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 ***REDACTED PUBLIC VERSION***

PLAINTIFF AMGEN INC.'S BRIEF IN SUPPORT OF ITS MOTION *IN LIMINE* NO. 17 TO EXCLUDE ROCHE FROM PRESENTING EVIDENCE TO CHALLENGE THE NON-OBVIOUSNESS OF THE DNA SEQUENCE ENCODING FOR HUMAN ERYTHROPOIETIN IN 1983

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I. INTRODUCTION

Amgen moves to exclude the three Roche Defendants (collective "Roche") from tainting the jury with evidence to challenge the non-obviousness of the DNA sequence encoding for human erythropoietin in 1983. That issue, and validity in general, of patent claims directed to the isolated DNA sequence for human erythropoietin were litigated years ago and decided against Roche's subsidiary, Chugai Pharmaceutical Co., Ltd. ("Chugai") and Genetics Institute ("GI") by this Court, the Federal Circuit, the Patent Office Board of Patent Appeals and Interferences ("Board") and the District of Delaware. These adjudications collaterally estop Roche from making the same assertions in this proceeding and from relitigating the factual findings essential to the issues decided in these prior adjudications.

For many years, Amgen battled with Chugai and GI concerning the validity of Dr. Lin's first patent (the "'008 Patent"), which was directed to an isolated DNA sequence encoding human erythropoietin. As part of their broad-based invalidity challenges, GI and Chugai expressly challenged the non-obviousness of the DNA sequence, which Dr. Lin cloned in 1983, specifically asserting that it was obvious to clone and isolate the DNA sequence from DNA libraries. This Court in 1989, the Federal Circuit in 1991, and the Board in 1991, all agreed that the DNA sequence and its cloning and isolation was not obvious. Further, on May 12, 1993, Amgen, GI, and Chugai settled the various lawsuits. All parties intended that the settlement agreement "***fully and finally settle and resolve all controversies*** and disputes between them which have been or ***could have been raised*** by either party against the other" in the various lawsuits. (Ex. 1 at AM-ITC 00799255-71.) GI acknowledge in an attachment to the settlement agreement, that ""[t]he '008 patent was duly and legally issued, is ***valid and enforceable*** in law and equity…" (Ex. 1 at AM-ITC 00799267.)[1] Pursuant to the Settlement Agreement, this Court entered a stipulated judgment stating that "[t]he '008 patent was duly and legally issued, is ***valid and enforceable*** in law and equity…" (Ex. 2 at AM44 2024651 (emphasis added).) The

[1] Paragraph 11 of the Settlement Agreement states that "This SETTLEMENT AGREEMENT and its attachment constitute a single, integrated written contract expressing the entire agreement." (Ex. 1 at AM-ITC 00799264).

Delaware Court entered a dismissal with prejudice of GI's claims. Thus, the inventions defined therein of an isolated DNA erythropoietin sequence are valid.

Chugai is now a subsidiary of Roche. Roche acquired Boehringer Mannheim GmBH ("Boehringer"), a licensee and joint venturer of GI. That entity is now known as named defendant Roche Diagnostics GmBH. Roche is in privity with Chugai and GI. Thus, Roche is bound by the prior adjudications and is collaterally estopped from raising any issue, including the underlying factual bases, that the erythropoietin DNA sequence and its cloning was obvious in 1983. Roche's experts intend to so testify, and Roche may attempt to introduce other evidence on this subject. Roche is also excluded from arguing that Dr. Lin's invention was obvious because it was derived from others (35 U.S.C. § 102(f) prior art) otherwise Roche will necessarily be allowed to attack the prior adjudications that Dr. Lin's erythropoietin DNA sequence and its cloning was non-obvious. Amgen requests that this Court exclude Roche from offering any evidence at trial that the DNA sequence directed to human erythropoietin was obvious, including the testimony of Drs. Lowe and Spinowitz that the cloning of the EPO DNA sequence was obvious and that the invention was obvious under § 102(f) prior art.

II. STATEMENT OF FACTS

As detailed below in Section III, Roche should be collaterally estopped to assert that the claims of the '008 Patent were obvious. As explained in that section, one of the requirements for a finding of collateral estoppel in a second litigation is that the party to the second action must be the same as or in privity with the parties in the first action. The facts that follow establish that Roche is in privity with Chugai, GI, and Boehringer, all of whom have challenged the validity of the '008 claims on the ground that they are obvious, and they have lost. Because of Roche's privity with those parties, Roche should now be bound by the prior findings of non-obviousness.

A. THE CHUGAI – GI RELATIONSHIP

On June 29, 1984, GI and Chugai entered into a license agreement under which GI purported to grant Chugai the exclusive right to use GI's technology for the manufacture and sale

of recombinant EPO (rEPO) in the United States.[2] (Ex. 3, AM-ITC 00078873-923 at AM-ITC 0078920; Ex. 4, AM-ITC 00049907.) GI also agreed to research and develop the technology to manufacture EPO, while Chugai worked on the commercialization (clinical tests and regulatory approval) of EPO using GI's technology. (Ex. 3 at AM-ITC 00078906.) The parties recognized that "the timing of the development of rEPO is critically important in light of the competition and the need for early market introduction." (Ex. 5 at AM-ITC 00435824.)

