UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

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

DEFENDANTS' MEMORANDUM IN SUPPORT OF MOTION FOR RECONSIDERATION AND OPPOSITION TO AMGEN'S MOTION TO COMPEL PRODUCTION OF ROCHE'S CELL LINE AND RELATED DOCUMENTS

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Dated: January 22, 2007

Defendants F. Hoffmann-La Roche Ltd, Roche Diagnostics GmbH, and Hoffmann-La Roche Inc. (collectively "Roche") respectfully submit this motion for reconsideration and opposition to the Motion to Compel production of Roche's cell line and related documents filed by Plaintiff, Amgen Inc. ("Amgen"), on January 10, 2007.

I. INTRODUCTION

On January 22, 2007, the Court granted Amgen's motion to compel Roche's cell lines. ("Order"). However, Amgen's motion was granted on an incomplete record because the Court did not allow Roche the opportunity to oppose the motion. Roche's opposition would have been due January 24th, 2007, and counsel for Roche communicated to the Court's clerks that an opposition would be filed by the allotted due date. Roche respectfully moves the Court to reconsider its Order until after review of Roche's opposition papers for purposes of fairness and due process. At the very least, Roche's position includes a compromise approach, which is outlined in the attached proposed order, whereby the Roche cell lines can be produced to Amgen under terms that will preserve Roche's trade secret and proprietary information. Due to the Court's ruling on Amgen's motion to compel without hearing Roche on the issue and in light of the extraordinarily sensitive nature of the materials sought in Amgen's motion and Amgen's mischaracterization of its purported need for these materials, the Court should grant reconsideration.

Amgen's latest motion to compel is but the latest example in a pattern of overreaching discovery demands, this time directed at some of Roche's most assiduously guarded trade secrets, Roche's proprietary cell lines used in connection with the production of MIRCERA™. The *only* reason that Amgen gives for needing access to Roche's cell line is to determine whether it is "capable of producing 100, 500 or 1000 units of EPO as measured by radioimmunoassay

(RIA) per 10^6 cells in a 48 hour period." Amgen Memo. at 1. Roche has not refused to provide information about the production levels of its cells. In fact, Roche's BLA for MIRCERA™ has been in Amgen's hands for more than six months. This document contains an entire section describing the production of the EPO starting material used to synthesize MIRCERA™, including cell line propagation and purification and characterization of the expressed EPO protein. To the extent Amgen contends that the BLA does not provide sufficient information regarding the production level of Roche's cell line, in response to this Court's order dated December 29, 2006, Roche is producing the European regulatory filing for Roche's EPO product sold in Europe. Roche uses the same cell line that is described in that document to produce the EPO starting material for MIRCERA™. Production of the European regulatory filing, which provides excruciating detail including protein production levels for Roche's cell line, began today with the production of particularly relevant pages.

In light of the ample documentary information provided or currently being provided containing the information that Amgen asserts is needed, Amgen cannot establish a compelling need for the cell line itself. Amgen wants Roche to admit that its cell line is "capable upon growth in culture of producing EPO in the medium of their growth in excess of 100U of erythropoietin per 106 cells in 48 hours as determined by radioimmunoassay." As Roche explained to Amgen in its supplemental response and related correspondence, this phrase, which is taken verbatim from the '349 patent claims, is indefinite and scientifically imprecise. Roche cannot admit or deny a limitation that it does not understand. As such, Roche reasonably requested an explanation as to how this test should be performed. Rather than responding to this reasonable inquiry, Amgen filed the instant motion. Amgen's inability to explain why Roche's documents are insufficient to show whether Roche's cells meet the claimed production levels

only confirms that the measure of EPO units required by the '349 claims is hopelessly indefinite and unsupported by any disclosure in the patent.

Amgen takes the position that since TKT produced its cell line, so should Roche. The circumstances under which TKT surrendered its cell line are completely inapplicable to this case. There, in the course of a summary judgment hearing, TKT attacked Amgen's assertions regarding the production levels of TKT's cell line and precipitated the need for Amgen to rebuff the attack through testing. As such, TKT readily ***agreed*** to produce its cell line. Here, Amgen's motion is not precipitated by a genuine need for Roche's cell line, but instead in the hope that by threatening Roche with having to hand over its cell line, it can pressure Roche into a crucial admission that Amgen cannot prove at trial.

