Exhibit 6

Declaration of Krista M. Rycroft in Support of Roche's Motion for Summary Judgment that Claim 1 of the '422 Patent Is Invalid Under 35 U.S.C. § 112

UNITED STATES DISTRICT COURT

DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, vs. HOECHST MARION ROUSSEL, INC. and TRANSKARYOTIC THERAPIES, INC., Defendants.	)	Civil Action No. 97-10814-WGY

EXPERT STATEMENT OF HARVEY F. LODISH, Ph.D.

CONFIDENTIAL

directly from the cells rather than from the cell culture medium, it would be apparent to someone experienced in the field of molecular biology that further purification would be required to improve the therapeutic utility of the final EPO product by removing incompletely or improperly processed EPO products. Thus, the claim construed even in this manner embraces subject matter that is substantially similar to Defendants' HMR4396 EPO product.

122. I understand that Defendants contend that, because their HMR4396 EPO product does not contain human serum albumin ("HSA"), whereas Amgen's EPOGEN® product does contain HSA, HMR4396 possesses some advantage over EPOGEN®. First, I am not aware of any advantage of excluding HSA from a pharmaceutical EPO composition. Furthermore, from my reading of the '422 patent and its claims, it is my understanding that the inclusion or exclusion of HSA is not encompassed by the claims, and thus is not relevant to whether this claim of the '422 patent encompasses Defendants' HMR4396 EPO product.

THE '080 PATENT

Claim 2

123. I understand Claim 2 of the '080 patent to recite:

> 2. An isolated erythropoietin glycoprotein having the in vivo biological activity of causing bone marrow cells to increase production of reticulocytes and red blood cells, wherein said erythropoietin glycoprotein comprises the mature erythropoietin amino acid sequence of FIG. 6 and is not isolated from human urine.

A. "the mature amino acid sequence of FIG. 6"

124. I understand this reference to "the mature erythropoietin amino acid sequence of FIG. 6" to mean the amino acids numbered 1-165 as set forth in Figure 6 of

Amgen's Patents. Although it was not known at the time the applications for Amgen's Patents were filed, it is now well-understood scientifically that mature human EPO has that 165-amino-acid sequence. This is the final form of human EPO that is produced by recombinant human cells, CHO cells and other mammalian cells. It is also the final form of human EPO found in human urine. *See* Recny *et al.*, "Structural Characterization of Natural Human Urinary and Recombinant DNA-derived Erythropoietin," *J. Biol. Chem.* 262:17156-17163 (1987), attached hereto as Exhibit J. As described in Amgen's Patents, the amino acids shown in Figure 6 were deduced from the EPO DNA that was cloned and sequenced by Dr. Lin. Amgen's Patents correctly identify the 27-amino-acid signal peptide (or "leader sequence"), and confirm its cleavage from the translated polypeptide. *See, e.g.,* 21:6-7 and 27:60-67. I understand that the "deduced" amino acid residue at position 166, while based on the correct DNA sequence for the EPO gene, is cleaved off of the EPO polypeptide during post-translational processing.

125. According to, *e.g.*, IND 19 and IND 2357, Defendants' HMR4396 EPO product has precisely this 165-amino-acid sequence. Thus, there is no question but that Defendants' HMR4396 EPO product meets this limitation.

126. I understand that Defendants contend that the mature EPO polypeptide product specified by this term must have all of the 166 amino acids which Dr. Lin "deduced" as constituting the "mature" protein. *See, e.g.,* 21:3-6. I find no scientific basis for this construction of the term. While correspondence of the N-terminal amino acids of Amgen's EPO product produced by CHO cells to those of

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

Executed on December 20, 1999 in Boston, Massachusetts.

Harvey F. Lodish, Ph.D.

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