UNITED STATES DISTRICT COURT
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.: 1:05-cv-12237 WGY

PLAINTIFF AMGEN INC.'S OPPOSITION TO ROCHE'S MOTION IN LIMINE TO PRECLUDE AMGEN FROM PRESENTING EVIDENCE REGARDING (1) A 1993 SETTLEMENT AGREEMENT BETWEEN GENETICS INSTITUTE AND (2) A 1989 DECISION THAT GENETICS INSTITUTE USED CELLS THAT INFRINGED THE '008 PATENT

I. INTRODUCTION

Roche attempts to preclude Amgen from introducing as evidence this Court's 1989 decision in *Genetics Institute*, the essential factual findings of that decision, and the 1993 Settlement Agreement under the guise that Roche will be prejudiced. However, Roche is simply trying to relitigate issues and facts decided in prior adjudications against three entities which Roche is now in privity with: Roche's subsidiaries, Chugai Pharmaceutical Co., Ltd. ("Chugai") and Boehringer Mannheim GmBH ("Boehringer"), and its licensor, Genetics Institute ("GI"). This Court, the Federal Circuit, the Patent Office Board of Patent Appeals and Interferences ("Board") and the District of Delaware have heard these issues against the Roche-related entities. Roche's interrogatory responses and Roche's expert reports indicate that Roche wants to retry these findings and admissions of validity. For these reasons, Amgen has moved this court to collaterally estop Roche from introducing such evidence at trial.[1]

Roche cannot disturb the prior findings and admissions because it is the owner or successor-in-interest to all three of the joint venture partners who contested these earlier litigations. A Roche entity, merged with Chugai, and Roche became its majority stakeholder. Thus, Roche is bound to this Court's 1989 decision as Chugai is bound. Roche is also bound to the 1989 decision because Roche's subsidiary Boehringer Mannheim (GI's joint venture partner) is also bound by it. Boehringer entered into a joint venture with GI to develop and commercialize EPO. The actions of one acting on behalf of the joint venture binds the other joint venture partners.[2] Thus, Boehringer was bound to the 1989 decision against its joint venture partner GI and to the terms of the 1993 settlement agreement as well. Of course, Roche uses the EPO cell-line it licensed from GI to make peg-EPO.

[1] Amgen Motion In Limine No. 17, Docket No. 876.

[2] *See Adams v. NVR Homes, Inc.*, 193 F.R.D. 257, 261 (D. Md. 2000) ("Because all partners are jointly liable for all debts and obligations of a partnership, members of a joint venture are jointly liable for all obligations undertaken by the venture, and the actions of the joint venture bind the individual partners.")

Moreover, although claiming prejudice, Roche has not provided any reasons why it would be unfairly prejudiced. Accordingly, the Court should deny Roche's motion in its entirety.

II. ARGUMENT

A. ROCHE SEEKS TO EXCLUDE THIS COURT'S 1989 DECISION FROM THE JURY SO IT CAN WASTE JUDICIAL RESOURCES AND THE JUROR'S TIME TO RELITIGATE THE ADJUDICATED ISSUE THAT DR. LIN'S EPO DNA SEQUENCE WAS NON-OBVIOUS AND THOSE ESSENTIAL FACTUAL FINDINGS

Amgen's Motion In Limine No. 17 (Docket No. 876) sets forth in detail the relationships of GI's, Boehringer GmBH, Chugai, and Roche.[3] In essence, Roche subsumed the joint venture by merging with Chugai, buying Boehringer, and licensing EPO from GI. Thus, it is bound by the 1993 Settlement Agreement, by this Court's 1989 decision that Dr. Lin's EPO sequence was not obvious, and the following factual findings essential to this Court's decision:

- "The unique probing and screening method employed by Dr. Lin in isolating the EPO gene was what distinguished the invention from the prior art." *Amgen*, 13 USPQ 2d at 1767.
- Amgen relied on "Dr Lin's use of two sets of 128 mixed probes to jointly probe the human genomic library, which previously has been announced as an 'impractical method' for isolating mammalian protein genes." *Id.*
- There was not a "'reasonable expectation of success' in cloning the EPO gene based on this probing strategy." *Id.*
- "No one had successfully screened a genomic library using fully degenerate probes of such high redundancy as the probes used by Dr. Lin." *Id.* at 1768.
- "Biogen did not begin to use the genomic library in screening for the EPO gene until the end of 1983 or the beginning of 1984, *after* Dr. Lin had already succeeded in cloning the gene." *Id.*
- "None of these prior art references suggests that the probing strategy of using two fully redundant set of probes, of relatively high degeneracy, to screen a human genomic library would be likely to succeed in pulling out the gene of interest." *Id.*
- To construct a cDNA library, "the tissue source for a given gene must be known." *Id*. at 1743.
- In 1981, there was no known tissue source available for EPO. *Id.* at 1750.

