Syllabus

MERCK KGaA *v.* INTEGRA LIFESCIENCES I, LTD., ET AL.

CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

No. 03–1237. Argued April 20, 2005—Decided June 13, 2005

It is not "an act of [patent] infringement to . . . use . . . or import into the United States a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the . . . use . . . of drugs." 35 U. S. C. § 271(e)(1). The Federal Food, Drug, and Cosmetic Act of 1938 (FDCA) is such a law. Under the FDCA, a drugmaker must submit research data to the Food and Drug Administration (FDA) in an investigational new drug application (IND) when seeking authorization to conduct human clinical trials, and in a new drug application (NDA) when seeking authorization to market a new drug. Respondents filed a patent-infringement suit, claiming, *inter alia,* that petitioner had willfully infringed their patents by supplying respondents' RGD peptides to other defendants for use in preclinical research. Petitioner answered, among other things, that § 271(e)(1) exempted its actions from infringement. The jury found otherwise and awarded damages. In post-trial motions, the District Court affirmed the jury's award and denied petitioner's motion for judgment as a matter of law. The Federal Circuit affirmed that denial, finding that § 271(e)(1)'s safe harbor did not apply. It reversed the District Court's refusal to modify the damages award and remanded for further proceedings.

Held: The use of patented compounds in preclinical studies is protected under § 271(e)(1) at least as long as there is a reasonable basis to believe that the compound tested could be the subject of an FDA submission and the experiments will produce the types of information relevant to an IND or NDA. The statutory text makes clear that § 271(e)(1) provides a wide berth for the use of patented drugs in activities related to the federal regulatory process, including uses reasonably related to the development and submission of any information under the FDCA. *Eli Lilly & Co.* v. *Medtronic, Inc.*, 496 U. S. 661, 665–669. This necessarily includes preclinical studies, both those pertaining to a drug's safety in humans and those related to, *e. g.,* a drug's efficacy and mechanism of action. Additionally, § 271(e)(1) exempts from infringement the use of patented compounds in preclinical research, even when the patented compounds do not themselves become the subject of an FDA submission.

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The "reasonable relation" requirement cannot be read effectively to limit § 271(e)(1)'s stated protection of activities leading to FDA approval for all drugs to those activities leading to FDA approval for generic drugs. Similarly, the use of a patented compound in experiments not themselves included in a "submission of information" to the FDA does not, standing alone, render the use infringing. Because the Federal Circuit applied the wrong standard in rejecting petitioner's challenge to the jury's finding that petitioner failed to show that its activities were covered by § 271(e)(1), the trial evidence has yet to be reviewed under the standard set forth in the jury instruction, and developed in more detail here. Pp. 202–208.

331 F. 3d 860, vacated and remanded.

SCALIA, J., delivered the opinion for a unanimous Court.

E. Joshua Rosenkranz argued the cause for petitioner. With him on the briefs were *M. Patricia Thayer*, *James N. Czaban*, and *Donald R. Dunner*.

Daryl Joseffer argued the cause for the United States as *amicus curiae* in support of petitioner. With him on the brief were *Acting Solicitor General Clement*, *Assistant Attorney General Keisler*, *Deputy Solicitor General Hungar*, *Douglas N. Letter*, *Mark S. Davies*, *Alex M. Azar II*, *Richard Lambert*, *John M. Whealan*, and *Heather F. Auyang*.

Mauricio A. Flores argued the cause for respondents. With him on the brief were *Raphael V. Lupo*, *Cathryn Campbell*, *Mark G. Davis*, *M. Miller Baker*, *Richard B. Rogers*, and *David M. Beckwith*.*

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*Briefs of *amici curiae* urging reversal were filed for AARP by *Sarah Lenz Lock*, *Bruce Vignery*, and *Michael Schuster;* for Eli Lilly and Co. et al. by *James J. Kelley*, *Thomas G. Plant*, and *John A. Cleveland, Jr.;* for Eon Labs, Inc., by *Shashank Upadhye;* for Genentech, Inc., et al. by *Carter G. Phillips*, *Virginia A. Seitz*, *Jeffrey P. Kushan*, and *Gary H. Loeb;* for the New York Intellectual Property Law Association by *David F. Ryan;* and for Pharmaceutical Research and Manufacturers of America by *Roderick R. McKelvie* and *Brooks Mackintosh*.

