

# EXHIBIT

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**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-12237 WGY

**CONTAINS CONFIDENTIAL  
INFORMATION SUBJECT TO  
PROTECTIVE ORDER**

**SECOND SUPPLEMENTAL EXPERT REPORT OF DR. LOWE**

**I, JOHN LOWE, M.D.**, submit this supplemental expert report on whether the claims asserted against Roche from certain of Amgen's United States Patents, as described below, would have been obvious in 1983.

**I. BACKGROUND**

1. I am the same John Lowe who submitted the April 6, 2007 Expert Report of John Lowe ("April 6, 2007 Exp. Rep."). My education and experience, compensation and prior testimony are set forth in my April 6 report, and a copy of my curriculum vitae is Exhibit A to that report. If called upon to do so, I will go through my curriculum vitae to discuss the contents, including any relevant professional experience and cited references.

**II. MATERIALS CONSIDERED**

2. In forming my opinions and preparing this report, I have considered the materials cited and listed in this report, as well as the materials listed in the attached Exhibit A-1. I have also relied on my professional scientific and clinical experience.

such as Biogen or Schering, which as Dr. Goldwasser admitted, with such material could have cloned the EPO gene or an EPO cDNA. (See for example, April 6, 2007 Lowe Report ¶ 52).

10. In this regard, a number of the findings made by the district court further strengthen my conclusion that in view of the evidence cited in my April 6, 2007 report, before October 1983, it would have been obvious to one of skill in the art to achieve this objective through cloning the cDNA for EPO. At the time, a finite number of practical approaches were available to clone the gene, essentially using cDNA libraries or using genomic libraries. The findings of the district court are consistent with my conclusion that the approach using cDNA libraries was both well within the routine technical knowledge of one of skill at the time and predictable, and therefore would have been an obvious choice. As discussed in my April 6, 2007 report, it is my opinion that Lin's only advantage over his contemporaries was his exclusive access to a sufficient amount of pure EPO which Dr. Goldwasser provided to Amgen. My opinion is consistent with the finding of the district court that "Amgen held an advantage over the other companies because it alone among the commercial biotechnical companies had access in usable amounts after 1981 to urinary source EPO, which was a 'rather rare commodity,' from Dr. Goldwasser, the primary person who had that material." Chugai I at \*35.

11. The district court's findings<sup>1</sup> confirm that Lin's successful cloning relied on material from Dr. Goldwasser, which allowed Dr. Lin to design a suitable oligonucleotide probe for screening:

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<sup>1</sup> To the extent I have referred to findings of the district court in this report in Chugai I and in TKT I, I reserve the right to specifically rely on any of the underlying evidence with respect to these findings cited in the court's opinion.

gene represented no more than the application of one of a small number of identified and predictable solutions to this problem, which one of skill would have routinely applied to achieve this objective. In my opinion, during prosecution, Amgen overcame the rejection of the claimed subject matter as obvious only by mischaracterizing the state of the art, in particular the purported unpredictability of expressing functional recombinant human glycoproteins, and by arguing that the predictable paths to cloning and expressing the human EPO gene would only have been obvious to try.

39. The only reason Amgen was first to achieve this objective was through its advantage in being the only company before 1984 that had access to amounts of purified urinary source human EPO sufficient to obtain protein sequence information required to design degenerate oligonucleotide probes. As of 1983, in view of the prior art and having a sufficient source of Dr. Goldwasser's purified EPO in hand, nothing in what Dr. Lin achieved would have required more than ordinary skill and common sense. For all the reasons discussed here as well as in my previous reports, it is my opinion that by October 1983, all the asserted claims of the Lin patents would have been obvious.

40. I declare that the foregoing is true and correct to the best of my knowledge and belief.

Dated: May 8, 2007



John Lowe, M.D.