UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

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

MEMORANDUM IN SUPPORT OF DEFENDANTS' MOTION TO COMPEL THE PRODUCTION OF DOCUMENTS, AND DEPOSITION TESTIMONY UNDER RULE 30(b)(6), RELATING TO PEGYLATION AND ARANESP®

Lee Carl Bromberg (BBO# 058480)
Julia Huston (BBO# 562160)
Keith E. Toms (BBO# 663369)
Nicole A. Rizzo (BBO# 663853)
BROMBERG & SUNSTEIN LLP
125 Summer Street
Boston, MA 02110
Tel. (617) 443-9292

Leora Ben-Ami (*pro hac vice*)
Mark S. Popofsky *(pro hac vice)*
Patricia A. Carson (*pro hac vice*)
Thomas F. Fleming (*pro hac vice*)
Howard S. Suh (*pro hac vice*)
Peter Fratangelo (BBO# 639775)
Vladimir Drozdoff (*pro hac vice*)
David L. Cousineau (*pro hac vice*)
KAYE SCHOLER LLP
425 Park Avenue
New York, New York 10022
Tel. (212) 836-8000

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

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I. INTRODUCTION

Roche respectfully asks the Court to compel Amgen to produce documents regarding its Aranesp® erythropoiesis stimulating agent ("ESA") and the pegylation of Aranesp® and EPO. Amgen should also be compelled to provide a knowledgeable witness pursuant to FRCP 30(b)(6) on pegylation of Aranesp®.

A. Amgen's Contentions Necessitate Discovery into the Pegylation of Aranesp®

Amgen has refused discovery into the pegylation of Aranesp®, yet Amgen has put the pegylation of Aranesp® squarely at issue in this case by contending in its interrogatory responses that its commercial Aranesp® product is covered by one or more claims in its asserted "EPO patents." Amgen also contends that Roche's MIRCERA™ product is covered by one or more claims of its asserted patents. Amgen's contentions that Roche's MIRCERA™ molecule is a type of pegylated EPO — an erroneous characterization because MIRCERA™ is a unique, new molecule created through chemical synthesis — that is covered by claims of the patents-in-suit, and that Aranesp® is covered by the patents-in-suit, entitle Roche to examine Amgen's underlying work and positions with regard to attempts at pegylation of Aranesp® to create what is referred to as "PEG-NESP." Amgen's success or failure with pegylation is germane to the issues of Roche's non-infringement defense in terms of the nature and difficulty of pegylation and its ability to create a new and distinct molecule. This discovery is also relevant to issues of invalidity, including whether Amgen's patents-in-suit enable pegylated molecules.

B. Pegylation of Aranesp® Is Within the Scope of Documents Compelled by the Court's January 3rd Order

Contrary to Amgen's position, this Court's Order of January 3, 2007 does not justify its withholding discovery related to "PEG-NESP." Amgen has placed Aranesp® and its attempted pegylation of Aranesp® at issue after the Court's order by claiming that Aranesp® is covered by

one or more of the of the patents-in-suit. In its Response to Roche's First Set of Interrogatories, which are dated January 9, 2007, Amgen contends that Aranesp® is a type of EPO product, which would place "PEG-NESP" within the scope of discovery ordered on the issue of "Pegylated EPO" in the January 3rd Order. Thus, the Court's January 3rd Order does not excuse Amgen's refusal to provide Roche legitimate discovery into "PEG-NESP" and, in fact, requires such discovery.[1]

C. Amgen Should Provide Its BLA for Aranesp®

In addition, Roche requests that the Court compel Amgen to produce its BLA for Aranesp. Although Amgen has already conceded the relevance of Aranesp® itself, which Amgen contends will be an adequate market substitute for MIRCERA™, Amgen has not produced the BLA for Aranesp®. Amgen attorneys had previously stated that they were planning on producing portions of the Aranesp® BLA, but almost a month later they have failed to do even this.[2] Roche has provided its full BLA for MIRCERA™ in the native format submitted to the FDA. The Court should direct that Amgen immediately do likewise and produce to Roche its BLA for Aranesp®, particularly its full Chemistry, Manufacturing and Controls ("CMC") section which contains crucial information regarding the structure and properties of the product.

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1 This discovery should include the designation of a knowledgeable witness as well as the production of documents relating to the research and development of "PEG-NESP"; documents relating to any comparisons of "PEG-NESP" with Aranesp®, Epogen®, Procrit®, MIRCERA™ and any other ESA's; as well as documents relating to U.S. Patent No. 6,586,398 directed to "PEG-NESP" (See Ex. A) and all patent applications relating to "PEG-NESP" including 08/108,016 and 08/479,892.

