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 BENCH MEMORANDUM CONCERNING THE APPROPRIATE JURY INSTRUCTION ON 35 U.S.C. § 271(g)

Amgen Inc. respectfully requests that the Court adopt Amgen's proposed jury instruction XIII.A.2 "Infringement of '868 Claims 1-2, '698 Claims 6-9, and '349 Claim 7."[1] Roche's corresponding proposed jury instruction, entitled "6.6 Material Change,"[2] is legally incorrect and unduly prejudicial to Amgen. Unlike Roche's proposed instruction, Amgen's instruction is impartial and accurately reflects Federal Circuit precedent concerning the application of § 271(g).

The inquiry under § 271(g) is whether Roche's importation of peg-EPO avoids infringement because the glycosylated EPO it contains has been (a) "materially changed by subsequent processes" or (b) is a "trivial and non-essential component of another product."

[1] Attached as Exhibit A is Amgen's amended proposed jury instruction XIII.A.2. "Proposed Instruction for Infringement of '868 Claims 1-2, '698 Claims 6-9, and '349 Claim 7."

[2] Docket No. 917 at 53-54.

Roche's proposed instruction misstates and over-extends the findings of a single district court case, *Eli Lilly and Co. v. Am. Cyanamid Co.*,[3] in order to justify an inaccurate statutory interpretation of the "materially changed" prong of the non-infringement test. Moreover, Roche's instruction does not even mention the "trivial and non-essential component" prong of the test. Roche's instruction identifies four "factors [that] support a finding of material change." But the *Lilly* district court did not actually identify the "factors" proposed by Roche. Rather, Roche selectively quotes the *Lilly* district court's analysis of the specific facts of that case, as opposed to any "factors" of general application. Importantly, these "factors" were not identified in the precedential Federal Circuit decision in *Lilly*.[4] And contrary to the impression left by Roche's proposed instruction, the Federal Circuit in *Lilly* expressly declined "to define with precision what classes of changes would be material and what would not . . . ."[5] Rather, § 271(g) has to be resolved on a case-by-case basis.[6] Roche's instruction is therefore legally incorrect because it would confuse the jury by conflating the particular facts of another case with the legal rule itself.

Even assuming the *Lilly* district court's factual analysis were applicable here, Roche has misstated and over-extended that court's findings. For example, Roche's instruction identifies

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[3] 66 F. Supp. 2d 924, 932 (S.D. Ind. 1999). This decision is a grant of summary judgment of non-infringement after the Federal Circuit affirmed the district court's earlier denial of a preliminary injunction under § 271(g). *Eli Lilly & Co. v. American Cyanamid Co*., 82 F.3d 1568 (Fed. Cir. 1996).

[4] *Eli Lilly & Co. v. American Cyanamid Co*., 82 F.3d 1568 (Fed. Cir. 1996).

[5] *Id.* at 1573.

[6] *Bio-Technology Gen. Corp. v. Genentech, Inc.*, 80 F.3d 1553, 1561 (Fed. Cir. 1996) ("The statute does not specify what products will be considered to have been 'made by' the patented process, apparently because Congress wanted the courts to resolve this critical question of proximity to the product of the patented process on a case-by-case basis. See S. Rep. No. 83, 100th Cong., 1st Sess. 46 (1987) ('Inevitably the courts will have to assess the permutations of this issue of proximity to or distance from the process on a case-by-case basis.'); *id*. at 49 ('The Committee expects the courts to exercise careful judgment in distinguishing those products that are too far removed from the patented process, and those that have been changed only in insignificant ways.').".

"subsequent processes [that] confer significant structural differences to the product of the patent processes such as the removal and/or addition of certain chemical groups of a compound" as a factor for finding material change. But this "factor" is entirely circular and self-fulfilling because it suggests that all additions or subtractions from a chemical compound are significant changes to that compound. If this were the case, there would be no need for the "materially changed" test at all, because ***any*** change to the chemical structure of a product of a patented process would be exempt from infringement. Rather, the Federal Circuit in *Lilly* noted that some changes to the chemical structure of a compound are ***not*** material:

> While the addition or removal of a protective group, standing alone, might not be sufficient to constitute a "material change" between two compounds (even though it could dramatically affect certain of their properties), the conversion process between compound 6 and cefaclor involves considerably more than the removal of a protective group.[7]

As the holding in *Lilly* makes clear, this statement was made in the context of chemical substitutions and additions that transformed the non-functional starting compound into a useful antibiotic.

