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Merck KGaA v. Integra Lifesciences I, Ltd.: Does the Breadth of Safe Harbor Protection Toll the Death Knell For Biotech Research Companies?

In *Merck KGaA v. Integra Lifesciences I, Ltd.*,[1] the United States Supreme Court held that use of patented inventions during research where there was a reasonable basis for believing that the experiments would produce information relevant to Food and Drug Administration ("FDA") approval was protected from patent infringement lawsuits under 35 U.S.C. § 271(e)(1),[2] commonly referred to as the "safe harbor" provision.[3] This decision affirmed almost two decades of judicial decisions affording broad interpretation to the safe harbor provision and reversed the Federal Circuit's creation of a bright-line test limiting the scope of section 271(e)(1).[4]

1. 125 S. Ct. 2372 (2005).
2. 35 U.S.C. § 271(e)(1) (2003).
3. *Merck*, 125 S. Ct. at 2383.
4. *Id.* at 2383-84.

I. FACTUAL BACKGROUND

Integra Lifesciences I, Ltd. ("Integra") owned five patents related to a compound that promoted wound healing, biocompatibility of prosthetic devices, and growth of new blood vessel branches.[5] The compound was a short tri-peptide segment of fibronectin having the sequence Arg-Gly-Asp ("RGD peptide"). The RGD peptide attached to the <<alpha>>v<<beta>>3 receptors on cell surface proteins called integrins. This controlled interaction with integrins was responsible for the claimed beneficial results, such as new blood vessel growth.[6]

Dr. David Cheresh, a scientist at Scripps Research Institute ("Scripps") discovered that blocking <<alpha>>v<<beta>>3 receptors inhibits angiogenesis, the biological process that generates new blood vessels. He also found that blocking angiogenesis was a successful method to stop tumor growth by starving rapidly dividing tumor cells. After the discovery, Merck KGaA ("Merck") hired Scripps and Dr. Cheresh to identify potential drug candidates that might inhibit angiogenesis. In 1997 the Scripps research team chose a derivative of this cyclic peptide for clinical development.[7]

After learning of the agreement between Scripps and Merck, Integra believed the angiogenesis research was a commercial activity that infringed on its RGD peptide patents. Integra offered Merck licenses to the patents-in-suit, which Merck declined following lengthy negotiations. As a result, Integra sued Merck for infringement of its RGD peptide patents.[8] At trial, the court found that Merck's actions were not exempt from infringement under the safe harbor of section 271(e)(1).[9] Without the safe harbor protection, Merck was found liable for infringing four of the five Integra patents.[10]

On appeal, the Federal Circuit affirmed the trial court's ruling that Merck's research activities were not exempt from infringement liability under the safe harbor.[11] To reach this conclusion, the Federal Circuit adopted a narrow interpretation of section 271(e)(1) that excluded protection of drug development activities not solely for uses reasonably related to clinical testing for FDA approval.[12] Clinical testing differs

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5. Integra Lifesciences I, Ltd. v. Merck KGaA, 331 F.3d 860, 863 (Fed. Cir. 2003).
6. *Id.* at 862-63.
7. *Id.* at 863.
8. *Id.*
9. *Id.* at 864.
10. *Id.* at 863-64.
11. *Id.* at 868.
12. *Id.* at 866.

from preclinical research because a drug manufacturer must file an investigational new drug application ("IND") to obtain approval to conduct clinical trials (tests on humans) as part of FDA approval for a new drug.[13] An IND describes preclinical tests (e.g., tests on animals) performed with the drug to justify the proposed clinical testing.[14] Based on the difference between clinical and preclinical research, the court created a bright-line test to assess whether the activity was protected by the safe harbor.[15]

The Supreme Court granted Merck's petition for writ of certiorari to determine whether preclinical research is exempt from infringement under section 271(e)(1).[16]

II. LEGAL BACKGROUND

In 1984 the Second Circuit Court of Appeals impeded the flow of generic drugs into the market with its decision in *Roche Products, Inc. v. Bolar Pharmaceutical Co.*[17] Generally, this decision forced generic drug manufacturers to wait until the patent expired on name-brand drugs before performing any tests on those drugs as part of the FDA approval process.[18] Because it takes years to develop new drugs, prohibiting research that involved patented drugs effectively extended the duration of the patent.[19] Development could begin only when the patent expired. As a result, *Roche* gave pioneer drug manufacturers a *de facto* extension of their patents, because generic drug companies could not begin their research on a competing product until *after* the patent expired.[20]

