UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC.,	)	
	)	
Plaintiff,	)	
v.	)	Civil Action No.: 05 Civ. 12237 WGY
	)	
F. HOFFMANN-LA ROCHE LTD, ROCHE DIAGNOSTICS GmbH, and HOFFMANN-LA ROCHE INC.,	)	
Defendants.	)	

DEFENDANTS' MEMORANDUM IN SUPPORT OF THEIR MOTION TO COMPEL THE PRODUCTION OF DOCUMENTS

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December 15, 2006

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Defendants F. Hoffmann-La Roche Ltd, Roche Diagnostics GmbH, and Hoffmann-La Roche Inc. (collectively "Roche") respectfully submit this memorandum in support of their motion to compel the production of certain documents from Plaintiff Amgen Inc. ("Amgen"). For the reasons discussed below, Roche's motion to compel should be granted.

I. INTRODUCTION

Amgen has objected to producing numerous clearly relevant documents responsive to Defendants' First Set of Requests for The Production of Documents and Things (Nos. 1-123) ("Roche Requests"). While Amgen has objected to producing a wide host of categories of documents, this motion to compel is limited to two discrete subjects of documents. For the Court's convenience, these subjects, the affected specific Requests for Production, and these subjects' relevance are presented in chart form below.

Document Topic	Relevance	Doc. Requests
Documents relating to and demonstrating Amgen's efforts in developing pegylated compounds, including pegylated GCSF, pegylated MGDF, and pegylated NESP.	MIRCERA™ , the accused drug, is a pegylated compound. Amgen's infringement position is that pegylating a compound is nothing more than a trivial and routine matter which does not change the structure and function of the compound. To the extent that Amgen has developed pegylated compounds showing that this was not the case, this evidence is relevant and necessary to challenge Amgen's infringement theory.	19, 20, 27-35, 58, 59, 70, and 105-112.
Documents relating to and identifying the research and development of Amgen's Aranesp®, including those identifying its structure and biological activity.	Amgen has indicated in prescribing information that Aranesp® may be covered by at least one of the patents-in-suit, but not others. Therefore, comparisons between Aranesp® and MIRCERA™ are relevant not only to claim construction issues, but also those involving noninfringement. Moreover, to the extent there are documents showing that Aranesp® is covered by the asserted claims but not described in the patents, this information is critical to Roche's written description and enablement defenses. Finally, Aranesp® competes directly in the marketplace with Amgen's other EPO product, Epogen®, and eventually, with Roche's MIRCERA™ upon its FDA approval. Therefore, documents in connection with Aranesp®'s market power are relevant to Roche's pending antitrust counterclaims.	20, 24-26, 31, 33-35, 42, 43, 45, 55, 56, 58-74, 78, 86, 87, 105-112, 114, 117, and 118.

Roche discussed Amgen's objections with respect to these topics in a meet and confer on December 11, 2006. During the meet and confer, Roche explained the relevance and need of these documents. While maintaining reluctance, Amgen indicated that it would consider Roche's request. Following the meet and confer, both sides sent letters memorializing its version of the meet and confer. (*See* Letter of Howard Suh to William G. Gaede III, dated Dec. 13, 2006, and attached hereto as Ex. A; *see also* Letter No. 1 of William G. Gaede III to Howard Suh dated Dec. 13, 2006, and attached as Ex. B). However, later that same day, Amgen stated that at least with respect to the two topics at issue above, the parties were at an impasse, thus necessitating the filing of this motion. (*See* Letter No. 2 of William G. Gaede III to Howard Suh, dated December 13, 2006, and attached as Ex. C).

II. AMGEN SHOULD PRODUCE DOCUMENTS RELATED TO ITS OWN PEGYLATED COMPOUNDS AND ATTEMPTS AT PEGYLATION

In Defendants' First Set of Requests for The Production of Documents and Things (Nos. 1-123) (attached hereto as Ex. D), Roche propounded several requests which called for, *inter alia*, production of documents concerning "Pegylated Compounds," which are defined as "any substance, drug or pharmaceutical incorporating into its chemical structure one or more polyethylene glycol polymers." The active pharmaceutical ingredient of MIRCERA™, the accused product in this case, is a molecule that is synthesized using polyethylene glycol polymer (PEG) and EPO as starting materials. Amgen's patents-in-suit claim, *inter alia*, erythropoietin (EPO) molecules. Nowhere in the specifications of the patents-in-suit or the patent claims are any pegylated compounds mentioned. Nonetheless, Amgen claims that MIRCERA™, a pegylated compound, infringes Roche's EPO patents. In Amgen's view, pegylation is simple, well known in the art, and does nothing to alter the starting material in any appreciable way.

Therefore, according to Amgen, although MIRCERA™ comprises a pegylated compound, it infringes Amgen's EPO patents, which do not claim nor even mention any pegylated compounds.

Roche, in agreement with the generally accepted view of those of skill in the art of pegylation, understands that synthesis reactions using PEG molecules and proteins as starting materials creates entirely new compounds, distinct from the starting materials used.[1] The new compound has a fundamentally different structure and function than the starting materials. Even if the starting protein for Roche's MIRCERA™ infringes Amgen's patents, a point Roche disputes, once the synthesis reaction is complete, a new, entirely different compound results that does not meet the limitations of Amgen's patent claims, and does not infringe. This is a fundamental part of Roche's defense of non-infringement. The process of pegylation, the ease with which it is done, and the physical, chemical and biological effects of synthesizing compounds using PEG and protein as starting materials are thus clearly relevant issues in this litigation, and Roche has propounded discovery relevant to these issues.