2 Teleconference meet and confer of February 27, 2007 with William Gaede, III for Amgen and attorneys for Roche including Thomas Fleming and Manvin Mayell.

D. Amgen Should Provide Complete Production of Documents Relating to Amgen's "PEG-EPO" Work

Finally, the Court should Compel Amgen to produce missing documents relating to "Pegylated EPO" in accordance with the Court's January 3rd Order. Amgen's attorneys have represented to Roche that they have produced "any" documents relating to "Amgen's peg-EPO work." (See Ex. B, Letter of Gaede to Carson, dated March 14, 2007; Ex. C, Letter of Gaede to Fratangelo, dated March 14, 2007). Notably, however, not a single document from the files of Thomas Boone, Amgen's designated 30(b)(6) witness for this topic, have been produced to Roche. Particularly, it has come to Roche's attention that key lab notebooks describing this work have not been produced. These notebooks are essential to Roche's preparation for the deposition of Amgen's 30(b)(6) witness on Amgen's "PEG-EPO" work and Amgen should be compelled to search for and produce them, along with any other documents relating to Amgen's "PEG-EPO" work that Amgen has withheld.

II. AMGEN SHOULD PRODUCE DOCUMENTS AND A KNOWLEDGEABLE WITNESS RELATED TO PEGYLATION AND ATTEMPTED PEGYLATION OF ARANESP®

In light of Amgen's contention that Aranesp® is covered by the patents-in-suit, documents relating to Amgen's attempted pegylation of NESP, the active ingredient in the Aranesp® drug product, have become highly relevant to Roche's counterclaims and defenses of invalidity and non-infringement. Amgen created the compound referred to as "PEG-NESP" in order to make a longer-lasting version of Aranesp® but these efforts ultimately proved unsuccessful. (See Ex. A, U.S. Pat. No. 6,586,398; Ex. D, 2003 Am. Soc'y of Hematology Annual Meeting, Abstract #4364). Even though Amgen now contends that Aranesp® is covered by the patents-in-suit, Amgen has refused to provide any discovery at all regarding pegylation of Aranesp®. Lack of this discovery substantially prejudices Roche's preparation of its case

especially as fact discovery is rapidly waning. Amgen contends that the NESP molecule used to make the commercial Aranesp® product is an "erythropoietin product" within the meaning of Amgen's asserted patents. Thus, the characteristics of any pegylated NESP compounds, and Amgen's successes or failures in pegylating NESP, are legitimate areas of discovery for Roche to test Amgen's allegations of infringement of these patents by MIRCERA™. Specifically, Amgen asserts in this case that pegylation does not create a new molecule distinct from the starting materials. Amgen's own efforts to perform pegylation reactions with an alleged "erythropoietin product" — and particularly its failures at doing so — are at the heart of Amgen's infringement claim, yet Amgen seeks to obstruct Roche from examining these efforts.

Additionally, because Amgen contends that the NESP molecule of Aranesp® is covered by the asserted patents (which all share the same specification), Amgen's ability or inability to use pegylation to create a new molecule using NESP while allegedly in possession of the claimed inventions of the patents-in-suit provides evidence on whether these patents' specifications teach the use of pegylation to create a particular molecule. Thus, "PEG-NESP" is also relevant to the issues of enablement and written description under 35 U.S.C. § 112.

Moreover, Amgen's positions taken in its Markman briefing show that Amgen believes the claims in the patents-in-suit do not exclude the attachment of structures other than gylcosylation. Thus, the reaction of a peg molecule with NESP would, according to Amgen, not render the end product outside the scope of "erythropoietin products" which Amgen contends NESP is. In Amgen's Supplemental Response to Roche's Interrogatory No. 8, Amgen has specifically identified claim 1 of the '698 patent as covering Aranesp®. Claim 1 of the '698 describes "a process for the preparation of an in vivo biologically active ***erythropoietin***

product...." (emphasis added).[3] Amgen has argued in its claim construction briefing that the claims in the patents-in-suit should not be "construed to exclude the attachment of structures other than glycosylation to the *erythropoietin products recited in the claims.*" (emphasis added) (*See* Amgen Inc.'s Response to Defendants' Claim Construction Brief at 2). Thus, it is Amgen's position that pegylation of Aranesp® would not take it outside the scope of the claims. Amgen's "PEG-NESP," therefore, is just as relevant to this case as its Epogen® product which it also contends is covered by claims of the asserted patents and for which Amgen has already provided discovery. By the logic of Amgen's general contentions in this case, there is no reason to read the January 3rd Order regarding "Pegylated EPO" as not including "PEG-NESP". Amgen misreads the January 3rd Order now in order to skirt its obligations to provide full and meaningful discovery.