Roche's application of the "factors" it derives from the *Lilly* district court decision is also incorrect because it presumes that the facts of the *Lilly* case are directly analogous to those here. That is not the case. At issue in *Lilly* were claims to a method of making a chemical precursor to the antibiotic cefaclor. Four subsequent process steps were necessary to convert the precursor into cefaclor, the product that was imported into the United States. These steps each physically altered the structure of the precursor molecule: a hydroxy group was removed and replaced with a chlorine atom, a phenylacetyl group was removed and replaced with a phenylglycyl group, and a para-nitrobenzyl carboxylate ester group was removed.[8] The only commonality between the precursor of the claimed process and the imported product was the cephem nucleus, which is

[7] *Eli Lilly & Co.*, 82 F.3d 1568, 1573 (Fed. Cir. 1996).

common to thousands of compounds and has no antibiotic activity.[9] Each of the substitutions made to the structure of the precursor also changed the function of the precursor, transforming it from an ineffective antibiotic into an orally effective antibiotic: the carboxyl group was important for antibacterial activity; the chlorine atom increased the antibiotic potency; and the phenylglycyl group enabled the imported cefaclor to be effective when taken orally.[10] Before those changes, the ***precursor itself had no utility*** as an antibiotic.[11] Under these facts, the Federal Circuit held that "a change in the chemical structure and properties as significant as the change between compound 6 and cefaclor cannot lightly be dismissed as immaterial."[12]

Here, there can be no doubt that none of the changes effected by Roche to the EPO product of Lin's claimed process transforms the basic utility of the EPO product. The glycosylated EPO product of Lin's claimed process, which Roche incorporates into its peg-EPO product, has the identical basic utility as Roche's product — to cause bone marrow cells to increase production of reticulocytes and red blood cells.[13] Moreover, unlike the four significant changes between the product of the claimed process and the imported product in *Lilly*, here only a single chemical bond is altered in EPO by the addition of peg.[14]

There is no dispute over the explanatory language for "materially changed" proposed by Amgen: "A change is not a material change unless it is a significant change in the EPO product's structure and properties, which changes the basic utility, or use for, the EPO product." Amgen's

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[8] *Id.* at 1570.

[9] *Id.* at 1573.

[10] *Id.* at 1570.

[11] *Id.* at 1577 ("Cefaclor is a powerful oral antibiotic, with a set of chemical and biological properties that give it great utility in that regard; compound 6 has no such properties, and it has no significant utility as an antibiotic.").

[12] *Id.* at 1573.

[13] 10/4/07 Trial Tr. 2488:10-2490:5.

[14] 10/4/07 Trial Tr. 2460:3-7.

language is consistent with the case law and the more general portion of Roche's instruction. In particular Roche's instruction similarly states: "In the chemical context, a material change in a compound is most naturally viewed as significant change in the compound's structure and properties." In *Eli Lilly & Co. v. American Cyanamid*, the Federal Circuit stated, "In the chemical context, a 'material' change in a compound is most naturally viewed as a significant change in the compound's structure and properties."[15] Quoting the legislative history, the Federal Circuit also stated: "A product will be considered to have been made by a patented process if the additional processing steps which are not covered by the patent do not change the physical or chemical properties of the product in a manner which changes the ***basic utility of the product*** [produced] by the patented process.[16] Likewise, in the *Lilly* district court decision relied upon by Roche, the court stated: "The 'material change' exception to process patent infringement under § 271(g) applies when an intermediate product is significantly different from the end product in its chemical structure, properties and basic utility."[17]

Roche's instruction is also insufficient in that it omits another legal test under § 271(g) that has been identified and applied by the Federal Circuit. Specifically, even a significant change to the structure and properties of the EPO product will not be a "material change" if it would not be possible or commercially viable to make the EPO product but for the use of Amgen's patented processes. The *Lilly* court paraphrases the legislative history as ***allowing "significant changes***" if such a but for relationship exists:

> "[U]nder certain circumstances, ***significant changes*** in the properties or structure of a chemical product ***do not render*** the product 'materially changed' within the meaning of the statutory language. . . . [A] hypothetical chemical product,

[15] 82 F.3d 1568, 1573 (Fed. Cir. 1996). The Federal Circuit has employed several different tests, while noting that none are conclusive. *Id.* at 1578.

[16] *Id.* at 1577 *quoting* S.Rep. No. 83 100th Cong., 1st Sess. 49 (1987) at 50.

[17] *Eli Lilly & Co.*, 66 F. Supp. 2d 924, 934 (D. Ind. 1999).

