

EXHIBIT B**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

EXPERT REPORT OF CHARLES G. ZAROULIS, M.D.

1. I have been asked by counsel for Defendants¹ to provide my opinion regarding the validity of claims of U.S. Patent No. 5,756,349 (the “ ‘349 patent”). I have prepared this report in anticipation of providing my testimony at trial on the subject matter set forth below.

I. BACKGROUND

2. I am a practicing hematologist with a subspecialty in blood banking. Since 1992, I have been an attending physician in the Department of Medicine, Division of Hematology & Oncology, at University Hospital in Staten Island, New York. Until 2002, I served as director of the division and oversaw our clinical research. I also serve as the Director of Marrow Transplantation, and the Director of the Blood Bank and Tranfusion-Medicine Service. I received my undergraduate degree from the University of Virginia and my medical degree from

¹ F. Hoffmann-La Roche, Ltd., Roche Diagnostics GmbH and Hoffmann-La Roche, Inc. (collectively “Roche”).

radioimmunoassay as required by the claims because different standards would give different results.

F. Claim 7 is Invalid for Indefiniteness and Lack of Enablement

74. Claim 7 of the '349 patent claims a process for producing erythropoietin using vertebrate cells "which are capable ... or producing erythropoietin ... in excess of 100 [500, 1000] U of erythropoietin per 10^6 cells in 48 hours as determined by radioimmunoassay."⁵⁶ One skilled in the art would instantly understand that "U of erythropoietin" is a measure of biological activity alone, and would know that radioimmunoassays cannot measure biological activity. The only way to measure biological activity of EPO and obtain a value for Units of EPO is with an *in vivo* bioassay. Therefore I conclude that under no circumstance could one of skill in the art at the time of the invention have understood the clear boundaries of this limitation present in claims 1-6 of the '349 patent.

75. In my opinion, the '349 patent does not enable one skilled in the art to make (and use) the claimed invention because one could not practice the claimed method and obtain the required number of units of erythropoietin as determined by radioimmunoassay. Because the details of the RIA and the methods for preparing or obtaining the necessary components for the RIA are not disclosed in the '349 patent, and because the nature of the "U of erythropoietin" claimed is not described or defined, and no information describing how to correlate RIA results with biological assay results or how to calculate or estimate biological activity from RIA results is provided, someone of ordinary skill in the art would be unable to make and use the invention claimed in the '349 patent.

⁵⁶ U.S. Patent No. 5,756,349, col. 38, lines 9-12.