A. The Origin of "Safe Harbor" Protection Under Section 271(e)(1): Hatch-Waxman Act

In response to the *Roche* decision, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman"),[21] which amended the Patent Act[22] and the Federal Food, Drug,

13. *Merck*, 125 S. Ct. at 2377.
14. *Id.*
15. *Integra*, 331 F.3d at 866.
16. *Merck*, 125 S. Ct. at 2376.
17. 733 F.2d 858 (1984).
18. *Id.* at 863.
19. Eli Lilly v. Medtronic, Inc., 496 U.S. 661, 670 (1990).
20. *Id.*
21. Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. §§ 301, 355, 360cc (2003); 28 U.S.C. § 2201 (1993); 35 U.S.C. §§ 156, 271, 282 (2003)).
22. 35 U.S.C. §§ 1-376 (2000).

and Cosmetic Act[23] ("FDCA") to remove the obstacle created by *Roche*.[24] Specifically, the Act created an exemption for generic competitors to test patented drugs for FDA approval before the patent expires,[25] thus effectively overturning *Roche*.[26] The exemption, codified as 35 U.S.C. § 271(e)(1), is commonly referred to as the "safe harbor" for pharmaceutical research because it protects researchers from patent infringement liability.[27]

Further, the safe harbor enactment effectively stripped the pioneering drug companies of the *de facto* extensions of their patents by allowing generic drugs to reach the market faster.[28] To compensate those drug companies for the *de facto* loss, Congress also created 35 U.S.C. § 156, which extended the life of patents subjected to a lengthy regulatory approval process.[29]

B. Defining The Scope of Section 271(e)(1): Which Patented Inventions Are Protected?

Courts have struggled to define where the limits of safe harbor protection fall within the FDA approval process for generic drugs. This limit is a critical question, because competitors can proceed with developing generic equivalents prior to expiration of the patent only to the extent that the boundaries of the safe harbor are clear. Generally, courts have defined the scope of safe harbor protection by two criteria: (1) the type of patented invention and (2) the proximity of the infringing research phase to downstream FDA approval. Most of the early litigation focused on the first criterion.

1. Early Judicial Interpretation of Section 271(e)(1): Limited Inclusion of Patented Inventions. Following the enactment of section 271(e)(1), the Northern District of California, in *Scripps Clinic & Research Foundation v. Genentech*,[30] made the first attempt to define the scope of the safe harbor provision. There, the court addressed whether a foreign patent could be protected by section 271(e)(1).[31]

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23. 21 U.S.C. § 301-395 (1994).

24. Ann K. Wooster, J.D., Annotation, *Construction and Application of Hatch-Waxman Act*, 180 A.L.R. FED. 487, 508 n.3 (2002).

25. 35 U.S.C. § 271(e)(1) (2003).

26. Wooster, *supra* note 24, at 508 n.3.

27. Elizabeth Stotland Weiswasser & Scott D. Danzis, *The Hatch-Waxman Act: History, Structure, and Legacy*, 71 ANTITRUST L.J. 585, 586 (2003).

28. *Eli Lilly*, 496 U.S. at 671.

29. *Id.* at 670-71.

30. 666 F. Supp. 1379 (N.D. Cal. 1987).

31. *Id.* at 1396.

Scripps developed a process for purifying and concentrating Factor VIII:C, an essential protein that allows the body to produce blood clots.[32] While using Scripps's patented product for research, Genentech independently developed its own process to produce Factor VIII:C and applied for both a U.S. and European patent for its product.[33] Consequently, Scripps sued Genentech for infringement.[34] Genentech claimed that its infringing activities fell within section 271(e)(1) because, even though Genentech had used Scripps's patented product to obtain its European patent, the research had also been used to obtain FDA approval.[35]

The court refused to interpret section 271(e)(1) as broadly as Genentech desired.[36] Under Genentech's interpretation, research bearing a reasonable relationship to the purpose of FDA testing, though not "solely for" that purpose, would be noninfringing under section 271(e)(1).[37] The court rejected this interpretation because it would defy the plain meaning of the statute and the intent of Congress by eliminating the express statutory limitation "solely for."[38] Instead, the court focused on the term "solely for" to conclude that the research must be done "solely for" the purpose of meeting FDA reporting requirements and not for any other purpose.[39] Thus, under *Scripps*, an activity must be performed *solely for* the purpose of obtaining FDA approval to fall within the safe harbor.[40]