In Amgen Inc.'s Objections and Responses to Defendants' First Set of Requests for The Production of Documents and Things (Nos. 1-123) ("Amgen's Responses") (attached hereto as Ex. E), Amgen generally objects to Roche's definition of "Pegylated Compounds" to the extent it is "not limited to pegylated substances, drugs or pharmaceuticals that are the subject matter described in the patents which Amgen asserts in this action or encompassed by some other defense or claim in this action." (Ex. E, General Objection ¶ 11). In Amgen's view, pegylated

[1] *See, e.g.*, Graham Molineux, *Pegfilgrastim: Using Pegylation Technology to Improve Neutropenia Support in Cancer Patients*, Anti-Cancer Drugs 2003, 14:259-64 at 259, and Steven G. Elliott, *New Molecules and Formulations of Recombinant Human Erythropoietin*, in Erythropoietins and Erythropoiesis: Molecular, Cellular, Preclinical, and Clinical Biology, G. Molineux, M.A. Foote & S.G. Elliott, eds. (2003) at 252-53, attached hereto as Exs. F and G, respectively.

erythropoietin is relevant to this lawsuit, but Amgen refuses to produce documents relevant to any other pegylated compound, including most significantly, pegylated compounds and attempts at creating pegylated compounds undertaken by Amgen. This completely ignores the fact that pegylation itself, and the effects of synthesis reactions involving PEG are crucial to Roche's defense of non-infringement. On the one hand, Amgen wants to say that even though Roche's accused product is pegylated, it still infringes Amgen's patents, yet it claims that documents detailing Amgen's own attempts, both successful and unsuccessful, to pegylate proteins to create new drugs, which relate to the difficulty of pegylation, and the effects on the structure, composition and properties of a molecule that has been pegylated are not relevant. Amgen has created new drugs by pegylating existing drugs, and has patented and currently markets them as separate and distinct from their non-pegylated counterparts. Documents related to these pegylated drugs, for example, are relevant to the question of whether pegylation creates an entirely new molecule, as Roche contends, or is merely an insignificant change, easily carried out, that does nothing to alter the nature of the starting material. Amgen's product line and marketing contradict Amgen's position on pegylation taken in this lawsuit, and Amgen should have to produce responsive documents related to these other pegylated compounds.

In response to Amgen's objection, and in an attempt to avoid needing the Court's intervention on this issue, Roche agreed in a December 11 conference call with Amgen to narrow its requests calling for documents related to pegylated compounds to documents related to Amgen compounds "PEG-GCSF," "PEG-MGDF," and "PEG-NESP" (pegylated darbepoetin alfa, an analog of human erythropoietin). These are all molecules developed by Amgen, and Amgen's work on characterizations of these molecules are relevant to the issue of pegylation.

GCSF stands for granulocyte colony stimulating factor, and is a product sold by Amgen in the U.S. under the trade name "Neupogen." Amgen developed a pegylated version, PEG-GCSF, for which it holds patents, and which it markets for sale in the U.S. as an entirely different drug under the trade name "Neulasta." These drugs both induce the rapid proliferation and release of certain white blood cells into the bloodstream, which helps the body fight infection. Just as PEG-GCSF is different from GCSF, the active pharmaceutical ingredient of MIRCERA™ differs from the product covered by Amgen's patents: erythropoietin.

MGDF stands for megakaryocyte growth and development factor, and is a product which induces the rapid production and release of platelets into the bloodstream. It is not marketed by Amgen in the U.S., but Amgen tried unsuccessfully to develop a pegylated version (PEG-MGDF) as a therapeutic drug. Clinical trials[2] were halted when patients developed potentially harmful side effects, and formed antibodies to the drug.[3] In surprising contrast to most pegylated proteins, PEG-MGDF remained immunogenic. Amgen's failure to produce a safe and effective pegylated MGDF product, and the work Amgen did on pegylated MGDF is clearly relevant to Amgen's contention that pegylation is easy, simple, and does not significantly alter the nature of the molecule that is reacted with the PEG molecule.

Similarly, Amgen created[4] and evaluated[5] a compound called "PEG-NESP," a pegylated version of Amgen's long-lasting erythropoiesis stimulating agent, Aranesp®.[6] As with PEG-

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[2] *See* Michael Fanucci, et al., *Effects of Polyethylene Glycol-Conjugated Recombinant Human Megakaryocyte Growth and Development Factor on Platelet Counts After Chemotherapy for Lung Cancer*, 336 New Engl. J. Med. 404-09 (1997), attached as Ex. H

[3] *See* AM-ITC 00527339, Amgen Press Release, "Amgen Discontinues Development of MGDF", dated Sep. 11, 1998, and attached as Ex. I.

[4] *See* U.S. Patent No. 6,586,398 (issued Jul. 1, 2003), attached as Ex. J.

[5] *See* 2003 Am. Soc'y of Hematology Annual Meeting, Abstract #4364, attached as Ex. K.

