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Legal Update

Biotechnology Update

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I. *Bio-Technology General Corp. v. Genentech, Inc.*

1. On April 8, 1996, the United States Court of Appeals for the Federal Circuit affirmed the ruling in *Bio-Technology General Corp. v. Genentech, Inc.*, holding that the District Court for the Southern District of New York had not abused its discretion in granting a preliminary injunction.¹ The District Court's order enjoined Bio-Technology General Corp. ("BTG")² from making, using, selling, or offering for sale or distribution human growth hormone in the United States.³ On October 7, 1996, the United States Supreme Court denied BTG's petition for writ of certiorari.⁴

2. The infringement issue involves two patents assigned to Genentech⁵ concerning human growth hormone ("hGH"), therapeutic in treatment of hypopituitary dwarfism in children.⁶ The first patent is for a recombinant DNA

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¹ *Bio-Technology Gen. Corp. v. Genentech, Inc.*, 80 F.3d 1553, 1556 (Fed. Cir. 1996), *aff'g* 886 F. Supp. 377 (S.D.N.Y. 1995).

² Bio-Technology General Corp. ("BTG") is a health care company specializing in designing products for endocrine, ophthalmic, dermatologic, and cardiovascular disorders. For more information on BTG, see *Bio-Technology General Corp.* (visited Mar. 25, 1997) <<http://www.westergaard.com:8080/Med/btgc.html>>.

³ *See Bio-Technology*, 80 F. 3d at 1556.

⁴ *See Bio-Technology Gen. Corp. v. Genentech, Inc.*, 117 S. Ct. 274 (1996).

⁵ Genentech, Inc. is an industry leader in developing pharmaceuticals, including growth hormones, for significant medical needs. For more information on Genentech, see (visited Mar. 25, 1997) *Genentech, Inc.* <<http://www.bio.com/co/gene.html>>.

⁶ *See Bio-Technology*, 80 F.3d at 1556.

method for producing a 191- or 192-amino acid hGH product that is essentially identical and functionally equivalent to the natural hormone.⁷ The second patent is for a method of constructing a replicable cloning vehicle, capable in a microbial organism of expressing a particular polypeptide, such as hGH.⁸ In Israel, BTG manufactures hGH by similar recombinant DNA methods and had licensed its product for sale in the United States.⁹

3. In January 1995, BTG sued Genentech in the District Court of New York in order to obtain a declaratory judgment that the United States Patent Nos. 4,601,980 ('980) and 4,348,832 ('832) were invalid and not infringed by BTG.¹⁰ Genentech counterclaimed for infringement and moved for a preliminary injunction against BTG for infringement of the two patents.¹¹ The court found in favor of Genentech and granted a preliminary injunction against BTG.¹² Specifically, the court found that (1) BTG's process for producing hGH fell within the literal scope of Claim 2 of the '980 patent; (2) BTG's process for making a plasmid fell within the literal scope of Claim 1 of the '832 patent; and (3) BTG's infringement defenses lacked merit.¹³ Accordingly, BTG appealed to the Court of Appeals for the Federal Circuit.

4. The Federal Circuit affirmed the lower court's grant of a preliminary injunction, finding that the court did not abuse its discretion.¹⁴ Judge Lourie, who authored the opinion, rejected BTG's challenges to the likelihood of success on the merits.¹⁵

5. With respect to Claim 2 of the '980 patent, the Federal Circuit dismissed BTG's three non-infringement arguments.¹⁶ First, the court rejected BTG's claim

⁷ See *id.* (referencing U.S. Pat. No. 4,601,980).

⁸ See *id.* at 1557 (referencing U.S. Pat. No. 4,348,832).

⁹ See *id.*

¹⁰ See *id.*

¹¹ See *Bio-Technology Gen. Corp. v. Genentech, Inc.*, 886 F. Supp. 377, 379 (S.D.N.Y. 1995).

¹² See *id.* at 384.

¹³ See *Bio-Technology Gen. Corp. v. Genentech, Inc.*, 80 F.3d 1553, 1557 (Fed. Cir. 1996).

¹⁴ See *id.* at 1556.