2. The Turning Point in Interpretation of Section 271(e)(1): *Eli Lilly v. Medtronic*. The Supreme Court provided the foundation for a broad interpretation of the safe harbor's scope with its decision in *Eli Lilly v. Medtronic*.[41] In *Eli Lilly*, the Court decided whether the safe harbor provision was limited only to drugs.[42] Eli Lilly sued Medtronic for infringement of its patents related to an implantable cardiac defibrillator, a medical device used in the treatment of heart patients.[43] Medtronic claimed that its activities were "'reasonably related to the

32. *Id.* at 1383.
33. *Id.* at 1384-85.
34. *Id.* at 1385.
35. *Id.* at 1396.
36. *Id.*
37. *Id.*
38. *Id.*
39. *Id.*
40. *Id.*
41. 496 U.S. at 661.
42. *Id.* at 663-64.
43. *Id.* at 664.

development and submission of information under' the FDCA", and thus protected by the safe harbor.[44] The district court rejected Medtronic's argument and held that the safe harbor was limited to drug research.[45] The Federal Circuit reversed, stating that activities undertaken to develop information reasonably related to obtaining FDA approval were protected from infringement liability.[46] The Supreme Court affirmed the Federal Circuit, holding that the safe harbor protected pre-market development of medical devices as well as drugs.[47]

To reach this conclusion, the Court relied on statutory construction principles to determine Congress's intent regarding the application of the safe harbor provision to medical device research.[48] In particular, a point that weighed heavily in the decision was the fact that section 271(e)(1) was intended to be the counterpart to section 156,[49] which extended the life of patents subject to lengthy FDA approvals.[50] Section 156 included medical devices in the list of items eligible for such an extension.[51] The Court reasoned that Congress likely would not have given both drugs and medical devices the benefit of a patent extension under section 156 without burdening both with infringement protection under section 271(e)(1).[52] As a result, the Court interpreted section 271(e)(1), in light of section 156, to determine whether an infringing activity was protected by the safe harbor.[53] By looking beyond the text of section 271(e)(1) to find congressional intent, the Supreme Court established the principle that the safe harbor provision should be interpreted broadly.[54]

3. Judicial Interpretation of Section 271(e)(1) Following *Eli Lilly*: Broad Inclusion of Patented Inventions. Following the Supreme Court's decision in *Eli Lilly* to broadly interpret section 271(e)(1), courts have progressively extended the protection afforded by section 271(e)(1).[55]

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44. *Id.*
45. *Id.*
46. *Id.*
47. *Id.* at 678-79.
48. *Id.* at 673.
49. *Id.*
50. *Id.* at 670-71.
51. *Id.* at 673-74.
52. *Id.* at 672-73.
53. *Id.* at 672-74.
54. *Id.*
55. *See* Abtox v. Exitron, 122 F.3d 1019 (Fed. Cir. 1997); Telectronics Pacing Sys. Inc. v. Ventritex, 982 F.2d 1520 (Fed. Cir. 1992); Wesley Jessen Corp. v. Bausch & Lomb, Inc., 235 F. Supp. 2d 370 (D. Del. 2002).

In *Intermedics v. Ventritex*,[56] Intermedics alleged that Ventritex's manufacture of defibrillators, its sale to hospitals, and demonstration of the device at trade shows, infringed its patents.[57] To determine whether an activity was within safe harbor protection, the Northern District of California created a two-part test: (1) whether the actual use was infringing, and (2) whether it would be reasonable for a party in the defendant's situation to believe that its uses would contribute to the kinds of information the FDA would consider relevant when deciding to approve a product.[58]

Under part one, the court limited the types of activities subject to infringement analysis.[59] The court objectively looked at the actual use to assess whether the act was an infringing activity, without considering a party's motive or intent behind an act.[60] The objective application was based on the statutory language "solely for *uses* reasonably related."[61] The word "uses", rather than "purposes", provided clear evidence of Congress's intent to apply the exemption objectively.[62] The court determined that, under part one of the test, none of Ventritex's activities constituted an infringing activity, thus obviating the need to analyze the scope of safe harbor protection.[63]

Under part two, the court did not limit the exemption to infringing uses that actually result in information for submission to the FDA.[64] Instead, the test asks objectively whether the use in question could reasonably contribute to the generation of information of the type that would likely be required for FDA approval, thus providing innovators with a more generous safe harbor protection.[65] This test is based on Congress's intent not to punish a competitor if some of its activities generated information that did not interest the FDA, or generated more information than was necessary to obtain FDA approval.[66]

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56. 775 F. Supp. 1269 (N.D. Cal. 1991).
57. *Id.* at 1282.
58. *Id.* at 1281.
59. *Id.* at 1279.
60. *Id.* at 1275.
61. *Id.* at 1278 (emphasis added).
62. *Id.*
63. *Id.* at 1281-88.
64. *Id.* at 1280-81.
65. *Id.*
66. *Id.* at 1280.