On November 27, 1985, GI and Chugai entered into a second manufacturing agreement to "expedite the market introduction of erythropoietin" by jointly working on a project for the "commercial production processes" of erythropoietin. (Ex. 6 at AM-ITC 00435789) Chugai took an exclusive license of GI's manufacturing patents in the United States. (Ex. 6 at AM-ITC 00435789-93.) Chugai's efforts culminated in the filing of a Product License Application filed with the FDA in September 1988 to obtain approval to sell rEPO in the United States. (Ex. 7 at R10-000061368.)

B. THE BOEHRINGER MANNHEIM - GENETICS INSTITUTE JOINT VENTURE

In the fall of 1984, GI commenced discussions with Boehringer (now Roche) to develop and commercialize EPO in Europe. *Trustees of Columbia University v. Roche Diagnostics GmbH*, 272 F. Supp. 2d 90, 97 (D. Mass. 2002). Europe was a territory excluded from the GI-Chugai License Agreement. *Id*. After months of negotiation, GI and Boehringer reached an agreement on the venture and entered into a Development and License Agreement on October 8, 1985, describing their relationship as follows:

> 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).

[2] Chugai also received the exclusive rights to use GI's technology in Japan, Canada, Mexico, and Asia (except China). (Ex. 3 at AM-ITC 0078920; Ex. 4, AM-ITC 00049907.)

(Ex. 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.)

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

(Ex. 9 at AM-ITC 00445791.)

On January 11, 1988, Boehringer and GI entered into a further agreement concerning the production of EPO. (Ex. 10, AM-ITC 00789541-61.) That same year, Boehringer agreed to supply GI with EPO reformulated in Germany for a study involving Jehovah's Witnesses. (Ex. 11 at AM-ITC 00787113.)

C. THE 1987 AMGEN V. GI/CHUGAI LITIGATION

1. This Court Found, and the Federal Circuit Agreed, that GI/Chugai Failed to Prove Obviousness

On October 27, 1987, Amgen filed suit against Chugai and GI in the District of Massachusetts, alleging that GI infringed Amgen's '008 Patent, and that Chugai, as a result of its collaborative relationship with GI, had induced and/or contributed to GI's direct infringement of the '008 Patent. *Amgen Inc. v. Chugai Pharm. Co., Ltd.*, No. 87-2617-Y, 1989 U.S. Dist. LEXIS 161110, 13 U.S.P.Q. 2d 1737 (D. Mass. 1989) *affirmed in part*, 927 F.2d 1200 (Fed. Cir. 1991). Specifically, Amgen alleged that the defendants making of EPO infringed claim 2, 4 and 6 of the '008 Patent. Claim 2 of the '008 Patent provides:

> 2. A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin.

'008 Patent, col. 40, ll. 1-3. Clam 2 is plainly directed to an isolated DNA sequence that encodes for human erythropoietin. The '008 Patent claimed a priority date of December 13, 1983, and reflected the work of Dr. Lin in cloning and isolating the gene encoding for human erythropoietin in approximately October 1983.

Both GI and Chugai answered and counterclaimed, asserting affirmative defenses of invalidity. These included allegations that claim 2 of the '008 Patent was invalid under 35 U.S.C § 103 ("obviousness") because in 1983, when Dr. Lin cloned the EPO gene, "'*the probing strategies*' used by him had been disclosed in the prior art references and were widely practiced in the biotechnology industry." *Id*. at 1764 (emphasis added). This Court considered in detail Chugai and GI's evidence of the alleged obviousness of the erythropoietin DNA sequence claimed and held that Chugai and GI had failed to prove that claim 2 of the '008 Patent was obvious. More specifically, this Court found that the evidence did not show that there was a reasonable expectation of success in cloning the EPO gene based on the *probing strategy*. *Id*. at 1767 (emphasis added).

This Court found that:

- "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.
- "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.

Amgen, 13 USPQ 2d at 1767-1769. The Federal Circuit did not disturb this Court's findings of fact on appeal. *Amgen*, 327 F.2d at 1200.

Chugai and GI appealed. *Amgen*, 927 F.2d at 1200. On March 5, 1991, the Federal Circuit affirmed this Court's holding that claim 2 of the '008 Patent was valid and nonobvious and rejected Chugai and GI's arguments. *Id*. The Federal Circuit stated, "[w]e agree with the district court's conclusion, which was supported by convincing testimony." *Id*. at 1208. The case was remanded back to this Court on other grounds. *Id*.

