

**IN THE UNITED STATES DISTRICT COURT
FOR THE 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,

Defendants.

Civil Action No. 05-12237 WGY

**ROCHE'S MEMORANDUM IN SUPPORT OF ITS MOTION *IN LIMINE* TO
PRECLUDE AMGEN FROM INTRODUCING TESTIMONY OF VLADIMIR
TORCHILIN RELATED TO PEGYLATION OF NON-EPO COMPOUNDS**

After refusing to provide discovery related to pegylation of compounds other than EPO, and consistent with this Court's ruling that "No Witness May Rely On Evidence Withheld From Discovery," Amgen should be precluded from presenting any evidence or testimony from its expert witness Valdimir Torchilin relating to the following topics:

- (1) chemical reactions of polyethylene glycol reagents (hereinafter "pegylation") with any compounds other than EPO, and
- (2) whether pegylation of compounds is a routine process that does not materially affect the structure, composition, or properties of a molecule.

This evidence and testimony should not be allowed for the following reasons:

- Amgen refused to provide any discovery whatsoever into Amgen's work on pegylation of its own molecules such as GCSF, NESP and MGDF, arguing that "whether pegylation is simple or difficult or whether pegylation affects the structure, composition or properties of specific molecules that are not accused of infringement" is not at issue in this case.¹ In response to Amgen's opposition to providing this

¹ Amgen Inc.'s Opposition to Defendants' Motion to Compel Production of Documents, D.I. 201, filed 12/12/06 ("Amgen's 12/6/07 Opp."), at *2.

discovery, this Court ruled that “The Case Involves EPO, Including Pegylated EPO, Not Other Pegylated Compounds.”²

- Consistent with this Court’s ruling that “No Witness May Rely On Evidence Withheld From Discovery,” Amgen should be barred now from raising this evidence before the jury.
- The Court previously ruled during Dr. Lodish’s testimony that testimony of pegylation of compounds besides erythropoietin was not permitted when the Court sustained an objection at sidebar to a question asking Dr. Lodish about pegylation of such compounds.³ The Court noted that it was aware from Roche’s previously submitted bench memos on the issue (D.I. 1260 and 1298) that Amgen refused to provide discovery of pegylation of non-EPO products and sustained objection to the question “Do you have an understanding as to whether or not other proteins have been pegylated before peg-EPO?”⁴

During fact discovery, Amgen took the position that pegylation with any compound other than EPO was not relevant to this litigation, successfully preventing Roche from obtaining any discovery into Amgen’s work on pegylation of its own molecules such as GCSF, NESP (Amgen’s attempts to pegylate its ESA Aranesp[®]), and MGDF by arguing to this Court that “whether pegylation is simple or difficult or whether pegylation affects the structure, composition or properties of specific molecules that are not accused of infringement” is not at issue in this case.⁵ Following the close of fact discovery, however, Amgen served several expert reports, including reports by Amgen expert Vladimir Torchilin, which claimed that pegylation is a routine process that does not materially affect the structure, composition, or properties of a molecule. These expert reports cite to and rely upon documents and information of pegylation of

² Court’s Order dated 1/3/07 on Motion (D.I. 170).

³ Trial Tr., Day 17, 2457:25 - 2458:16

⁴ Id.

⁵ Amgen’s 12/6/07 Opp. at *2.

compounds other than EPO. Amgen has now indicated that it intends to call Dr. Torchilin as a live witness on Monday, October 15. It is clear that it was Amgen's plan all along to deny Roche discovery into Amgen's attempts, including mostly failures to successfully pegylate compounds other than EPO, and then present expert testimony that pegylation is simple and routine, and point to pegylation of other compounds as evidence. Having engaged in this duplicitous behavior and successfully prevented Roche from obtaining what Amgen characterized as irrelevant discovery, Amgen should be precluded from offering any evidence, including the testimony of Dr. Torchilin, on the topic it described as irrelevant - pegylation of compounds other than EPO.

I. AMGEN REFUSED DISCOVERY RELATED TO PEGYLATION OF NON-EPO COMPOUNDS ARGUING SUCH DISCOVERY WAS NOT RELEVANT

During the fact discovery phase of this case, Roche propounded several document requests relating to Amgen's efforts to develop pegylated versions of its compounds, including GCSF, MGDF and NESP (Aranesp[®]).⁶ Amgen refused to provide this discovery on the grounds that documents related to "any Pegylated Compound" other than erythropoietin" was "not reasonably calculated to lead to the discovery of admissible evidence."⁷ Roche also propounded an interrogatory to Amgen seeking Amgen's contention as to whether Mircera[®] was materially changed within the meaning of 35 U.S.C. § 271(g), to which Amgen provided a conclusory one-line statement about pegylation with no further elaboration on whether it would argue that

⁶ Defendants' First Set of Requests for the Production of Documents and Things to Amgen, Inc. (Nos. 1-123) dated October 30, 2006.