This test, which has been adopted by subsequent courts,[67] opened the door to the inclusion of other types of patented inventions beyond the narrow list originally intended by Congress.[68] It is this judicially created test that has inspired many proposals to limit the scope of section 271(e)(1) to include only those activities within congressional intent.[69]

Courts have adhered to the doctrine of broad interpretation set forth in *Eli Lilly*, even when presented with clear opportunities to narrow the scope of section 271(e)(1) protection. For example, in *Abtox v. Exitron*,[70] the Federal Circuit chose to enlarge the safe harbor provision beyond the limits set forth in *Eli Lilly*.[71] Abtox was accused of infringing a patent covering a plasma sterilizer[72] categorized as a Class II medical device.[73] While the Supreme Court's decision in *Eli Lilly* established that medical devices were covered by the safe harbor generally, the device at issue in *Eli Lilly* had been a Class III medical device.[74] Only Class III medical devices are subject to a lengthy regulatory approval process, which is the requirement to qualify for a patent extension under section 156.[75] In contrast, an abbreviated FDA approval process applied to Class I and II medical devices.[76] Under the *Eli Lilly* test, the safe harbor did not protect Class II medical devices because they did

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67. *See, e.g.*, *Telectronics Pacing Sys.*, 982 F.2d at 1525 n.5 (citing the second part of the *Intermedics* test as a "carefully reasoned and exhaustive analysis" of congressional intent regarding use of derived test data for fund raising and other business purposes).

68. William Feiler & Paula Wittmayer, *Expanding Exemptions for Generics*, MANAGING INTELL. PROP., June 1, 2003, at 48.

69. *Id.*

70. 122 F.3d 1019 (Fed. Cir. 1997).

71. *Id.* at 1029.

72. *Id.* at 1022.

73. *Id.* at 1027. The FDCA, through the Medical Device Amendments of 1976, classifies medical devices into three categories based on the risk posed by their use. *Abtox*, 122 F.3d at 1028. Class I includes devices that present no unreasonable risk of illness or injury, which are subject to minimal regulation by "general controls." *Id.* Class II devices are those that are more harmful but may be marketed without advance approval, which are subject to federal performance regulations known as "special controls." *Id.* Class III includes devices that either "present a potential unreasonable risk of illness or injury," or are "purported or represented to be for a use in supporting or sustaining life or for a use which is of substantial importance in preventing impairment of human health." *Id.* (quoting 21 U.S.C. § 360c(a)(1)(C)). Class III medical devices must undergo a rigorous premarket approval process, whereas Class I and II devices experience an abbreviated approval process. *Id.*

74. *Id.* at 1029. The device at issue in *Eli Lilly* was an implantable cardiac defibrillator, a medical device used in the treatment of heart patients. *Id.* at 1028.

75. *Id.* at 1028-29.

76. *Id.* at 1028.

not qualify for patent extension under section 156.[77] The Federal Circuit, however, characterized the Supreme Court's analysis interpreting section 271(e)(1), in light of section 156, as narrow.[78] Instead, the Federal Circuit focused on the Supreme Court's broad reasoning that section 271(e)(1) applies to any use reasonably related to regulation under the FDCA.[79] By applying this broad reasoning, the court concluded that the safe harbor extended to Class II medical device research.[80] By adopting the Supreme Court's broader policy reasoning over its narrower interpretation of section 271(e)(1) in light of section 156, the Federal Circuit reinforced the policy of broadly interpreting safe harbor protection.[81]