2. Boehringer Was Substantively Involved in the Chugai/GI Litigation

Boehringer was substantively involved in this Court's *Amgen v. Chugai* proceeding through its partner GI. Boehringer paid damages of over $5 million for GI when this Court ordered that all profits from GI's sale of EPO be placed into an escrow account.[3] (*See* Ex. 12 at AM-ITC 00789762 (citing Bundle 4, Tab 1 at p. 5).) Moreover, Boehringer was substantially involved in negotiations regarding the amount of damages which GI was going to pay. (Ex. 12 at AM-ITC 00789762, Ex. 13 at AM-ITC 00787126.)

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* Ex. 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).)

Finally, when the suits were ultimately settled by way of a settlement agreement and stipulated judgment, *infra*, GI stated that it required Boehringer's approval before it could be finalized. (Ex. 14 at AM-ITC 00119908.) This requirement was consistent with the terms of the

[3] Boehringer was also very much involved with GI in foreign disputes concerning their joint venture. In an Australian litigation, Boehringer provided Dr. Hasselbeck, now head of Anemia Research for Roche, in a dispute between litigation between Genetics Institute and Kirin-Amgen. (*See* Ex. 15 at AM-ITC 00809294, 00809296.) In UK litigation, Boehringer and GI retained the same law firm to represent their business ventures in a multi party dispute. (Ex. 16 at AM-ITC 00789904; see also Ex. 17, AM-ITC 00790194 (Plaintiffs Boehringer and GI v. Defendant Cilag Limited).)

GI/Boehringer 1985 agreement requiring Boheringer's approval for any settlement of a case. (Ex. 18 at AM-ITC 00815935.)

D. THE FRITSCH ET AL (GI) V. LIN (AMGEN) INTERFERENCE

On June 1, 1989, GI requested an interference between its U.S. Patent Application No. 693,258 ("Fritsch Application") and Dr. Lin's 1987 issued '008 Patent. Months later, on September 6, 1989, GI requested an interference between its Fritsch Application with Lin's U.S. Patent Application No. 113,179, that was directed to processes for making the recombinant erythropoietin. On May 9, 1989 the Board declared Interference Nos. 102,096 and 102,097 and suspended the prosecution of the patent applications before the PTO. (Ex. 19 at AM-ITC 00332532.) GI requested a third interference between its Fritsch Application and Lin's U.S. Patent Application No. 113,178, that was directed to the recombinant erythropoietin. On February 9, 1990, the Board declared Interference No. 102,334.

The '096 interference addressed whether Fritsch, the junior party, was the prior inventor of a "purified and isolated" DNA sequence encoding for erythropoietin (EPO), over Lin, the senior party. (Ex. 20 at AM-ITC 00816003.) In addition to asserting priority, Fritsch argued, like Chugai and GI did previously in the litigation, that Dr. Lin's claims directed to the DNA sequence were unpatentable under 35 U.S.C. § 103 (obviousness) as it would have been obvious to clone the EPO DNA. (*Id*. at AM-ITC 00816004.) Fritsch made the same contentions in the '097 interference. (Ex. 21, AM-ITC 00337751-58.)[4]

On December 3, 1991, following the 1991 Federal Circuit's opinion affirming this Court's decision that claim 2 of the '008 Patent was nonobvious under the DNA probing and cloning prior art, the United States Board of Patent Appeals and Interferences rendered a ruling that the Federal Circuit decision was binding on the issue of obviousness:

> We are bound by the Federal Circuit decision . . . According to the Federal Circuit and district court decisions, at the time of Lin's invention a person of ordinary skill in the field of gene cloning, armed with knowledge available in the prior art, would have found it "obvious to try" to isolate the EPO gene using the probing technique employed by Lin but, in view of a difference of opinion among the experts, the evidence was found to be insufficient to establish that there was a

[4] The '097 interference involved Amgen's '179 Application. Four of the five patents in suit, U.S. Patent Nos. 5,441,868, 5,618,698, 5,756,349, and 5,955,422 issued from continuation applications of the '179 application.

> "reasonable expectation of success" in cloning the EPO gene based on the *probing strategy* disclosed in the prior art. (Ex. 20 at AM-ITC 00816012 (emphasis added).)

The Board adopted this Court's factual findings in deciding that the '008 Patent was not obvious. (Ex. 20 at AM-ITC 00816012-13.) The Board's decision in the '096 interference was never appealed. (Ex. 22 at AM-ITC 00816316.) *See Meritor Transmission Corp. v. Eaton Corp.*, Civil No. 1:04-CV-178, 2006 U.S. Dist. LEXIS 95409 at * 9-*12 (W.D.N.C. Sep. 26, 2006) (Board decision that is final can serve to collaterally estop a party). GI filed an appeal under 35 U.S.C. § 146 to the United States District Court for the District of Delaware on the two other interferences. (Ex. 23; AM-ITC 00816284-89.)