MGDF, Amgen's attempts to develop PEG-NESP into a commercial product have proved unsuccessful. Such efforts are relevant to the nature of pegylation, the difficulty in doing it successfully, and the effect pegylation has in creating a new molecule different from the starting protein – all issues relevant to Amgen's infringement claims and Roche's defense of non-infringement. Since Amgen marks its commercial Aranesp® product with some of the patents-in-suit, it strains credulity for Amgen to argue that PEG-NESP is not relevant to the issues in this case.

Documents related to these Amgen drugs are relevant to the issue of pegylation – what it means, how it works, how difficult or easy it is, how it affects proteins, and whether pegylating a drug creates a new molecule or has a negligible effect on proteins. These documents are relevant to Amgen's claim that Roche's pegylated drug in MIRCERA™ infringes Amgen's EPO patents, and Roche's defense of non-infringement, and at minimum Amgen should be required to produce documents related to PEG-GCSF, PEG-MGDF, and PEG-NESP.

Amgen's general objection also affects a number of specific Requests for Production where Amgen has objected to producing documents relevant to its pegylated compounds. These include Requests for Production Nos. 6, 19, 20, 27-35, 58, 59, 70, and 105-112. Following are some representative samples, but the same reasoning applies to all of the Requests affected by this objection. A complete list and recitation of the Requests for Production and Amgen's Responses are contained in Appendix A filed simultaneously. Representative examples:

[6] *See* Joan C. Egrie & Jeffrey K. Browne, *Development and Characterization of Darbepoetin Alfa*, 16 Oncology, Supp. no. 10, 13-22 (Sept. 2002), attached as Ex. L.

REQUEST FOR PRODUCTION NO. 19:

All Documents and Electronic Data Concerning any communications with Lawrence Souza and/or his researchers or assistants, that Concern the subject matter disclosed or claimed in Amgen's EPO Patents, or to the design, development and manufacture of pegylated erythropoietin or pegylated G-CSF.

AMGEN RESPONSE:

In addition to the foregoing General Objections, Amgen makes the following Specific Objections to this request: Amgen objects to the Request to the extent that it seeks production of documents and electronic data concerning "the design, development and manufacture of . . . pegylated G-CSF" on the grounds that it is overly broad, unduly burdensome, and not reasonably calculated to lead to the discovery of admissible evidence.

Subject to and without waiver of these Specific Objections and General Objections set forth above which are incorporated herein by reference, Amgen responds as follows: Amgen will produce relevant, responsive, non-privileged documents regarding erythropoietin.

Amgen thus refuses to produce communications with Lawrence Souza or his research assistants related to pegylated GCSF. Roche believes that Lawrence Souza is an Amgen scientist that has worked extensively on the compounds contained in the request, including pegylated GCSF. These documents are relevant to show the work done by Amgen in pegylating GCSF, the effects of those attempts, the difficulty in developing a pegylated drug, and the differences between pegylated drugs and the starting materials.

REQUEST FOR PRODUCTION NO. 20:

All Documents and Electronic Data Concerning any communications with Joan C. Egrie and/or her researchers or assistants, that Concern the subject matter disclosed or claimed in Amgen's EPO Patents, or to the design development and manufacture of any erythropoiesis stimulating agent other than human erythropoietin, or to the design, development and manufacture of any Pegylated Compound.

AMGEN RESPONSE:

In addition to the foregoing General Objections, Amgen makes the following Specific Objections to this request: Amgen objects to the Request to the extent that it seeks production of documents and electronic data concerning "the design, development and manufacture of any erythropoiesis stimulating agent" or "any Pegylated Compound" other than erythropoietin, on the grounds that it is overly broad, unduly burdensome, and not reasonably calculated to lead to the discovery of admissible evidence.

Subject to and without waiver of these Specific Objections and General Objections set forth above which are incorporated herein by reference, Amgen responds as follows: Amgen has produced and will produce relevant, responsive, non-privileged documents.

Just as with No. 19 above, Roche believes that Joan C. Egrie is an Amgen scientist that has worked extensively on many of Amgen's drugs, including pegylated compounds. To the extent that there are documents responsive to this request which relate to work by Joan C. Egrie and/or her research assistants which concern pegylated GCSF, pegylated MGDF, or pegylated NESP, Amgen should be required to produce these documents.

REQUEST FOR PRODUCTION NO. 32:

All Documents and Electronic Data Concerning the preparation and publication of the following articles, Including all drafts, underlying data and lab notebooks, and all communications referring or relating thereto:[7]

AMGEN RESPONSE

In addition to the foregoing General Objections, Amgen makes the following Specific Objections to this request: To the extent that this Request seeks production of documents unrelated to erythropoietin, Defendants' accused product, the patents-in-suit, or any claim or

