EXHIBIT E

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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

EXPERT REPORT OF DR. LOWE

I, JOHN LOWE, M.D., declare as follows:

I offer this expert report on whether the claims asserted against Roche from certain of Amgen's United States Patents, as described below, are invalid for obviousness and lack of novelty.

I. QUALIFICATIONS

1. I am currently the Professor and Chair of the Department of Pathology at Case Western Reserve University School of Medicine in Cleveland, Ohio. I have held this position since March 1, 2005. Prior to March 1, 2005, I was a Professor of Pathology at the University of Michigan Medical School, and was an Investigator of the Howard Hughes Medical Institute. I held the medical school faculty position at the University of Michigan and my position with the Howard Hughes Medical Institute since October 1, 1986. In my prior position at the University of Michigan, I spent approximately 80% of my time and effort in scientific research activities. In

my current position, I spend approximately 40% of my time and effort in scientific research activities.

2. My past and current scientific research has focused on understanding how a protein modification termed glycosylation contributes to the function of several specific proteins of relevance to the mammalian immune system. These proteins include: (1) the Notch family of cell surface receptors; (2) the proteins that bind to Notch proteins (Notch ligands); (3) the selectins, which are three members of a family of proteins that mediate adhesion of white blood cells to the inside of the blood vessel; and (4) selectin ligands. My role in this research continues to consist of formulating hypotheses, designing experiments, supervising the completion of these experiments by laboratory personnel comprised of PhD students, research technicians, and junior faculty members, interpreting the data forthcoming from these experiments, and helping to compose the manuscripts that report these data and their conclusions.

3. In addition to my laboratory research responsibilities, I currently administer the Pathology Department at the Case Western Reserve School of Medicine and the University Hospitals of Cleveland. This Department has as its missions the provision of clinical laboratory and surgical pathology services to the physicians and patients at University Hospitals of Cleveland, the teaching of medical students, PhD students, and physicians in training at the Case Medical Center, and basic and applied research in biomedicine.

4. I am the sole author of four issued United States patents and two issued foreign patents, and a coauthor of five issued United States patents. These patents include claims for novel methods for molecular cloning of genes and cDNAs encoding mammalian proteins that control glycosylation, for DNA and protein sequences derived from such cloning activities, or for the expression of a soluble recombinant molecule whose state of glycosylation is essential to

does not provide any patentable distinction over the DNA and host cell claims 2, 4, 6, 7, 25 and 27 of the ‘008 patent. As described above, the prior art described numerous examples of promoters and various expression vectors including such promoters where such promoters were operably linked to drive expression of exogenous genes, and use of viral promoters, such as promoters from the SV40 virus. It would have been obvious to one of skill in using either the claimed DNA or host cells expressing such DNA to use such promoters to express DNA encoding human erythropoietin in a mammalian or other vertebrate cell, such as a COS cell or CHO cell.

184. Moreover, the use of cells comprising amplified marker DNA as recited by ‘698 patent claim 7, and specifically, amplified maker DNA corresponding to the DHFR gene, does not provide any patentable distinction over the DNA and host cell claims 2, 4, 6, 7, 25 and 27 of the ‘008 patent. As described above, prior to October 1983, the prior art described numerous examples of using amplification for transient and for stable expression of human glycoproteins in host cells such as COS cells or CHO cells, and expression vectors encoding various marker genes such as the DHFR gene for use in such methods. It would have been obvious to use such expression vectors and amplification methods to express human erythropoietin in such host cells, resulting in host cells comprising amplified marker DNA, including amplified DHFR marker gene DNA.

C. Claim 7 of the ‘349 Patent is not Patentably Distinct from Claims 2, 4, 6, 7 and 25 of the ‘008 Patent

185. Dependent claim 7 of the ‘349 patent is directed to “a process for producing erythropoietin” comprising culturing, “under suitable nutrient conditions” vertebrate cells described by claims 1, 2, 3, 4, 5 or 6. These claims specify that the cells can be propagated in vitro and are capable of producing human erythropoietin in excess of 100, 500 or 1000 U per 10^6

cells in 48 hours. Claim 7 however does not require a specific rate of EPO production to be achieved when using these cells in the process.

186. Claims 25 and 27 of the ‘008 patent are directed to a recombinant mammalian host cell, transformed in such a manner as to allow the host cell to express an erythropoietin with the “biological property of causing bone marrow cells to increase production of reticulocytes and red blood cells.” In my opinion, there is no patentable distinction between the host cell claims 25 or 27 of the ‘008 patent, and the process recited by ‘349 patent claim 7 of producing erythropoietin by culturing, “under suitable nutrient conditions” vertebrate cells capable of producing human erythropoietin in excess of 100, 500 or 1000 U per 10^6 cells in 48 hours.