¹⁵ See *id.* at 1558.

¹⁶ See *id.*

that its product was not human growth hormone.¹⁷ BTG claimed that in its process the bacterial host cell product was not hGH as mentioned in Claim 2, but instead was insoluble met-hGH in the form of biologically-inactive inclusion bodies.¹⁸ The Federal Circuit looked to the '980 patent and found that the specification indicated that the product of the process was met-hGH which could or could not be converted to hGH.¹⁹ The court concluded that BTG's biologically-inactive met-hGH that formed inclusion bodies was still "hGH" for purposes of the '980 patent.²⁰

6. Second, BTG claimed that it used its own patented purification process to recover biologically active hGH from the inclusion bodies of met-hGH and that this process was not disclosed in the '980 patent.²¹ The court also rejected this argument, finding that BTG's purification process fell clearly within the broad, generic language of Claim 2's isolation and purification steps.²²

7. Third, BTG argued that its process did not infringe under 35 U.S.C. § 271(g) because it materially changes the product claimed by the patented process.²³ That is, the BTG process materially changes the met-hGH produced by Genentech's process before import into the United States.²⁴ The court again found BTG's argument of a material change invalid based on the '980 patent encompassing both hGH and met-hGH.²⁵

8. The court also discussed BTG's non-infringement argument regarding Claim 1 of the '832 patent.²⁶ BTG constructed the plasmid in question prior to the enactment of section 271(g). Therefore, BTG argued that the lower court erred in retroactively applying the statute.²⁷ The court stated that infringement under

17 *See id.*

18 *See id.*

19 *See id.* at 1559.

20 *See id.* (basing this conclusion on expert testimony).

21 *See id.*

22 *See id.*

23 35 U.S.C. § 271(g) (1994).

24 *See id.*

25 *See id.* at 1559-60.

26 *See id.* at 1560.

27 *See id.*

section 271 does not attach upon the making of the product by a process patented in the United States.²⁸ Instead it involves importing for sale the product made by such a process.²⁹ Thus, the court held that BTG's intent to import and sell hGH in the United States during the term of the '832 patent amounts to infringement.³⁰

9. The court discussed the issue of whether hGH is a product made by a patented process even though Claim 1 of the '832 patent does not specifically cover hGH but covers a method for producing a replicable cloning vehicle (plasmid).³¹ The court noted that the statute does not directly answer this question, but legislative history provides that courts should decide on a case-by-case basis.³² Drawing on similar cases, the court found that infringement of a process for making a plasmid is not avoided by using that plasmid to make its intended product.³³ Furthermore, since the patent detailed the production of hGH through the claimed steps, as a matter of law the production of hGH was not too remote from the claimed process of making the plasmid.³⁴

10. The Federal Circuit affirmed the preliminary injunction because it found BTG's met-hGH was hGH under Claim 2 of the '980 patent. BTG's purification process also fell under the isolation and purification steps of Claim 2. The court found that BTG violated section 271(g) because it intended to import and sell hGH in the United States during the '832 patent term. Finally, the court held that an infringement occurred when BTG used the patented plasmid to make its intended product.

II. *Eli Lilly & Co. v American Cyanamid Co.*

11. In a case involving 35 U.S.C. § 271(g),³⁵ the Federal Circuit Court of Appeals affirmed the ruling in *Eli Lilly & Co. v. American Cyanamid Co.*³⁶ In so

²⁸ *See id.*

²⁹ *See id.*

³⁰ *See id.*

³¹ *See id.* at 1561.

³² *See id.* (citing S. REP. NO. 83, 100th Cong., 1st Sess. 46 (1987)).

³³ *See id.*

³⁴ *See id.*

³⁵ 35 U.S.C. § 271(g) (1994).

