Roche attempted to buttress Dr. Fromm's arguments in the "Second Supplemental Expert Report of Dr. Thomas Kadesch" and the "Third Supplemental Expert Report of Dr.

[3] *See* 1986 Lai *et al*. paper, Exh. 1, at 3116 (emphasis added).

[4] *Id*. (emphasis added).

[5] *Id*. at 3120 (emphasis added).

[6] *Id.* at 3119-20 (emphasis added) (citing an "in press" paper and a 1984 paper).

Lowe" (both dated June 13, 2007). Drs. Kadesch and Lowe addressed Dr. Fromm's argument and the 1986 Lai *et al*. paper -- for the first time each – in those reports. However, neither disputed that Lai *et al*. relied on Dr. Lin's DNA sequence for erythropoietin and the then-unpublished "improved method" of "compositional analysis."

The unavoidable conclusion is that the 1986 Lai *et al*. paper is not probative of the level of skill in the art on 1983 or 1984, and it is therefore irrelevant and inadmissible under FRE 402.

V. AMGEN WILL BE UNFAIRLY PREJUDICED IF THE 1986 LAI *ET AL.* PAPER IS ADMITTED INTO EVIDENCE

Amgen submits that it would be legal error for the jury to consider the 1986 Lai paper in determining the obviousness of Dr. Lin's inventions. Apparently, Roche hopes to mislead the jury into thinking that a person of ordinary skill in the art in 1983 or 1984 would have reasonably expected to succeed in obtaining a result similar to that which the authors of the 1986 Lai *et al*. paper performed, and then reported over two years later. But, Roche's argument must be proven based on prior art; not on after-developed art, and not on art that was after-developed through the use of the claimed inventions (reduced to its most basic form, Roche's argument is that it was obvious in 1983-84 to obtain results later achieved through the use of Dr. Lin's DNA sequence so as to obtain the same or a similar DNA sequence). Nor is the 1986 Lai *et al*. paper a fair measure for comparison; the jury will be in no position (indeed, Roche has presented no evidence on this) to determine the degree of success that a person of ordinary skill in the art in 1983 or 1984 would have reasonably expected to accomplish in comparison to 1986 Lai *et al*. paper. Indeed, the jury will be presented with a difficult task at trial, to determine the state of the art of protein sequencing in 1983 or 1984, and the 1986 Lai *et al*. paper can only make that task more confusing. Accordingly, the Court should bar introduction of the 1986 Lai *et al*. paper under FRE 403 to avoid the substantial prejudice and confusion that will be caused by Roche

importing the 1986 technology described in the 1986 Lai *et al*. paper into the jury's 1983-84 analysis.

VI. CONCLUSION

Amgen requests that the Court exclude from evidence the 1986 Lai *et al*. paper since it is not prior art and has not been proven to relate what was known in the art by the time of the Lin inventions.

Respectfully Submitted,

Date: August 21, 2007

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 on August 21, 2007.

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