> chemical X, is not 'materially changed' if 'chemical X is an important intermediate product, such as a polymer, which can be materially changed into an end product, ***albeit by trivial or conventional processes.*** In this respect, a product will be considered made by the patented process, regardless of any subsequent changes, if it would not be possible or commercially viable to make that product ***but for the use of the patented process***. In judging the commercial viability, the courts shall use a flexible standard which is appropriate to the competitive circumstances.'[18]

Roche's instruction contains another legal error. Roche suggests that the appropriate comparison is between the "product of the patented process" and the "the imported product."[19] The appropriate legal test, however, is whether the product of the process — not the imported product — has been materially changed by subsequent processes prior to importation. The two-part test in § 271(g) focuses on the differences, if any, between the EPO product of the claimed process and that EPO product as it is contained in peg-EPO, not differences between the product of the claimed process and the totality of the imported product.

The statutory language makes this clear. Section 271(g) asks whether the product of the process — not the imported product — has been materially changed by subsequent processes prior to importation. Alternatively, the statute asks whether the product of the process has become merely a trivial and nonessential component of the imported product. If, as Roche contends, the relevant legal inquiry were to compare the product of the process (EPO) with the totality of the imported product (peg-EPO), the second statutory test would be superfluous.

Tellingly, Roche does not even mention the second statutory test in its instruction. If Roche's view were the relevant legal analysis, then a "material change" would occur every time a product of a claimed process was incorporated into a larger product, and there would be no

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[18] *Eli Lilly & Co.*, 82 F.3d at 1575 quoting H.R. Rep. No. 60, 100th Cong., 1st Sess. 13-14 (1987) (emphasis added). Also cited for the same rule: S. Rep. No. 83, 100th Cong., 1st Sess. 49, 50 (1987); H.R. Conf. Rep. No. 576, 100th Cong., 2d Sess. 1087 (1988) *See also Bio-Technology Gen. Corp. v. Genentech, Inc.*, 80 F.3d 1553, 1561 (Fed. Cir. 1996).

[19] "To determine material change, one must look to the substantiality of the change between the product of the patented process and the imported product." Roche's Proposed Jury Instructions, Docket No. 917 at 53.

purpose served by inquiring whether the incorporated product had become a "trivial and non-essential component" of the imported product. But that is not the law.

The recent decision in *Oki America, Inc. v. Advanced Micro Devices, Inc.*[20] is instructive. In that case, the patent claim at issue related to a process for making a semiconductor wafer with smooth edges. As a result, the semiconductor wafers had less debris leading to less defects in the semiconductor chips that were diced from the wafers. Moving for summary judgment of non-infringement, the defendant conceded it used the claimed process outside the United States. However, it argued that it materially changed the product of the process (semiconductor devices from a wafer substrate lacking certain debris) by performing subsequent processing steps. The court, however, rejected the argument:

> Oki also argues that the numerous other wafer processing steps (mask placement, photolithography, resist development and removal, dicing, encapsulation) required for fabrication would anyway constitute a material change. As stated above, however, ***the product is a device lacking certain debris, and this aspect of the product remains unchanged by any subsequent processing***. . . . The ***subsequent processing steps***, such as photolithography, resist development and removal, dicing, and encapsulation, ***do of course make material changes to the physical and electrical properties of the semiconductor substrate, but these changes do not impact the product of Allen process, a debris-free device***.[21]

Here, prior to importation, Roche makes EPO using Lin's claimed processes and then pegylates the EPO, by attaching a peg chain to the EPO polypeptide. The peg chain forms a single amide bond at either the N-terminal alanine or the side chain of an internal lysine.[22] This reaction does not alter the amino acid sequence or the carbohydrate composition of the glycoprotein.[23] In fact, in efforts to gain FDA approval, Roche told the FDA the EPO in peg-EPO is "identical" to the EPO that is used as a starting material in the pegylation process. Thus,

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[20] No. C-04-03171, 2006 WL 2711555 (N.D. Cal. Sept. 21, 2006).

[21] *Id.* at *14 (emphasis added).

[22] 10/4/07 Trial Tr. 2460:16-25.

[23] Trial Exh. 53 at 4027 ("Both EPO starting material and RO0503821 have the identical amino

like the debris-free wafer in *Oki*, the EPO product of the process is not "changed" as a result of subsequent processing.

Because Amgen's instruction fairly summarizes the prevailing case law concerning § 271(g) while Roche's instruction is inaccurate and unduly prejudicial to Amgen, Amgen respectfully requests that the Court adopt Amgen's instruction.

Dated: October 9, 2007

AMGEN INC.,

By its attorneys,

/s/ Michael R. Gottfried

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