

**UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS**

AMGEN INC.,

Plaintiff,

v.

F. HOFFMANN-LAROCHE
LTD., a Swiss Company, ROCHE
DIAGNOSTICS GmbH, a German
Company and HOFFMANN LAROCHE
INC., a New Jersey Corporation,

Defendants.

Civil Action No.: 05-12237 WGY

**AMGEN'S OPPOSITION TO ROCHE'S BENCH MEMORANDUM
(D.N. 1273) REGARDING AMGEN'S DEMONSTRATION OF THE REQUISITE
NEXUS REGARDING SECONDARY CONSIDERATIONS OF NON-OBVIOUSNESS**

Roche asserts all of the claims-in-suit are obvious and therefore invalid. The United States Supreme Court, however, has made plain that in assessing whether a patent claim is obvious, it is necessary to consider, among other things, objective evidence of non-obviousness.¹ Accordingly, in addition to other proofs, Amgen has presented evidence of long-felt need, solution of that long-felt need by the commercial embodiments of the asserted claims, failure of

¹*Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966) (listing commercial success, long-felt need, and failure of others as objective evidence of non-obviousness). Evidence of skepticism or disbelief before the invention, public praise, unexpected results, industry acceptance also has been considered by courts assessing the non-obviousness of inventions. *See, for example, Envil. Designs, Ltd. v. Union Oil Co. of Cal.*, 713 F.2d 693, 697-98 (Fed. Cir. 1983) (considering skepticism or disbelief before the invention as highly probative evidence of nonobviousness); *Allen Archery, Inc. v. Browning Mfg. Co.*, 819 F.2d 1087, 1092 (Fed. Cir. 1987) (copying by others, public praise, unexpected results, and industry acceptance); *Micro Motion Inc. v. Exac Corp.*, 741 F. Supp. 1426, 16 U.S.P.Q.2d 1001, 1008 (Cal. 1990) (praise); *In re Piasecki*, 745 F.2d 1468, 1474 (Fed Cir. 1984) (praise); *Diversitech Corp. v. Century Steps, Inc.*, 850 F.2d 675, 679 (Fed. Cir. 1988) (copying); *Metabolite Laboratories, Inc. v. Laboratory Corp. of Am. Holdings*, 370 F.3d 1354, 1368, 71 U.S.P.Q.2d (BNA) 1081 (Fed. Cir. 2004) (skepticism and licensing).

others to solve the problem, skepticism or disbelief before the invention, public praise, unexpected results, and industry acceptance.²

Recognizing that such evidence makes ineluctable the conclusion that the claimed inventions are anything but obvious, Roche seeks to preclude Amgen from arguing its import to the jury. It asserts that Amgen has failed to prove a nexus between the success of Amgen's commercial product — EPOGEN[®] — and Dr. Lin's specification. Roche, however, misapprehends the law. Nexus is *prima facie* established by showing that Amgen's commercial product falls within the scope of its *claims-in-suit*.³ Once nexus has been *prima facie* established, Roche must rebut the presumption of nexus by clear and convincing evidence, not mere argument or conjecture.⁴

At trial, Amgen made a *prima facie* showing that EPOGEN[®] and its use meet every limitation of at least '422 claim 1 and '933 claims 3, 7, 8, 9, 11, 12, and 14.⁵ It was therefore

² Trial Tr. (Spinowitz) 941:9-942:7, 944:2-7, (Friedman) 1431:8-15, (Spaeth) 1531:25-1532:6 (long felt need); Trial Tr. (Friedman) 1426:23-1427:15, (Spaeth) 1530:23-1531:22 (solution to the unmet need), Trial Tr. (Friedman) 1426:23-1428:11, 1436:8-16 (unexpected advantages and results); Trial Exh. 11 at AM-BER-ERB000001; Trial Exh. 2012 at AM-ITC 000953154 (commercial success); Trial Tr. (Spinowitz) 945:23-946:2, (Goldwasser) 2012:4-8, 18-21, (Friedman) 1497:10-18, (Lowe) 460:25-461:5, (Spinowitz) 929:4-9, 930:17-931:10 (failure of others); Trial Ex. 20 at AM-ITC 00076147-8, Trial Tr. (Friedman) 1438:21-1440:8 (skepticism).

