UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, v. F. HOFFMANN-LA ROCHE LTD., a Swiss Company, ROCHE DIAGNOSTICS GmbH, a German Company and HOFFMANN-LA ROCHE INC., a New Jersey Corporation, Defendants.	**Exhibit A** C. A. No.: 05-CV-12237-WGY

PUBLIC VERSION

Exhibit 36

to the Declaration of Cullen N. Pendleton in Support of Amgen's Opposition to Roche's Motion for Summary Judgment that Claim 7 of the '349 Patent is Invalid Under 35 § USC 112 and is Not Infringed

Redacted

CONTROL OF MATERIALS

IDENTITY OF THE WORKING CELL BANK (WCB) 29.04.93: PHENOTYPIC ANALYSIS

1. SUMMARY

Phenotypic properties of the Working Cell Bank (WCB) 29.04.93 derived Chinese hamster ovary (CHO) cells were analyzed by testing methotrexate (MTX) resistance. The presence of the dihydrofolate reductase (DHFR) gene, correlated to the MTX resistance, was shown in the end-of-production cells (EPC) by their ability to grow in the presence of MTX.

For this purpose CHO cells were harvested [redacted] as EPC from a 10 L-laboratory scale fermentation. During this 10 L-laboratory scale fermentation the CHO cells were cultivated in the absence of MTX which reflects the full scale fermentation process. The EPC were grown [redacted] in spinner flasks without MTX. Then the EPC were split into cultures without and with [redacted] MTX in the medium. The EPC were then cultivated for additional [redacted] cycles to evaluate MTX resistance.

Without MTX the specific Epoetin beta (EPO) productivity amounted to about 3.4 µg EPO/10^6 cells/day [redacted]. During further cultivation without MTX the specific productivity decreased to about 50 % of the initial specific EPO productivity. Thus, in the extended cultivation [redacted], a specific productivity of about 2 µg EPO/ 10^6 cells/ day was found. However in the presence of MTX the specific productivity remained at a constant level of about 3.7 µg EPO/10^6 cells/day.

In respect to growth expressed as doubling times the WCB 29.04.93 derived CHO cells showed the same behavior as the CHO cells used for the serum containing EPO production process.

Regarding specific productivity the WCB 29.04.93 derived CHO cells showed in the absence of MTX the same reduction [redacted] of the original specific EPO productivity as the CHO cells used for the serum containing EPO production process.

2. OBJECTIVE

The medium for the cultivation of the CHO cells contains no nucleosides. For the biosynthesis of nucleosides the CHO cells have to synthesize appropriate amounts of the enzyme dihydrofolate reductase (DHFR) for cell growth. MTX inhibits the DHFR. Thus, only if the gene coding for DHFR is available in adequate copy numbers the cells can grow in the presence of MTX.

The objective of the phenotypic analysis was to prove MTX resistance of WCB 29.04.93 derived CHO cells in extended serum-free culture.