

Exhibit 38

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

NOTICE OF
CLAIMED INVESTIGATIONAL EXEMPTION
FOR A NEW DRUG

ERYTHROPOIETIN (EPOCH)

CHUGAI PHARMACEUTICAL CO., LTD.

VOLUME 1.3

Plaintiff's Exhibit 19

CONFIDENTIAL SUBJECT TO
PROTECTIVE ORDER C.A. NO. 87-
2617-Y (D.C.MA.) C.A. NO. 87-
07200 TJH(DC.CA)CHUGAI 639

PLAINTIFF'S
EXHIBIT
19

A 119740

Chugai Pharmaceutical Co., Ltd.
1-9, Kyobashi 2-chome
Chuo-Ku, Tokyo 104, Japan

Section 4.2.6.8 Biological Tests for Identity and Potency

An in vivo test employing polycythemic mice was used to identify and determine the potency of recombinant human erythropoietin (EPOCH) in direct comparison with the Second International Reference Preparation of naturally occurring, human, urinary erythropoietin (Annable A., Cotes P.M. and Mussett M.V., The second international reference preparation of erythropoietin, human, urinary, for bioassay. Bull. Org. mond. Sante-Bull. W.H.O., 1972, 47, 99-112). This test established a preparation (R-ST, an abbreviation of recombinant erythropoietin standard) derived from one of EPOCH lots (R6F02) as a secondary reference standard. The data recorded in Table 4.2.6.8-1 for other EPOCH lots are based on the use of R-ST. The in vivo polycythemic mouse bioassay method used is described in Section 4.2.7. The value of this in vivo potency was expressed in International Units (IU) per mg EPOCH polypeptide, the latter having been determined on the basis of Glx content (19 residues per one molecule of EPOCH) by amino acid composition analysis (see Section 4.2.7).

Since no statistically significant lot-to-lot difference was found in potency, the weighted mean log-potency (\bar{M}) was computed on the basis of available values obtained from individual assays on 5 lots of bulk EPOCH (R6F02, R6G01, R6J03, R6K01 and R6K02) according to Equations (41) and (42), p1177, USP XXI, and translated by taking its anti-logarithm into the mean potency (\bar{P}) expressed in IU/mg EPOCH polypeptide. The mean potency value resulting from this computation was 180×10^3 IU/mg EPOCH polypeptide. It was decided to use this value as conversion constant to convert the weight of EPOCH polypeptide in μg or mg to the potency value in IU for all bulk EPOCH lots. This conversion constant is used throughout this submission. At the time of this decision the values for R6E02 were not available and were not included in the computation.

CONFIDENTIAL SUBJECT TO
PROTECTIVE ORDER C.A. NO. 87-
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