UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN, INC., Plaintiff, v. F. HOFFMANN-LAROCHE LTD., a Swiss Company, ROCHE DIAGNOSTICS GMBH, a German Company, and HOFFMANN LAROCHE INC., a New Jersey Corporation, Defendants.	)	Civil Action No. 05 CV 12237 WGY

BRIEF IN SUPPORT OF AMGEN'S MOTION *IN LIMINE* NO. 5: EXCLUDE EXPERT TESTIMONY REGARDING AMGEN'S REPLICATION OF ROCHE'S CELL CULTURE MEDIA

I. INTRODUCTION

To prove infringement, Amgen's expert, Dr. Richard Kolodner, performed experiments on Roche's EPO-producing cell line. In his June 13, 2007 Fourth Supplemental Expert Report, Roche's expert, Dr. Richard Flavell, criticized the conditions under which Amgen's expert, Dr. Kolodner, grew the cells that Roche uses to produce the recombinant EPO in its accused product. In his report, Dr. Flavell suggested that Dr. Kolodner's failure to grow the cells in exact cell culture medium that Roche uses to grow its cells in Germany calls into question the radioimmunoassay tests Amgen performed with Roche's cells to establish proof of infringement of '349 claim 7.[1]

Dr. Flavell fails to mention ***why*** Dr. Kolodner did not use Roche's exact culture medium. It is Roche's fault – not Amgen's or Dr. Kolodner's – that Dr. Kolodner could not use the exact medium that Roche says it uses to grow its cells in Germany. First, despite its counsel's repeated assurances that Roche would supply its "special" cell culture medium to Dr. Kolodner, Roche never did so (even to this day, despite continued requests by Amgen).[2] Second, Roche delayed sending its instructions as to how Dr. Kolodner could re-create the culture medium until so late in the expert discovery period that it was not possible for Dr. Kolodner to exactly replicate Roche's medium before submitting his report.[3] Third, because Roche had marked the document containing the recipe for making its cell culture medium as "RESTRICTED ACCESS CONFIDENTIAL BLA/IND - LOCKED ROOM ACCESS ONLY," Dr. Kolodner could not simply send the recipe for Roche's medium to a commercial vendor (or to scientists at Amgen)

[1] Fourth Expert Statement of Richard A. Flavell, Ph.D. at p. 9, ¶ 20.

[2] *See* Exhs. 1 (email exchanges between P. Carson and K. Flowers between April 19, 2007 and May 4, 2007) and 2 (Carson letter to Flowers dated April 19, 2007) to Declaration of Cullen N. Pendleton In Support of Amgen's Motion *In Limine* No. 5 (hereinafter "Pendleton Decl.").

[3] Expert Statement of Richard D. Kolodner, Ph.D. at ¶ 12.

to have the medium custom-formulated. Instead, Dr. Kolodner was forced to supplement a standard, pre-made cell culture medium (called "DMEM/F12") with additional components.[4]

Dr. Kolodner replicated the conditions Roche says it uses as closely as possible, given the time constraints imposed upon him by Roche's delayed production. Dr. Flavell criticized Dr. Kolodner's work in a supplemental expert report submitted a full month-and-a-half after Dr. Kolodner submitted his report describing his work, and 3 weeks after this Court's deadline for Roche to submit its expert reports rebutting Dr. Kolodner's report. Dr. Flavell could not say for certain whether the differences in the culture medium affected the production of EPO by Roche's cells one way or another.[5]

Because Roche's failure to comply with its discovery obligations resulted in Dr. Kolodner's inability to exactly replicate the cell culture medium that Roche says its uses to grow its cells in Germany, Roche should not be permitted to rely upon any difference in the cell culture medium used by Dr. Kolodner and that which Roche says its uses to support its argument of non-infringement. Consequently, any testimony by Roche's expert witnesses regarding any such difference, including but not limited to testimony by Dr. Flavell, as well as cross-examination of any Amgen expert on this issue, should be excluded.

II. ARGUMENT

A. Roche's delay in complying with its discovery obligations resulted in Dr. Kolodner's inability to replicate the exact culture medium used by Roche

Roche's improper delay in producing (i) the cell line it uses to make the recombinant EPO in its accused MIRCERA product; (ii) the instructions for formulating the cell culture

[4] *Id.*

[5] As Dr. Kolodner testified in his deposition, there were only minor differences between the medium he used and that specified by Roche. *See* Transcript of Deposition of Dr. Richard D. Kolodner at 35:25-36:3.

medium Roche says it uses to grow those cells; and (iii) the instructions for growing those cells in that medium is well documented. Amgen requested that Roche provide a viable sample of its DN2-3α3 cell line, along with the instructions for growing those cells, in Amgen's very first set of Requests for Production of Documents and Things, served on October 30, 2006.[6] Roche refused to comply with Amgen's request for months thereafter, requiring Amgen to file a motion to compel production of the cell line on January 10, 2007.[7] This Court granted Amgen's motion on January 23, 2007, ordering Roche to comply with Amgen's request. A month later, with Roche still refusing to comply, Amgen was forced to file a second motion to enforce this Court's order.[8]

