



UNITED STATES DISTRICT COURT  
DISTRICT OF MASSACHUSETTS

AMGEN INC., )

Plaintiff, )

v. )

F. HOFFMANN-LA ROCHE )  
LTD., a Swiss Company, ROCHE )  
DIAGNOSTICS GmbH, a German )  
Company and HOFFMANN-LA ROCHE )  
INC., a New Jersey Corporation, )

Defendants. )

Civil Action No.: 05-12237 WGY

**SUPPLEMENTAL EXPERT REPORT OF HARVEY F. LODISH, Ph.D.**

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BLA/IND Restricted Access*

phenol red (a pH-indicator dye), and containing thymidine and hypoxanthine) than they would when grown by Roche in Germany.

66. Contrary to Dr. Kadesch's assertion, this statement does not mean that "if Amgen during litigation can find some conditions that force a Defendants' cells to produce EPO at the claimed levels Amgen concludes there is infringement." Dr. Kolodner did not "find some condition" that "forced" Roche's cells to produce EPO at the claimed rates. Rather, because Roche did not send him the medium it actually uses in its accused process, and because he was under a time constraint that prevented him from exactly replicating that medium, he used a medium formulation that was as close to that used by Roche as practical. Like Dr. McLawhon, I do not believe that any of the minor differences between Roche's medium and the medium used by Dr. Kolodner could have materially affected the rate at which Roche's cells produced EPO in the medium of their growth, particularly given the fact that Roche's cells produced EPO at levels many times greater than 100 U per  $10^6$  cells in 48 hours. As stated in the April 30, 2007 Expert Statements of Drs. Kolodner and McLawhon, Dr. Kolodner grew the cells under the conditions specified by Roche and in a culture medium that did not differ in any materially significant aspect from that used by Roche, and Dr. McLawhon's experiments established that the cells were capable of meeting the claimed EPO production rates as determined by radioimmunoassay.

67. Furthermore, given the other evidence that I cited in my Infringement Expert Report and Addendum that corroborates that Roche's cells produce EPO at levels several times in excess of the 100 U per  $10^6$  cells in 48 hours requirement of Claim 7, all of the evidence that I have reviewed supports my opinion that Roche's DN2-3 $\alpha$ 3 cells, under the conditions used by Roche in its manufacturing process in Germany, produce EPO at the level required by '349 Claim 7. While we do not have direct RIA measurements taken from the DN2-3 $\alpha$ 3 cells in

Roche's fermentors in Germany (Roche did not provide such access), all of the available evidence supports an inference that the same cells grown under the conditions used by Roche in its manufacturing plant would produce EPO at a rate greater than 100 U per  $10^6$  cells over 48 hours as measured by RIA.

68. I note that Roche has offered no evidence to the contrary. Since Roche owns and controls the manufacturing plant in Germany, Roche could easily perform the RIA measurements on its production cell line. As far as I know, Roche has not performed such experiments, or Roche has chosen not to share the results with Amgen. The absence of any contradictory data from Roche further supports my opinion that Roche's production cell line satisfies the EPO production level requirement of '349 Claim 7.

**VI. IT WOULD NOT HAVE BEEN OBVIOUS TO CLONE THE EPO GENE IN OCTOBER 1983.**

69. I have reviewed the Supplemental Expert Report of Stuart Orkin, M.D. responding to certain arguments raised by Dr. Lowe in his Second Supplemental Report regarding whether Lin's cloning of the EPO gene was obvious. I agree with the points raised by Dr. Orkin in his supplemental expert report. I therefore incorporate by reference Dr. Orkin's supplemental report. At trial, I may address some or all of the points raised by Dr. Orkin in his supplemental report, which I incorporate by reference.

**VII. THE CLAIMS-IN-SUIT ARE NOT OBVIOUS IN LIGHT OF THE '008 PATENT BECAUSE ONE OF ORDINARY SKILL IN THE ART IN OCTOBER 1983 WOULD NOT HAVE HAD A REASONABLE EXPECTATION OF SUCCESS IN EXPRESSING *IN VIVO* BIOLOGICALLY ACTIVE GLYCOSYLATED EPO.**

**A. LIN'S DECEMBER 1983 PATENT APPLICATION DOES NOT DEMONSTRATE ONE OF ORDINARY SKILL IN THE ART WOULD HAVE HAD A REASONABLE EXPECTATION OF SUCCESS.**

70. In his Supplemental Report, Dr. Lowe suggests that Dr. Lin's December 1983

Executed this 4<sup>th</sup> day of June, 2007 at Boston, Massachusetts.



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HARVEY F. LODISH, Ph.D.