³⁶ 82 F.3d 1568 (Fed. Cir. 1996), *aff'g* 896 F. Supp. 851 (S.D. Ind. 1995) The district court had denied Eli Lilly's request for a preliminary injunction against appellee's importation and

deciding, the court applied its interpretation of "materially changed" under section 271(g) to include an intermediate compound.³⁷

12. Eli Lilly³⁸ ("Lilly") developed and patented cefaclor in 1975.³⁹ Each of the known patented processes for creating cefaclor involves production of an intermediate cephem compound known as an enol.⁴⁰ Once the enol cephem intermediate is produced, several steps are required to convert it to cefaclor.⁴¹ In 1995, Lilly purchased the patent at issue in this case.⁴² Claim 5 of the patent defines a method of producing the enol cephem intermediate known as "compound 6."⁴³ Production of cefaclor from compound 6 involves four separate steps.⁴⁴

13. On April 27, 1995, defendants American Cyanamid and Zenith Laboratories obtained FDA approval to distribute domestically the cefaclor produced by Biochimica Opus, S.p.A. of Italy.⁴⁵ Immediately, Lilly obtained the rights to the patent and filed suit for infringement against Cyanamid and Biocraft under several patents including the patent at issue.⁴⁶ Additionally, Lilly requested a preliminary injunction against the appellees to bar importation of the cefaclor produced by Opus, based on alleged infringement of Claim 5.⁴⁷

14. Reviewing Lilly's claim, the district court found that the product imported by defendants was sufficiently "materially changed" under section 271(g)⁴⁸ to avoid

distribution of the generic form of cefaclor, a broad-spectrum antibiotic. *See id.* at 1570.

³⁷ *See id.*

³⁸ Eli Lilly & Co. is a global pharmaceutical research company focused on developing pharmaceuticals to cure central nervous system disorders, cancer, endocrine diseases, infectious diseases, and cardiovascular disorders. For more information on Eli Lilly, see (visited Mar. 25, 1997) *Lilly* <<http://www.lilly.com/>>.

³⁹ *See id.* at 1570.

⁴⁰ *See id.*

⁴¹ *See id.*

⁴² *See id.* (referencing U.S. Pat. No. 4,160,085).

⁴³ *See id.*

⁴⁴ *See id.*

⁴⁵ *See id.*

⁴⁶ *See id.* at 1571.

⁴⁷ *See id.*

⁴⁸ 35 U.S.C. § 271(g) provides that a product is not made by a process if "1) it is materially changed by subsequent processes, or 2) it becomes a trivial and nonessential component of another

infringing Lilly's patent.⁴⁹ The court's justification was that compound 6 and cefaclor differ significantly in their structure and properties, including their biological activity.⁵⁰ Second, the processing steps used to alter compound 6 to cefaclor change the physical or chemical properties of the product in a manner that changes the basic utility of the product.⁵¹ The district court observed that compound 6 must undergo four complex steps to create cefaclor.⁵² In this process, three chemical groups are removed from compound 6 and two groups are added.⁵³ This structural difference results in different properties.⁵⁴ For example, cefaclor has high antibiotic activity while compound 6 has none.⁵⁵ The district court concluded that these biological and molecular differences illustrate the different uses of cefaclor and compound 6.⁵⁶ For example, the only known utility of compound 6 is as an intermediate in production of a variety of cephem compounds, while cefaclor is used as an antibiotic.⁵⁷ The district court concluded that these differences evinced "material change" under section 271(g).⁵⁸ Lilly then appealed to the Federal Circuit Court of Appeals.

15. The Federal Circuit affirmed the lower court's finding that a product produced abroad by a patented process, but modified or incorporated into another product before import, does not infringe the patented process.⁵⁹ Under section 271(g) such a product would not be infringing if it was either materially changed by a subsequent process, or it was a trivial and non-essential compound of another

product."

⁴⁹ See *Eli Lilly & Co. v. American Cyanamid Co.*, 896 F. Supp. 851, 857 (S.D. Ind. 1995).

⁵⁰ See *id.*

⁵¹ See *id.*

⁵² See *id.* at 856.

⁵³ See *id.*

⁵⁴ See *id.*

⁵⁵ See *id.* at 857.