Amgen has also withheld key witnesses and documents in their possession relating to Aranesp® and Amgen's attempted pegylation of Aranesp®.[4] Topic Five in Roche's Rule 30(b)(6) Notice ("Topic Five") requests that Amgen produce a person or persons with knowledge regarding the pegylation of EPO and ESA compounds.[5] In response, Amgen

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3 It is irrelevant that Amgen has not asserted this particular claim in the present litigation because this discovery remains relevant to Roche's asserted counterclaims of invalidity against all the claims of the asserted patents.

4 Amgen's withholding of documents in this context reflects a larger pattern of stonewalling evident most recently in Amgen's Objections to Roche's First 30(b)(6) Notice. Amgen's refusal to provide witnesses on other topics is the subject of another motion presently before the Court.

5 Topic Five of Roche's First 30(b)(6) Notice states in full "Research, development and evaluation of Pegylated Compounds by Amgen, including attempts by Amgen to modify EPO proteins or any ESA, including attempts successful or otherwise to create Pegylated Compounds using EPO or any ESA such that any chemical, physical, pharmacological and/or pharmacokinetic properties of the chemically modified compound differs from the EPO or ESA, and including attempts by Amgen to chemically modify the EPO protein such that its pharmacological and/or pharmacokinetic profile is different from the active drug product in EPOGEN®, including increased half life and different erythropoiesis activity."

designated Thomas Boone as its 30(b)(6) designee on Topic Five. (*See* Ex. E, Letter of Gaede to Drozdoff, dated March 9, 2007). However, Amgen has not produced a single document from Mr. Boone, even though he is listed as one of the inventors of U.S. Patent No. 6,586,398 directed to pegylated NESP. (*See* Ex. F, Letter of Carson to Fishman, dated March 12, 2007; Ex. G, Letter of Fratangelo to Fishman, dated March 12, 2007). Amgen claims that development of "PEG-NESP" is not relevant to any claim or defense in this case. (*See* Ex. B; Ex. H, Letter of Gaede to Carson, dated March 6, 2007). However, it is Amgen's own contentions that provide the rationale for discovery into "PEG-NESP".

Amgen's interrogatory responses put in issue the very subject matter that it now contends is irrelevant by claiming that Aranesp® is covered by the patents-in-suit. Amgen also claims that MIRCERA™ is covered by one or more claims of the patents-in-suit. Amgen then takes the logically irreconcilable position that although its Aranesp® product and Roche's MIRCERA™ are both alleged to be covered by the patents-in-suit, "PEG-NESP" is nonetheless irrelevant to this case. To the contrary, if Aranesp® is covered by the patents-in-suit as Amgen claims, then Roche is entitled to discovery regarding the characteristics of "PEG-NESP", Amgen's attempts to pegylate NESP, any related patent applications, and any comparisons between any pegylated NESP molecules and MIRCERA™ or other ESA's to examine Amgen's contentions in this case. Similarly, if Aranesp® is covered by claim 1 of the '698 patent as an "erythropoietin product," as Amgen stated in its supplemental interrogatory response, then the pegylation of NESP clearly falls within the January 3 Order that "Pegylated EPO" is discoverable. This is also consistent with the claim construction Amgen now urges upon the Court.

Roche has attempted to resolve this issue with Amgen and repeatedly advised Amgen that its refusal to produce documents relating to legitimate discovery would prejudice Roche.

(*See* Ex. I, Letter of Heckel to Gaede, dated March 19, 2007). Amgen should immediately produce responsive documents on "PEG-NESP" as the deposition of Amgen's designated witness on pegylation, Mr. Boone, listed inventor on Amgen's patent directed to "PEG-NESP," quickly approaches. Amgen should also designate a witness that is familiar with the issues for which this discovery is sought. In its March 14 letter, Amgen attempts to shield Mr. Boone from testifying on these issues by highlighting that he "will not be prepared on, and will not testify on 'other pegylated compounds.'" *See* Ex. B. However, for the same reasons noted above, Amgen has placed attempts at pegylating Aranesp® and the characteristics of the resulting molecules at issue and therefore must designate one or more witnesses that are knowledgeable as to this subject matter.