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[7] (1) Ankeny, et al., Exp. Neurol. 170, 85 - 100 (2001); (2) Archimbaud, et al., Blood 94, 3694-3701 (1999); (3) Basser, et al.,Blood 89, pp 3118 - 28 (1997); (4) Beveridge, et al., Pharmacotherapy 23, 101S - 109S (2003); (5) Bukowski, et al., Investigational New Drugs 11, pp 211 - 17 (1993); (6) Callahan, et al., Pharm. Res. 18, pp 261 - 266 (2001); (6) Crawford, Seminars in Oncology 30 (Suppl. 13), 24 - 30 (2003); (7) Crawford, Cancer Treatment Rev. 28 (Suppl. A.), 7 - 11 (2002); (7) De Boer, et al., Growth Factors 18, pp 215 - 226 (2000); (8) Fanucchi, et al., N.E.J.M. 336, pp 404 - 409 (1997); (9) Farese, et al., Stem Cells 21, pp 79 - 89 (2003); (10) Green, et al., Annals of Oncology 14, 29 - 35 (2003); (11) Guerra, et al., Pharm. Res. 15, pp 1822 - 1827 (1998); (12) Harker, et al., Blood 95, pp 2514 - 22 (2000); (13) Harker, et al., Blood 89, pp 155 - 165 (1997); (14) Harker, et al., Blood 88, pp 511 - 21 (1996); (15) Jensen-Pippo, et al., Pharm. Res. 13, pp 102 - 107 (1996); (16) Kendrick, et al., Analytical Biochemistry 299, pp 136 - 146 (2001); (17) Kerwin, et al., Protein Science 11, pp 1825 - 1833 (2002); (18) Kerwin, et al., Protein Science 11, pp 1825 - 1833 (2002); (19) Kinstler, et al., Adv. Drug Deliv. Rev. 54, pp 477 - 485 (2002); (20) Kinstler, et al., Pharm. Res. 13, pp 996 - 1002 (1996); (21) Long, et al., Exp. Hematol. 34, pp 697 - 704 (2006); (22) Lord, et al., Cancer Res. 7, 2085 - 90 (2001); (23) Molineux, Anti-Cancer Drugs 14, 259 - 264 (2003); (24) Molineux, Pharmacotherapy 23, 3S - 8S (2003); (25) Molineux, et al., Experimental Hematology 27, pp 1724 - 34 (1999); (26) Molineux, et al., Stem Cells 15, pp 43 - 49 (1997); (27) Molineux, et al., Blood 88, pp 366 - 376 (1996); (28) Molineux, et al., Blood 88, pp 1509 - 1514 (1996); (29) Morstyn, et al., Acta Haematol. 105, 151 - 55 (2001); (30) Nichol et al., J. Clin. Invest. 95, pp 2973 - 2978 (1995); (31) Niven, et al., Pharm. Res. 12, pp 1343 - 1349 (1995); (32) O'Malley et al., Blood 88, pp 3288 - 3298 (1996); (33) Pettit, et al., J. Biol. Chem. 272, 2312 - 2318 (1997); (34) Rajan, et al., Protein Sci. 15, pp 1063 -1075 (2006); (35) Sarkar, et al., Molecular Pharmacology 63, 147 - 158 (2003); (36) Schiffer et al., Blood 95, pp 2530 - 2535 (2000); (37) Ulich, et al., Exp. Hematol. 27, pp 117 - 130 (1999); (38) Ulich et al., Blood 87, pp 5006 - 5015 (1996); (39) Verdijk & Kuter et al., Blood 99, pp 3867 - 3868 (2002); (40) Zimmerman, et al., Can. Res. 49, pp 6521 - 6528 (1989).

defense in this action, it is overly broad, unduly burdensome, and not reasonably calculated to lead to the discovery of admissible evidence.

This is a list of articles authored at least in part by employees of Amgen or its affiliates. These articles relate to work done by Amgen to either produce or characterize molecules relevant to this litigation. In a conference call on December 11, Amgen represented that article no. 23 by Long *et al.* was not written by anyone associated with Amgen or its affiliates. With that representation, Roche withdraws the request for documents related to that article. Roche also agreed to narrow this request to articles authored by individuals associated with Amgen or its affiliated companies or institutions which relate to pegylated GCSF, pegylated MGDF, and PEG-NESP. These are articles nos. 2-4, 7-17, 21-22, 24-34 and 36-40. The documents relating to the publication and publication of these articles, including the scientific work underlying the articles are relevant to the issue of pegylation, and the effects of pegylation.

REQUEST FOR PRODUCTION NO. 33:

All Documents and Electronic Data Concerning the preparation and publication of any articles not listed in Request for Production No. 32 that refer or relate to any ESA, any Pegylated Compounds, pegylation or any related methods, Including all drafts, underlying data and lab notebooks, and all Communications referring or relating thereto.

AMGEN RESPONSE:

In addition to the foregoing General Objections, Amgen makes the following Specific Objections to this request: To the extent that this Request seeks production of documents unrelated to erythropoietin, Defendants' accused product, the patents-in-suit, or any claim or defense in this action, it is overly broad, unduly burdensome, and not reasonably calculated to lead to the discovery of admissible evidence.

This request captures articles not specifically known to Roche which concern the same topics as the articles listed in Request No. 32, and Amgen should be required to produce the requested documents with respect to any articles authored by individuals associated with Amgen concerning pegylated GCSF, pegylated MGDF, and PEG-NESP that are not specifically listed in Request No. 32.

REQUEST FOR PRODUCTION NO. 34:

All Documents and Electronic Data Concerning any ESA, any Pegylated Compounds, pegylation or any related methods maintained by Graham Molineux, Olaf Kinstler and/or Stephen Elliot and/or their researchers or assistants.