Briefs of *amici curiae* urging affirmance were filed for Applera Corp. et al. by *Edward R. Reines;* for Benitec Australia Ltd. by *Eric A. Kuwana*, *Marc R. Labgold*, and *Kevin M. Bell;* for Invitrogen Corp. et al. by *Drew S. Days III*, *Beth S. Brinkmann*, *Seth M. Galanter*, *David C. Doyle*,

JUSTICE SCALIA delivered the opinion of the Court.

This case presents the question whether uses of patented inventions in preclinical research, the results of which are not ultimately included in a submission to the Food and Drug Administration (FDA), are exempted from infringement by 35 U. S. C. §271(e)(1).

I

It is generally an act of patent infringement to "mak[e], us[e], offe[r] to sell, or sel[l] any patented invention . . . during the term of the patent therefor." §271(a). In 1984, Congress enacted an exemption to this general rule, see Drug Price Competition and Patent Term Restoration Act of 1984, §202, 98 Stat. 1585, as amended, 35 U. S. C. §271(e)(1), which provides:

> "It shall not be an act of infringement to make, use, offer to sell, or sell within the United States or import into the United States a patented invention (other than a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Act of March 4, 1913) . . .) solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs . . . ."

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and *Andrea L. Gross;* for Vaccinex, Inc., by *Kenneth C. Bass III* and *Linda Alcorn;* and for the Wisconsin Alumni Research Foundation et al. by *Rolf O. Stadheim* and *George C. Summerfield.*

Briefs of *amici curiae* were filed for the American Intellectual Property Law Association by *Donald R. Ware*, *Denise W. DeFranco*, and *Melvin C. Garner;* for the Biotechnology Industry Organization by *Richard J. Oparil;* for the Consumer Project on Technology et al. by *Joshua D. Sarnoff;* for Intellectual Property Professors by *John Fitzgerald Duffy* and *Katherine J. Strandburg;* for the Patent, Trademark & Copyright Section of the Bar Association of the District of Columbia by *Lynn E. Eccleston* and *Susan M. Dadio;* for the San Diego Intellectual Property Law Association by *Madison C. Jellins*, *Doug E. Olson*, and *John E. Peterson;* and for Sepracor Inc. by *Kenneth J. Burchfiel* and *Michael R. Dzwonczyk.*

The Federal Food, Drug, and Cosmetic Act (FDCA), ch. 675, 52 Stat. 1040, as amended, 21 U. S. C. § 301 *et seq.*, is "a Federal law which regulates the manufacture, use, or sale of drugs." See § 355(a); *Eli Lilly & Co.* v. *Medtronic, Inc.*, 496 U. S. 661, 665–666, 674 (1990). Under the FDCA, a drugmaker must submit research data to the FDA at two general stages of new-drug development.[1] First, a drugmaker must gain authorization to conduct clinical trials (tests on humans) by submitting an investigational new drug application (IND). See 21 U. S. C. § 355(i); 21 CFR § 312.1 *et seq.* (2005).[2] The IND must describe "preclinical tests (including tests on animals) of [the] drug adequate to justify the proposed clinical testing." 21 U. S. C. § 355(i)(1)(A); see 21 CFR §§ 312.23(a)(5) and (a)(8) (specifying necessary information from preclinical tests). Second, to obtain authorization to market a new drug, a drugmaker must submit a new drug application (NDA), containing "full reports of investigations which have been made to show whether or not [the] drug is safe for use and whether [the] drug is effective in use." 21 U. S. C. § 355(b)(1). Pursuant to FDA regulations, the NDA must include all clinical studies, as well as preclinical studies related to a drug's efficacy, toxicity, and pharmacological properties. See 21 CFR §§ 314.50(d)(2) (preclinical studies) and (d)(5) (clinical studies).

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[1] Drugmakers that desire to market a generic drug (a drug containing the same active ingredients as a drug already approved for the market) may file an abbreviated new drug application (ANDA) with the FDA. See 21 U. S. C. § 355(j). The sponsor of a generic drug does not have to make an independent showing that the drug is safe and effective, either in preclinical or clinical studies. See § 355(j)(2)(A). It need only show that the drug includes the same active ingredients as, and is bioequivalent to, the drug that it is mimicking. See §§ 355(j)(2)(A)(ii) and (iv); § 355(j)(8)(B).