III. AMGEN SHOULD BE COMPELLED TO PRODUCE ITS ARANESP® BLA

Just as "PEG-NESP" is relevant, the commercial Aranesp® product itself is relevant as well to Amgen's claims of infringement and Roche's counterclaims of invalidity and unenforceability. Further, on the issue of injunctive relief, Amgen has touted its product as an adequate market substitute for MIRCERA™ that is capable of meeting relevant public health and economic needs. To test this claim, Roche must make comparisons between Aranesp® and MIRCERA™ in structure, composition, and mechanism of action. However, Amgen has still not produced its BLA for Aranesp® which describes many of the structural and functional characteristics of the product and the clinical data underlying its indications. Amgen's failure to produce its BLA is indefensible in light of Roche's production of its own voluminous BLA for MIRCERA™ both in TIFF and then native format. Further, Amgen's own attorneys have indicated that they would produce portions of Amgen's BLA several weeks ago and have not

done so.[6] Amgen should have produced this BLA for a product already approved and on the market long ago, as it has had Roche's BLA for the MIRCERA™ product still pending before the FDA for almost ten months now. Thus, Amgen should be compelled to produce its BLA for Aranesp® in a native format like the format in which Roche has produced its BLA.

IV. AMGEN SHOULD BE COMPELLED TO PROVIDE COMPLETE PRODUCTION OF DOCUMENTS RELATING TO ITS WORK ON "PEG-EPO" INCLUDING KEY NOTEBOOKS

Consistent with the Court's January 3 Order, Amgen must provide full discovery relating to Amgen's research and work concerning "PEG-EPO" including production of responsive documents and the designation of a knowledgeable witness. However, Amgen's discovery on this subject matter already appears lacking. A confidential report produced by Amgen refers to Lab Notebooks #1938, #2112 and #1041 as containing information regarding "PEG-EPO". (AM440003873-74).[7] Despite its representations that is has provided complete discovery on "PEG-EPO", Amgen has not produced these notebooks to Roche and should be compelled to search for them and provide them. Moreover, Amgen has designated Mr. Boone as its knowledgeable 30(b)(6) witness yet has produced zero documents from his custodial files and only a few that list him as an author. This lack of production from Mr. Boone undermines Roche's ability to depose a witness with relevant knowledge on the subject matter of "PEG-

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6 Teleconference meet and confer of February 27, 2007 with William Gaede, III for Amgen and attorneys for Roche including Thomas Fleming and Manvin Mayell.

7 Amgen has not produced the three PEG-EPO lab notebooks numbered #1938, #2112, and #1041 that are referenced in Amgen's confidential document No. AM44 0003873. Roche does not feel it is necessary at this time for the Court to review this confidential document in its entirety, as Roche summarizes the information it contains that is relevant to the present motion. If Amgen wishes to contest Roche's characterization of the substance of this confidential document, however, Roche will assent to Amgen's motion to file it under seal for further review by the Court.

EPO". Amgen should provide complete discovery of its work on "PEG-EPO" including all relevant documents from Mr. Boone's files.

V. CONCLUSION

For all the foregoing reasons, the Court should order Amgen: (1) to produce all documents relating to the pegylation and attempted pegylation of Aranesp®; (2) to designate one or more witnesses who are fully prepared to testify regarding the pegylation and attempted pegylation of Aranesp®; (3) to produce its Aranesp® BLA; and (4) to provide complete production of documents relating to its wok on "PEG-EPO".

Dated: March 23, 2007
Boston, Massachusetts

Respectfully submitted,

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

By their Attorneys,

/s/ Keith E. Toms
Lee Carl Bromberg (BBO# 058480)
Julia Huston (BBO# 562160)
Keith E. Toms (BBO# 663369)
Nicole A. Rizzo (BBO# 663853)
BROMBERG & SUNSTEIN LLP
125 Summer Street
Boston, MA 02110
Tel. (617) 443-9292
ktoms@bromsun.com

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Thomas F. Fleming (*pro hac vice*)
Howard S. Suh (*pro hac vice*)
Peter Fratangelo (BBO# 639775)
Vladimir Drozdoff (*pro hac vice*)
David L. Cousineau (*pro hac vice*)
KAYE SCHOLER LLP
425 Park Avenue
New York, New York 10022
Tel. (212) 836-8000

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/s/ Keith E. Toms
Keith E. Toms

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