Amgen's argument that the cell lines are essential to its case leaves Roche in an untenable position; Amgen claims it must perform a certain test prescribed in these claims on the cell line but has refused to tell Roche how to perform this test or measure its results. In pressing its request for Roche's cell line, Amgen should be able to identify the test that it needs to perform. Inexplicably, it refuses to share this information with Roche. Until Amgen articulates what experiments must be performed and how to measure the results under the '349 patent, there can be no legitimate discovery purpose that outweighs Roche's strong interest in keeping its trade secret materials out of the hands of a competitor.

At minimum, Roche respectfully submits that resolution of this motion before Roche produces documents pursuant to this Court's order is premature and should be deferred. However, if, upon reconsideration, this Court is inclined to grant Amgen's motion, Roche respectfully requests that certain restrictions and safeguards be put in place. Each of these safeguards set forth in the accompanying proposed order will provide Roche's proprietary

information with the necessary protection while in no way impeding Amgen's ability to perform any allegedly necessary tests.

II. RECONSIDERATION IS WARRANTED

A court should grant reconsideration where there is evidence that was not before the court in its initial decision. *See Davis v. Lehane*, 89 F. Supp.2d 142, 147 (D. Mass 2000). In entering its initial decision the Court lacked substantial evidence concerning 1) the value of Roche's cell lines and the ease with which that value may be misappropriated, described below in Section III and in the attached declaration of Reinhard Franze, and 2) the unreliability of Amgen's stated need for the cell lines, described below in Section IV with respect to the indefiniteness of the claims of the '349 patent. Without this evidence, the Court's determination was premature and based solely on Amgen's misrepresentations. Amgen's motion completely glosses over the sensitive nature of Roche's proprietary cell lines and fails to appropriately address the risks associated with the production of microscopic living materials. Amgen also asserts the relevance of the production to the limitations of the '349 patent but never once explains how the measurements of the EPO production levels described in those limitations will be extracted from Roche's cells. The Court should consider Roche's new evidence and arguments contradicting Amgen's obfuscations and oversimplifications before granting the drastic discovery Amgen seeks.

Additionally, the Court has not heard Roche's proposed compromise measures which would at least provide for reasonable restrictions on the use of Roche's cell lines should the cells be produced. (See Attached Proposed Order). Without these proposed measures before it, the Court ordered production of Roche's cell line subject only to the general Protective Order in this

case, which due to the dynamic nature of living cells cannot provide adequate protection to Roche's cell line.

Reconsideration is also justified where the initial decision would work a manifest injustice. *Christianson v. Colt Indus. Operating Corp.*, 486 U.S. 800, 817, (1988); *Greene v. Union Mountain Life Ins. Co.*, 764 F.2d 19, 22-24 (1st Cir 1985) (ability to grant reconsideration of a non-final judgment derives from "the inherent power of the rendering district court to afford such relief from interlocutory judgments . . . as justice requires."**)**. Roche respectfully submits that this is just such an instance. Ordering production of Roche's proprietary cells without allowing Roche to be heard on the importance and secrecy of its cell line and the fallacies in Amgen's claimed justification for production of the cell line disserves the fairness of the discovery process. Roche should at least be given the opportunity to rebut these arguments before it is made to hand over its trade secrets to a competitor. In light of the extremely confidential nature of the materials at stake and Amgen's spurious and misleading arguments supporting its motion to compel, the Court's Order substantially prejudices Roche both in terms of this litigation and its business interests. Therefore, the interests of justice warrant reconsideration to allow Roche a fair hearing to protect its intellectual property and preserve its arguments in this case.