[2] We cite the current versions of federal statutes and regulations. The provisions cited are materially unchanged since the period of petitioner's alleged infringement.

II

A

Respondents, Integra Lifesciences I, Ltd., and the Burnham Institute, own five patents related to the tripeptide sequence Arg-Gly-Asp, known in single-letter notation as the "RGD peptide." U. S. Patent Nos. 4,988,621, 4,792,525, 5,695,997, 4,879,237, and 4,789,734, Supp. App. SA11–SA19. The RGD peptide promotes cell adhesion by attaching to $\alpha_v\beta_3$ integrins, receptors commonly located on the outer surface of certain endothelial cells. 331 F. 3d 860, 862–863 (CA Fed. 2003).

Beginning in 1988, petitioner Merck KGaA provided funding for angiogenesis research conducted by Dr. David Cheresh at the Scripps Research Institute (Scripps). *Telios Pharmaceuticals* v. *Merck KGaA*, Case No. 96–CV–1307 (SD Cal., Sept. 9, 1997), App. 30a. Angiogenesis is the process by which new blood vessels sprout from existing vessels; it plays a critical role in many diseases, including solid tumor cancers, diabetic retinopathy, and rheumatoid arthritis. 331 F. 3d, at 863. In the course of his research, Dr. Cheresh discovered that it was possible to inhibit angiogenesis by blocking the $\alpha_v\beta_3$ integrins on proliferating endothelial cells. *Ibid.* In 1994, Dr. Cheresh succeeded in reversing tumor growth in chicken embryos, first using a monoclonal antibody (LM609) he developed himself and later using a cyclic RGD peptide (EMD 66203) provided by petitioner.[3] App. 190a. Dr. Cheresh's discoveries were announced in leading medical journals and received attention in the general media. See Altman, Scientists Report Finding a Way to Shrink Tumors, N. Y. Times, Dec. 30, 1994, p. A1; Brooks et al., Integrin

[3] In the proceedings below, the Court of Appeals held that respondents' patents covered the cyclic RGD peptides developed by petitioner. 331 F. 3d 860, 869 (CA Fed. 2003). Petitioner does not contest that ruling here.

$\alpha_v\beta_3$ Antagonists Promote Tumor Regression by Inducing Apoptosis of Angiogenic Blood Vessels, 79 Cell 1157 (Dec. 30, 1994); Brooks, Clark, & Cheresh, Requirement of Vascular Integrin $\alpha_v\beta_3$ for Angiogenesis, 264 Science 569 (Apr. 22, 1994).

With petitioner's agreement to fund research at Scripps due to expire in July 1995, Dr. Cheresh submitted a detailed proposal for expanded collaboration between Scripps and petitioner on February 1, 1995. App. 95a–107a. The proposal set forth a 3-year timetable in which to develop "integrin antagonists as angiogenesis inhibitors," *id.*, at 105a, beginning with *in vitro* and *in vivo* testing of RGD peptides at Scripps in year one and culminating with the submission of an IND to the FDA in year three, *id.*, at 106a–107a. Petitioner agreed to the material terms of the proposal on February 20, 1995, *id.*, at 124a–125a, and on April 13, 1995, pledged $6 million over three years to fund research at Scripps, *id.*, at 126a. Petitioner's April 13 letter specified that Scripps would be responsible for testing RGD peptides produced by petitioner as potential drug candidates but that, once a primary candidate for clinical testing was in "the pipeline," petitioner would perform the toxicology tests necessary for FDA approval to proceed to clinical trials. *Id.*, at 127a; see 21 CFR § 312.23(a)(8)(iii) (2005) (requirement that "nonclinical laboratory study" include a certification that it was performed under good laboratory practices); see also § 58.3(d) (2004) (defining "[n]onclinical laboratory study"). Scripps and petitioner concluded an agreement of continued collaboration in September 1995. Case No. 96–CV–1307, App. 31a.