E. CHUGAI AND GI ADMITTED TO THE VALIDITY OF THE '008 PATENT AND ENTRY OF JUDGMENT

On May 12, 1993, almost two years after the Federal Circuit affirmed this Court's holding that the '008 Patent is valid as nonobvious, Chugai and GI entered into a Settlement Agreement with Amgen resolving all pending litigation, and admitting to the validity of the '008 Patent. (Ex. 1, AM-ITC 00799255-71.) Pursuant to the Settlement Agreement, there was an entry of judgment in this Court in which the Court stated that "[t]he '008 Patent was duly and legally issued, is valid and enforceable in law and equity…" (Ex. 2, AM44 2024650-52.) The Section 146 action filed in Delaware was "dismissed with prejudice" and the right to appeal "waive[d]." (Ex. 1 at AM-ITC 00799269).

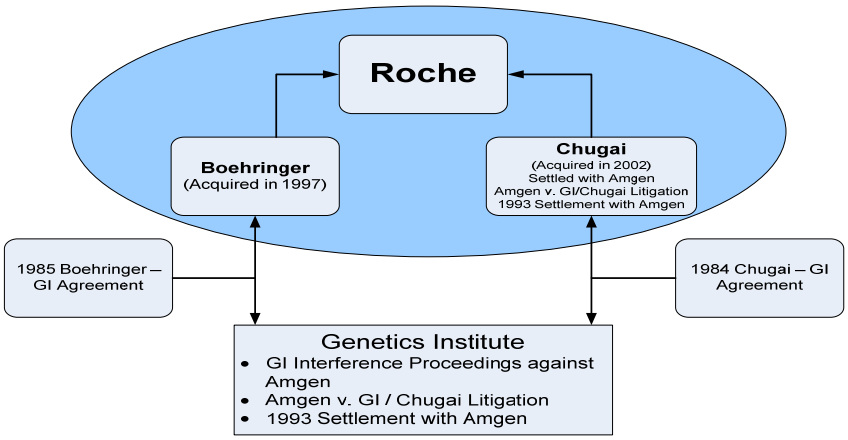
F. ROCHE ACQUIRED BOEHRINGER IN 1997 AND CHUGAI IN 2002

In 1997, Roche acquired Boehringer. (*See* Ex. 24.) Boehringer became Roche Diagnostics GmBH, a named defendant in the present action. *Id.* Roche continued on with the business venture with Genetics Institute and to this day makes EPO in Germany and sells it under the trade name "NeoRecormon." (*See* Ex. 25, Amgen's Opposition to Roche's Mot. To Dismiss For Lack of Personal Jurisdiction at 2.)

On October 1, 2002, Chugai became a member of the "Roche Group." (Ex. 26, R007090626-36) Through the merger, Roche acquired the majority ownership, or 50.1%, of Chugai. In a press release, the companies jointly explained: "Named 'Chugai, a member of the Roche Group,' the new company will be Roche's exclusive pharma representative in Japan and

will have rights to develop and market all pharmaceutical products which the Roche group decides to commercialize in Japan." (Ex. 27.)

Below is a figure summarizing the relationships of Roche, Chugai, and Boehringer in relation with GI.



G. ROCHE INTENDS TO OFFER EVIDENCE THAT THE CLONING OF THE EPO DNA IN 1983 SEQUENCE WAS OBVIOUS

Roche's Fifth Supplemental Responses and Objections to Plaintiff Amgen Inc.'s First Set of Interrogatories to Defendants (Nos. 9-11.) and the expert reports of Drs. Lowe and Spinowitz show that 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. (Exs. 28-30, Fifth Supplemental Responses to First Set of Interrogatories to Defendants (Nos. 9-11).) Lowe Expert Report, Spinowitz Supplemental report.) 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. (Ex. 31, '008 Patent.)

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.)

Roche served expert reports with similar statements. For example, three out of the four expert reports of Dr. Lowe contain opinions regarding the alleged obviousness of Dr. Lin's inventions in the '008 Patent. (Ex. 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*." (Ex. 29 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.

(Ex. 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*

[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." (Ex. 28 at 44). Roche should be collaterally estopped from making such an argument to the jury.

> *human erythropoietin* and express such a cDNA in a mammalian host cell, such as a CHO cell." (Ex.. 30, Supplemental Report of Spinowitz dated 5/1/07 at ¶ 36 (emphasis added).)

Simply stated, Roche intends to make the same argument that Chugai and GI lost many years ago, namely that the erythropoietin DNA sequence cloned many years ago by Dr. Lin was obvious.

