EXHIBIT B

UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff,	)	Civil Action No. 05-CV-12237 WGY
v.	)	
F. HOFFMAN-LA ROCHE, LTD., ROCHE DIAGNOSTICS, GmbH, and HOFFMAN-LA ROCHE, INC. Defendants.	)	

REBUTTAL REPORT OF RALPH A. BRADSHAW, PH.D.

Contains Amgen Confidential Information Subject To Protective Order

REDACTED

1. I have been retained as an expert in this case by counsel on behalf of Amgen Inc. ("Amgen"). If called to testify at trial, I expect to provide testimony regarding the matters set forth in this Report.

Qualifications

2. I am a Professor Emeritus in the Department of Physiology & Biophysics at the University of California at Irvine. I am also a Professor (Recall) in the Department of Pharmaceutical Chemistry at the University of California, San Francisco. Additionally, I serve as the Deputy Director of Mass Spectrometry Facility at the University of California, San Francisco. During the nearly 40 years I have been a faculty member, I have trained more than 20 students, advised dozens more and lectured to thousands of medical and graduate students in areas of molecular and cell biology. Most of the students who did their research in my laboratory now hold positions in either academia or industry.

3. In addition to fulfilling my duties at the Irvine and San Francisco campuses of the University of California, I am a Co-Editor and Associate Editor of Molecular & Cellular Proteomics and Growth Factor, respectively. Regarding Molecular & Cellular Proteomics, I was also the publication's founding Editor-in-Chief. In addition to these journals, I currently serve on the Editorial Boards of the journals Biotechnology and Applied Biochemistry, Cancer Communications/Oncology Research, and IN VITRO Rapid Communications in Cell Biology. In the past, I have served as an Associate Editor of the Journal of Biological Chemistry and of Protein Science and as Editor-in-Chief of Trends in Biochemical Sciences. Over the course of my career, I have served on a total of seventeen Editorial Boards of academic journals.

4. I am (or have been) a member of a total of eighteen scientific societies, including the American Chemical Society, the American Society for Biochemistry and Molecular Biology,

the Endocrine Society, the American Society for Cell Biology, the Society for Neuroscience, the International Society of Neurochemistry, the American Peptide Society, the Protein Society, the Association of Biomolecular Resource Facilities and the American Society of Bone and Mineral Research. I am an elected fellow of the AAAS and I also have served as the President of the Federation of American Societies of Experimental Biology, the Treasurer of the American Society for Biochemistry and Molecular Biology, and was the founding President of the Protein Society.

5. I have organized over three dozen national and international meetings on the structure and function of proteins, with a particular emphasis on growth factors. In addition, I have served on the Board of Directors of the Keystone Symposia on Molecular and Cell Biology for the past ten years and in the capacity of Treasurer for nine of those years. I have also been a member of the U. S. National Committee on Biochemistry of the National Academy of Sciences-National Research Counsel for almost ten years, serving as that Committee's Chairman for four years.

6. Finally, I have served on a number of international advisory committees including the Hagedorn Institute in Denmark and the Australian Health and Medical Research Strategic Review Committee, a group that was charged with reviewing all of that country's biomedical research. In addition, I served on the Executive Committee of the International Union of Biochemistry and Molecular Biology for six years.

7. I received my undergraduate degree in chemistry in 1962 from Colby College. I was awarded my doctorate degree in biochemistry from Duke University in 1966. I have edited twelve scientific treatises and books and am the author or co-author of more than 300 articles or reviews and more than 150 abstracts in the area of protein chemistry and cell biology. A copy of

my *curriculum vitae* is attached to this Report as Exhibit A.

8. In the course of my over 40 years of research experience, I have isolated, characterized and/or determined the sequence of some fifty proteins, including several polypeptide growth factors and glycoproteins. I determined the first amino acid sequence of a growth factor (nerve growth factor) and I have contributed substantially to the development of this field.

Information Considered

9. In forming the opinions expressed in this Report, I have considered the following things:

- U.S. Patent No. 5,547,933 ('933 Patent) (I have been informed that the specification of this patent is the same as that of all six patents involved in this litigation);
- The claims of U.S. Patent Nos. 5,621,080 ('080 Patent); 5,955,422 ('422 Patent); 5,547,933 ('933 Patent); 5,441,868 ('868 Patent); 5,756,349 ('349 Patent); and 5,618,698 ('698 Patent);
- The April 6, 2007 Expert Report of Richard A. Flavell, and the references cited therein;
- The April 6, 2007 Expert Report of Edward Everett Harlow, Jr., and the references cited therein;
- The March 16, 1990 Declaration of Joan Christine Egrie and the documents cited therein (AM-ITC 00406047-079); and
- Excerpts from Amgen Laboratory Notebooks 1135, 3416, and 9136. (AM-ITC 00068734-839; AM-ITC 00188055-111; AM-ITC01081006-047)
- The publications, references, and Expert Reports cited in this Report.

In forming my opinions, I additionally have relied upon the knowledge, training, and experience that I have acquired during my over 40 years as a protein chemist.

Compensation

10. I have been retained by counsel for Amgen as a consultant in connection with this action. I am being paid my usual consulting rate of $300.00 per hour.

Previous Testimony

11. I have not testified as an expert at trial within the preceding four years. I was deposed in the matter Abbott GmbH & Co. KG v. YEDA Research and Development Co., Ltd., Case No. 1:00CV01720 (D.D.C.) in 2004.

