**UNITED STATES DISTRICT COURT**
**DISTRICT OF MASSACHUSETTS**

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| AMGEN INC.,<br><br>Plaintiff,<br><br>v.<br><br>F. HOFFMANN-LA ROCHE LTD., a Swiss Company, ROCHE DIAGNOSTICS GmbH, a German Company and HOFFMANN-LA ROCHE INC., a New Jersey Corporation,<br><br>Defendants. | ) | Civil Action No.: 05-12237 WGY |

**AMGEN INC.'S OPPOSITION TO ROCHE'S MOTION IN *LIMINE* TO PRECLUDE AMGEN FROM INTRODUCING EVIDENCE REGARDING THE SAFETY OF MIRCERA®**

Roche's Motion in *Limine* to preclude Amgen from introducing evidence regarding the safety of peg-EPO is a transparent attempt to enable Roche to present a misleading and one-sided view of the purported clinical advantages of Roche's pegylation of EPO. Roche has indicated that it intends to rely on results from its clinical studies to suggest that pegylation of EPO results in a product that stimulates red blood cell production like EPO does (the function of Roche's product is indisputably provided by the EPO) and has the purported clinical advantage of requiring fewer doses. By opening this Pandora's Box, Roche cannot allege that it is unfair for Amgen to use this very same information to rebut Roche's claim. Indeed, as Roche's own clinical studies show, pegylation of EPO is not clinically advantageous and has resulted in a product, that, while equivalent in it ability to "increase a patient's reticulocytes and red blood cells," is more dangerous and less efficacious than EPO.

Furthermore, Roche has already opened the door regarding alleged safety issues. During

Roche's examination of Dr. Spinowitz, Roche was allowed, over Amgen's objection, to ask questions concerning the safety of ESAs currently on the market. Specifically, Mr. Fleming asked Dr. Spinowitz about the FDA Advisory Committee's review of the safety of Amgen's products. Dr. Spinowitz also responded to questions about whether he observed adverse effects with ESAs on the market. Now that Roche has injected the issue of product safety into the case, before the jury, it would be highly prejudicial and grossly unfair to preclude Amgen from presenting the reality that Roche's pegylated EPO product is less safe for patients than Amgen's products. Unless Amgen is allowed to present the safety evidence on Roche's product the jury will be mislead to believe that Roche's product is superior to Amgen's products, which it is not.

## I. Amgen Should Be Permitted to Introduce Evidence About Peg-EPO's Negative Clinical Profile to Counter Roche's Claim That Peg-EPO is Clinically Superior to ESAs Currently on the Market.

It is Roche, not Amgen, that seeks to affirmatively introduce information about the safety profile of ESAs currently on the market and the purported clinical benefits of pegylated EPO. During its examination of Dr. Spinowitz, Roche asked him about the FDA advisory committee's review of Amgen's products and adverse effects of ESAs currently on the market.[1] It is clear that Roche intends to compliment these misleading questions and testimony with an incomplete picture of pegylated EPO's safety profile. Thus, Dr. Gregory Longmore, a Roche expert, opines in his expert report that "treatment with CERA provides substantial and advantageous clinical benefits over traditional [EPO]."[2] He further opines that "a significant benefit" of peg-EPO is its ability "to maintain safe and stable hemoglobin levels over time, at least comparable to the hemoglobin stability achieved with epoetin beta administered over much shorter dosing

[1] 9/12/07 Trial Transcript, pp. 979-983.
[2] 5/11/07 Expert Report of Gregory D. Longmore ¶ 168 [hereinafter Longmore Report].

intervals."[3] Roche has indicated that it intends to call Dr. Longmore at trial. In its trial brief, Roche even goes so far as to suggest that if pegylated-EPO infringes Amgen's patents, this Court should ignore this infringement because it would be "wholly inequitable to hold Roche liable" when the "prolonged half-life of CERA translates into a result that will make a significant difference to patients."[4]

Since Roche has already introduced evidence about the safety of ESAs and intends to introduce information about the purported clinical benefits that result from pegylating EPO, Amgen should be permitted to counter this evidence, and the jury should be permitted to evaluate the entirety of Roche's alleged claims. The non-inferiority studies that Roche claims show peg-EPO is clinically superior, in fact show that peg-EPO, while able to effect erythropoiesis, is less safe – negating any so-called convenience offered to patients.[5] For example, in Roche's May 18, 2007 press release announcing receipt from the FDA of an approvable letter for peg-EPO, Roche also reported that patients taking peg-EPO experienced 6 times as many incidents of "serious gastrointestinal hemorrhages" than patients taking other erythropoiesis-stimulating agents.[6] There is no doubt that this information is directly relevant to any Roche claim that its pegylation resulted in a clinically superior product. Roche should not be allowed to mislead the jury by tarnishing Amgen's products and providing a one-sided and misleading presentation to the jury about pegylated EPO.

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[3] Longmore Report ¶ 173.

[4] 8/31/07 Roche's Trial Brief, at 25 (Docket No. 919).

[5] Amgen does not dispute that Roche's product will have a similar effect on hemoglobin levels as EPO. This is because, of course, Amgen's EPO is at the core of Roche's pegylated EPO.

[6] Hoffmann-La Roche Inc., Roche Receives Approvable Letter for MIRCERA® in the United States (May 18, 2007), http://www.rocheusa.com/newsroom/current/2007/pr2007051801.html ("Serious gastrointestinal hemorrhages were observed in 1.2% of patients treated with Mircera and 0.2% for patients receiving other ESAs.")

## II. Evidence About MIRCERA®'s Safety Profile Is Not Unduly Prejudicial Under FRE 403.

Furthermore, since Roche intends to raise the issue of clinical superiority of pegylated EPO — and has already raised the issue about the safety of EPO — there is no basis under FRE 403 to preclude Amgen from rebutting those claims. FRE 403 is not intended to insulate a party from facts that directly contradict assertions that the party affirmatively raises.[7] Indeed, without such information, the jury will asses Roche's claims of superiority in isolation – using incomplete and discrete evidence. This is precisely the type of confusion that FRE 403 is designed to avoid.[8]

Amgen is entitled to submit evidence of the negative side effects associated with pegylated EPO because Roche is claiming its pegylation has resulted in a clinically superior product. Under these circumstances, evidence about the clinical disadvantages of pegylation is relevant and not unfairly prejudicial. Accordingly, this court should deny Roche's Motion in *Limine* to Preclude Amgen from Introducing Evidence Regarding The Safety of MIRCERA®.

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[7] *Iacobucci v. Boulter*, 193 F.3d 14, 21 (1st Cir. 1999) (FRE 403 "does not aspire to eliminate prejudice -- after all, most evidence is offered precisely because the proponent believes it will prejudice the factfinder in his favor -- but only to eliminate unfair prejudice."); *Polec v. Northwest Airlines (In re Air Crash Disaster)*, 86 F.3d 498, 538 (6th Cir. 1996) ("Rule 403 does not exclude evidence because it is strongly persuasive or compellingly relevant . . . . The truth may hurt, but Rule 403 does not make it inadmissible on that account.").

[8] *United States v. Woodward*, 149 F.3d 46, 72 (1st Cir. 1998), citing *United States v. Aguilar-Aranceta*, 58 F.3d 796, 800 (1st Cir. 1995) (Under Rule 403, "if the evidence brings … a cognizable risk of confusing the jury, and if the baggage's weight substantially overbalances any probative value, then the evidence must be excluded.").

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Respectfully Submitted,

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