⁷ Amgen Inc.'s Objections and Responses to Defendants' First Set of Requests for the Production of Documents and Things (Nos. 1-123) dated December 4, 2006 at Responses to Requests Nos. 20, 31, 34-35, 105. (Exhibit A to Declaration of Alfred H. Heckel ("Heckel Decl."), D.I. 427, submitted in conjunction with Roche's 4/30/07 Memo); *See also* Responses to Requests Nos. 19, 58-59, 106-112. (Heckel Decl., Exh. A).

pegylation does not materially change a compound. Roche was forced to move to compel documents relating to pegylation from Amgen, arguing that they were relevant to both validity and infringement in this litigation because Amgen would take the position that pegylation of compounds was a routine, well-known process, easy to do, which did little to alter the starting compound. Amgen's own, internal documents showing the long, laborious, often unsuccessful, process to pegylate its own compounds would contradict Amgen's contention that pegylation is a simple process.

In its opposition to Roche's motion to compel, Amgen asserted that "documents relating to Amgen's pegylated proteins other than EPO are not relevant" and specifically with regard to GCSF and MGDF that "discovery regarding these proteins is therefore in no way related to the subject matter of Lin's patents - or this litigation."⁸ Amgen's current attempts to deny that it argued that pegylation of compounds other than EPO, or pegylation in general for that matter, were not relevant to this litigation are revisionist history belied by its own documents in which it stated "whether pegylation is simple or difficult or whether pegylation affects the structure, composition or properties of specific molecules that are not accused of infringement" is not at issue in this case.⁹ The Court adopted Amgen's position in its January 3 Order, denying discovery into pegylation and non-EPO compounds.¹⁰

⁸ Amgen Inc.'s Opposition to Defendants' Motion to Compel the Production of Documents, D.I. 201, at 7, 9-10.

⁹ Amgen's 12/6/07 Opp. at *2. Likewise, Amgen's arguments that it didn't take the position that documents relating to pegylation of non-EPO compounds were not relevant, but the real objection was that Roche's document requests were burdensome and too far-reaching are similarly undermined by Amgen's 12/6/07 Opp. and the fact that Amgen objected to producing any of its documents relating to pegylation of its GCSF, NESP and MGDF compounds.

¹⁰ Order of the Court on Motion D.I. 170, 1/03/07.

Amgen strictly interpreted the Court's Order and refused any discovery whatsoever into pegylation as it related to other compounds. Amgen even instructed its witnesses not to answer questions involving pegylation, such as pegylation of GCSF, during depositions.¹¹ Amgen even refused to allow any questioning or provide any discovery into Amgen's attempts to pegylate its second-generation erythropoietin-stimulating agent, Aranesp[®], though it contends that Aranesp[®] is covered by at least one unasserted claim of the patents-in-suit.

II. DR. TORCHILIN'S OPINIONS BASED ON PEGYLATION OF NON-EPO COMPOUNDS SHOULD BE PRECLUDED

After successfully arguing that pegylation of other compounds was irrelevant during fact discovery, Amgen submitted expert reports, including the April 6, 2007 and May 10, 2007 reports of Dr. Vladimir Torchilin, replete with assertions that pegylation with molecules was common practice at the time Roche developed Mircera[®], and would yield predictable, expected results.¹² At least paragraphs 20, 28, 32, 33, 65, 73, 78, 82-89, 91, 95-96 and 109-111 of Dr. Torchilin's April 6 report, and almost all of Dr. Torchilin's May 10, 2007 report, relate to characteristics of pegylation. In contradiction of Amgen's arguments to block discovery, at his deposition, Dr. Torchilin stated that pegylation of non-EPO compounds was relevant to this case:

Q: And do you think that the PEGylation of non-EPO compounds are relevant to your opinions in this case?

A: Yes, it certainly is relevant.¹³

¹¹ Molineux Depo. Trans., 3/28/07, 24:20-25:22 and 29:12-30:1.

¹² See First Expert Report of Dr. Vladimir P. Torchilin, Ph.D., D. Sc., dated April 6, 2007; Second Expert Report of Dr. Vladimir P. Torchilin, Ph.D., D. Sc., dated May 10, 2007.

¹³ Torchilin Dep. Trans., 7/25/07, 384:17-20.

Amgen's own difficulties in modifying other compounds with pegylation could provide crucial rebuttal evidence to the assertions of Amgen's experts, but Roche does not have this information since companies do not generally publish their experimental failures and Amgen refused to provide it during discovery. Amgen effectively blocked any opportunity for Roche to develop evidence through Amgen documents or testimony that would show pegylation was not a routine, simple process.

