CONTAINS RESTRICTED ACCESS CONFIDENTIAL BLA/IND MATERIAL
PURSUANT TO PROTECTIVE ORDER

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,	:	Civil Action No.: 05-12237 WGY
Defendants.	:	

DEFENDANTS' RESPONSES AND OBJECTIONS TO PLAINTIFF AMGEN INC.'S FIRST SET OF INTERROGATORIES TO DEFENDANTS (NOS. 1-15)

Defendants F. Hoffmann-La Roche Ltd., Roche Diagnostics GmbH, and Hoffmann-La Roche Inc. (collectively "Roche") make the following objections and responses to Plaintiff Amgen Inc.'s ("Amgen") First Set of Interrogatories (Nos. 1-15).

GENERAL OBJECTIONS

The following general objections apply to all of Defendants' responses and shall be incorporated in each response as if fully set forth therein. 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.

Defendants object to each and every interrogatory to the extent it seeks information protected by the attorney-client privilege, the attorney work product doctrine and/or any other applicable privilege. All answers herein shall be subject to this objection, and no provision of information herein may act as a waiver of these objections.

(b) the purpose(s) of each such use; and

(c) each document (excluding only patient-specific information) recording or reflecting any communication, agreement, or understanding between each such individual or entity and Roche or its agents or attorneys regarding such use; and

(d) each person, other than counsel, who furnished information or was consulted regarding your response to this interrogatory including the nature and substance of each such person's knowledge or information; and

(e) the three individuals affiliated with Roche, other than counsel, most knowledgeable regarding the subject matter of this interrogatory, stating the nature and substance of each such person's knowledge or information.

RESPONSE:

See Objections and Response To Interrogatory No. 7 above.

INTERROGATORY NO. 9

Separately, in claim chart form for each claim of Amgen's patents-in-suit that you contend in your Fifth and Sixth Affirmative Defenses or Tenth Counterclaim is invalid, identify:

(a) on a limitation-by-limitation basis, the legal and factual grounds on which you contend that such claim is invalid;

(b) the level of skill of a person having ordinary skill in the art to which the subject matter of the patents-in-suit pertains at the time of the claimed inventions;

(c) all evidence on which you rely in support of each contention, including all documents, testimony, prior knowledge, or public uses tending to support your contention(s), every test, experiment, and/or data upon which you rely in support of each contention that a claim is invalid;

(d) each person, other than counsel, who furnished information or was consulted regarding Roche's response to this interrogatory including the nature and substance of each such person's knowledge or information; and

(e) the three individuals affiliated with Roche, other than counsel, most knowledgeable regarding the subject matter of this interrogatory, stating the nature and substance of each such person's knowledge or information.

RESPONSE:

Defendants object to this interrogatory as unduly vague, ambiguous and overly broad. Moreover, Defendants object to this interrogatory to the extent that it calls for information

protected by the attorney-client privilege or work-product immunity. Defendants also object to this interrogatory because it constitutes multiple interrogatories and should be counted against Amgen as such for purposes of the 40 interrogatory limit imposed by the Court.

Defendants also object to this interrogatory because it is premature and calls for expert testimony. The asserted claims of the patents-in-suit have not been construed and the Court does not expect a *Markman* hearing on these claims until April 2, 2007.

Defendants reserve the right to modify or supplement this response at any time upon receipt of relevant materials from any source during discovery.

Subject to and without waiver of these Specific Objections and General Objections set forth above which are incorporated herein by reference, Defendants respond as follows.

A. Obviousness-Type Double Patenting and Same Invention Double Patenting under Section 101

All of the asserted claims of the patents-in-suit are invalid for obviousness-type double patenting over Amgen's now expired U.S. Patent No. 4,703,008 ("the '008 patent"). The '008 patent claims, among other things, the isolated DNA sequence encoding EPO as well as mammalian host cells transformed with this DNA sequence in a manner allowing these cells to express biologically active and glycosylated EPO protein. The '008 patent and the patents-in-suit all share the same specification and single inventor, and demonstrate that Amgen possessed only a single invention with minor obvious variations: mammalian host cells that can express the EPO protein using recombinant DNA technology to produce reliable quantities of EPO.

Amgen already convinced the Board of Patent Appeals of PTO during interference proceedings with Genetics Institute and Chugai, that once the skilled worker had isolated the EPO gene - as claimed in the '008 patent - there was nothing novel or inventive in the process of expressing that gene in host cells and then isolating the biologically active glycoprotein - as

Roussel, Inc., 457 F.3d 1293, 1303 (Fed. Cir. 2006). For example, the patients participating in the clinical study showed an increase in reticulocyte count, an increase in erythroid cells in the marrow and an increase in red cell mass, all of which are signs that the pharmaceutical composition had therapeutic effects. Accordingly, the EPO disclosed by Goldwasser also had "the in vivo biological activity of causing bone marrow cells to increase production of reticulocytes and red blood cells" as that phrase is properly construed.