III. ROCHE, THROUGH BOTH CHUGAI AND GI, HAD A FULL AND FAIR OPPORTUNITY TO LITIGATE THE VALIDITY OF THE OBVIOUS EPO DNA SEQUENCE, AND SHOULD BE PRECLUDED FROM RE-LITIGATING ITS OBVIOUSNESS BEFORE THIS COURT

Collateral estoppel is a question of law. *Keystone Shipping Co. v. New England Power Co.*, 109 F.3d 46, 49 (1st Cir. 1997). Collateral estoppel prevents relitigation of issues which have been fully and fairly litigated in a prior proceeding. *See Grella v. Salem Five Cent Savs. Bank*, 42 F.3d 26, 30 (1st Cir. 1994). The purpose of the doctrine is to "relieve parties of the cost and vexation of multiple lawsuits, conserve judicial resources, and, by preventing inconsistent decisions, encourage reliance on adjudication." *Allen v. McCurry*, 449 U.S. 90, 94 (1980).

Invalidity is an "issue" for the purposes of collateral estoppel. *See Pall Corp., v. Fisher Scientific Co.*, 962 F. Supp. 210, 213 (D. Mass. 1997); *Applied Med. Resources Corp., v. United States Surgical Corp.*, 352 F. Supp. 2d 1119, 1124 (C.D. Cal. 2005). Once an issue is raised and determined, it is the entire issue that is precluded, not just the particular arguments raised in support of the first case. *See Applied*, 352 F. Supp. 2d at 1124 (rejecting a party's attempt to escape collateral estoppel on the issue of invalidity by raising anticipation and obvious arguments not previously raised).

Moreover, a collaterally estopped party cannot relitigate findings of fact necessary for the determination of an issue. *Allen*, 449 U.S. at 94 ("once a court has decided an **issue of fact or law necessary to its judgment,** that decision may preclude relitigation of the issue in a suit on a different cause of action involving a party to the first case.") (citing *Montana v. U.S.*, 440 U.S. 147, 153, n.5 (1979); *see also In re Relafen Antitrust Litigation*, 286 F. Supp. 2d 56, 68-69 (D. Mass. 2003) (precluding a party from relitigating findings essential to an invalidity ruling).

The First Circuit has determined that for collateral estoppel to apply five requirements must be met. They are:

(1) the issue sought to be precluded must be the same as that involved in the prior action;

(2) the issue must have been actually litigated;

(3) the issue must have been determined by a valid and binding final judgment;

(4) the determination of the issue must have been essential to the judgment;

(5) the party to the second action must be the same as or in privity with the parties in the first action.

See Boston Scientific Corp. v. Schneider (Europe) AG, 983 F. Supp. 245, 255 (D. Mass. 1997).

A. INVALIDITY IN GENERAL AND SPECIFICALLY OBVIOUSNESS OF THE ERYTHROPOIETIN DNA SEQUENCE DR. LIN CLONED IN 1983 WERE LITIGATED IN THE CHUGAI/GI LITIGATION AND THE GI INTERFERENCE

The first four requirements of collateral estoppel are clearly met. First, the issues sought to be precluded are the same. Roche seeks to reargue that with the "*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*." (Exs. 28-29, Fifth Supplemental Interrogatory Response No. 9 at 43 and the Lowe report.) This very issue was decided by this Court and the Federal Circuit: "The evidence did not show that there was a reasonable expectation of success *in cloning* the EPO gene based on the *probing strategy*.[6]" *Amgen*, 13 U.S.P.Q. 2d at 1767. Moreover, the fact that Roche does not state that it is expressly challenging the validity of Claim 2 of the '008 Patent directed to the DNA sequence is irrelevant: The issue of whether it was obvious to clone the erythropoietin DNA sequence was decided years ago, and all arguments and facts necessary and attendant to that which were made or could have been made fell under the issue of invalidity (specifically obviousness). *See Pall Corp.*, 962 F. Supp. at 213; *Applied Med. Resources Corp.*, 352 F. Supp. 2d at 1123. Experts cannot come into this Court today and argue as obvious the cloning of the erythropoietin DNA sequence when this very Court considered and rejected such arguments by experts years ago.

[6] Judge Saris considered both cDNA and the gDNA libraries, which were essential facts to the conclusion that Dr. Lin's EPO DNA sequence was not obvious. Roche is estopped from challenging both the issue of fact and law from this prior adjudication. In fact, GI described both cDNA and gDNA libraries in its Proposed Findings of Facts in the interference proceeding, including Fritsch's decision not to use a cDNA library to clone the EPO gene, and to use a gDNA library instead, showing that the issue was essential to the determination. (*See* Ex. 32 at AM ITC 00330547, 556-57.)

Second, the validity of the '008 Patent was actually litigated in both this Court and the Federal Circuit and that includes all arguments relating to validity that were or could have been made. *Id*.; s*ee also Hartley v. Mentor Corp*., 869 F.2d 1469 (Fed. Cir. 1989) (The court found that the prior case's stipulated judgment operated as an adverse adjudication on the merits and the ruling on the patent's invalidity became a necessary part of the final judgment and was a basis for the collateral estoppel.)