³ *Demaco Corp. v. F. Von Langsdorff Licensing Ltd.*, 851 F.2d 1387, 1392 (Fed. Cir. 1988) ("A *prima facie* case of nexus is generally made out when the patentee shows both that there is commercial success, and that the thing (product or method) that is commercially successful is the invention disclosed and claimed in the patent."); *J. T. Eaton & Co. v. Atlantic Paste & Glue Co.*, 106 F.3d 1563, 1571 (Fed. Cir. 1997) ("When a patentee can demonstrate commercial success, usually shown by significant sales in a relevant market, and that the successful product is the invention disclosed and claimed in the patent, it is presumed that the commercial success is due to the patented invention."). Furthermore, any showing is made relative to the claims at issue: as stated in *WMS Gaming, Inc. v. Int'l Game Tech.*, 184 F.3d 1339, 1359 (Fed. Cir. 1999), the nexus must be drawn to "the claimed features of the invention" and the objective evidence.

⁴ *Demaco*, 851 F.2d at 1393 ("When the patentee has presented a *prima facie* case of nexus, the burden of coming forward with evidence in rebuttal shifts to the challenger, as in any civil litigation."); *J.T. Eaton & Co.*, 106 F.3d at 1571. See also *Demaco*, 851 F.2d at 1393 (noting that "argument" and "conjecture" are insufficient to overcome objective evidence of non-obviousness). *Rosemount, Inc. v. Beckman Instruments, Inc.*, 727 F.2d 1540, 1546 (Fed. Cir. 1984) (argument and conjecture are inadequate to overcome objective evidence).

⁵ See AMGEN'S BENCH BRIEF ON DOCUMENTS ALREADY IN EVIDENCE THAT DEMONSTRATE A

incumbent upon Roche to show by clear and convincing evidence that EPOGEN[®]'s success is caused by a factor other than the inventions' features as claimed. But rather than attempting such a showing, Roche instead argues that manufacture of the EPOGEN[®] involves steps other than those set forth in the specification. Roche's position, however, fails because this assertion is legally irrelevant and in any event there is no evidence, much less clear and convincing evidence, that such additional steps exclusively account for EPOGEN[®]'s success.

First, Roche argues that, since the specification's Example 10 provides for a "genetically heterogeneous population" of cell culture, whereas the FDA required EPOGEN[®] to be produced from a homogeneous population of cell culture, EPOGEN[®] is not "embraced" by Example 10. But, as noted, Roche posits a red herring. The legally salient question is whether there is a nexus between EPOGEN[®] and *the claims-in-suit*. Roche has provided no evidence that EPOGEN[®]'s success was exclusively attributable to matters other than the limitations of '422 claim 1 and '933 claims 3, 7, 8, 9, 11, 12, and 14. In any event, Roche's suggestion that FDA requirements resulted in changes to EPOGEN[®]'s manufacture allegedly not described in Example 10 is mere conjecture, belied by the uncontroverted testimony of Dr. Browne that EPOGEN[®] is in fact produced from a cell of Example 10.⁶

Second, once again misdirecting focus away from the pivotal fact of EPOGEN[®]'s possession of the limitations of the claims at issue, Roche asserts that Dr. Strickland's purification technique "necessarily affects the final EPO product." But this is exactly the type of "argument and conjecture" that the Federal Circuit has rejected as "insufficient" to rebut a *prima*

NEXUS BETWEEN EPOGEN[®] AND AT LEAST ONE CLAIM OF A PATENT-IN-SUIT, D.N. 1126. See Exhibit A – NEXUS BETWEEN EPOGEN[®] AND CLAIMS-IN-SUIT.

⁶ Trial Tr. (Browne) 1958:6-25, 1962:14-1963:21. Additionally, the Federal Circuit has previously affirmed the finding of fact that EPOGEN[®] is the product of Example 10. *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1321 (Fed. Cir. 2003).

facie case of nexus.⁷ Even assuming these statements were expressly connected to EPOGEN[®] — which they are not⁸ — Roche failed to present any evidence, much less clear and convincing evidence, as to whether or how EPOGEN[®]'s commercial success could be due to any of these alleged differences and is **not** attributable to its possession of the limitations of the claims-in-suit.

