Exhibit A

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-CV-12237WGY

DEFENDANTS' [PROPOSED] REPLY MEMORANDUM IN FURTHER SUPPORT OF DEFENDANTS' MOTION *IN LIMINE* TO INVOKE ISSUE PRECLUSION AS TO FINDINGS FROM PRIOR LITIGATION [D.N. 820]

Defendants F. Hoffmann-LaRoche, Ltd., Roche Diagnostics GmbH and Hoffmann-LaRoche Inc. (collectively "Roche") submit this reply memorandum in further support of their motion *in limine* to invoke the doctrine of issue preclusion to prevent Amgen from arguing contrary to certain determinations made in prior litigation.

In an attempt at obfuscation, Amgen in its opposition conflates the concept of claim preclusion (*res judicata*) with the concept of issue preclusion (collateral estoppel). Nevertheless, the two factual issues identified in Roche's motion—(1) that rEPO cannot be distinguished from uEPO on the basis of glycosylation, and (2) that the common specification of the patents-in-suit does not support claims to analogs of EPO beyond the few disclosed in the patent specifications—clearly satisfy the four requirements of issue preclusion. These two issues have

been finally decided in prior litigations and thus cannot be re-litigated in this case. If Roche's motion *in limine* is not granted, not only will precious time be wasted before the jury re-litigating these well-trodden issues, but Amgen will be allowed to make arguments directly contrary to findings made by this Court and adopted by the Federal Circuit

Notably, Amgen does not dispute that three of the four requirements for issue preclusion are met for each of these two issues, namely "…(2) the issue was actually litigated in the first action; (3) resolution of the issue was essential to a final judgment in the first action; and (4) the party against whom estoppel is invoked had a full and fair opportunity to litigate the issue in the first action." *Amgen, Inc. v. F. Hoffman-La Roche Ltd.*, ---F.Supp.2d---, 2007 WL 1893058 *2 (D. Mass. 2007). Amgen's sole basis for opposing Roche's motion is that the issues in the prior litigations are irrelevant or unrelated to the issues in the present litigation. However, as discussed in Roche's original motion and as discussed below, these two factual issues in the prior litigations are identical to factual issues in the present litigation. Amgen in its opposition raises a series of red herrings in an attempt to make the factual issues finally decided in the prior litigations sound different from the identical factual issues in the present case. The fact that these factual issues had previously arisen for different claims, for different patents and/or in a different context does not prevent them from being identical issues. *See, e.g., Amgen, Inc. v. Genetics Institute, Inc.,* 877 F.Supp. 45 (D.Mass. 1995)(Young, J.), *aff'd Amgen, Inc. v. Genetics Institute, Inc.,* 98 F.3d 1328 (Fed. Circ. 1996).

I. THE FACTUAL ISSUE "rEPO CANNOT BE DISTINGUISHED FROM uEPO ON THE BASIS OF GLYCOSYLATION" IS IDENTICAL IN THE PRIOR LITIGATION AND THE PRESENT LITIGATION

In *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 165 (D. Mass. 2001), this Court held that "Claims 1, 2, and 9 of the '933 patent are not infringed, and, if this

finding is error, those claims are invalid for lack of an adequate written description, indefiniteness, and lack of enablement." Essential to this holding was the factual finding that rEPO cannot be distinguished from uEPO on the basis of glycosylation. *Id.* at 155 ("[T]he glycosylation of human urinary erythropoietin is a standardless standard. ... As a result, making comparisons between the glycosylation of recombinant EPO and that of human urinary EPO is virtually impossible."). The Federal Circuit affirmed this Court's holding that the '933 patent is invalid. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1358 (Fed. Cir. 2003). In doing so, the Federal Circuit adopted this Court's finding that rEPO cannot be distinguished from uEPO on the basis of glycosylation. *See, e.g., id.* at 1341-1342.