Following the service of the expert reports by Amgen, including Dr. Torchilin's report, offering the opinion that pegylation is routine and does not affect structure, composition or properties in any meaningful way based upon pegylation of compounds other than EPO, Roche moved to strike these infringement allegations and opinions in Amgen's expert reports.¹⁴ In ruling on Roche's motion, this Court stated, "Motion Denied Without Prejudice Depending On How the Evidence Develops At Trial. No Witness May Rely On Evidence Withheld From Discovery."¹⁵ Amgen should be precluded from offering the testimony of Dr. Torchilin on the subject of whether pegylation is routine or affects the structure, composition or properties of the molecule in a significant way.¹⁶

¹⁴ Memorandum in Support of Defendants' Motion to Strike Infringement Allegations in Amgen's Expert Reports on Which Amgen Did Not Provide Discovery and to Preclude Discovery, D.I. 426, filed 4/30/07 ("Roche's 4/30/07 Memo").

¹⁵ Order of the Court on D.I. 425, 5/16/07.

¹⁶ The other two Amgen witnesses who included opinions regarding pegylation of compounds other than EPO were Dr. Lodish and Dr. Katre. Amgen did not list Dr. Katre on its potential trial witness list as one of its ten experts, and Dr. Lodish has already testified. During Dr. Lodish's testimony, the Court correctly sustained an objection at sidebar to a question asking Dr. Lodish about pegylation of other compounds besides erythropoietin. Trial Tr., Day 17, 2457:25 - 2458:16.

Amgen has argued that its experts, including Dr. Torchilin, do not rely on any documents not produced during discovery other than scientific journal articles in support of their opinions regarding pegylation of non-EPO compounds. This is exactly the point - Amgen not only denied discovery to Roche into its own difficulties with pegylation of its compounds, but did not give these documents to its own experts to review in forming their opinions. When asked how much effort and time it took by Amgen to attempt to pegylate, successfully or not, any of Amgen's non-EPO compounds, Dr. Torchilin made clear that he did not know and did not take this into account in his opinion, stating that "How exactly many hours was used to make PEGinterferon or PEG whatever, monoaminoxidase, no, I don't know."¹⁷ It is precisely Amgen's internal documents that Amgen argued were irrelevant and refused to provide in discovery that would provide this type of information that Amgen has tried to hide from Roche and even from its own experts:

"QUESTION: You didn't have access to all the trial and error experimentation that went into Amgen's work to PEGylate other proteins other than EPO?"

Mr. Gaede: Same objections.

A: No, I didn't have access to all the documents regarding Amgen's failed or successful attempts to PEGylate other proteins.¹⁸

The First Circuit has made clear:

The purpose of discovery is to make a trial less a game of blind man's bluff and more a fair contest with the basic issues and facts disclosed to the fullest practicable extent. Once a proper discovery request has been seasonably propounded, we will not allow a party sentimentally to avoid its obligations by filing misleading or evasive responses, or by failing to examine records within its control.¹⁹

¹⁷ Torchilin Dep. Trans., 7/25/07, 386:12-14.

¹⁸ Torchilin Dep. Trans., 7/25/07, 388:20-389:2.

¹⁹ *Anderson v. Cryovac, Inc.*, 862 F.2d 910, 929 (1st Cir. 1988).

It is also clear that Courts may preclude expert opinion where it constitutes surprise or a shift in a litigant's previous position. See *Thibeault v. Square D Co.*, 960 F.2d 239, 246-47 (1st Cir. 1992); *Freund v. Fleetwood Enterprises, Inc.*, 956 F.2d 354, 358 (1st Cir. 1992). Judicial fairness dictates that such conduct should not be countenanced. "[T]he doctrine of judicial estoppel prevents a litigant from pressing a claim that is inconsistent with a position taken by that litigant either in a prior legal proceeding or in an earlier phase of the same legal proceeding." *InterGen N.V. v. Grina*, 344 F.3d 134, 144 (1st Cir. 2003). "In line with this prophylactic purpose, courts typically invoke judicial estoppel when a litigant is 'playing fast and loose with the courts.'" *Id.* (citing *Patriot Cinemas, Inc. v. Gen. Cinema Corp.*, 834 F.2d 208, 212 (1st Cir. 1987)).

Amgen refused to provide discovery relating to pegylation of non-EPO compounds to Roche, and told this Court that the difficulty of pegylation and whether pegylation affects the structure, composition or properties of specific molecules other than EPO was not relevant or discoverable.²⁰ Amgen should be held to its original position that documents relating to pegylation of compounds other than EPO are not relevant to this case, and should be precluded from offering any testimony or evidence at trial discussing the characteristics of pegylation or whether it is routine, either now, at the time of the development of Mircera[®], or at the time of Amgen's claimed invention. On this very topic, this Court has already ruled that "Motion Denied Without Prejudice Depending On How the Evidence Develops At Trial. No Witness May Rely On Evidence Withheld From Discovery."²¹ Amgen should be precluded from offering Dr. Torchilin's testimony, or any other evidence, on whether pegylation was a routine, simple

²⁰ Amgen's 12/6/07 Opp. at *2.

²¹ Order of the Court on Motion D.I. 425, 5/16/07.

procedure that did not substantially affect the structure, composition or properties of the starting compound based on pegylation of any compound other than EPO.

Dated: October 14, 2007
Boston, Massachusetts

Respectfully submitted,

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

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