Third, Roche argues that, since the patents-in-suit were not issued at the time EPOGEN[®] “hit the market,” its commercial success must be exclusively attributed to the ‘008 patent, the only issued patent at the time of EPOGEN[®]'s approval in 1989. This argument, however, is legally unsupported and nonsensical as the determination of non-obviousness under *Graham v. John Deere Co.* applies equally to “subject matter *to be patented*” in applications submitted to the Patent Office, as it does to issued claims and patents.⁹ Under Roche’s articulation of the test, an applicant could never provide evidence of secondary considerations of commercial success to the Patent Office to prove the non-obviousness of his or her inventions, because claims had not yet issued. In fact, the inventions claimed in the patents-in-suit and disclosed in Dr. Lin’s 1984 applications are the very foundation of Amgen’s commercial product, EPOGEN[®] and its subsequent commercial success. Without Dr. Lin’s *in vivo* biologically active man-made human EPO, there would be no EPOGEN[®]. In any event, EPOGEN[®] — an *in vivo* biologically active human EPO **glycoprotein** — does not fall within the scope of the ‘008 claims which are directed to an isolated and purified **DNA molecule** and host cells containing that molecule.¹⁰

⁷ *Demaco*, 851 F.2d at 1393.

⁸ The testimony by Dr. Strickland upon which Roche relies is not specific to EPOGEN[®]. Trial Tr. 2157:12-2165:4.

⁹ *Graham v. John Deere Co.*, 383 U.S. 1, 18-19 (1966).

¹⁰ Furthermore, it cannot be said that EPOGEN[®]'s success is attributable to the right to exclude conferred by the ‘008 patent because, as the decision of the International Trade Commission made plain, the claims of that patent did not prevent the importation of a competing product. *See* Certain Recombinant Erythropoietin, Inv. No. 337-TA-281, Order of the USITC Commission (April 10, 1989).

Contrary to Roche's citation, neither *Merck*¹¹ nor *Weatherchem*¹² relates to whether a patent must have issued at the time of the commercial product's success for there to be a nexus between the success and the claimed invention. In both *Merck* and *Weatherchem*, parties presented evidence that the success of the commercial product was attributable to factors external to the claimed features of the invention, such as the ability of a party to exclude others from practicing a method of treatment claim as a result of having another patent directed to the administration of the same compound, or the incorporation in the commercial embodiment of a limitation disclosed in an unrelated patent to which the commercial success of the product was due. *Merck* and *Weatherchem* are simply inapposite as Roche cannot make a showing that the '008 conferred on Amgen a right to exclude others from selling a pharmaceutical product that meets the limitations of the patents-in-suit as the '008 claims were not directed to a pharmaceutical product or its use. In any event, it should be noted that the '008 did not issue before the filing of the applications giving rise to the claims-in-suit.

Fourth, Roche argues that any public praise for Amgen's cloning of the EPO gene is irrelevant because the EPO gene is not claimed in any of the patents-in-suit. But once again Roche misdirects the focus away from the legally salient question as to the nexus between the claims-in-suit and EPOGEN[®]'s success. On that question, as Dr. Friedman and even Roche's Dr. Spinowitz testified, the evidence is uncontroverted that there was and continues to be huge public praise for recombinant human EPO — Dr. Lin's *in vivo* biologically active man-made glycoprotein and its use to treat anemic dialysis patients in correcting their anemia and improving quality of life by increasing their hematocrit, a product and use falling four square within the scope of the claims-in-suit.¹³ In any event, since it was Roche who made the blanket

¹¹ *Merck & Co., Inc. v. Teva Pharm. USA, Inc.*, 395 F.3d 1364 (Fed. Cir. 2005).

¹² *Weatherchem Corp. v. J.L. Clark, Inc.*, 163 F.3d 1326 (Fed. Cir. 1998).

¹³ Trial Tr. (Spinowitz) 941:23-942:7; 943:4-13; 941:17-21; 944:2-7; (Friedman) 1426:23-

charge that the claims-in-suit are somehow rendered obvious by the assertion of Roche's Dr. Lowe that cloning the human EPO gene was obvious,¹⁴ Roche not Amgen put into play the question of what the objective evidence shows as to the non-obviousness of cloning the human EPO gene. Having opened the door, far be it from Roche to attempt to preclude Amgen from providing the jury with the facts regarding the whole picture.

CONCLUSION

A prima facie nexus having been established and Roche having failed to discharge its heavy burden of proof to rebut that nexus, Amgen respectfully requests that the Court reject all requests by Roche to preclude Amgen from relying upon or arguing to the jury the import of the objective evidence of non-obviousness in this case.

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Respectfully Submitted,

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1427:15, 1434:19-1435:9, 1448:4-13.

¹⁴ Trial Tr. (Lowe) 145, 256:20-258:12.

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CERTIFICATE OF SERVICE

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