Third, a valid and binding judgment came: (1) after the Federal Circuit upheld this Court's determination that claim 2 of the '008 Patent was valid as nonobvious; (2) when GI failed to appeal on the '096 interference; (3) when Chugai and GI signed the 1993 Settlement Agreement admitting to the '008 Patent's validity and this Court entered judgment thereon with such express findings;[7] and (4) when, pursuant to the Settlement Agreement, GI dismissed with prejudice its appeal of the '097 interference in the District of Delaware. *See Freedman & Co., Inc. v. Marvin RAAB,* Civ. No. 06-3723 (RBK), 2007 U.S. Dist. LEXIS 44532, *10 (D.N.J. June 18, 2007) (*citing Gambocz v. Yelencsics*, 468 F.2d 837, 840 (3d. Cir. 1972) (A dismissal "with prejudice" is treated as an adjudication of the merits and thus has preclusive effect.)).

Fourth, the determination of non-obviousness of claim 2 of the '008 Patent directed to the isolated DNA sequence was essential to both (1) the judgment of validity by this Court and at the Federal Circuit and (2) the settlement agreement and subsequent entry of judgment. (Ex. 1, 1993 Settlement Agreement.) Three tribunals have already decided the issue that Dr. Lin's invention, the isolated DNA sequence, was not obvious.

Moreover, a party collaterally estopped from relitigating an issue is also collaterally estopped from relitigating facts that were essential to the determination of the issue. *Allen*, 449 U.S. at 94; *see also In re Relafen*, 286 F. Supp. 2d at 68-69. There is no question that Judge Saris considered the essential factual questions of whether it was obvious for one of skill as of December 1983 priority date to clone the EPO gene by way of cDNA or gDNA library as the facts in Section II.C.1 above show. Roche may not relitigate the essential factual issues as to whether it was obvious to clone from a DNA library the gene for human erythropoietin even for the patents-in-suit. Collateral estoppel prevents what exactly may happen if Roche is not

[7] *Amgen, Inc*., 13 U.S.P.Q. 2d 1737, 927 F.2d 1200; Ex. 1, 1993 Settlement Agreement.

estopped – contradictory factual findings. Specifically, that in the case of the '008 Patent it was not obvious to clone from a DNA library gene for human erythropoietin but that it would be obvious to clone from a DNA library gene for human erythropoietin for the purposes of this present litigation. Collateral estoppel prevents Roche from creating contradictory facts.

B. ROCHE IS IN PRIVITY WITH CHUGAI AND GI AND IS THUS BOUND BY THE ADJUDICATIONS

The remaining issue is whether the party to the current action, Roche, is in privity with the parties to the first action, Chugai and/or GI. "The term 'privity' is now used to describe various relationships between litigants that would not have come within the traditional definition of that term." *Boston Scientific*, 983 F. Supp. at 257, (*citing Richards v. Jefferson City*, 517 U.S. 793 (1996)). Traditionally, privity has been found where the non-party controlled the previous litigation; where the non-party is a successor in interest to the prior party; or where a non-party interests were adequately represented by a party in the first action under the doctrine of virtual representation. *See Gonzalez v. Banco Central Corp.*, 27 F.3d 751, 758, n.5 (1st Cir. 1994), *Tyus v. Schoemehl*, 93 F.3d 449, 453-454 (8th Cir. 1996). Roche is in privity with Chugai and GI: (1) under the doctrine of virtual representation; (2) as Chugai's parent; and (3) by virtue of its joint venture with GI. *See Boston Scientific*, 983 F. Supp. at 258.

1. Both Chugai and GI were Virtual Representatives of Roche

Virtual representation is applied when a court finds the existence of some special relationship between the parties justifying preclusion. *See Tyus*, 93 F.3d at 455. A party is bound under the doctrine of virtual representation, even when not a party to the original action, if "… one of the parties to the suit is so closely aligned with [the parties] interests as to be his virtual representative." *AeroJet-General Corp. v. Askew*, 511 F.2d 710 (5th Cir. 1975). As there is no straightforward test, virtual representation remains an *equitable theory* and its application is to be determined on a case by case basis. *See Gonzalez*, 27 F.3d at 761. A non-party such as Roche will be barred from bringing its claim if "the balance of the equities tips in favor of preclusion." *Id*.

In *Boston Scientific*, the District Court of Massachusetts examined whether a company was in privity for purposes of collateral estoppel with a company it had recently acquired. *See Boston Scientific*, 983 F. Supp. at 258. Defendant Boston Scientific was estopped from

relitigating the validity of plaintiff's patents as a result of a judgment against a company with which Boston Scientific merged. In finding that the parties were virtual representatives, this Court considered three factors, all of which confirm that the doctrine should apply to find that Roche is in privity with Chugai and GI.