Further, the claim limitation "wherein said erythropoietin is purified from mammalian cells grown in culture" is a source or process limitation which the Federal Circuit stated would not confer patentability to the claimed product over human erythropoietin isolated from a different source. *See Amgen Inc. v. Hoechst Marion Roussel*, 314 F.3d 1313, 1354 n.20 (Fed. Cir. 2003). Similarly, any source or process limitations found in the '933 claims or in the '080 claims would not confer patentability to those claimed products over human erythropoietin isolated from a different source.

G. Lack of Written Description and Enablement Under Section 112 – Pegylated Compounds

Amgen has taken the position that the asserted claims of the patents-in-suit cover and claim pegylated compounds, which Amgen contends MIRCERA™ to be. The asserted claims of the patents-in-suit are invalid for lack of written description and enablement because it is undisputed that there is no written description of the techniques for pegylating proteins within the patent specifications. As a result, Amgen has failed to adequately describe its contended full scope of its asserted claims.

H. Lack of Written Description and Enablement Under Section 112 – DNA Claims

To the extent that Amgen contends that the patents-in-suit cover proteins expressed from cDNA, those claims are invalid for failure to provide an adequate written description and lack of enablement. Amgen's claims directed to the production of EPO are only supported by examples to human genomic DNA, rather than screening a human cDNA library.

The German Federal Patent Court (BPG) held in December 2000 that Amgen's European patent disclosure, which is identical to the specification of the patents-in-suit, does not adequately teach cDNA encoding human EPO and required an express disclaimer in the DNA claims in that case stating that they were "excluding [the] cDNA sequence encoding human EPO." *See* BPG Decision, dated December 14, 2000.

I. Lack of Definiteness Under Section 112 – "Glycosylated Erythropoietin"

The asserted claims of the patents-in-suit that contain the terms "glycosylated erythropoietin," "erythropoietin glycoprotein," and similar variants, are invalid under 35 U.S.C. § 112 as indefinite because one skilled in the art is unable to comprehend the bounds of the claim language considering that multiple glycosylation forms can exist from a single host cell when cultured under different conditions.

A particular glycoprotein may occur in forms that differ in the structure of one or more of its carbohydrate units, especially when cultured under differing conditions, including a different glucose concentration, a different ammonium ion concentration, or the addition of hormones. The language "a glycosylated erythropoietin" and its variants are vague and indefinite in light of the microheterogeneity of glycoproteins and therefore Amgen has failed to set out with the requisite degree of precision and particularity the bounds of the invention which it has claimed and has failed to provide the necessary clear warning to others as to what constitutes infringement of the patent.

J. Lack of Definiteness Under Section 112 – "capable upon growth in culture of producing erythropoietin in the medium of their growth in excess of 100 U of erythropoietin per 10^6 cells in 48 hours as determined by radioimmunoassay"

Asserted claim 7 of the '349 patent depends from claims 1-6, each directed to vertebrate cells capable of producing erythropoietin in the medium of their growth. The claims require that claimed cells produce a specified number of "U of erythropoietin," either 100, 500, or 1000, per 100,000 cells in 48 hours. Claims 1-6 further require that "U of erythropoietin" be determined by radioimmunoassay. It is Roche's contention that the phrase as used in the claims is indefinite, cannot be properly defined in view of the patent specification and is otherwise scientifically inaccurate, as radioimmunoassay alone cannot measure erythropoietin units ("U") as required by the claim phrase. The specification does not define "U of erythropoietin" nor does it disclose any method for measuring "U of erythropoietin." Without further guidance that the specification fails to provide, the proper metes and bounds of this limitation cannot be determined. Because claim 7 depends from claims 1-6, each of which contains this limitation, claim 7 itself is indefinite under § 112 for failing to distinctly claim the subject matter in a manner that enables one skilled in the art to understand its true scope.

INTERROGATORY NO. 10

Separately, in claim chart form for each claim of Amgen's patents-in-suit that you contend is invalid under 35 U.S.C. § 102, identify and describe on a limitation-by-limitation basis for each claim:

(a) where, on a limitation-by-limitation basis, you contend each claim limitation is disclosed in the prior art;

(b) how each such limitation is disclosed in the prior art, including specific references to pages, claims, columns and/or line numbers (if applicable) in each document supporting such contention;

(c) all evidence on which you rely in support of each contention, including all documents, testimony, prior knowledge, or public uses tending to support your contention(s), and

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Defendants.	:	

DEFENDANTS' SECOND SUPPLEMENTAL RESPONSES AND OBJECTIONS TO PLAINTIFF AMGEN INC.'S FIRST SET OF INTERROGATORIES TO DEFENDANTS (NOS. 1-15)

Defendants F. Hoffmann-La Roche Ltd., Roche Diagnostics GmbH, and Hoffmann-La Roche Inc. (collectively "Roche") make the following Second Supplemental Objections and Responses to Plaintiff Amgen Inc.'s ("Amgen") First Set of Interrogatories (Nos. 1-15).

