

UNITED STATES DISTRICT COURT  
DISTRICT OF MASSACHUSETTS

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

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**ROCHE’S OPPOSITION TO AMGEN’S MOTION *IN LIMINE* NO. 5 [DN 832]:  
EXCLUDE EXPERT TESTIMONY REGARDING AMGEN’S REPLICATION OF  
ROCHE’S CELL CULTURE MEDIA**

**INTRODUCTION**

The inability of Amgen’s expert to reproduce Roche’s cell culture conditions is the fault of Amgen, not Roche. Roche timely responded to Amgen’s discovery requests regarding its cell lines and the cell culture media needed to grow those cells. In contrast, Amgen failed to exercise even minimal diligence in obtaining the cell culture media. Amgen’s attempt to use its own failure to preclude Roche from defending against infringement does not withstand scrutiny and should be rejected.

Amgen fails to mention that it never made a formal discovery request to Roche for a sample of the cell culture media -- either prior to the end of discovery, or even afterwards. What Amgen did request, namely the *instructions* for culturing the cells and the recipe for the cell culture media, was provided to it in August 2006, over *six months* before Amgen claims its expert’s experiments were hindered by the lack of those media.

During that time Amgen was free to share Roche's culture media recipe with any one of its many experts who had signed the protective order. Those experts could have followed the recipe and faithfully reproduced the cell culture media. Instead, Amgen opted at the eleventh hour to try to obtain the actual media from Roche. Roche's counsel responded to Amgen's last-minute, informal request by attempting to procure the cell culture media from Roche's manufacturing facility in Germany. Due to production cycles, Roche does not keep its cell culture media in stock and when Amgen made its request, Roche had none in stock. The earliest Roche would have had cell culture media available to ship to Amgen was May 2, after Amgen's expert reports were due. Given the last-minute nature of Amgen's request, Roche could not provide the cell culture media to Amgen's expert in sufficient time.

Roche plans to defend this case by questioning the scientific reliability of the infringement experiments that Amgen may use in its case. Roche should not be denied the opportunity to offer such evidence simply because Amgen was negligent in conducting discovery and in conducting the experiments.

### **ARGUMENT**

#### **A. Amgen Did Not Request A Sample Of The Media During Discovery.**

In its recitation of the history of discovery regarding Roche's cell lines, Amgen either glosses or neglects to mention key facts. In its October 2006 document requests, Amgen sought a sample of Roche's DN2-3 $\alpha$ 3 cell line, but notably did *not* request a sample of Roche's cell culture media, requesting only instructions for culturing such cells.<sup>1</sup>

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<sup>1</sup> Amgen's First Request for Production of Documents and Things, Oct. 30, 2006, at 9.

Roche responded to Amgen's demand for instructions by pointing Amgen directly to a section of Roche's BLA (biologics license application) for MIRCERA<sup>®</sup> containing the instructions for reproducing the culture media for its DN2-3α3 line.<sup>2</sup> In fact, the portion of the BLA containing the media instructions was produced to Amgen in August 2006 in connection with the related ITC investigation. Thus, contrary to Amgen's assertion, Roche did not delay in providing Amgen instructions for making the media.

The instructions in the BLA contained a full list of components and conditions required to reproduce the customized media in which Roche grows its cell line. Amgen thus was on notice since August 2006 that it would need to create or otherwise obtain this media in order to duplicate Roche's production conditions. Despite this notice, Amgen never requested either more information about the media or a sample. Likewise, none of Amgen's motions involved any request for cell culture media samples. Even Amgen's motions to compel focused only on the cell line itself, not the media, and the resulting order of this Court similarly pertained only to the cell lines.<sup>3</sup>

When Roche delivered a sample of its cell line to Dr. Kolodner, Roche also sent him the instructions from the BLA, at Amgen's request, to assist him in reproducing the culture media.<sup>4</sup> Dr. Richard Kolodner had been designated as Amgen's expert a month earlier and was not barred by the protective order from seeing the media instructions in the BLA. Amgen's oversight in failing to send these instructions to its own expert cannot be ascribed to delay or inaction on the part of Roche, which had not only supplied the

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<sup>2</sup> Roche's Responses and Objections to Amgen's First Set of Requests for Production of Documents and Things, Dec. 4, 2006, at 14.

<sup>3</sup> See Modified Order, February 27, 2007, DN 298.

<sup>4</sup> Ex. A to Declaration of Gregg T. Brooks in Support of Roche's Opposition to Amgen's Motion in Limine No. 5 (filed herewith), 3/20/07 email from Denise Lopez to Deborah Fishman.

instructions in August 2006, but had reminded Amgen of that fact in a December discovery response, and had again supplied the instructions directly to Dr. Kolodner. Despite having the instructions from the BLA, Amgen's expert did not recreate the cell media (Amgen Br. at 1-2).

Only after the close of discovery, in an informal request, did Amgen seek a sample of the cell culture media for the first time. Roche made good faith efforts to provide a sample to Amgen, but was not able, because no inventory of the media was available in Roche's production facility.<sup>5</sup> The earliest Roche could have cell culture media available to ship to Amgen was May 2, after Amgen's expert reports were due. Roche should not pay the price in evidentiary exclusion for Amgen's failure to either produce the cell culture media according to Roche's instructions or to timely request the media.

**B. Roche Has a Right to Introduce Testimony Impeaching the Scientific Credibility of Amgen's Infringement Experiments**

Amgen's expert, Dr. Kolodner, conducted experiments on cell lines received from Roche designed to recreate the conditions in which Roche cultivates its DN2-3 $\alpha$ 3 cell line, which Roche uses to produce the starting material for MIRCERA.<sup>6</sup> He erred, however, by using a culture medium that differed from Roche's. Dr. Kolodner conducted these experiments to investigate whether Roche's cell lines meet the limitations of claim 7 of Amgen's U.S. Patent No. 5,756,349.<sup>7</sup> Dr. Kolodner's inability to use culture media

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<sup>5</sup> 4/25/07 email from P. Carson to K. Flowers, Exhibit A to Declaration of Cullen N. Pendleton (DN 834).

<sup>6</sup> Expert Statement of Richard D. Kolodner, Ph.D, dated April 30, 2007 ¶ 6.

<sup>7</sup> The erythropoietin production of these cell lines is also the subject of Dr. Harvey S. Lodish's report and likely testimony.

equivalent to those used by Roche is a deficiency that, in the opinion of Roche's expert Dr. Richard Flavell, undermines Dr. Kolodner's conclusions.

Evidence that casts doubt on the scientific credibility of experiments is admissible under Fed. R. Evid. 402 as impeachment evidence. Dr. Flavell may provide testimony concerning the credibility of Dr. Kolodner's reproduction of the cell lines, and in turn of Dr. McLawhon's radioimmunoassay measurements of EPO production from those cells. Specifically, such testimony will concern the dissimilarity of Dr. Kolodner's experiments from Roche's production protocols.

Roche is entitled to rebut Amgen's evidence of infringement, whether by the testimony of Dr. Flavell, or by cross-examination of Amgen's experts concerning the cell culture conditions of Dr. Kolodner's experiments. Amgen should not be able to preclude such critical testimony on infringement because of lack of diligence in its own investigations of Roche's cell lines.

### **CONCLUSION**

For the foregoing reasons, Amgen's Motion *in Limine* No. 5 should be denied in all respects.

Dated: September 4, 2007  
Boston, Massachusetts

Respectfully submitted,

F. HOFFMANN-LA ROCHE LTD,  
ROCHE DIAGNOSTICS GMBH,  
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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/ Kregg T. Brooks  
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