Like the Federal Circuit in *Abtox*, other courts have interpreted section 271(e)(1) broadly.[82] Contrary to the trend of expanding protection under the safe harbor, the Western District of Wisconsin in *Infigen, Inc. v. Advanced Cell Technology, Inc.*[83] refused to follow the Federal Circuit's reasoning in *Abtox*.[84] Instead, the district court returned to the Supreme Court's *Eli Lilly* test, stating that section 271(e)(1) extended protection only to those patents offered extensions under section 156.[85] In that case, one patent at issue was directed to a process for activating bovine oocytes for use in cloning cattle.[86] This activity was not subjected to a lengthy FDA approval process, and thus, did not qualify for an extended patent term under section 156.[87] The court found that section 271(e)(1) did not protect the activity under the *Eli Lilly* test, which required interpretation of section 271(e)(1) in light of section 156.[88] In support of this result, the court stated that "the patent extension is the quid pro quo for the protection from infringement actions and vice versa."[89]

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77. *Id.*
78. *Id.* at 1029.
79. *Id.*
80. *Id.*
81. *Id.*
82. *See Telectronics Pacing Sys.*, 982 F.2d at 1523-24 (holding that trade show demonstrations are an exempt use under section 271(e)(1)); *Wesley Jessen Corp.*, 235 F. Supp. 2d at 376 (interpreting section 271(e)(1) to allow an infringer to continue to sell a product after FDA approval was received).
83. 65 F. Supp. 2d 967 (W.D. Wis. 1999).
84. *Id.* at 980.
85. *Id.*
86. *Id.* at 970.
87. *Id.* at 980.
88. *Id.*
89. *Id.*

The district court's decision in *Infigen* is contrary to the Federal Circuit's holding in *Abtox*.[90] Thus, it is likely that the Federal Circuit would have reversed *Infigen* on appeal.[91] The *Infigen* case, however, settled before reaching the appellate level.[92] For this reason, this rare decision narrowing the scope of section 271(e)(1) has largely been ignored.[93]

C. Defining The Scope of Section 271(e)(1): Expanding Safe Harbor Protection To Upstream Research

In recent years, litigation over safe harbor protection has shifted to the second criterion: the relationship between the infringing research phase and the downstream FDA approval. Under this criterion, courts have gradually extended safe harbor protection further upstream in the drug discovery process.[94] For example, in *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*,[95] the District Court of Massachusetts adopted the broad interpretation rationale to extend safe harbor protection to activities performed in the initial stages of drug development.[96] Hoechst used Amgen's patented protein product ("EPO") to facilitate development of a competing product.[97] Hoechst's infringing activities included: (1) exporting a batch of EPO to Japan to evaluate an alternative manufacturing process, (2) performing EPO purity studies, (3) producing commercial scale batches of EPO, (4) characterizing the carbohydrate structure of EPO, (5) performing tests for European regulatory approval, and (6) planning to conduct testing for Japanese regulatory approval.[98] The court extended protection to all of these infringing activities because they might "bear reasonable prospects of yielding information that might be relevant in the FDA approval process."[99] The court concluded that Hoechst's activities were within the safe harbor by emphasizing that while use of a patented invention must be *reasonably related* to FDA approval, it need not be for the *exclusive purpose* of FDA approval.[100]

Amgen extended safe harbor protection to early use of patented drugs in generic drug research but did not address use of other patented

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90. Feiler & Wittmayer, *supra* note 68, at 48.
91. *Id.*
92. *Id.*
93. *Id.*
94. *Id.* at 50.
95. 3 F. Supp. 2d 104 (D. Mass. 1998).
96. *Id.* at 110.
97. *Id.* at 106.
98. *Id.* at 108-11.
99. *Id.* at 108.
100. *Id.*

products in the drug discovery process. By following and expanding *Amgen*'s holding, the Southern District of New York, in *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*,[101] extended safe harbor protection to cover patented biotech research tools used in the drug discovery process.[102] Bristol-Myers had used Rhone-Poulenc's patented intermediate chemical compounds during research and development of its end-product drug.[103] The court determined that the safe harbor covered use of patented intermediate chemical compounds, a biotech research tool, in the development of new drugs.[104] The court reasoned that even though each use of the biotech research tool by Bristol-Myers in early stage research might not have yielded information that could be submitted to the FDA, the uses related to this preliminary activity could facilitate the generation of information that later would be submitted.[105]