GENERAL OBJECTIONS

The following general objections apply to all of Defendants' responses and shall be incorporated in each response as if fully set forth therein. 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.

Defendants object to each and every interrogatory to the extent it seeks information protected by the attorney-client privilege, the attorney work product doctrine and/or any other

See Objections and Response To Interrogatory No. 7 above.

INTERROGATORY NO. 9

Separately, in claim chart form for each claim of Amgen's patents-in-suit that you contend in your Fifth and Sixth Affirmative Defenses or Tenth Counterclaim is invalid, identify:

(a) on a limitation-by-limitation basis, the legal and factual grounds on which you contend that such claim is invalid;

(b) the level of skill of a person having ordinary skill in the art to which the subject matter of the patents-in-suit pertains at the time of the claimed inventions;

(c) all evidence on which you rely in support of each contention, including all documents, testimony, prior knowledge, or public uses tending to support your contention(s), every test, experiment, and/or data upon which you rely in support of each contention that a claim is invalid;

(d) each person, other than counsel, who furnished information or was consulted regarding Roche's response to this interrogatory including the nature and substance of each such person's knowledge or information; and

(e) the three individuals affiliated with Roche, other than counsel, most knowledgeable regarding the subject matter of this interrogatory, stating the nature and substance of each such person's knowledge or information.

RESPONSE:

Defendants object to this interrogatory as unduly vague, ambiguous and overly broad. Moreover, Defendants object to this interrogatory to the extent that it calls for information protected by the attorney-client privilege or work-product immunity. Defendants also object to this interrogatory because it constitutes multiple interrogatories and should be counted against Amgen as such for purposes of the 40 interrogatory limit imposed by the Court.

Defendants also object to this interrogatory because it is premature and calls for expert testimony. The asserted claims of the patents-in-suit have not been construed and the Court does not expect a *Markman* hearing on these claims until April 2, 2007.

Defendants reserve the right to modify or supplement this response at any time upon receipt of relevant materials from any source during discovery.

With respect to double patenting, Roche contends that at least claims 1, 2, 4, 5, 6, 7, 8, 23, 24, 25, 26, and 27 of U.S. Patent No. 4,703,008 render the asserted claims of the patents-in-suit invalid as identified above.

SECOND SUPPLEMENTAL RESPONSE

Roche also refers Amgen to the deposition transcript from the Deposition of Eugene Goldwasser held in this action on February 14 and 26, 2007.

INTERROGATORY NO. 10

Separately, in claim chart form for each claim of Amgen's patents-in-suit that you contend is invalid under 35 U.S.C. § 102, identify and describe on a limitation-by-limitation basis for each claim:

(a) where, on a limitation-by-limitation basis, you contend each claim limitation is disclosed in the prior art;

(b) how each such limitation is disclosed in the prior art, including specific references to pages, claims, columns and/or line numbers (if applicable) in each document supporting such contention;

(c) all evidence on which you rely in support of each contention, including all documents, testimony, prior knowledge, or public uses tending to support your contention(s), and every test, experiment, and/or data upon which you rely in support of each contention that a claim is invalid;

(d) each person, other than counsel, who furnished information or was consulted regarding your response to this interrogatory including the nature and substance of each such person's knowledge or information; and

(e) the three individuals affiliated with Roche, other than counsel, most knowledgeable regarding the subject matter of this interrogatory, stating the nature and substance of each such person's knowledge or information.

RESPONSE:

See Objections and Response To Interrogatory No. 9 above.

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DEFENDANTS' THIRD SUPPLEMENTAL RESPONSES AND OBJECTIONS TO PLAINTIFF AMGEN INC.'S FIRST SET OF INTERROGATORIES TO DEFENDANTS (NOS. 1-15)

Defendants F. Hoffmann-La Roche Ltd., Roche Diagnostics GmbH, and Hoffmann-La Roche Inc. (collectively "Roche") make the following further supplemental objections and responses to Plaintiff Amgen Inc.'s ("Amgen") First Set of Interrogatories (Nos. 1-15).

GENERAL OBJECTIONS

The following general objections apply to all of Defendants' responses and shall be incorporated in each response as if fully set forth therein. 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.

Defendants object to each and every interrogatory to the extent it seeks information protected by the attorney-client privilege, the attorney work product doctrine and/or any other applicable privilege. All answers herein shall be subject to this objection, and no provision of information herein may act as a waiver of these objections.