a. Amgen is a competitor of Roche, Chugai and GI

The *Boston Scientific* Court assessed whether at the time of the previous litigation there was a clear identity of interest, *i.e.*, "the validity and enforceability of a patent, held by a common competitor, which was potentially infringed by both companies." *Id* at 258. Such an identity exists here where Amgen was and is a common competitor of both Roche, Chugai and GI and the patents arise out of the common application Amgen filed in December 1983. Moreover, the identity of the issue is the same then and now: whether the EPO gene was obvious in 1983 in view of the prior art cloning techniques.

b. Roche had notice of the *Amgen v. Chugai* litigation

Second, the Court explained, "there can be no doubt that BSC had actual notice of the Minnesota litigation while it was being conducted, and BSC certainly had such notice when it decided to merge with SciMed." *Id*. Likewise, there can be no doubt that Roche had notice of the litigation. Roche, a multinational corporation, would have performed due diligence before it acquired Boehringer and Chugai. Additionally, because GI, Roche, Boehringer and Chugai are all competitors with Amgen, Roche would have followed the heated litigation between Amgen, GI and Chugai in this Court. In fact, Roche had copies of Amgen's 1990 and 1991 annual reports, which referenced the litigation. (Exs. 33 at R10-000235812; Ex. 34 at R10-001303916.)

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c. The balance of equities tips in favor of preclusion

Lastly, but most importantly, the "balance of equities tips decidedly in favor of preclusion." Failure to hold Roche to the prior adjudications would allow Roche to relitigate issues which have already been decided and would serve as a fundamental miscarriage of the public policies behind the doctrine of collateral estoppel. *See id*. at 259-260. Allowing Roche to attack the obviousness of the EPO DNA and its cloning by couching its position as a factual

matter would allow the relitigation of the issue that Roche's predecessors lost several times over. Amgen entered into the 1993 Settlement Agreement to "fully and finally settle and resolve all controversies and disputes [.]" (Ex. 1, AM-ITC 00799257.) Relitigating the issues now harms Amgen by forcing it to incur expenses and waste time to address these issues that were put to rest in 1993. Effectively, it would allow Roche to enjoy the benefit of judgments Chugai and GI have won without suffering the burden of those it has lost. *See Mars, Inc. v. Nippon Conlux Kabushiki-Kaisha*, 58 F.3d 616, 619 (Fed. Cir. 1995) (courts also focus on whether the relationship between the parties is such that one party should enjoy the benefit, or suffer the burden, of a judgment for or against another).

There is no question as to the adequacy of the representation in the prior proceedings. *See Tyus*, 93 F.3d at 455-456. "One party 'adequately represents' the interests of another when the interests of the two parties are very closely aligned and the first party had a strong incentive to protect the interests of the second party." *Id*. The interests of both Chugai and GI were identical to the interest of Roche in this litigation – to invalidate Amgen's patents as a defense to patent infringement by contending, in part, that it was obvious to clone the EPO DNA in 1983 based on known techniques in the prior art.

Moreover, the record is clear that Boehringer, now named defendant Roche Diagnostics GmBH, was actively involved in the litigations, including approving the settlement and entry of judgment against GI stating that the '008 Patent was valid. (Ex. 12, AM-ITC 00789762, Ex. 13, AM-ITC 00787126, Ex. 8, AM-ITC 00119908.)

Roche's close ties with GI, and its acquisition of Boehringer and Chugai, all warrant the equitable finding that Roche is in privity with the prior adjudications.

2. As Chugai's Parent, Roche is in Privity with Chugai

Roche should also be bound by the prior adjudication of validity and particularly the non-obviousness of the erythropoietin DNA because Roche is Chugai's parent. *See Boston Scientific*, 983 F. Supp. at 259. The Federal Circuit, in *Boston Scientific*, explained "as parent and wholly-owned subsidiary, BSC and SciMed clearly have the type of close relationship which, if not indicating privity per se, at the very least contributes significantly to a finding that BSC should be held to have assumed the burden of a judgment against SciMed." *Id*. *citing Mars*, 58 F.3d at

619 (applying claim preclusion based in part on fact that present and former defendants were parent and wholly-owned subsidiary); *Nordhorn v. Ladish Co*., 9 F.3d 1402, 1405 (9th Cir. 1993) ("Corporate affiliations may be relevant in determining whether two parties are in privity for purposes of issue or claim preclusion."); *G & T Terminal Packaging Co. v. Consolidated Rail Corp*., 719 F. Supp. 153, 159 (S.D.N.Y. 1989) (Subsidiaries are in privity with principal for res judicata purposes when, as here, they sufficiently represent the principal's interest,") Similarly, on October 1, 2002 Roche acquired Chugai and Chugai became Roche's subsidiary. (Ex. 26, R007090626-36, press release.) Through the merger, Roche acquired the majority ownership, or 50.1%, of Chugai. As Chugai's parent, Roche is bound by the issues adjudicated in the earlier proceedings and the factual findings essential to the issues adjudicated.

3. Roche Is Bound Because It Has A Joint Venture With GI

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).

