

**UNITED STATES DISTRICT COURT  
DISTRICT OF MASSACHUSETTS**

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 AMGEN INC., :  
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 Plaintiff, :  
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 v. :  
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 F. HOFFMANN-LA ROCHE LTD, a Swiss : Civil Action No.: 05-12237 WGY  
 Company, ROCHE DIAGNOSTICS GmbH, a :  
 German Company and HOFFMANN-LA ROCHE :  
 INC., a New Jersey Corporation, :  
 Defendants. :  
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**DEFENDANTS’ SUPPLEMENTAL RESPONSES AND OBJECTIONS TO PLAINTIFF  
AMGEN INC.’S THIRD SET OF INTERROGATORIES TO DEFENDANTS (NO. 26)**

Defendants and Counterclaim-plaintiffs F. Hoffmann-La Roche Ltd., Roche Diagnostics GmbH, and Hoffmann-La Roche Inc. (collectively “Roche”) hereby object and respond to Plaintiff and Counterclaim-defendant Amgen Inc.’s (“Amgen”) Third Set of Interrogatories (No. 26).

**GENERAL OBJECTIONS**

The following general objections apply to all of Roche’s responses and shall be incorporated in each response as if fully set forth therein (“General Objections”). To the extent specific General Objections are cited in response to a specific interrogatory, those specific General Objections are provided because they are believed to be particularly applicable to the specific interrogatory and are not to be construed as waiver of any other General Objections applicable to the interrogatory.

acknowledged that its process and resulting *in vivo* biologically active erythropoietin was merely an obvious and inherent result of expressing the DNA sequence encoding human erythropoietin in a host cell: “the particular type of glycosylation linkages was simply a result of the type of host cell used to produce the recombinant erythropoietin.” (EP 411 678 Opposition Proceedings, Statement of Grounds submitted by Amgen 10/8/1992).\*

Amgen’s consistent pattern of failing to apprise the United States examiners of material information from European proceedings is similarly shown through its failure to disclose arguments that were raised during the opposition proceedings to its Kirin-Amgen European Patent Application No. 0 148 605 regarding the high materiality of errors in the data corresponding to Example 10 of its US patent application. (European Tech. Board of Appeals 11/21/1994 (“[A]s admitted by the Respondents, the carbohydrate analysis performed in Example 10 was erroneous.”); *see also* 9/6/2000 Borun Trial Tr. 2854:9-25 (incorrect hexose/fucose values in U.S. Patents)).

Amgen also asserted that it was inappropriate for the examiner to consider prior art (the Yokota 4,695,542 patent) in conjunction with the claims of the ’008 patent to show that the pending claims were obvious arguing that “as noted in the decisional authorities, [double patenting] must be determined through consideration of the *claims* of the pending application and issued patent -- and not with reference to the prior art.” (AM-

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\* In addition, Amgen also failed to disclose inconsistent arguments made during the following proceedings in Europe: (1) Ortho Pharmaceutical Corp. v. Boehringer Mannheim GmbH (Landgericht Dusseldorf (4 O 150/91)) (Patent infringement action for E 0 148 605), (2) Boehringer Mannheim GmbH v. Janssen-Cilag GmbH (4 O 229/91, Landgericht Dusseldorf) (Cilag I), EP 0 205 564 (3) Boehringer Mannheim GmbH v. Janssen-Cilag GmbH (4 O 58/92, Landgericht Dusseldorf) (Cilag II), EP 0 411 678; (4) Boehringer Mannheim GmbH v Kirin-Amgen, (3 Ni 32/93, Bundespatentgericht (BPG)) and appeals therefrom and (5) Kirin-Amgen and Ortho Pharmaceuticals v. Boehringer Mannheim GmbH and Boehringer Mannheim UK Ltd., The High Court Of Justice Chancery Division, Patents Court (CH 1993-K-No. 937).

demonstration that all of the carbohydrate structures in r-HuEPO are also found in u-EPO.”); AM-ITC 00092884; AM-ITC 00092981-83). Nor did Amgen explain to the examiner(s) that purported differences in glycosylation and carbohydrate composition were not due to differences between CHO rEPO and urinary EPO, but because of different purification techniques in certain instances and variability and error in testing techniques. These documents and information were not submitted to the examiners.

Furthermore, after Amgen learned of the error in its reporting of the carbohydrate analysis of CHO rEPO and urinary EPO in example 10 (‘933 patent 28:51-67), it did not make that error known to the various examiners or the public by disclosing the mistake in any response or amendment in the file history. But for Amgen’s misconduct conduct at least claims 1, 2 and 6 of the ‘933 patent and claim 1 of the ‘080 patent would not have issued. Accordingly, the ‘933 patent and the related ‘080 patents are unenforceable for inequitable conduct.

#### **Amgen’s Affirmative Misrepresentations and Omissions Regarding Molecular Weight**

In addition to the information outlined above regarding COS rEPO and CHO rEPO (hereby incorporated), in 1995 Mr. Borun presented for the first time a claim requiring that “said product has a higher molecular weight than human urinary EPO as measured by SDS-PAGE.” (AM-ITC 00941545), and the claim was allowed without a rejection or any amendment. (‘933 patent). Relevant literature, as well as Lin’s specification, acknowledged that human urinary erythropoietin is a glycoprotein with a molecular weight of approximately 34,000 daltons (*e.g.* ‘933, col. 5:48-52 (“Erythropoietin, an acidic glycoprotein of approximately 34,000 dalton molecular weight, may occur in three forms:  $\alpha$ ,  $\beta$  and asialo. The  $\alpha$  and  $\beta$  forms differ slightly in carbohydrate components, but have the same potency, biological activity and molecular weight.”); AM-ITC 00987639-49 (“The human asialo hormone has an apparent molecular

*et al.*, “Inducible Production of Erythropoietin by a Human Yolk Sac Tumor Cell Line”, *Am. Fed. Clin. Res.* 31:307A (1983) (“We have identified a human yolk sac tumor-derived cell line (1411H) which can be induced to produce significant amounts of Ep.”); Ascensao *et al.*, “Erythropoietin Production by a Human Testicular Germ Cell Line”, *Blood* 62(5):1132-34 (1983) (“We have identified a human testis germ cell line 1411-H, that produces significant amounts of Ep. The erythropoietic activity was demonstrated by the ability of cell-free supernatants to stimulate erythropoiesis in exhypoxic polycythemic mice.”)).

Amgen’s inequitable conduct in securing the ‘008 claims infects all the patents-in-suit, rendering each unenforceable.

No individual affiliated with Roche, other than counsel, furnished information or is “most knowledgeable regarding the subject matter of this Interrogatory.”

Roche expressly reserves the right to amend and/or supplement its interrogatory response as fact discovery and expert discovery progresses (including the availability of finalized deposition transcripts with errata).

DATED: April 2, 2007

F. HOFFMANN-LA ROCHE LTD,  
ROCHE DIAGNOSTICS GMBH, and  
HOFFMANN-LA ROCHE INC.

By its attorneys,

/s/ Thomas F. Fleming

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CERTIFICATE OF SERVICE

I hereby certify that a copy of DEFENDANTS' RESPONSES AND OBJECTIONS TO PLAINTIFF AMGEN INC.'S THIRD SET OF INTERROGATORIES TO DEFENDANTS (NO. 26) was served upon the attorneys of record for the plaintiff (as listed below) by email on the above date.

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