

# EXHIBIT C

UNITED STATES DISTRICT COURT  
DISTRICT OF MASSACHUSETTS

AMGEN INC., )  
 )  
 Plaintiff, )  
 ) Civil Action No.: 05-12237 WGY  
 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. )  
\_\_\_\_\_)

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

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21. First, as noted above, Lin made clear that it was the sequence of amino acid residues of mammalian-produced EPO provided by the illustrative examples that essentially defined the primary structural conformation, or amino acid sequence, of human EPO

22. Second, it was not possible in 1984 (nor would it be today) to deduce the cleavage of arginine 166 based on the EPO DNA sequence.

23. Third, the technology for carboxy-terminal (as opposed to amino-terminal) protein sequencing was not well developed in the 1983-1984 time frame, which explains why Dr. Lin could not carry out an analysis of the C-terminus of recombinant EPO and thus why he was unaware of this processing step.

24. Fourth, the human EPO produced in Example 10 of Dr. Lin's patents has the 1-165 amino acid recited in Figure 6.<sup>15</sup> This is because the CHO cells used to produce EPO possess the appropriate enzyme(s) to recognize and cleave arginine 166 from EPO. This reaction occurs as the consequence of expression in a vertebrate cell line. The efficiency of the carboxy-terminal cleavage is inherent in and dependent on the particular cell expressing EPO. The CHO cells of example 10 in the patent are highly efficient at the cleavage of the carboxy-terminal arginine. Thus, the specification inherently demonstrates 165 amino acid human EPO. In other words, if a person skilled in the art followed Example 10, they would be in possession of a 165 amino acid human EPO.

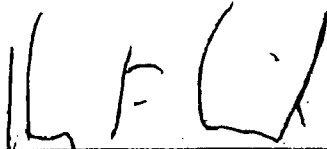
25. On the other hand, not all host cells cleave arginine 166 as efficiently as CHO cells. For example, Roche's EPO produced in human host cells ("EPO-EGA") was not cleaved with 100 percent efficiency, resulting in a mixture of 165 and 166 amino acid EPOs.<sup>16</sup> Likewise,

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<sup>15</sup> 9/28/99 Declaration of Jeffrey K. Browne, Ph.D. ¶ 3.

<sup>16</sup> U.S. Patent No. 6,544,748 at Col. 6:27-31 ("human EPO can be isolated from HeLa S3 cells, which is mainly a polypeptide with a length of 165 amino acids, which is formed by C-terminal

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



HARVEY F. LODISH, PH.D.