[3] *See* Docket No. 877.

- "Isolation of the monkey cDNA occurred based on Dr. Lin's successful isolation of the EPO gene from the human genomic library using nonobvious procedures." *Id.* at 1769.

These above essential findings of fact were first raised in Amgen's Motion In Limine No. 17. Roche did not challenge that the above factual findings were essential to this Court's ruling that Dr. Lin's EPO DNA sequence was not obvious. Instead, Roche claims that the Settlement Agreement, the prior adjudication and essential findings are not relevant to the invalidity phase of the upcoming trial. That is not the case. Roche's strategy belies its representation to the Court. Roche's challenge of the validity of the patents-in-suit necessarily disturbs the prior adjudications and the Court's essential findings of fact.

Roche intends to offer evidence at trial that the isolated DNA sequence for human erythropoietin claimed in the expired '008 Patent is obvious under the prior art.[4] Specifically, Roche intends to assert that the probing and the cloning of the EPO DNA from a cDNA library would have been obvious to one of ordinary skill in the art in 1983, rendering the isolated EPO DNA sequence that was patented in claim 2 of the '008 Patent obvious. (Docket No. 878-31.)

Roche's interrogatory responses stated:

- "*Prior to October 1983 it would have been obvious for the skilled practitioner* with access to sufficient quantities of purified human EPO to construct a cDNA library from one of several EPO producing human cell lines and *to isolate a human EPO cDNA* by screening such a library with the appropriate oligonucleotide probe based on knowledge of the partial amino acid sequence. *Using techniques known in the art and described in the available literature, the skilled practitioner would have had a reasonable expectation of success in obtaining a cDNA clone encoding EPO*." (Ex. 28 at 43 (emphasis added).)[5]

- "Provided one skilled in the art had a sufficient amount of hEPO protein, one would have had a reasonable expectation of success in isolating cDNA clones for EPO using degenerate oligonucleotide probe screening." (*Id*. at 44.)

[4] Docket No.878-28 – 878-30 (Fifth Supplemental Responses to First Set of Interrogatories to Defendants); Docket No. 878-9 -878-11 (Lowe Expert Report, Spinowitz Supplemental report).

[5] Furthermore, Roche's Interrogatory Responses and Roche's Statement of Contested Issues of Fact (Docket No. 807-B) shows that Roche intends to challenge at trial the prior finding that Dr. Lin's EPO DNA sequence was non-obvious by arguing that Dr. Lin's invention is obvious under 35 U.S.C. §103 in view of § 102(f) prior art. (Docket No. 807-B at 3.) Such an argument necessarily disturbs the prior adjudication that Dr. Lin's EPO DNA sequence was non-obvious, including the argument that had Dr. Goldwasser made his "purified EPO protein or tryptic fragment, available to the public, the Lin Patents would have been obvious." Roche should be collaterally estopped from making such an argument to the jury.

Roche served expert reports with similar statements. For example, Dr. Lowe, who will be Roche's first witness, has opinions in three of his four expert reports regarding the alleged obviousness of Dr. Lin's inventions in the '008 Patent. (Docket No. 878-29, First Lowe report.) For example, Dr. Lowe opined:

- "As described below, *prior to October 1983 it would have been obvious for the skilled practitioner with access to sufficient quantities of purified human EPO* to construct a cDNA library from one of several EPO producing human cell lines and to isolate a human cDNA by screening such a library with an appropriate oligonucleotide probe based on the partial DNA sequence of the protein. Using techniques known in the art and described in the available literature, *the skilled practitioner would have had a reasonable expectation of success in obtaining a cDNA clone encoding EPO.*" (*Id.* at ¶30.)