AMGEN RESPONSE:

In addition to the foregoing General Objections, Amgen makes the following Specific Objections to this request: To the extent that this Request seeks production of documents and electronic data concerning 'any ESA, any Pegylated Compounds, pegylation or any related methods" not directed to erythropoietin, it is overly broad, unduly burdensome, and not reasonably calculated to lead to the discovery of admissible evidence.

Subject to and without waiver of these Specific Objections and General Objections set forth above which are incorporated herein by reference, Amgen responds as follows: Amgen has produced and will produce relevant, responsive, non-privileged documents regarding erythropoietin. Amgen is willing to negotiate with Defendants regarding narrowing this Request to a reasonable scope of documents relevant to a claim or defense in this action.

This request seeks documents concerning, *inter alia*, documents regarding pegylated compounds and methods maintained by specific Amgen employees. Despite Amgen's claim that it is willing to negotiate with Roche regarding production of documents responsive to this request, on a conference call discussing this issue Amgen rejected Roche's suggestion that, with respect to Amgen's objection on "Pegylated Compounds," Amgen only produce documents maintained by these Amgen employees which relate to pegylated GCSF, pegylated MGDF, and PEG-NESP. For the reasons documents relating to these compounds in general are relevant, as discussed in the section on pegylated compounds, Amgen should be required to produce these documents.

REQUEST FOR PRODUCTION NO. 35:

All Documents and Electronic Data Concerning any ESA, any Pegylated Compounds, pegylation or any related methods currently or previously maintained by the following people[8]:

[8] Thomas Boone, David N. Brems, Robert Briddell, William J. Callahan, Byeong S. Chang, Art Cohen, Randolph B. DePrince, Stephen P. Eisenberg, Gary S. Elliott, Christine E. Farrar, Frederick A. Fletcher, MaryAnn Foote, Nancy E. Gabriel, Sheila Gardner, Colin V. Gegg, V. Goldshteyn, Alan D. Habberfield, James B. Hamburger, Cynthia Hartley, R. Wayne Hendren, Jerry M. Housman, Anna Y. Ip, Kathleen E. Jensen-Pippo, Brent S. Kendrick, Brent Kern, Bruce A. KerwinPatrick Kerzic, Elliot Korach, Andrew A.

(continued...)

AMGEN RESPONSE:

In addition to the foregoing General Objections, Amgen makes the following Specific Objections to this request: To the extent that this Request seeks production of documents and electronic data concerning "any ESA, any Pegylated Compounds, pegylation or any related methods" not directed to erythropoietin, Defendants' accused product, the patents-in-suit, or any claim or defense in this action, it is overly broad, unduly burdensome, and not reasonably calculated to lead to the discovery of admissible evidence.

Subject to and without waiver of these Specific Objections and General Objections set forth above which are incorporated herein by reference, Amgen responds as follows: Amgen has produced and will produce relevant, responsive, non-privileged documents regarding erythropoietin.

This request seeks documents concerning, *inter alia*, documents regarding pegylated compounds and methods maintained by specific Amgen employees. Despite Amgen's claim that it is willing to negotiate with Roche regarding production of documents responsive to this request, on a conference call discussing this issue Amgen rejected Roche's suggestion that, with respect to Amgen's objection on "Pegylated Compounds," Amgen only produce documents maintained by these Amgen employees which relate to pegylated GCSF, pegylated MGDF, and PEG-NESP. For the reasons documents relating to these compounds in general are relevant, as discussed in the section on pegylated compounds, Amgen should be required to produce these documents.

These are representative of the requests concerning pegylated Amgen compounds for which Amgen refuses to produce documents. A complete copy of all of the Requests for Production and Amgen's Response relevant to this issue of pegylated GCSF, pegylated MGDF, and pegylated NESP is provided in Appendix A, filed simultaneously.

Kosky, David Ladd, Scott L. Lauren, Tiansheng Li, B. C. Liang, Pamela Lockbaum, Alexis M .K. Lueras, Patricia McElroy, Eugene S. Medlock, Mary Ann Miller-Messana, Russell T. Migita, George Morstyn, Linda O. Narhi, Ralph W. Niven Amiee G. Paige, Rahul S. Rajan, Lloyd Ralph, J. Renwick, Gisela Schwab, Linda Shaner, Christopher Sloey, Greg Stoney, Weston Sutherland, Lisa D. Trebasky, T. Tressel, Michael Treuheit, Tom Ulich, Tim Walker, K. Lane Whitcomb, J. Wilson, D. Winters, Qiao Yan, Heather Yeghnazar, John D. Young, V. Zani

III. AMGEN SHOULD PRODUCE DOCUMENTS RELATED TO ARANESP

Amgen generally objects to Roche's definition of "Erythropoiesis Stimulating Agent" or "ESA" as "any substance, drug or pharmaceutical composition that is capable of stimulating the production of red blood cells by bone marrow," and to each specific request using those terms to the extent those requests "seek to encompass information concerning substances, drugs or pharmaceutical compositions that are not within the subject matter claimed in the patents which Amgen asserts in this action, the prior art, or Defendants' definition of any market" as overbroad, unduly burdensome, and not reasonably calculated to lead to the discovery of admissible evidence. (Ex. E, General Objection ¶ 10). In particular, Amgen claims this definition "would include an unlimited universe of undefined substances other than erythropoietin or compositions comprising erythropoietin." (*Id.*).