Finally, on March 20, 2007, Roche supplied Dr. Kolodner with a sample of its cell line, as well as the cell culture media recipe. By this point, this Court's allotted period for submitting expert reports was drawing to a close. However without the Roche's unique culture medium, Dr. Kolodner was unable to grow the cells under the exact conditions that Roche uses in its manufacturing process. Roche, however, repeatedly promised, between April 19 and April 25, that they would supply Dr. Kolodner with a sample of Roche's culture medium – not directions as to how to grow it, but a sample itself.[9] Roche even went so far as to ask which of its two types of media Dr. Kolodner needed.[10] Despite repeated follow-up emails from Amgen, Roche never

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[6] Docket Nos. 156-12 and 156-13 (Amgen's First Set of Requests for the Production of Documents and Things) at pp. 9-10, Nos. 11-14.

[7] Docket No. 223 (Amgen's Memorandum in Support of Its Motion to Compel Production of Roche's Cell Line and Related Documents).

[8] Docket No. 294 (Amgen Inc.'s Memorandum in Support of Its Motion to Enforce the Court's January 23, 2007 Order Compelling Roche to Produce Its Cell Line and to Extend the Time for Amgen to Submit its Infringement Expert Report Regarding the Testing of Roche's DN2-3α3 Cell Line).

[9] *See* Exhs. 1 (email exchanges between P. Carson and K. Flowers between April 19, 2007 and May 4, 2007) and 2 (Carson letter to Flowers dated April 19, 2007) to Pendleton Decl.

[10] *Id.*

sent the sample – instead, it supplied Dr. Kolodner with instructions for how to grow the medium. As Dr. Kolodner stated in his expert report, although he eventually received the list of components in Roche's recommended medium, it was not feasible to precisely re-create that medium using off-the-shelf components, and Roche refused to supply the medium itself.[11] Therefore, Dr. Kolodner was forced to attempt to re-create the medium as closely as possible by supplementing a standard, commercially available pre-made medium with solid supplementary medium components in a compressed period of time.[12]

Dr. Kolodner's inability to use the exact cell culture medium that Roche says it uses in Germany was caused by three factors: Roche's delay in supplying the instructions for formulating that medium until very late in the expert report period, Roche's designation of the document setting out the recipe for that cell culture medium as "RESTRICTED ACCESS CONFIDENTIAL BLA/IND - LOCKED ROOM ACCESS ONLY," which prevented Dr. Kolodner from having a commercial vendor (or scientists at Amgen) formulate the medium "from scratch," and Roche's refusal to supply Dr. Kolodner with the medium itself. Although Amgen first requested that Roche produce its cells and culture medium in October 2006, and this Court ordered Roche to produce them in January – Roche did not comply with that order until late March 2007, almost five months after the first request was made. Roche therefore should not be permitted to challenge Amgen's test results on that medium on the basis that the cell culture medium that Dr. Kolodner ultimately used to grow Roche's cells was not exactly identical to the medium that Roche says it uses in Germany.

[11] Expert Statement of Richard D. Kolodner, Ph.D., at ¶ 12.

[12] *Id.* at ¶ 13.

B. This Court made it clear that a party would bear the fault for its lack of cooperation in discovery

This Court has made it very clear in several orders that the parties should cooperate in discovery in order to ascertain the truth.[13] Roche's prolonged, unjustified refusal to produce its cell line and culture medium to Amgen fly in the face of these orders. Considering Roche's numerous delays, stall tactics, and refusals to comply with the Court's order to produce these materials, Roche's witnesses should not now be allowed to criticize the cell growth and testing conducted by Amgen's experts Drs. Kolodner and McLawhon.

III. CONCLUSION

Amgen requests an order excluding any testimony by a Roche witness, including but not limited to Dr. Flavell, or any cross-examination of any Amgen witness, regarding any difference between the cell culture medium used by Dr. Kolodner to grow Roche's cells and the cell culture medium that Roche says it uses in Germany, as any such difference resulted from Roche's failure to comply with the Court's orders on Amgen's motions to compel production of Roche's cells.

[13] *See* 5/2/07 Court Order ("Discovery Is Not A Game And Court Orders Are Not To Be Altered. What Is Expected And Required Is A Cooperative Venture To Ascertain The Truth. Should Any Party Have Wrongfully Failed To Make Discovery, The Appropriate Sanction Is A Preclusion Order, The Drawing Of Adverse Inferences, Or Both."), 5/16/07 Court Order ("No Witness May Rely On Evidence Withheld From Discovery"), and 1/22/07 Court Order ("No Party May Introduce In Evidence Any Document Called For In Discovery And Not Produced, Nor Any Data Derived From Such Document.").

Respectfully Submitted,

Date: August 17, 2007

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By its attorneys,

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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 and paper copies will be sent to those indicated as non-registered participants on August 17, 2007.

/s/ Michael R. Gottfried
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