In the present case, Roche intends to show that the rEPO of the claims-in-suit is anticipated by or obvious in light of naturally occurring EPO, i.e., uEPO. Amgen will undoubtedly attempt to show that its claimed rEPO is distinguishable from the prior art uEPO. If Amgen were to attempt to do so by arguing that the glycosylation of the claimed rEPO differed from that of prior art uEPO, Amgen would be re-litigating the identical factual issue that has been fully litigated and finally decided against Amgen in the prior litigation. However, the doctrine of issue preclusion prevents Amgen from re-litigating this factual issue. That different claims or different patents were involved in the prior litigation is of no avail to Amgen, since the factual issue is identical. *Amgen, Inc. v. Genetics Institute, Inc.,* 877 F.Supp. 45 (D.Mass. 1995), *aff'd Amgen, Inc. v. Genetics Institute, Inc.,* 98 F.3d 1328 (Fed. Circ. 1996). The doctrine of issue preclusion only requires that the identical issue have been previously litigated; it does <u>not</u> require that the issue have been litigated in the identical context. Indeed, if the issue had been litigated in the identical context, the doctrine of claim preclusion would be the appropriate doctrine, not issue preclusion.

Amgen in its opposition does not attempt to explain why this factual issue is not identical to that of the prior litigation; Amgen merely argues that different claims were litigated in the prior litigation—which argument is of no avail to Amgen, as noted above.

Amgen also argues that this factual issue has been decided against Roche on summary judgment pursuant to this Court's Electronic Order of August 27, 2007 granting in part the Amgen motion designated as D.N. 531. This argument is incorrect and misleading. Amgen had moved *inter alia* that "non-naturally occurring" was definite. Whether this term is definite or not, Roche is not prevented from showing that claims containing this term are anticipated by or obvious in light of prior art uEPO. (Furthermore, it should be noted that the term "non-naturally" only occurs in the claims of the '933 patent, and Amgen's anticipation and obviousness defenses based on uEPO are also directed to the '422 patent.)

Roche's subject motion *in limine* does not re-open the issue of whether "non-naturally occurring" is indefinite. Rather, it prevents Amgen from re-litigating whether rEPO is distinguishable from uEPO on the basis of glycosylation, and thus prevents Amgen from using this faulty and inappropriate basis to rebut Roche's showing of anticipation and obviousness. Although Amgen cannot distinguish rEPO from uEPO on the basis of glycosylation, Amgen would not be foreclosed from asserting a different basis for distinguishing rEPO from uEPO—if a different basis were available to Amgen.

As of the time this reply is being written, the parties do not yet have the Court's written opinion explaining its rationale for its Electronic Order of August 27, 2007, which held that "non-naturally occurring" was definite. Nevertheless, it should be safe to assume that the rationale for the holding that "non-naturally occurring" was definite will not be that rEPO can be distinguished from uEPO on the basis of glycosylation. Such a rationale would be (i) directly

contrary to this Court's prior determination that "making comparisons between the glycosylation of recombinant EPO and that of human urinary EPO is virtually impossible" (*Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 155 (D. Mass. 2001)) and (ii) directly contrary to the Federal Circuit's reliance on this determination (*Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1341-1342 (Fed. Cir. 2003)). Thus, unless and until a written opinion is provided holding "non-naturally occurring" is definite because rEPO can be distinguished from uEPO on the basis of glycosylation, it is inappropriate for Amgen to argue that this factual issue has been decided against Roche in the Court's August 27, 2007 Electronic Order. As it stands now, Roche is not prevented from showing that claims containing the term "non-naturally occurring" (as well as other claims) are anticipated by or obvious in light of prior art uEPO. And there is no indication that this Court has reversed its prior factual finding that rEPO cannot be distinguished from uEPO on the basis of glycosylation.

II. THE FACTUAL ISSUE "THAT THE COMMON SPECIFICATION OF THE PATENTS-IN-SUIT DOES NOT SUPPORT CLAIMS TO ANALOGS OF EPO BEYOND THE FEW DISCLOSED IN THE PATENT SPECIFICATIONS" IS IDENTICAL IN THE PRIOR LITIGATION AND THE PRESENT LITIGATION

In its opposition, Amgen argues that this issue—which was thoroughly litigated and finally decided in the *Chugai* litigation—is irrelevant to the current litigation because "Amgen is not asserting a claim regarding analogs as part of this litigation because Roche's accused product is not an analog; it has exactly the same amino acid sequence as human erythropoietin." D.N. 896, p. 6. However, the nature of Roche's accused product is irrelevant to the validity of Amgen's claims. For example, if one were to attempt to practice the subject matter of '349 claim 7, the radioimmunoassay technique of that claim would measure fragments of EPO; however, these fragments of EPO are EPO analogs that are not fully enabled or described by the patent specification.