Pursuant to the agreement, Dr. Cheresh directed *in vitro* and *in vivo* experiments on RGD peptides provided by petitioner from 1995 to 1998. These experiments focused on EMD 66203 and two closely related derivatives, EMD 85189 and EMD 121974, and were designed to evaluate the suitability of each of the peptides as potential drug candidates. 331 F. 3d, at 863. Accordingly, the tests measured the efficacy,

specificity, and toxicity of the particular peptides as angiogenesis inhibitors, and evaluated their mechanism of action and pharmacokinetics in animals. *Ibid.* Based on the test results, Scripps decided in 1997 that EMD 121974 was the most promising candidate for testing in humans. *Ibid.* Over the same period, Scripps performed similar tests on LM609, a monoclonal antibody developed by Dr. Cheresh.[4] App. 277a, 285a–298a. Scripps also conducted more basic research on organic mimetics designed to block $\alpha_v\beta_3$ integrins in a manner similar to the RGD peptides, *id.*, at 223a–224a; it appears that Scripps used the RGD peptides in these tests as "positive controls" against which to measure the efficacy of the mimetics, *id.*, at 188a.

In November 1996, petitioner initiated a formal project to guide one of its RGD peptides through the regulatory approval process in the United States and Europe. *Id.*, at 129a. Petitioner originally directed its efforts at EMD 85189, but switched focus in April 1997 to EMD 121974. Case No. 96–CV–1307, App. 31a. Petitioner subsequently discussed EMD 121974 with officials at the FDA. *Id.*, at 397a. In October 1998, petitioner shared its research on RGD peptides with the National Cancer Institute (NCI), which agreed to sponsor clinical trials. *Id.*, at 214a–217a. Although the fact was excluded from evidence at trial, the lower court's opinion reflects that NCI filed an IND for EMD 121974 in 1998. 331 F. 3d, at 874 (Newman, J., dissenting).

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[4] Scripps licensed the patent for the monoclonal antibody to Ixsys, a California biotechnology company. App. 271a. Based on research conducted at Scripps and at Ixsys in consultation with Dr. Cheresh, an IND application for a humanized version of the antibody called Vitaxin was filed with the FDA on December 30, 1996. *Id.*, at 271a–274a, 404a. In addition to toxicology tests, the application included information from Dr. Cheresh's *in vitro* and *in vivo* experiments related to the antibody's mechanism of action and efficacy as an inhibitor of angiogenesis. *Id.*, at 399a–404a. Ixsys began clinical testing of the antibody as an angiogenesis inhibitor in February 1997. *Id.*, at 304a.

B

On July 18, 1996, respondents filed a patent-infringement suit against petitioner, Scripps, and Dr. Cheresh in the District Court for the Southern District of California. Respondents' complaint alleged that petitioner willfully infringed and induced others to infringe respondents' patents by supplying the RGD peptide to Scripps, and that Dr. Cheresh and Scripps infringed the same patents by using the RGD peptide in experiments related to angiogenesis. Respondents sought damages from petitioner and a declaratory judgment against Dr. Cheresh and Scripps. *Id.*, at 863. Petitioner answered that its actions involving the RGD peptides did not infringe respondents' patents, and that in any event they were protected by the common-law research exemption and 35 U. S. C. § 271(e)(1). 331 F. 3d, at 863.

At the conclusion of trial, the District Court held that, with one exception, petitioner's pre-1995 actions related to the RGD peptides were protected by the common-law research exemption, but that a question of fact remained as to whether petitioner's use of the RGD peptides after 1995 fell within the § 271(e)(1) safe harbor. With the consent of the parties, the District Court gave the following instruction regarding the § 271(e)(1) exemption:

> "To prevail on this defense, [petitioner] must prove by a preponderance of the evidence that it would be objectively reasonable for a party in [petitioner's] and Scripps' situation to believe that there was a decent prospect that the accused activities would contribute, relatively directly, to the generation of the kinds of information that are likely to be relevant in the processes by which the FDA would decide whether to approve the product in question.
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> "Each of the accused activities must be evaluated separately to determine whether the exemption applies.

> "[Petitioner] does not need to show that the information gathered from a particular activity was actually submitted to the FDA." App. 57a (one paragraph break omitted).