Amgen also specifically objects to the production of any documents concerning the design, development or manufacture of any ESA that is not erythropoietin. (*See id.*, Amgen's Responses and Objections to Roche's First Set of Document Requests Nos. 20, 24-26, 31, 33-35, 45, 55, 56, 58-74, 78, 86, 87, 105-112, 114, 117 and 118). In response to Amgen's objection that the term ESA would include an infinite number of documents, Roche agreed to limit the request to marketed ESAs. Amgen rejected this proposal. (*See* Ex. B, Letter No. 1 of William G. Gaede III to Howard Suh, dated Dec. 13, 2006). The real issue here is that Amgen refuses to produce certain documents related to its second generation ESA, darbepoetin alfa, sold under the tradename Aranesp®. Amgen's Aranesp® product, and in particular the reasons that it has successfully argued that Aranesp® is not covered by the patents-in-suit, are particularly relevant to this case for the reasons discussed below. Accordingly, Amgen should be compelled to produce its Aranesp® documents to Roche without further delay.

Through years of research Roche developed a third generation ESA product: MIRCERA™. As Amgen is aware, Roche contends that the active pharmaceutical ingredient in MIRCERA™ is not covered by the patents-in-suit. Amgen's EPO patents disclose and claim erythropoietin and methods to manufacture erythropoietin. MIRCERA™ comprises a molecule that was never contemplated by the inventor of the patents-in-suit Dr. Lin, and that is neither described nor claimed in those patents. In particular, MIRCERA™ is not and does not contain a "human erythropoietin," "erythropoietin glycoprotein," or "glycosylated erythropoietin polypeptide" as claimed in the patents-in-suit. The Roche document requests that Amgen refuses to comply with seek discovery regarding Roche's defense of non-infringement.

While Amgen was still developing its erythropoietin product, it sold the rights to the lion's share of the erythropoietin market to its licensee Ortho Biotech Products, L.P. ("Ortho"). By the terms of its license with Ortho, Amgen is prevented from selling its erythropoietin product, Epogen®, in the non-dialysis and diagnostic markets. In order to compete in this market, Amgen developed its second generation ESA, Aranesp®. In that regard, Amgen claims that Aranesp® is different from erythropoietin and not covered by its license with Ortho. Not surprisingly, the question of whether Aranesp® is covered by the patents-in-suit and the Ortho/Amgen Product License Agreement was hotly contested by Amgen and Ortho. Apparently, Amgen was successful in showing that Aranesp® was not covered by the patents-in-suit, likely for at least some of the same reasons that Roche contends that MIRCERA™ does not infringe the patents-in-suit. Specifically, Amgen showed that Aranesp® was not erythropoietin. In light of Amgen's position, Amgen's documents related to the research, design, and development of Aranesp®, plus documents related to the dispute between Amgen and Ortho over Aranesp® are highly relevant to Roche's non-infringement defense.

On the other hand, if there are documents that demonstrate that Amgen's Aranesp® is covered by one of more claims of the patents-in-suit, this would be critical to Roche's invalidity defenses. For example, in its prescribing information, Amgen marks Aranesp® with at least one of the patents-in-suit.[9] Therefore, to the extent that Amgen's patent claims cover Aranesp®, those claims may be invalid for lack of enablement or lack of written description because such molecules are not adequately described in the patents.

In addition, Amgen is also proceeding on a theory of infringement under the doctrine of equivalents. Thus, discovery should also reach matters involving the use of pharmaceutical and biological compounds that are similar to erythropoietin. Consequently, the structure, function, and other characteristics of Aranesp® are also relevant to the inquiry of whether ESAs different from erythropoietin, including the active pharmaceutical ingredient in MIRCERA™, are covered by the patents-in-suit under the doctrine of equivalents.

Moreover, Amgen seeks a permanent injunction and perhaps a preliminary injunction in this case. Thus, the nature of the harm to Amgen, if any, if MIRCERA™ is allowed to enter the market is clearly at issue. Information concerning Aranesp® sales, costs and marketing are relevant to the effect MIRCERA™ may have on both Amgen's bottom line and the ESA market as a whole. These types of documents are also relevant to Roche's antitrust counterclaims. Accordingly, Amgen should be ordered to produce documents related to ESAs other than erythropoietin, including responsive documents related to Aranesp® . These include documents related to Aranesp® responsive to Request Nos. 20, 24-26, 31, 33-35, 45, 55, 56, 58-74, 78, 86,

[9] Aranesp®'s labeling information states that "[t]his product, or its use, may be covered by one or more US Patents, including US Patent No. 5,618,698, in addition to others including patents pending. *See* http://www.amgen.com/medpro/aranesp_pi.html

87, 105-112, 114, 117, and 118. These requests and Amgen's responses are presented in their entirety in Appendix A.

It should be noted that Amgen has already produced selected documents in the related ITC action which relate to Aranesp®. This is curious in light of Amgen's current position that documents relating to Aranesp® are not relevant to the claims and defenses in this action. Clearly, Amgen recognizes the relevance of these documents but does not wish to engage in the effort to provide a full and fair production of all such relevant documents. Amgen cannot unilaterally decide to produce only a limited sample of Aranesp® documents and then foreclose all other production of these documents in order to lighten its discovery obligations or to cut off Roche from learning more significant information about Aranesp®.