Moreover, entry of an order requiring Roche to produce its trade secrets without a hearing on the issue impinges upon Roche's due process rights. Trade secrets are held to be property that is afforded constitutional protection. *Ruckelshaus v. Monsanto Co.*, 467 US 986, 1003-04 (1984) ("To the extent that Monsanto has an interest in its health, safety, and environmental data cognizable as a trade-secret property right under [state] law, that property right is protected by the Taking Clause of the Fifth Amendment."). Entry of an order adverse to

a party before the party may be heard on an issue does not accord with that party's constitutionally guaranteed due process rights. *See Jenkins ex rel. Jenkins v. Mo.*, 216 F.3d 720, 726 (8th Cir 2000) ("procedural niceties equate with due process and must be afforded the parties. ... The parties are entitled to notice and an opportunity to prepare for a unitary status hearing"). Thus, due process weighs in favor of reconsideration of the Order so that the Court may hear Roche's arguments on the matter.

III. AMGEN HAS NOT ESTABLISHED A COMPELLING NEED FOR ROCHE'S PROPRIETARY CELL LINES

Amgen seeks access to Roche's secret and proprietary DN2-3(α)3 cell line used to create the MIRCERA™ starting material, which was painstakingly developed through countless man-hours and millions of dollars. (See Attached Franze Decl. at ¶ 9). Should these cells fall into the hands of a competitor, competitive and financial harm to Roche is virtually inevitable. The cell line that Amgen seeks is the same cell line that Roche currently uses to supply its EPO drug to Europe. Unlike the United States, where Amgen has maintained a more than twenty year stranglehold on the EPO market, in Europe, numerous companies, including Amgen, its licensee Johnson & Johnson, and generic competitors are jockeying for market position. Roche's established cell-line, generating commercial quantities of EPO, would be an invaluable piece of proprietary information for any of Roche's competitors, including Amgen. Even Amgen acknowledges that the materials it seeks to discover by this motion are trade secrets (Amgen Memo. at 7). As such, the burden shifts to Amgen "to establish that the requested information is relevant and necessary to the cause of action." *Coca Cola Bottling Co. v. Coca Cola Co.*, 107 F.R.D. 288, 293 (D.Del 1985); *Centurion Industries Inc. v. Warren Steurer and Assocs.* 665 F.2d 323, 325 (10th Cir. 1981).

Conspicuously absent from Amgen's motion is any explanation as to why the only information that Amgen asserts that Roche's proprietary cell line is needed for, i.e., production levels, cannot be derived from Roche's BLA or other Roche documents. Roche's entire Biologics License Application ("BLA") for MIRCERA™ has been in Amgen's hands for more than six months. ITC-R-BLA-00000001-00122307. Within the BLA is The Chemistry, Manufacturing, and Control ("CMC") chapter containing a section entitled "Drug Substance – EPO Starting Material." ITC-R-BLA-00004651-00006253. This section gives complete information regarding the fermentation, purification and characterization processes used to create this starting material. For example, the section provides both the concentration and the weight of starting material harvested from each of 81 separate production batches, together with values for the viable cell density and harvest volume. ITC-R-BLA-00005200-00005211. In addition, the section provides results of biological assays that establish the specific *in vivo* biological activity of starting material obtained from each of 38 individual production batches. ITC-R-BLA-00005792-00005793. Amgen has produced no evidence that the production levels of Roche's cell line cannot be derived from this document.

Moreover, to the extent that Amgen may contend that Roche's BLA is insufficient, this Court has ordered Roche to produce documents responsive to the following Amgen document requests, by or before January 29, 2007:

> 1. Documents sufficient to show for each cell line used to produce "the EPO component of peg-EPO" the amount of EPO produced in culture over 24 hours as measured by RIA. See Amgen Request No. 14.
>
> 2. "Documents sufficient to show each cell line considered, evaluated and/or used by Roche to produce the EPO component of peg-EPO." Amgen Request No. 16.

Amgen's assertion that Roche has not yet produced any documents regarding its cell line is demonstrably false in light of Roche's production of its BLA. (Amgen Memo. at 1, 6). It is further disingenuous since Amgen is fully aware that Roche has been ordered to produce documents responsive to the above requests. Specifically, Roche will produce, among other responsive documents, the regulatory document filed in connection with gaining approval for Roche's EPO product marketed in Europe. Roche uses the same EPO that is the subject of that application filed with the European Medicines Agency ("EMEA"), as a starting material to synthesize MIRCERA™. That document, particularly relevant pages of which were produced today, provides the specific EPO productivity of Roche's cell line, harvested over various generation cycles, calculated to ug EPO/10^6 cells per day. In addition to providing specific values, specific EPO productivity in ug/10^6 cells /day against the number of generation cycles is graphically depicted. Those documents indisputably provide all of the information regarding the source, structure, growth conditions and production levels of Roche's cell line needed by Amgen.