Summary of My Opinions

12. I have reviewed the April 6, 2007 Expert Reports of Drs. Richard Flavell and Edward Harlow, as well as the documents cited therein. In those reports, Dr. Flavell offers the opinion that Dr. Lin's specification fails to teach or describe how to purify recombinant human erythropoietin for use in a pharmaceutical composition. Dr. Harlow offers a like opinion. I have been asked to consider these opinions.

13. Based on my review of the above-referenced documents, as well as my over 40 years of experience as a protein chemist, it is my opinion that:

Opinion 1: As of 1983-1984, before Dr. Lin's patent disclosure, the ordinarily skilled person could not have purified EPO to apparent homogeneity from blood and cell culture samples, using any procedure reporting the purification of EPO from urine, with a reasonable expectation of success.

Opinion 2: From the outset of 1984, with Dr. Lin's abundant EPO starting material and the benefit of his teachings in hand, the ordinarily skilled person would have been able to purify recombinant human EPO to apparent homogeneity.

14. I note that at paragraph 12 of his Report, Dr. Flavell, in addition to offering an opinion regarding protein purification, also offers the same opinions set forth in Dr. Lowe's Report:

"12. I have reviewed the expert report of Dr. John Lowe in this case

> which describes how these claims were disclosed in the prior art and Dr. Lin's previous patent on this subject matter, U.S. Patent No. 4,703,008 ("the '008 patent"). I agree with Dr. Lowe's conclusions that these claims are obvious in view of the prior art and also not patentably distinct from the claims of the '008 patent and are therefore invalid."

It is my understanding that Dr. Lowe' Report does not address protein purification. Rather, it refers to, among other things, whether the cloning and expression of human erythropoietin would have been obvious before Dr. Lin's inventions. Because the cloning issues involved in this case are outside my area of expertise, I will not be offering any opinion as to Dr. Flavell's wholesale adoption of Dr. Lowe's Report and opinions.

Tutorial

15. Protein chemical studies include the elucidation of the structure/function relationship of a protein. In more recent times, protein chemistry has evolved to include the field of proteomics, a field that deals with the relationship between proteins in a sample and their functions (as compared to the reductionist approach — reducing samples to their component parts prior to considering their function).

16. As a general matter, protein chemical studies usually focus on the elucidation of the structure/function relationship of a protein(s). In more recent times, protein chemistry has evolved to include the field of proteomics, an area of study that deals with the broader description of proteins and their functions in larger, more complex samples (as compared to the reductionist approach that has largely characterized the last forty years of biochemical studies — reducing samples to their component parts and studying them as isolated entities).

17. In order to eliminate the confounding contributions of other entities, proteins are usually isolated before their structure/function relationships are elucidated. The types and number of procedures needed to purify a particular protein from a sample will depend on what other

its commercial purification process does not undermine these teachings.

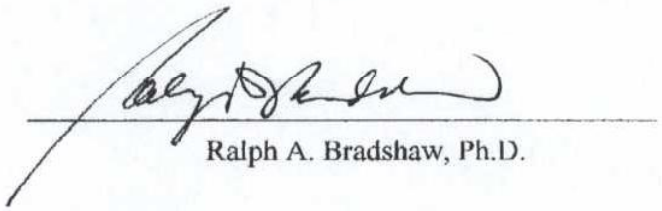
80. It appears to me that Amgen's efforts, and particularly the efforts of Dr. Strickland and another Amgen scientist, Dr. Por Lai, were directed to finding an easier and more economical way to purify human erythropoietin from cell culture media. That Drs. Strickland and Lai received a patent for these efforts does not make Dr. Lin's teaching, or the Miyake *et al.* protocol, less trustworthy. Nor does it serve as a basis for asserting that Dr. Lin did not teach a means for purifying human erythropoietin to apparent homogeneity, or change my opinion.

81. In my opinion, Dr. Strickland and Dr. Lai's claims are directed to a new and non-obvious combination — a specific process comprising a defined set of steps. In the anion exchange step, material is loaded at a neutral pH and the column then washed with a urea solution at a pH of 4.5. The acidic urea wash was added to inactivate proteases and thus minimize the formation of EPO fragments (as set forth in the patent). The resulting combination was and is an improvement over any of the processes previously described in the art (whether by Drs. Lin, Miyake and Goldwasser, or any others). The ordinarily skilled person would not necessarily have found Drs. Lai and Strickland's process intuitive. One of ordinary skill in the art would not have thought to use a urea wash to inactivate proteases because urea was not typically used for that purpose and was known to cause carbamylation of the protein in alkaline conditions, Drs. Strickland and Lai avoided the carbamylation issue by conducting the step under acidic conditions.

82. This work, and the novelty of Drs. Strickland and Lai's approach to use urea under acidic conditions does not change my opinion that one of ordinary skill in the art would have been able to purify recombinant human erythropoietin from cell culture media to apparent homogeneity in light of Dr. Lin's teachings.

83. Based on both the data from Dr. Strickland and Dr.Egrie, I therefore agree with Judge Young when he notes that "[i]mportantly, it was Amgen's invention that opened the floodgates for EPO production and led to the first pharmaceutical composition containing EPO to obtain FDA approval." (*Amgen, Inc. v. Hoechst Marion Roussel, Inc.* 339 F. Supp. 2d 202, 319 (D. Mass, 2004) aff'd 457 F.3d 1293, 1308 (Fed. Cir. 2006)). Thus, before Dr. Lin's inventions, the problem confronting researchers and clinicians was not knowledge of purification methods, but rather the availability of a source from which to obtain EPO.

Dated: May 11, 2007



Ralph A. Bradshaw, Ph.D.