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. 4: EXCLUDE GENENTECH'S PLA FILING [ROCHE TRIAL EXH. NO. 1072] BECAUSE IT IS NOT PRIOR ART

I. INTRODUCTION

Amgen moves to exclude Roche's expected reference to and introduction of clinical trial data and techniques described in a confidential Product License Application ("PLA") [Roche Trial Exhibit No. 1072] submitted to the FDA by Genentech in 1986 — about two years after the effective filing dates for the asserted claims of the Lin patents in suit — as evidence of what would have been obvious as of 1983-1984. In his expert report, Roche's trial expert Dr. John Lowe used this 1986 Genentech PLA to argue that use of Chinese Hamster Ovary (CHO) cells grown in culture to produce *in vivo* biologically active EPO would have been obvious in 1983. Genentech's PLA filing, which is still not available to one of ordinary skill in the art, discusses techniques and data that were unknown to those skilled in the art at the time of Lin's invention, and concerns tissue-type plasminogen activator (tPA), not EPO. This PLA filing is not prior art and Roche has no evidence showing that the PLA reflects the relevant state of the art as it would have been understood by the ordinarily skilled artisan by the filing dates of the subject in Lin's claimed inventions. Accordingly, the Genentech PLA, as well as Dr. Lowe's opinions based thereon, are irrelevant to Roche's prior art defenses and should be excluded under FRE 402 and 403 because of the likely confusion of the jury.

II. ARGUMENT

A. Genentech's 1986 PLA Is Not Prior Art

Asserted in this case are claims 1 and 2 of the '868 Lin patent, claims 6-9 of the '698 Lin patent, claim 7 of the '349 Lin patent, claim 1 of the '422 Lin patent, and claims 3, 7-9, 11, 12, 14 of the '933 Lin patent. The latest possible effective filing date for all of the asserted claims is November 30, 1984, the date Amgen filed the last of its continuation-in-part applications. Dates on Genentech's confidential PLA indicate that it was assembled in March-April of 1986 and

submitted to the FDA on April 24, 1986,[1] almost two years after any of the attributable filing dates to the asserted Lin patent claims. The PLA comes too late to be prior art in this case.

Also, since submissions to the FDA are not made public,[2] the assumption must be that this Genentech PLA was ***never*** publicly disclosed. Indeed, even when Genentech produced these portions of the PLA to Amgen in 2007, it marked every page as "Genentech, Inc. – Confidential."[3] The earliest public disclosure of the therapeutic use of tPA produced using CHO cells cited by Dr. Lowe is a non-technical FDA press release dated November 13, 1987.[4]

The Genentech PLA thus does not qualify as prior art under the patent law (see 35 U.S.C. §§102 and 103).

B. Genentech's 1986 PLA Is Not Probative Of What Was Possible For One Of Ordinary Skill In The Art In 1983-1984

There was no explanation in Dr. Lowe's report as to how a person of ordinary skill in the art in 1983-1984 could possibly have known of the concealed techniques or clinical results discussed in the later submitted Genentech PLA. Since Genentech's PLA submitted in 1986 is not prior art, Dr. Lowe improperly relies on it to opine that well before 1986 the skilled artisan would have had a reasonable expectation of success in using CHO cells to produce a functional, *in vivo* biologically active recombinant human glycoprotein, such as erythropoietin.[5] Dr. Lowe's use of hindsight to reconstruct what would have been possible at the time of the invention, and thereby analyzing the obviousness in 1983-1984 using a blueprint that was assembled more than

[1] ROCHE-GNE 03009.

[2] 21 C.F.R. §§ 601.50 and 601.51.

[3] ROCHE-GNE 0001-3060.

[4] 4/6/07 Expert Report of Dr. Lowe at ¶ 126 (citing TPA Approval – Blood Clot Dissolver, http://www.fda.gov/bbs/topics/NEWS/NEW00191.html).

two years later.

While in some circumstances a later-dated reference may be evidence of the level of skill in the art at the time of an earlier-filed patent application, that is not so here. When a party like Roche fails to show that a later-dated reference such as the Genentech PLA is probative of the state of the art at the pertinent time, courts generally exclude such references from evidence.[6] Roche has not met its burden to show that the Genentech PLA is probative of the state of the art of using CHO cells to produce *in vivo* biologically active glycoproteins such as erythropoietin as of 1983-1984.

According to the Federal Circuit, even when there was later arising independent development of an invention identical to that claimed, there needs to be some showing that the later arising invention applies to the time the claimed invention was made.[7] Using events subsequent to the invention date to establish the level of ordinary skill in the art at the time the invention was made is improper and "is magnified in the context of rapidly evolving

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[5] 5/1/07 Supplemental Expert Report of John Lowe, M.D. ¶ 6-14.

[6] Amgen acknowledges it is not precedent, but in *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*), the Federal Circuit held "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." *See also 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].").

[7] *Stewart-Warner Corp. v. City of Pontiac, Michigan*, 767 F.2d 1563, 1570 (Fed. Cir. 1985) ("Development by others may also be pertinent to a determination of obviousness of an invention; but the evidence presented was of activities occurring well after the filing date of the '926 patent application, and was not shown to apply to the time the invention was made, as required by 35 U.S.C. §103." (internal cites omitted))

technology."[8] There is no dispute that biotechnology is a rapidly evolving technology. Roche has not shown that the technology described in the Genentech tPA, using CHO cells to produce biologically active glycosylated tPA, applies during 1983-1984 and thus it should be excluded and Roche precluded from referring to the PLA in its testimony, particularly through Dr. Lowe.

C. Amgen Will Be Unfairly Prejudiced If Genentech's PLA Is Admitted Into Evidence

Even if the Genentech PLA has any probative value in this case (which Amgen does not assume is true), that value will be substantially outweighed by the unfair prejudice that Amgen will suffer if the PLA is deemed admissible. Roche's introduction of the Genentech PLA would mislead the jury to think that a person of ordinary skill in the art in 1983-1984, two years before the submission of the PLA, would have reasonably expected to succeed in obtaining the expression of a biologically active glycoprotein such as erythropoietin. The Court should bar introduction of the Genentech PLA to avoid any such prejudice.

III. CONCLUSION

For the reasons above, Amgen requests this Court to exclude the confidential Genentech PLA [Roche Trial Exh.1072] and any testimony based thereon as irrelevant under FRE 402, or in the alternative as so lacking in probative value as to serve merely to confuse the jury under FRE 403.

[8] *Id.*

Respectfully Submitted,

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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 17, 2007.

/s/ Michael R. Gottfried
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