Moreover, Dr. Lowe's testimony that cloning EPO using the genomic library is obvious directly contradicts the findings of fact and law in the prior adjudications. Roche is trying to relitigate the issue. Dr. Lowe testified:

> Q. Dr. Lowe, are you offering any opinion in this case that it would have been obvious in 1983 to clone the EPO gene from a genomic library?
>
> A. Yeah, let me look at my expert report to make sure, to address that with certainty. I think that my report indicates that overall it would be obvious based on prior art and so on to clone a genomic fragment of the human EPO gene.
>
> Q To clone the DNA encoding EPO from a genomic library?
>
> A Yeah.

(Docket No.878-37, Lowe 6/25/07 Dep. Tr. at 198:14-25.) Further, Dr. Spinowitz offered similar opinions in his Supplemental Report:

- "As demonstrated in the April 6, 2007 Expert Reports of Dr. John Lowe and Dr. Rodney Kellems, one of skill in the art as of the *time of the application* of the patents-in-suit *would have found it obvious to create a DNA clone encoding human erythropoietin* and express such a cDNA in a mammalian host cell, such as a CHO cell." (Docket No. 878-30, Supplemental Report of Spinowitz dated 5/1/07 at ¶ 36 (emphasis added).)

Simply stated, Roche intends to make the same arguments that the GI-Chugai-Boehringer joint venture lost many years ago, namely that the erythropoietin DNA sequence cloned many years ago by Dr. Lin was obvious. Roche fails to explain why the Court's decision would be highly prejudicial.

B. ROCHE HAS COMPLETELY SUBSUMED THE OWNERSHIP OR INTERESTS OF EACH OF THE THREE JOINT VENTURE PARTNERS

1. Roche Merged With Chugai and Owns a Majority Stake

Roche is bound by the 1993 settlement agreement, this Court's 1989 decision and essential finding of facts under the doctrine of collateral estoppel because Chugai, in which Roche is a majority stakeholder, is bound by it.[6] In 2002, Roche's chairman of the board, described this merger as exploiting and combining Chugai's epogin assets with Roche's own pre-existing epo assets:

> Thanks to NeoRecormon (Roche) and Epogin (Chugai) we now control the global marketing rights to epoetin beta, a major anemia treatment, outside the United States. The smooth and seamless integration of Chugai in Japan will be of great importance for the future growth of our pharmaceutical business.

(Gaede Decl., Ex. 2.) In 2002, a Roche subsidiary merged with Chugai, giving Roche a 50.1% ownership. (*Id*.) Roche attempts to avoid collateral estoppel by claiming that none of the Roche defendants-in-suit bought the 50.1% stake in Chugai and it acquired Chugai by a separate corporate place holder, "Roche Pharmholding B.V., a Dutch affiliate of Roche Holding, Ltd., Switzerland, neither of which is a party to this case." (Roche Memo at 2.) Roche offers no evidence to support this assertion. Moreover, a press release issued by name Defendant, F. Hoffman-La Roche Ltd makes no mention that the acquisition was made by Roche Pharmholding B.V. Instead, F. Hoffman-La Roche's press release announced to the public that "Roche Group will become a majority shareholder with 50.1% interest in the new enterprise to be known as "Chugai, a member of the Roche Group." (Gaede Decl., Ex. 1 at 1.) The press release follows the fact of Roche's claims in its annual report that Roche owns and controls Chugai. The objective evidence indicates that F. Hoffman-La Roche was the entity controlling the Chugai acquisition, and used a Dutch corporation for convenience.[7]

[6] Amgen's Motion In Limine No. 17 provides the full analysis as to why Roche is bound by the 1993 Settlement Agreement.

[7] Even were it the case that a non-party Roche entity acquired Chugai, the F. Hoffman-La Roche press release clearly evidences that the entities do not operate separately as the entity that

Roche seeks to modify the Court's judgment that the "'008 Patent was duly and legally issued . . . was valid and enforceable in law and equity" by arguing that the Settlement Agreement limits the reach of a Court order. (Roche Memo at 2.) Roche offers no support that a settlement agreement can modify the scope of a court's later judgment. Moreover, Roche's view that GI and Chugai executed the Settlement Agreement without admitting to the validity of the '008 Patent is misplaced because Roche fails to quote the 1993 Settlement Agreement in its entirety. GI and Chugai explicitly admitted to the validity of the '008 patent. The 1993 Settlement Agreement stated that:

> This Settlement Agreement and its attachments hereto constitute a single, integrated written contract expressing the entire agreement of the parties and shall not be modified except by a writing signed by each of them.