Amgen's unfettered access to Roche's regulatory filings obviates any need to give Amgen access to Roche's proprietary cell line. The court's reasoning in *Friction Division Products, Inc. v. E.I. Dupont De Nemours & Co.*, 658 F. Supp. 998, 1006 (D. Del. 1987) is applicable. There, in denying discovery of "more specific technical information" regarding an allegedly infringing product, including chemical compositions that were "vital, major trade secrets" the court noted:

> "[t]he harm in disclosing such trade secrets would be the ability of technical representatives of . . . any other company which obtains the information to use the compositions and processes without identifying the source and thereby reap the benefits and profits that rightfully belong to Carlisle. Moreover, because of the

> difficulty in analyzing frictional products, it would be impossible for Carlisle to determine if their proprietary information was being used by others.[1]

Amgen's reliance on TKT's production of its cell line in the *Amgen v. HMR/TKT* litigation to justify production here is misleading and inapt. There, in the context of a summary judgment hearing, TKT attacked Amgen's evidence regarding the production levels of TKT's cell line as being insufficient. Implicitly acknowledging that it had produced no documentary evidence that could adequately address the issue, TKT *agreed* without protest to produce its cell line in order to refute the contentions of Amgen's expert. (See Exh. A to the accompanying Declaration of Patricia A. Carson ("Carson Decl."), December 15, 1999 Hearing Transcript from *Amgen v. Hoechst Marion Roussel, Inc. et al.*, Civil No. 97-10814-WGY). Moreover, at the time, since TKT had no approved EPO product, the cell line in question was not an established commercial cell line. Here, Amgen is seeking access to the very cell line that Roche uses to produce its product that competes with Amgen's products in Europe.

IV. AMGEN'S MOTIVATION IN SEEKING ROCHE'S CELL LINE IS SUSPECT

In light of the substantial documentary evidence regarding Roche's cell line that Amgen will receive through discovery, Amgen's true purpose in filing its motion is questionable. In the course of the parties' negotiations regarding Roche's responses to Amgen's First Set of Requests to Admit, Amgen offered to withdraw its request *provided* Roche admitted to Amgen's request No. 21, reading as follows:

> DN2-3α3 cells are capable upon growth in culture of producing EPO in the medium of their growth in excess of 100U of erythropoietin per 10^6 cells in 48 hours as determined by radioimmunoassay.

(Carson Decl., Exh. B, Letter dated Jan. 5, 2007 from Fishman to Carson).

[1] This District of Massachusetts also made a similar denial of discovery with respect to another non-party's technical composition trade secrets, which was affirmed by the Federal Circuit, reported at *Friction Division Products, Inc. v. E.I. DuPont de Nemours & Co., Inc.*, 795 F.2d 1019 (Fed. Cir. 1986).

In that Roche's paramount concern is protecting its proprietary cell line and ensuring that it does not fall into the hands of its competitors, Roche was willing to consider this heavy-handed "compromise". Consultation with scientific experts, however, raised questions as to how "capable upon growth in culture of producing EPO in the medium of their growth in excess of 100U of erythropoietin per 10^6 cells in 48 hours as determined by radioimmunoassay" would be properly measured.

Specifically, claim 7 of the '349 patent, alternatively dependent on claims 1-6, requires a minimum output of EPO "U" (or "units") as measured by radioimmunoassay ("RIA"). RIA is used to measure amounts of protein, while units are a measure of activity. Nowhere in the patent specification is a "unit" defined. The specification notes that RIA measures "units" of EPO based on a standard, but this standard is never disclosed. (Carson Decl., Exh. C, '349 Patent, col. 16, ln. 45 - col. 17, ln.7). Neither Roche nor this Court can understand Amgen's request without an explanation as to how the claim limitation is properly measured.