⁵⁶ See *id.*

⁵⁷ See *id.*

⁵⁸ See *id.*

⁵⁹ See *Eli Lilly & Co. v. American Cyanamid Co.*, 82 F.3d 1568, 1568 (Fed. Cir. 1996).

product.⁶⁰ The inquiry turned on whether the imported product was "materially changed" from the product produced by the patented process in regard to section 271(g).⁶¹

16. To determine "materially changed," Lilly advocated an economic value test.⁶² That is, Lilly argued that one should determine whether the infringing product depresses the commercial or economic value of the United States process patent.⁶³ If such an effect is found, Lilly reasoned that the import should be considered infringing under section 271(g).⁶⁴ Lilly argued that a product of a patented process is not materially changed if its principal commercial use is conversion into the product that is the subject of infringement.⁶⁵

17. The court rejected Lilly's argument, noting that the statutory text focuses on a "changed product" not economic consequences.⁶⁶ The court noted that Lilly's theory lacks a limiting factor based either on the structural differences or on the number of steps.⁶⁷ Therefore, the court reasoned, under Lilly's test, if the primary use of compound 6 was to create cefaclor, then compound 6 and cefaclor would be defined as not "materially changed" even if separated by 10 complex steps.⁶⁸ Additionally, the court pointed out Lilly's argument fails because as soon as compound 6 was used for some commercial product other than creating cefaclor, it would become "materially changed" even though its molecular and biological property stayed the same.⁶⁹

18. The court affirmed the lower court's determination that because the physical or chemical manner of the product had changed, which in turn changed its

⁶⁰ See 35 U.S.C. § 271(g).

⁶¹ *Eli Lilly*, 82 F.3d at 1572.

⁶² *See id.*

⁶³ *See id.*

⁶⁴ *See id.*

⁶⁵ *See id.*

⁶⁶ *See id.* at 1572-73 (referencing 35 U.S.C. § 271(g)).

⁶⁷ *See id.* at 1573.

⁶⁸ *See id.*

⁶⁹ *See id.*

utility, the product was "materially changed" for the purposes of section 271(g).⁷⁰ Therefore, appellee's importation of cefaclor did not infringe Lilly's patent for compound 6.⁷¹

19. Judge Rader concurred with the majority's decision because Lilly failed to show irreparable harm.⁷² He disagreed, however, with the majority's interpretation of the "material change" standard under section 271(g).⁷³ Acknowledging that the statute is vague, he criticized the majority's reliance on legislative history.⁷⁴ He pointed out that the House and Senate reports concerning interpretation of "material change" provide a number of tests but that none of these tests provide practical utility.⁷⁵ In his view, the majority should have concentrated on the overriding purpose of the statute to provide protection to United States patent holders.⁷⁶ Previously, foreign companies could import products created abroad by patented processes and escape patent infringement liability.⁷⁷ The statute closed this loophole.⁷⁸ Rader lamented that the majority's decision would produce yet another loophole: denying protection to holders of process patents on intermediate compounds.⁷⁹ He reasoned that in view of the statute's purpose, compound 6 and cefaclor are essentially the same product since compound 6 is only four steps removed from cefaclor and its sole commercial purpose is the production of cefaclor.⁸⁰ Rader argues that the majority decision, in effect, eliminates patent protection for intermediate processes whenever that process is not the only way to make the intermediate.⁸¹

70 *See id.*

71 *See id.*

72 *See id.* at 1579 (Rader, J., concurring).

73 *See id.*

74 *See id.*

75 *See id.* at 1580-81.

76 *See id.* at 1581.

77 *See id.*

78 *See id.*

79 *See id.*

80 *See id.*

81 *See id.*

20. By their unwillingness to grant exceptions to defendants, courts have recognized congressional intent to provide protection to patent holders under section 271(g).⁸² The result is that courts interpret "materially changed" to cover only substantial changes.⁸³ In *Eli Lilly*, the Federal Circuit interpreted substantial change to include an intermediate compound whose sole use was in a process for creating a commercial product.⁸⁴ The determination of whether it is "materially changed" from its final product depends on an analysis of the process steps, structural differences, and utility, not its commercial purpose.

⁸² See Anna M. Budde, *Liability of a Foreign Manufacturer Using a Patented Process for Indirect Infringement*, 42 WAYNE L. REV. 291, 309 (1995).

⁸³ See *id.* at 312.

⁸⁴ See *Eli Lilly*, 82 F.3d at 1578.