Thus, Roche intends to show that '349 claim 7 is not fully enabled or described. Roche is not barred from trying this defense before the jury; the question of whether or not Roche's product is an analog does not prevent Roche from pursuing such a 35 U.S.C. § 112, 1st ¶ defense. Since the previously litigated issue that the common specification of the patents-in-suit does not support claims to analogs of EPO beyond the few disclosed in the patent specifications is relevant to Roche's defense and is identical in the prior and current litigations, issue preclusion is appropriate.

Accordingly, Amgen's sole basis for opposing issue preclusion on this issue—namely, that "Amgen is not asserting a claim regarding analogs as part of this litigation because Roche's accused product is not an analog; it has exactly the same amino acid sequence as human erythropoietin"—is ill-founded and does not, in any way, address whether the issue is identical in the two litigations. As a result, Amgen's entire opposition on this issue collapses.

It should be noted that in attempting to oppose issue preclusion on this issue, Amgen misleadingly describes the nature of its motion for summary judgment designated D.N. 531. The Court's August 27, 2007 Electronic Order did not find that '349 claim 7 was fully enabled and described. Amgen's motion only addressed the enablement of so-called PEG-EPO (in point 4 of the motion), and with respect to the '349 claim 7 specifically, Amgen only moved (in point 2 of the motion) that it was definite in certain aspects. Specifically, Amgen moved

> (2) Dr. Lin's claim to a process for producing erythropoietin using cells that are "capable upon growth in culture of producing erythropoietin in the medium of their growth in excess of 100 U of erythropoietin per 10^6 cells in 48 hours, as determined by radioimmunoassay," as set forth at claim 7 of U.S. Patent No. 5,756,349, is definite because an ordinarily skilled artisan would understand this term to require:
>
> (a) The use of cells that produce in excess of 100 U of erythropoietin per 10_6 cells in 48 hours; and
>
> (b) A radioimmunoassay results in which one type of antibody and EPO sample are calibrated against a known EPO standard.

(It should also be noted that the Court did not grant point 3 of Amgen's motion, which relates to "human erythropoietin," a term also found in the '349 claims.)

Thus, whether the enablement and written-description requirements are fully satisfied for '349 claim 7 is a defense that Roche is allowed to pursue and intends to pursue at trial. Thus, contrary to Amgen's argument, the issue of whether EPO analogs are fully enabled and described is still a relevant issue in the current case, and furthermore, this issue is identical to the issue in the *Chugai* case.

III. THE PRIOR DETERMINATIONS SHOULD BE PROVIDED TO THE JURY

Amgen also opposes Roche presenting the prior judicial determinations listed in Exhibit A of Roche's motion *in limine* D.N. 820 to the jury as conclusive evidence (point 3 of the motion *in limine*). Amgen also cross-moved to preclude Roche from doing so. Roche's reply to Amgen's opposition on this particular point is set forth in Roche's opposition to said cross-motion.

CONCLUSION

For the reasons set forth above, Roche's motion *in limine* D.N. 820 should be granted, and Amgen should be prevented from re-litigating these two issues: (1) that rEPO cannot be distinguished from uEPO on the basis of glycosylation, and (2) that the common specification of the patents-in-suit does not support claims to analogs of EPO beyond the few disclosed in the patent specifications. These determinations are directly relevant to the claims in the instant litigation and have been fully and finally litigated by Amgen in prior proceedings.

Dated: September 3, 2007
Boston, Massachusetts

Respectfully submitted,

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

By their Attorneys

/s/ Timothy M. Murphy
Lee Carl Bromberg (BBO# 058480)
Robert L. Kann (BBO# 258025)
Timothy M. Murphy (BBO# 551926)
Julia Huston (BBO# 562160)
Keith E. Toms (BBO# 663369)
Nicole A. Rizzo (BBO# 663853)
Kregg T. Brooks (BBO# 667348)
BROMBERG & SUNSTEIN LLP
125 Summer Street
Boston, MA 02110
Tel. (617) 443-9292
tmurphy@bromsun.com

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

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 will be delivered to Amgen's trial counsel by electronic mail in the manner requested in the August 29, 2007, letter of Renee DuBord Brown to Thomas F. Fleming. Paper copies will be sent to those indicated as non registered participants on September 4, 2007.

/s/ Timothy M. Murphy
Timothy M. Murphy

03099/00501 732747.2