(Docket No. 878-1 at 10; Ex. A, attached to the 1993 Settlement Agreement, included language admitting to the validity of the '008 Patent) ("The '008 Patent was duly and legally issued, is valid and enforceable in law and equity.").)

Roche claims that the '008 Patent has no bearing to the issues in this case. This is wrong. As explained above, Roche's interrogatory responses and Roche's experts clearly show that Roche wants to relitigate the issue of whether Dr. Lin's EPO DNA sequence was obvious and facts about the probing and cloning from DNA libraries as part of its strategy to challenge the validity of the patents-in-suit. Aside from its conclusory assertion, Roche does not offer any explanation why introduction of the 1993 settlement agreement is prejudicial. Accordingly, Roche has not met its burden and its motion should be denied.

announced the press release was the Roche Group, not some other place holder. Further, the press release does not identify the Roche entity and thus strongly evidences that the Roche entities are not separate from one another. Instead they are members of a collective group, acting more like divisions within a corporation. This is best exemplified by Roche's description of itself, "Headquartered in Basel, Switzerland, Roche is one of the world's leading research-oriented healthcare groups in the fields of pharmaceuticals, diagnostics and vitamins. Roche's innovative products and services address prevention, diagnosis and treatment of diseases, thus enhancing people's well being and quality of life."

2. Roche Is Bound by the 1993 Settlement Agreement and This Court's 1989 Decision Because Defendant Roche Diagnostics GmBH Acquired Boehringer, Which Was Bound Because of Its Joint Venture With GI

Roche seeks to avoid the equitable reach of collateral estoppel by arguing that Roche was not a party to the case and "does not have (and never has had) any corporate relationship with GI." Roche admitted that named Defendant Roche Diagnostics GmbH acquired Boehringer in 1997.[8] Boehringer entered into a joint venture with GI in 1985. (Docket No. 877 at 17-18).

In October 8, 1985, GI and Boehringer described their relationship as:

> BM desires that ***GI, on behalf of and in collaboration with BM***, undertake a research and development project utilizing recombinant DNA technology for producing erythropoietin on a commercially feasible basis for use in humans. In return for certain rights under the patents and Know-how developed by GI, BM will financially support the research and development activities of GI and will pay GI the royalties provided for herein.
>
> GI and BM recognize that there exist third party patent positions of uncertain validity and applicability covering the production of recombinant erythropoietin as well as generic process steps. ***GI and BM are willing to share the risks*** that the project herein undertaken herein may be held to infringe one or more of these patent positions (in accordance with the terms of this Agreement).

(Docket No. 878-8 at AM-ITC 00119897.) The 1985 Agreement also stated that the parties would jointly own the intellectual property rights of technology jointly developed. (Ex. 8 at AM-ITC 00119905.)[9]

A 1985 GI report to its stockholders characterized the BM relationship in the following fashion:

> In human healthcare, European and South American rights to erythropoietin were licensed to Boehringer Mannheim. Under this agreement Genetics Institute will be responsible for developing a commercial process for EPO and also has the right to manufacture a substantial portion of Boehringer Mannheim's clinical trial and eventual commercial product requirements. Boehringer will be responsible

[8] Roche's Opp. To Amgen's Motion *In Limine* No. 17, Docket No. 904 at 3.

[9] Roche has argued that Boehringer did not enter into a joint venture with GI because the governing law section of the 1985 agreement indicates that Swiss law applies. The governing law section read properly addressed disputes between GI and Boehringer as it relates to the agreement. Moreover, joint venture does not require an explicit agreement. Under Massachusetts law, GI's activities with Boehringer for the research, development, and commercialization of EPO, strongly evidences the formation of a joint venture. (See Docket No. 877 at 17-18, *Petricca Development Limited Partnership v. Pioneer Development Co.,* 40 F. Supp. 2d 49, 53 (D. Mass. 1999).

> for the conduct of human clinical trials and eventual product marketing and distribution.

(Docket No. 878-9 at AM-ITC 00445791.)

Boehringer was actively involved in the litigation. Correspondence between GI and Boehringer concerning the Amgen suits shows Boehringer's heavy involvement. For example, a representative from Boehringer told GI in a letter dated July 2, 1991 that:

> We believe that we have not only worked cooperatively together in the past few months in initiating the serum free project and in responding to the patent situation, but it is ***our joint responsibility*** to even work closely ***to fight the Amgen club*** in every direction which seems reasonable and possible. (*See* Docket No. 878-12 at AM-ITC 00789764 (quoting Letter from Daum and Schuster of BMG to Leicher of GI dated July 2, 1991) (emphasis added) (Bundle 4, Tab 17, p. 274).)