In the end, Amgen's reason for not producing Aranesp® documents is similar to its reason for withholding documents related to pegylation. In both cases, Amgen's arguments hinges on its false premise that Roche's non-infringement defenses have no merit. Amgen simply wants to cut off Roche's non-infringement defenses before they get started. Roche obviously has a different view, and asks that its be given an opportunity to pursue discovery regarding these defenses which strike at the heart of Amgen's allegations of infringement.

Amgen's refusal to produce documents concerning any ESA other than erythropoietin affects a number of specific requests for production, including Requests for Production Nos. 20, 24-26, 31, 33-35, 45, 55, 56, 58-74, 78, 86, 87, 105-112, 114, 117 and 118. Following are some representative examples, but the same reasoning applies to all of these Requests. A complete list and recitation of the Requests for Production and Amgen's Responses are contained in Appendix A filed simultaneously. Representative examples:

REQUEST FOR PRODUCTION NO. 24

All Documents and Electronic Data Concerning any submissions to or communications with the United States Food and Drug Administration (FDA) by or on behalf of Amgen, with respect to any ESA, Including epoetin alfa, marketed and sold under the brand names Epogen®, Procrit®, Eprex®, and Erypo®, and darbepoetin alfa, marketed and sold under the brand name Aranesp®.

AMGEN RESPONSE:

In addition to the foregoing General Objections, Amgen makes the following Specific Objections to this request: To the extent that this Request seeks production of documents and electronic data concerning "any submissions to or communications with . . . FDA . . . with respect to any ESA" other than "epoetin alfa, marketed and sold under the brand names Epogen®, Procrit®, Eprex®, and Erypo®" it is irrelevant, overly broad, unduly burdensome, and not reasonably calculated to lead to the discovery of admissible evidence. To the extent that this Request also seeks production of "all" documents and electronic data concerning "any submissions to or communications with" the FDA with respect to epoetin alfa, it is overly broad and unduly burdensome. Amgen does not understand how the requested scope of documents is relevant to any claim or defense in this action; but, Amgen is willing to negotiate with Defendants to the extent Defendants believe otherwise in an effort to identify what, if any, subset of documents is relevant to this action…

Subject to and without waiver of these Specific Objections and General Objections set forth above which are incorporated herein by reference, Amgen responds as follows: Amgen has produced and will produce relevant, responsive, non-privileged documents.

This request seeks documents concerning, *inter alia*, Amgen's communications with the FDA regarding Aranesp®. As its objections suggest, Amgen refused during the meet and confer process to produce these types of regulatory documents related to Aranesp®. (*See* Ex. B, Letter No. 1 of William G. Gaede III to Howard Suh, dated Dec. 13, 2006). Amgen's communications with the FDA regarding Aranesp®, including any statement it may have made regarding whether Aranesp® was equivalent to erythropoietin or comparisons of the bioavailability, safety, efficacy and/or other properties of Aranesp® with other ESAs is relevant to the issues of validity in this case including obviousness. This information is also relevant to infringement for the reasons discussed above. Accordingly, Amgen should be required to produce these documents.

REQUEST FOR PRODUCTION NO. 63

All Documents and Electronic Data Concerning the structure or parameters of the markets and submarkets for any ESA products sold in the United States Including Documents or Electronic

Data Concerning actual or potential substitutes for ESAs in the treatment of ESRD or CKD and/or potential customers and patients in such markets or submarkets.

AMGEN RESPONSE:

In addition to the foregoing General Objections, Amgen makes the following Specific Objections to this request: Amgen objects to this request as overly broad and unduly burdensome as this request is not bounded in time and calls for the production of all documents in Amgen's possession.

Subject to and without waiver of these Specific Objections and General Objections set forth above, which are incorporated herein by reference, Amgen responds as follows: Amgen will produce relevant, responsive, non-privileged documents sufficient to show "the structure or parameters of the markets and submarkets" for recombinant human erythropoietin dating back to January 1, 2005.

REQUEST FOR PRODUCTION NO. 64

All Documents and Electronic Data Concerning the entry or potential entry of any ESA products into the markets and/or submarkets for any ESA products, Including Documents or Electronic Data discussing or reflecting costs of or barriers to entry, such as, for example, FDA approval and business relationships with potential or existing customers.

AMGEN RESPONSE:

In addition to the foregoing General Objections, Amgen makes the following Specific Objections to this request: To the extent that this Request seeks production of documents and electronic data concerning information unrelated to activities in the United States, it is overly broad and unduly burdensome and not reasonably calculated to lead to the discovery of admissible evidence. Amgen further objects to this request as being overly broad and unduly burdensome because it is not bounded in time and calls for the production of all documents in Amgen's possession.

Subject to and without waiver of these Specific Objections and General Objections set forth above, which are incorporated herein by reference, Amgen responds as follows: Amgen will produce relevant, responsive, non-privileged documents.

REQUEST FOR PRODUCTION NO. 65

All business plans, marketing plans, sales or market projections, market analyses, market share projections, pricing plans, pricing analyses, sales plans or projections for the sale or license of Aranesp® and/or Epogen® for treatment of patients with ESRD.