In joint ventures, every joint partner is an agent of the partnership and the act of every partner binds the joint venture. *See Great Hawaiian Financial Corp., v. Aiu*, 863 F.2d 617, 621 (9th Cir. 1988).

The first factor is met. In 1985, Boehringer and GI entered into a joint venture that has brought in over $100 million of revenue for GI and much more for Boehringer. ((*See* Ex. 25, Amgen's Opposition to Roche's Mot. To Dismiss For Lack of Personal Jurisdiction at 9, Gottfried Decl., Ex. B at pp. 796-799, and 814.) Boehringer and GI did not form a separate entity such as a partnership or corporation for their venture, but joined forces to develop and commercialize EPO in Europe.

The second factor, "a contribution of money, property, effort, skill, or other assets to a common undertaking," is met. GI contributed to the research and technology in this venture while Boehringer spent its money and efforts on the commercialization of EPO. (Ex. 8, 1985 Agreement at AM-ITC 00119902.)

The third factor, "a joint property interests in all or parts of the subject matter of the joint venture," is met because under the 1985 Agreement, Boehringer and GI "jointly own" the intellectual property rights to technology jointly developed. (Ex. 8, 1985 Agreement at AM-ITC 00119905.)

The fourth factor, "a right to participate in the control or management of the enterprise," is present. The 1985 Agreement gave each party the right to "visit the Other Party at its offices and laboratories and to discuss the Project work and its results in detail with the technical personnel and consultants of the Other Party." (Ex. 8 at AM-ITC 00119901.) Boehringer's involvement in the GI/Chugai litigation confirms its right to participate in the enterprise. Most telling, any settlement involving GI's technology required Boehringer's approval. (Ex. 8 at AM-ITC 00119908.) Boehringer had control.

The fifth and sixth factors, "an expectation of profit" and "share of profit," is present. The 1985 Agreement includes royalty payments from Boehringer to GI. (Ex. 8 at AM-ITC 00119912.) Moreover, the purpose of the agreement is for both parties to profit from the commercialization of EPO.

The seventh factor, "an express or implied duty to share in the losses," is met. The 1985 operating agreement expressly states that "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)." Accordingly, both parties expressly stated that they would share in the losses.

Finally, the eighth factor is present. Boehringer and GI's venture is limited to the research, development, and commercialization of EPO.[8]

[8] Thus, despite a clause claiming that there is no joint-venture, the presence of the eight factors in the Boehringer-GI relationship strongly evidence the formation of a joint venture.

When GI lost the litigations and further admitted to the validity of the '008 Patent with Boehringer's full knowledge and participation, that bound GI's joint venture partner, Boehringer, now defendant Roche Diagnostics GmBH. The acts of a joint venture binder in furtherance of the joint venture binds the other joint venture partners. Here, the evidence is undisputed that Boehringer was actively involved in the prior litigations. GI's settlement agreement required its joint venture partner, Boehringer's approval. 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. Moreover, Roche Diagnostics uses the EPO that Boehringer gained access to as a result of the Boehringer-GI 1985 Agreement in making CERA. In essence, what we have here is the Boehringer venture operating as Roche Diagnostics. Thus, Roche is estopped from challenging the non-obviousness of cloning the DNA sequence encoding for human erythropoietin, as it seeks to do here. Roche is also collaterally estopped from relitigating facts essential to the prior adjudication.[9]

IV. IN THE ALTERNATIVE, ROCHE IS CONTRACTUALLY ESTOPPED FROM CHALLENGING THE VALIDITY OF THE '008 PATENT

The 1993 Settlement Agreement also gives rise to contractual estoppel. *See Flex-Foot, Inc. v. CRP, Inc.*, 238 F.3d 1362 (Fed. Cir. 2001) (Federal Circuit precluded challenge of the validity of the patent based on contractual estoppel due to terms of the settlement agreement). On May 12, 1993, Chugai and GI entered into a Settlement Agreement with Amgen resolving all pending litigation, and admitting to the validity of the '008 Patent. (Ex. 1, AM-ITC 00799255-71.) Pursuant to the Settlement Agreement, there was an entry of judgment in this Court in which the Court stated that "[t]he '008 Patent was duly and legally issued, is valid and enforceable in law and equity…" (Ex. 36, AM44 2024650-52.) As discussed above, the relationship between Roche and Chugai and Roche and Boehringer, binds Roche to the 1993 Settlement Agreement with Amgen and Chugai and GI's admission of the validity of the '008 Patent. The Federal Circuit has held, like in the case here, where a party agrees to a dismissal

[9] The findings of facts essential to the district court's determination of non-obviousness is discussed in Section II.C.1. above.

with prejudice with an accompanying settlement agreement, the party is contractually estopped from challenging the patents validity. *Id*. at 1367.

V. CONCLUSION

For the reasons stated above, Roche should be excluded at trial from presenting evidence that the EPO DNA sequence and its cloning were obvious and from relitigating the factual findings essential to that prior adjudication.

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