Ultimately, GI settled the case in 1993 with Boehringer's approval. GI's development agreement with Boehringer required Boehringer's approval of any settlement related to the joint venture.[10] (Docket No. 878-14 at AM-ITC 00119908; Docket No. 878-18 at AM-ITC 00815935.) Accordingly, GI's admission of the validity of the EPO DNA sequence and the findings form the prior adjudications binds Boehringer. Since Roche merged with Boehringer, all Roche defendants too must be bound. *See Adams v. NVR Homes, Inc.*, 193 F.R.D. 257, 261 (D. Md. 2000) ("Because all partners are jointly liable for all debts and obligations of a partnership, members of a joint venture are jointly liable for all obligations undertaken by the venture, and the actions of the joint venture bind the individual partners."); *Hodges v. El Torito Restaurants*, No.C-96-2242,1998 U.S. Dist. LEXIS 11517, at *11 ("companies assume the liabilities of other

[10] Under Massachusetts law, a joint venture formed between GI and Boehringer. Massachusetts law considers the following factors in determining whether a joint venture exists:

> (1) an agreement by the parties manifesting their intention to associate for joint profit not amounting to a partnership or a corporation; (2) a contribution of money, property, effort, skill, or other assets to a common undertaking; (3) a joint property interests in all or parts of the subject matter of the joint venture; (4) a right to participate in the control or management of the enterprise; (5) an expectation of profit; (6) a right to share in the profit; (7) an express or implied duty to share in the losses; and (8) a limitation to a single undertaking (or possibly a small number of enterprises).

Petricca Development Limited Partnership v. Pioneer Development Co., 40 F. Supp. 2d 49, 53 (D. Mass. 1999); *see also* Docket No. 877 at 17-18.

companies they acquire"); *Okaw Drainage Dist. v. Nat'l Distillers & Chem. Corp.*, 739 F. Supp. 459, 461 (C.D. Ill. 1990). Moreover, Roche Diagnostics uses the EPO that Boehringer gained access to as a result of the Boehringer-GI 1985 Agreement in making CERA.[11] Roche has paid over $100 million to GI. (Docket No. 877 at 17.)

Roche's reliance on *Ecolab, Inc. v. Paraclipse, Inc.*, 285 F.3d 1362, 1376 (Fed. Cir. 2002) is not relevant to the issue of collateral estoppel.[12] *Ecolab* addressed the issue of whether res judicata applied to a party. Moreover, unlike *Ecolab*, the issues have been fully and fairly litigated, with decisions from the Board of Interference, a trial and adjudication with this Court, and a Federal Circuit decision. Thus, *Ecolab* is not germane to the issue in Roche's motion.

Similarly, Roche's reliance on res judicata cases to argue why it is not collaterally estopped from challenging the 1993 Settlement Agreement, the 1989 adjudication, and essential findings of fact should be given very little weight. Collateral estoppel and res judicata involve similar but distinct enough concepts. For example, Roche sought to attack Amgen's virtual representation analysis under the doctrine of collateral estoppel by citing *to Gonzalez v. Banco Central Corp.*, 27 F.3d 751 (1st Cir. 1994). *Gonzalez* addressed the issue of whether the district court's res judicata bar was in error. Amgen is asserting collateral estoppel. (*See* Amgen Motion In Limine No. 17, Docket No. 877.) Accordingly, Roche's reliance on res judicata cases is misplaced.

III. CONCLUSION

For the foregoing above reasons, Roche's motion should be denied.

[11] Roche again claims that the '008 Patent is not at issue here. As explained earlier, Roche is attempting to relitigate this Court's determination that Dr. Lin's EPO DNA sequence was non-obvious and the essential factual findings. Roche also argues that the prior finding that GI infringed Dr. Lin's '008 Patent is not relevant because it involved host cell claims which are not at issue. But the prior findings are relevant to this case to determine the merits of Roche's material change argument under 271(g)(1).

[12] Roche cited to *Ecolab* in its opposition to Amgen's motion *in limine* no. 17 as supporting its position that contractual estoppel does not apply.

DATED: September 4 2007

Respectfully Submitted,

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