AMGEN RESPONSE:

In addition to the foregoing General Objections, Amgen makes the following Specific Objections to this request: To the extent that this Request seeks production of documents and electronic data concerning information unrelated to activities in the United States, it is overly broad and unduly burdensome and not reasonably calculated to lead to the discovery of admissible evidence.

> Subject to and without waiver of these Specific Objections and General Objections set forth above, which are incorporated herein by reference, Amgen responds as follows: Amgen will produce relevant, responsive, non-privileged documents regarding 2007 and thereafter.

Requests Nos. 63-65 seek documents concerning, *inter alia*, markets and submarkets for ESA products. Amgen offers to produce documents sufficient to show what *Amgen* believes to be "the structure and parameters of the markets and submarkets for recombinant human erythropoietin" dating back to January 1, 2005. The limits Amgen tries to place on these requests are overly restrictive for a number of reasons. First, the federal rules do not allow Amgen to pick and choose from among the relevant documents it wants to produce. Amgen should produce all documents concerning the market for recombinant human erythropoietin in its possession. Second, MIRCERA™ is not recombinant human erythropoietin. It makes no sense to limit the scope of discovery to recombinant human erythropoietin when MIRCERA™ will be competing against other ESAs such as Aranesp®. Third, Amgen's time limitation is unreasonable. Important information about the effect MIRCERA™ might have on the market includes historical information about the effect the last new product had on the market. That product —Aranesp®— entered the United States market in 2001. Accordingly, Amgen should produce Aranesp marketing documents from at least as early as January 1, 2000.

These and other related requests are also relevant to Roche's antitrust counterclaims. Amgen does not dispute that it is withholding documents that are both relevant to Roche's counterclaims and responsive to Roche's requests. Instead, Amgen refuses to produce these documents until it receives a ruling on its recently filed motion to dismiss. In other words, Amgen has effectively granted its own motion. This is improper. As Amgen highlights in almost every brief it files with this Court, the discovery schedule in this case is "extremely tight." (*See, e.g.*, Amgen's Memorandum in Support of its Motion to Compel, D.I. #166, at 2). Document production must be completed by February 16, 2007. There is no guarantee that the

parties will get a ruling on Amgen's motion early enough to comply with that deadline if Amgen's motion is denied. Accordingly, Amgen should be compelled to produce all documents in its possession responsive to these requests.

REQUEST FOR PRODUCTION NO. 78

All minutes of and notes from Amgen's board of directors or committee meetings, or any other Amgen meeting Concerning the research, development, and marketing of any ESA designed, developed, produced, manufactured, marketed or licensed by Amgen.

AMGEN RESPONSE:

In addition to the foregoing General Objections, Amgen makes the following Specific Objections to this request: To the extent that this Request seeks production of, "All minutes and notes from . . . or any other Amgen meeting concerning the research, development, and marketing of any ESA designed developed, produced, manufactured, marketed or licensed by Amgen,"," it is overly broad, unduly burdensome, and not reasonably calculated to lead to the discovery of admissible evidence. Amgen further objects to this Request as being overly broad and unduly burdensome because it is not bounded by time. Amgen also objects to this Request on the grounds that it is duplicative of other Requests propounded by the Defendants. See e.g., Requests Nos. 9, 22, 23.

Subject to and without waiver of these Specific Objections and General Objections set forth above which are incorporated herein by reference, Amgen responds as follows: Amgen has produced and will produce relevant, responsive, non-privileged documents regarding erythropoietin.

This request seeks documents concerning, *inter alia*, Amgen's research, development and marketing of ESAs, including but not limited to Aranesp®. Again, Amgen improperly limits the documents it will agree to produce to those that specifically concern the molecule erythropoietin. Amgen's position that the patents-in-suit cover products like MIRCERA™ that are not erythropoietin, but that it will not produce any documents in this action other than those related to erythropoietin is curious, duplicitous and without any logic. As discussed above, Amgen work concerning second generation ESAs such as Aranesp® is particularly relevant to Roche's defenses in this action.

Indeed, even Amgen recognizes that its objections are overly restrictive. During the parties' meet and confer on December 11, Amgen agreed to produce documents concerning

"Amgen's statement regarding whether Aranesp® falls within the scope of the patents-in-suit" and documents sufficient to show the structure, pharmaceutical composition, FDA approved methods of use and manufacture of Aranesp®. These too are not reasonable limits on the scope of discovery in this case. For example, Amgen's proposal excludes documents related to whether Aranesp® is covered by the patents-in-suit that are not "statements" made on behalf of Amgen. Documents concerning the properties, function, safety and effectiveness of Aranesp® are also excluded. These and other types of similar documents are all relevant to the claims and defenses in this action. Accordingly, Amgen should produce all non-privileged documents responsive to this request.

IV. CONCLUSION

For all of the foregoing reasons, Roche respectfully requests that the Court compel Amgen to produce documents related to Aranesp® and Amgen's pegylated compounds in addition to pegylated erythropoietin as set forth in the Proposed Order accompanying this motion.

Dated: December 15, 2006
Boston, Massachusetts

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that this document filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF) and paper copies will be sent to those indicated as non registered participants on the above date.

/s/ Keith E. Toms
Keith E. Toms

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