187. As described above, prior to October 1983, mammalian cell lines such as COS cells and CHO cells had been widely used for recombinant expression. Conditions for culturing such cells were well described and routine. Also, as described above, it would have been obvious to express a human glycoprotein, including human EPO by expressing it in mammalian host cells such as COS cells or CHO cells. As further described above, prior to October 1983, the prior art described numerous examples of using amplification to achieve high level transient and stable expression of human glycoproteins in host cells such as COS cells or CHO cells, and expression vectors for use in such methods. For example, the Goeddel ‘075 patent describes use of amplification to generate recombinant host cells capable of expressing tPA in amounts of 28 to 98 μg per 10^6 cells/48 hours. (‘075 patent at col. 27, table 3).

188. Based on my review, the ‘349 patent does not define the standard against which the radioimmunoassay units recited in the ‘349 patent claims are to be defined, therefore leaving this term indefinite. The first mention of units however refers to erythropoietin with a specific activity of 70,400 units/mg of protein. ‘349 patent, col. 7. Assuming production of

erythropoietin with this specific activity, it would have been obvious to use known expression vectors and amplification methods to generate recombinant host cells capable of expressing in culture erythropoietin in the range of 100-1000 units (approximately 1.4 to 14 μg) per 10^6 cells/48 hours, as recited by '349 patent claim 7. (If one assumes a higher specific activity, the required level of protein expression would be correspondingly less). In particular, it would therefore have been obvious to one of skill to use a mammalian host cell as recited by '008 claim 25, or specifically the CHO host cell recited by '008 patent claim 27, transformed with an appropriate expression vector to allow one to generate a host cell capable of expressing human EPO at levels recited by '349 claim 7.

189. Similarly, in my opinion there is no patentable distinction between claim 2 of the '008 patent to a DNA sequence "consisting essentially of a DNA sequence encoding human erythropoietin, and the process recited by '349 patent claim 7 for producing a human erythropoietin. Having a DNA sequence encoding human erythropoietin, as discussed above, it would have been obvious to one of skill to choose a mammalian host cell such as a CHO cell to express the human EPO protein encoded by such a DNA sequence, to use known expression vectors and amplification techniques to generate cells capable expressing human EPO at levels recited by the '349 claim 7, and to culture such cells under suitable nutrient conditions in order to produce human EPO as recited by '349 patent claim 7. Moreover, for the same reasons, there is no patentable distinction between claims 4 or 6 of the '008 patent to recombinant host cells, in particular host cells transformed with the DNA sequence encoding human erythropoietin of '008 claim 2 and the claimed process as recited by '349 patent claim 7.

face of these documents. For the purpose of brevity, in this report I may not repeat or discuss the dates on the face of each article, patent, and document cited to herein.

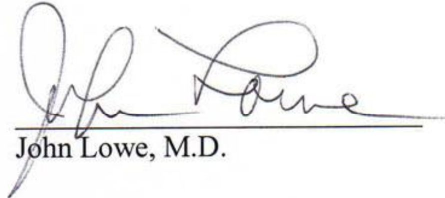
246. I reserve the right to rely upon other materials generated in the further discovery proceedings or presented at trial. In connection with my testimony, I may also use certain graphic and/or demonstrative materials to illustrate my testimony at trial, including those materials listed at Exhibit C, and perhaps other demonstratives and graphics that have not yet been prepared and those based on documents identified in this report. I assume copies of these exhibits will be provided to Amgen as required. I reserve the right to rely upon testimony or other materials generated in further discovery proceedings or presented at trial.

247. In the last four years I have not testified at any trial, deposition or court proceeding.

248. My fee for consulting with Roche's attorneys during this case is $475 per hour. I have not testified at trial or by deposition during the last four years.

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

Dated: April 6, 2007



John Lowe, M.D.

CERTIFICATE OF SERVICE

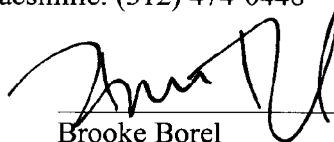
I hereby certify that a copy of this document was served upon the attorneys of record for the plaintiff (as listed below) by email and overnight mail on the below date.

Lloyd R. Day, Jr. (*pro hac vice*)
David A. Madrid (*pro hac vice*)
Linda A. Sasaki-Baxley (*pro hac vice*)
DAY CASEBEER MADRID &
BATCHELDER LLP
20300 Stevens Creek Boulevard, Suite 400
Cupertino, CA 95014
Telephone: (408) 873-0110
Facsimile: (408) 873-0220

D. Dennis Allegretti (BBO#545511)
Michael R. Gottfried (BBO#542156)
Patricia R. Rich (BBO# 640578)
DUANE MORRIS LLP
470 Atlantic Avenue, Suite 500
Boston, MA 02210
Telephone: (617) 289-9200
Facsimile: (617) 289-9201

William G. Gaede III (*pro hac vice*)
McDERMOTT WILL & EMERY
3150 Porter Drive
Palo Alto, CA 94304
Telephone: (650) 813-5000
Facsimile: (650) 813-5100

Kevin M. Flowers (*pro hac vice*)
Thomas I. Ross (*pro hac vice*)
MARSHALL, GERSTEIN & BORUN
LLP
233 South Wacker Drive
6300 Sears Tower
Chicago IL 60606
Telephone: (312) 474-6300
Facsimile: (312) 474-0448



Brooke Borel
April 6, 2007