Safe harbor protection has also been granted to biotech research tools in the development of medical devices.[106] In *Nexell Therapeutics, Inc. v. AmCell Corp.*,[107] AmCell had been seeking FDA approval for a stem cell separator designed to separate good stem cells from malignant stem cells.[108] AmCell's separator performed this function by utilizing a monoclonal antibody, which adhered to the desired stem cells.[109] Nexell owned the patent on the monoclonal antibody[110] and sued for infringement.[111] AmCell claimed that safe harbor protection extended to cover the use of biotech tools necessary to use the stem cell separator in the FDA approval process.[112] The District Court of Delaware focused on the activities performed to obtain FDA approval of the cell separator and found that only those activities reasonably related to that approval were exempt under the safe harbor provision.[113]

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101. 2001 WL 1512597 (S.D.N.Y. Nov. 28, 2001) (unpublished opinion).
102. *Id.* at *3.
103. *Id.* at *1.
104. *Id.* at *6.
105. *Id.* at *7.
106. *See* Nexell Therapeutics, Inc. v. AmCell Corp., 143 F. Supp. 2d 407, 422-23 (D. Del. 2001).
107. 143 F. Supp. 2d 407 (D. Del. 2001).
108. *Id.* at 410-11, 420. Stem cells are undifferentiated cells that have the potential of becoming red blood cells, white blood cells, or platelets. *Id.* at 410. In cancer patients, the good stem cells are returned to the patient after treating the marrow to destroy the malignant cells. *Id.*
109. *Id.* at 411.
110. *Id.* at 413.
111. *Id.* at 418.
112. *Id.*
113. *Id.* at 422-23.

III. COURT'S RATIONALE

The Supreme Court granted certiorari in *Merck KGaA v. Integra Lifesciences I, Ltd.*[114] to consider whether preclinical research is exempt from infringement under section 271(e)(1).[115]

Writing for a unanimous Court, Justice Scalia relied on the plain meaning of the text of section 271(e)(1) to determine the scope of activities included in the safe harbor.[116] The Court held that the statutory text did not support a bright-line exclusion of preclinical research from the types of activities that fell under the "reasonably related" language of the statute.[117] In particular, the Court determined that "the statutory text makes clear that it provides a wide berth for the use of patented drugs in activities related to the federal regulatory process."[118]

The Court's holding affirmed a line of cases preceding the Federal Circuit's decision in *Integra Lifesciences I, Ltd. v. Merck KGaA*.[119] In effect, the decision reiterates the general principle established in *Eli Lilly* that the safe harbor provision should be interpreted broadly.[120] Specifically, the Court held that:

> [W]here a drugmaker has a reasonable basis for believing that a patented compound may work, through a particular biological process, to produce a particular physiological effect, and uses the compound in research that, if successful, would be appropriate to include in a submission to the FDA, that use is "reasonably related" to the "development and submission of information under . . . Federal law."[121]

Thus, a potentially infringing use could be protected under section 271(e)(1) regardless of whether a researching company actually submits to the FDA specific preclinical or clinical data from the scientific research process attendant to that use, as long as the researcher had a reasonable belief that the information would be appropriate to include in a regulatory submission in some manner.[122]

The Supreme Court reversed the Federal Circuit's holding because the lower court erroneously relied on legislative history to conclude that

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114. 125 S. Ct. 2372 (2005).
115. *Id.* at 2376.
116. *Id.* at 2383.
117. *Id.*
118. *Id.* at 2380.
119. 331 F.3d 860 (2003).
120. *Merck*, 125 S. Ct. at 2383 (quoting 35 U.S.C. § 271(e)(1)).
121. *Id.*
122. *Id.*

Congress had intended to provide a narrow exemption for infringing activities related to drug research.[123] The Federal Circuit stated in its opinion that the legislative record showed the section 271(e)(1) exemption had been narrowly tailored to have only a *de minimis* impact on the patentee's right to exclude.[124] With this intent in mind, the Federal Circuit focused on the "solely" language to achieve a narrow interpretation of section 271(e)(1) that prevented extension of "'reasonably related' to embrace the development of new drugs because those new products will also need FDA approval."[125] This interpretation made a significant break from preceding cases that refused to read any such limitations into the "reasonably related" language.[126] The Federal Circuit's opinion noticeably restricted the activities that qualified as being reasonably related to the FDA approval process.[127] Essentially, the Federal Circuit drew a line between clinical and preclinical experimentation to create a bright-line rule as to when the exemption applies.[128]

In contrast to the Federal Circuit's analysis, the Supreme Court reasoned that scientific testing is a process of trial and error.[129] The Federal Circuit's interpretation of the safe harbor excluded protection of research conducted on patented compounds for which an IND is not ultimately filed.[130] Such an interpretation limited the safe harbor protection to situations where the researcher knows at the outset that a particular compound will be the subject of an eventual application to the FDA.[131] A researcher would only have such insight where "the active ingredient in the drug being tested is identical to that in a drug that has already been approved."[132]

