

EXHIBIT G

**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

**CONTAINS CONFIDENTIAL
INFORMATION SUBJECT TO
PROTECTIVE ORDER**

REDACTED

SECOND SUPPLEMENTAL EXPERT REPORT OF DR. THOMAS KADESCH

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I, Dr. Thomas Kadesch, hereby declare the following:

1. I have been retained by F. Hoffmann-La Roche, Ltd, Roche Diagnostics GmbH and Hoffmann-La Roche, Inc. (collectively “Roche”) to provide my further opinions regarding the validity of certain of the asserted claims of U.S. Patent Nos. 5,756,349 (the “349 patent”), U.S. Patent No. 5,618,698 (the “698 patent”), U.S. Patent 5,547,933 (the “933 patent”), U.S. Patent 5,621,080 (the “080 patent”), U.S. Patent 5,441,868 (the “868 patent”), and U.S. Patent 5,955,422 (the “422 patent”). I will refer to these patents as the “patents-in-suit” or “the Lin patents”. I herein incorporate by reference my two prior expert reports, dated April 6, 2007 and May 1, 2007.

I. MATERIALS REVIEWED

2. In forming my opinions and preparing this report, I have reviewed and relied upon the materials cited and listed in Exhibit A, attached to this report, as well as on my many years of experience in the field of molecular biology. This work is reflected in my curriculum vitae.

II. SUMMARY OF OPINIONS

A. Claims of the ‘349 and ‘698 Patents Are Indefinite And/Or Lack Written Description

3. I have reviewed the Supplemental Expert Report of Harvey F. Lodish, Ph.D., dated June 4, 2007, and specifically those sections that purport to rebut my opinions set forth in my prior reports. Nothing in Dr. Lodish’s supplemental report has changed my opinion that the patents do not adequately describe the following claim terms:

- “non-human DNA sequences which control transcription” (‘349 Patent, claim 1);

19. Finally, Dr. Lodish states that the claims of the '349 patent are not indefinite based on the terms "capable upon growth culture" or "upon growth in culture [that] are capable of producing." (Lodish Supp. at ¶48). However, his conclusions of definiteness are based on completely reading out the claim term "capable." He states that:

If someone produces EPO by performing the step of "culturing under suitable nutrient conditions," genetically engineered cells that satisfy at least one of Claim 1-6 in a manner that produces at least 100 Units of EPO in the medium of their growth per 10^6 cells in 48 hours as measured by radioimmunoassay, they have literally infringed Claim 7. If someone produces EPO by culturing cells under suitable nutrient conditions that do not produce at least 100 Units or less of EPO, they do not literally infringe.

(Lodish Supp. at ¶50). As I pointed out in my Supplement Report, there is no way for persons of skill in the art to determine whether they infringed this claim because these claims do not require an actual production level. The claims only require that the cells be "capable" of making a certain amount. This is compounded by the fact that the claim does not specify what nutrient conditions be used to grow the cell. Thus, someone could produce 75 Units of erythropoietin under one set of conditions, but would not know whether this infringed the '349 patent claims, because under different nutrient conditions, these same cells could be capable of producing 100 Units. (This would apply particularly to promoters whose expression can be induced by specific culture conditions.) As a result, I maintain my opinion that these claims are indefinite.³

³ In response to Dr. Lodish's June 4th Report, I will clarify the opinion I gave in my prior report. Roche's counsel asked me to consider whether or not the EPO production level requirement of Claim 7 of the '349 patent was achievable using methodology that was known in the prior art. This production level is unclear and indefinite. However, the additional limitation of a minimum production level is not linked to anything that was not
(continued...)

VI. INVALIDITY DUE TO INDEFINITENESS OF “U OF ERYTHROPOIETIN...AS DETERMINED BY RADIOIMMUNOASSAY.”

20. As someone of skill in the art who practiced enzymology and biochemistry in 1983, the phrase “U of erythropoietin...as determined by radioimmunoassay,” as recited in the claims of the ‘349 patent, would have confounded me for the reasons set forth in my prior reports. In trying to make sense of these terms, I would have consulted the patent. However, rather than clarify the scope of the claims, the patent specification only confirms that these claims are indefinite.

21. I first note that the patent defines erythropoietin as an acidic glycoprotein of approximately 34,000 daltons (‘349 patent, col. 5, ln. 47), and that the invention describes a protein having one or more of the biological properties of naturally-occurring erythropoietin (‘349 patent, col. 10, ln. 8-15).

22. However, it becomes very clear that the patent acknowledges the inherent limitations that prevent an RIA from actually measuring whether a particular sample actually contains biologically active erythropoietin. For example, the “Background” section of the patent states quite clearly that:

In co-owned, co-pending U.S. patent application Ser. No. 463,724, filed Feb. 4, 1983, by J. Egrie, published Aug. 22, 1984 as European Patent Application No. 0 116 446, there is described a mouse-mouse hybridoma cell line (A.T.C.C. No. HB8209) which produces a highly specific monoclonal, anti-erythropoietin antibody which is also specifically immunoreactive with a polypeptide comprising the following

already well known in the art. For example, the use of methotrexate to amplify and increase expression had already been reported before 1983. *See e.g.*, Ringold et al., *Co-expression and amplification of dihydrofolate reductase cDNA and the Escherichia coli XGPRT gene in Chinese hamster ovary cells*, J Mol Appl Genet. 1981;1(3):165-75.

influenza haemagglutinin genes that code for intracellular and secreted from of the protein,” Nature 300: 598-603, December 1982; see also Shen *et al.* 1982; Devos *et al.*, 1982; Bock *et al.* 1982; Mantei *et al.* 1980; P.Hobart *et al.* 1980; Walter *et al.*, 1981; Drickamer 1981).

66. For these reasons, it is my opinion that as of 1983, one could have determined the amino acid sequence of EPO, synthesized DNA encoding EPO, attached DNA encoding a signal peptide, and transfected the DNA into mammalian cells and thereby produce glycosylated and secreted EPO.

June 13, 2007

A handwritten signature in black ink, consisting of a large, stylized initial 'T' followed by 'Kadesch' in a cursive script. The signature is positioned above a horizontal line.

Thomas Kadesch, Ph.D.