In light of this ambiguity, Roche informed Amgen that it could not admit nor deny Amgen's request, but left open the potential for a further response if Amgen provided additional guidance. (Carson Decl., Exh. D, Letter dated Jan. 8 from Carson to Fishman). Amgen responded by filing this motion.

Undoubtedly, Amgen knows how it plans to test Roche's proprietary cell line to determine whether it meets the production levels of the '349 patent claims. Amgen must explain this test to Roche so that Roche will at least know what must be admitted in an effort to avoid being coerced to give its proprietary cell line to a key competitor. While any such admission will necessarily be premised on assurances that Amgen will not resurrect its cell line request in the future and reserve Roche's right attack the '349 claims on various grounds under

35 U.S.C. § 112, based on Amgen's previous representations, such an admission may render this motion to compel moot.

At minimum, even if Amgen's motion is granted upon reconsideration, Amgen should be compelled to provide the details regarding any and all tests that it plans to perform on Roche's cell line. Granting Amgen free reign to perform tests on Roche's proprietary cell line without explanation or justification will both threaten the secrecy of the cell line and substantially prejudice Roche in this litigation. Without understanding of the tests to be performed, particularly with respect to the '349 claims, Roche will be deprived of any means to contradict or defend the test results.

V. ACCESS TO ROCHE'S PROPRIETARY CELL LINE MUST BE CONTINGENT ON HEIGHTENED SECURITY PROVISIONS

In the event that this Court is inclined to give Amgen access to Roche's proprietary cell line, it must be under conditions far more stringent than pursuant to the general Protective Order in this case. Given the microscopic and self-propagating nature of cells, misappropriation of this material is difficult if not impossible to control and/or detect. (Franze Declaration at ¶ 10). These facts, together with the extreme value and proprietary nature of Roche's cell line mandate that any production must be under strict security provisions tailored to protect this type of material.

Under FRCP 26(C)7 Courts use a sliding scale to provide protection for such highly confidential material that takes into account the proprietary nature of the material and the commercial relationship of the parties. *See Ares-Serono, Inc. v. Organon Int'l B.V.*, 151 F.R.D. 215, 220 (D. Mass 1993). Here, Amgen seeks to physically possess the microscopic means of production of not only the MIRCERA™ starting material, but also the NeoRecormon product, which is not at issue in this case and is sold outside the U.S. in direct competition with Amgen's

products that stimulate erythropoiesis ("ESA's"). Moreover, in Europe the competitive situation is considerably different since Amgen's patents have no effect there and generic companies compete with ESA products. Thus, the danger of exposing Roche's proprietary cell line is enhanced.

Given the nature of the material, any protective order cannot fully protect Roche's trade secret. In the hands of a competitor, the incentives to defy the protective order are great, while Roche has virtually no means of effectively policing the order. Amgen or any other Roche competitor could easily misappropriate Roche's cell line to derive a commercial advantage in the European ESA market. Therefore, if this Court is still inclined to grant Amgen's request for Roche's proprietary cell line, Roche respectfully requests that the Court order production pursuant to the security measures as set forth in the proposed order submitted herewith. These restrictions *inter alia*, provide for testing only by an approved third party expert, place strict limits on access by outside counsel and clearly define how the cell-line is to be stored and handled.

Even with all the restrictions proposed by Roche in place, it is indisputable that Amgen has little incentive to be as diligent in guaranteeing the security of Roche's cell line as its owner. Therefore, Roche respectfully requests that if Amgen's request is not denied upon reconsideration of its Order, this Court defer its decision until Amgen receives further documents responsive to Amgen's requests 14 and 15. The most unjust result of this disposition would be to order Roche to compromise the confidentiality of their cell lines, risking great competitive and economic risk, before it is clear that production of Roche's cell line is warranted.

VI. CONCLUSION

For the foregoing reasons, Roche requests that the Court grant reconsideration of its January 22, 2007 Order and deny Amgen's motion to compel production, as Amgen has failed to demonstrate sufficient need for Roche's proprietary cell lines, and the motion is premature pending document discovery.

Dated: January 22, 2007

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CERTIFICATE OF SERVICE

I hereby certify that this document filed through the ECF system will be sent electronically on the above-referenced date 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 January 23, 2007.

/s/ Keith E. Toms
Keith E. Toms