In rejecting the Federal Circuit's interpretation, the Supreme Court stated that the plain language of the statute does not support such a narrow interpretation.[133] Rather, the statute "exempted from infringement *all* uses of patented compounds 'reasonably related' to the process of developing information for submission under *any* federal law

123. *Id.*
124. *Integra*, 331 F.3d at 867.
125. *Id.*
126. *See, e.g.*, Intermedics, Inc. v. Ventritex, Inc., 775 F. Supp. 1269, 1279 (N.D. Cal. 1991).
127. *Integra*, 331 F.3d at 866-67.
128. *Id.* at 866.
129. *Merck*, 125 S. Ct. at 2382.
130. *Id.* at 2383.
131. *Id.*
132. *Id.*
133. *Id.*

regulating the manufacture, use, or distribution of drugs."[134] As a result, the Supreme Court stated that section 271(e)(1) "leaves adequate space for experimentation and failure on the road to regulatory approval. . . ."[135]

IV. IMPLICATIONS

The Supreme Court's decision in *Merck KGaA v. Integra Lifesciences I, Ltd.*[136] reversed the Federal Circuit's decision to exclude preclinical use of patented compounds in drug research from the safe harbor of section 271(e)(1).[137] By exempting infringing activities performed early in the research process, the safe harbor protection is granted to users of any patented invention, including biotech research tools, that may be used in connection with the generation of information to the FDA.[138] The breadth of protection afforded by section 271(e)(1) has serious implications for pharmaceutical companies and the biotech industry.

From the perspective of the pharmaceutical industry, the Court's opinion allows generic drug makers to bring new drug therapies to the market quicker, cheaper, and with less risk of infringement suits.[139] By allowing generic drug companies to conduct preclinical research on patented compounds without fear of patent infringement suits, those companies can accelerate the time to develop new drugs and make drug discovery more efficient.[140]

From the biotech industry's perspective, the expansive interpretation of section 271(e)(1) may be quite harmful.[141] The Federal Circuit "suggested that a limited construction of section 271(e)(1) is necessary to avoid depriving so-called 'research tools' of the complete value of their patents."[142] Although the Supreme Court declined to expressly address the issue raised by the Federal Circuit regarding biotech research tools, the implications of a broad interpretation of the safe harbor provision raises serious concern among the biotech companies.[143] Examples of biotech research tools that may be impacted by this decision are DNA sequences, stem cell lines, monoclonal antibodies, reagents, animal

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134. *Id.*
135. *Id.*
136. 125 S. Ct. 2372 (2005).
137. *Id.* at 2383-84.
138. Feiler & Wittmayer, *supra* note 68, at 50.
139. Robert W. Esmond & Robert A. Schwartzman, *The Patent Infringement Exemption Land Grab*, 17 NO. 6 INTELL. PROP. & TECH. L.J. 11, 14 (June 2005).
140. *Id.*
141. *Id.*
142. *Merck*, 125 S. Ct. at 2382 n.7.
143. *Id.*

models, growth factors, clones and cloning tools, laboratory equipment and machines, databases, and computer software.[144] A broad exemption from patent infringement could seriously harm biotech companies whose business is limited to these types of products, which have little use outside of biomedical research.[145] By removing the possibility of infringement lawsuits, researchers will have little incentive to pay licensing fees for these research tools.[146] Without a means to encourage license fee payment for patented research tools, the biotech industry will no longer try to develop and patent new drug discovery tools.[147]

Alternatively, these companies may try to conceal their inventions from the public under "trade secret" protection.[148] The removal of public availability of such inventions not only will lead to a significant reduction in new inventions relating to drug discovery, but also will strike a major blow against small pharmaceutical companies whose patented drugs are often used in the discovery of other drugs.[149] In the end, the decision will effectively destroy an entire industry dedicated to developing new drug discovery tools.[150]

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144. Report of the National Institutes of Health (NIH) Working Group on Research Tools 3 (June 4, 1998), *available at* http://www.nih.gov/news/researchtools/index.htm.

145. Esmond & Schwartzman, *supra* note 139, at 14.

146. *Id.*

147. *Id.*

148. *Id.*

149. *Id.*

150. *Id.*

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