The jury found that petitioner, Dr. Cheresh, and Scripps infringed respondents' patents and that petitioner had failed to show that its activities were protected by § 271(e)(1). It awarded damages of $15 million.

In response to post-trial motions, the District Court dismissed respondents' suit against Dr. Cheresh and Scripps, but affirmed the jury's damages award as supported by substantial evidence, Civ. Action No. 961307 JMF (SD Cal., Mar. 26, 2001), App. to Pet. for Cert. 52a, and denied petitioner's motion for judgment as a matter of law, Civ. Action No. 96CV–1307 JMF (SD Cal., Mar. 6, 2001), App. to Pet. for Cert. 50a. With respect to the last, the District Court explained that the evidence was sufficient to show that "any connection between the infringing Scripps experiments and FDA review was insufficiently direct to qualify for the [§ 271(e)(1) exemption]." *Id.*, at 49a.

A divided panel of the Court of Appeals for the Federal Circuit affirmed in part and reversed in part. The panel majority affirmed the denial of judgment as a matter of law to petitioner, on the ground that § 271(e)(1)'s safe harbor did not apply because "the Scripps work sponsored by [petitioner] was not clinical testing to supply information to the FDA, but only general biomedical research to identify new pharmaceutical compounds." 331 F. 3d, at 866. It reversed the District Court's refusal to modify the damages award and remanded for further proceedings.[5] *Id.*, at 872. Judge Newman dissented on both points. See *id.*, at 874, 877. The panel unanimously affirmed the District Court's ruling

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[5] On remand, the District Court reduced the damages award to $6.375 million. Civ. Action No. CV.96 CV 1307–B(AJB), 2004 WL 2284001, *1 (SD Cal., Sept. 7, 2004).

that respondents' patents covered the cyclic RGD peptides developed by petitioner. *Id.*, at 868–869; *id.*, at 873, n. 7 (Newman, J., dissenting). We granted certiorari to review the Court of Appeals' construction of § 271(e)(1). 543 U. S. 1041 (2004).

III

As described earlier, 35 U. S. C. § 271(e)(1) provides that "[i]t shall not be an act of infringement to . . . use . . . or import into the United States a patented invention . . . solely for uses reasonably related to the development and submission of information under a Federal law which regulates the . . . use . . . of drugs." Though the contours of this provision are not exact in every respect, 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.

As an initial matter, we think it apparent from the statutory text that § 271(e)(1)'s exemption from infringement extends to all uses of patented inventions that are reasonably related to the development and submission of *any* information under the FDCA. Cf. *Eli Lilly*, 496 U. S., at 665–669 (declining to limit § 271(e)(1)'s exemption from infringement to submissions under particular statutory provisions that regulate drugs). This necessarily includes preclinical studies of patented compounds that are appropriate for submission to the FDA in the regulatory process. There is simply no room in the statute for excluding certain information from the exemption on the basis of the phase of research in which it is developed or the particular submission in which it could be included.[6]

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[6] Although the Court of Appeals' opinion suggests in places that § 271(e)(1)'s exemption from infringement is limited to research conducted in *clinical* trials, see 331 F. 3d, at 866, we do not understand it to have adopted that position. The Court of Appeals recognized that information included in an IND would come within § 271(e)(1)'s safe harbor. *Ibid.* Because an IND must be filed *before* clinical trials may begin, such information would necessarily be developed in preclinical studies.

Respondents concede the breadth of § 271(e)(1) in this regard, but argue that the only preclinical data of interest to the FDA is that which pertains to the safety of the drug in humans. In respondents' view, preclinical studies related to a drug's efficacy, mechanism of action, pharmacokinetics, and pharmacology are not reasonably included in an IND or an NDA, and are therefore outside the scope of the exemption. We do not understand the FDA's interest in information gathered in preclinical studies to be so constrained. To be sure, its regulations provide that the agency's "primary objectives in reviewing an IND are . . . to assure the safety and rights of subjects," 21 CFR § 312.22(a) (2005), but it does not follow that the FDA is not interested in reviewing information related to other characteristics of a drug. To the contrary, the FDA requires that applicants include in an IND summaries of the pharmacological, toxicological, pharmacokinetic, and biological qualities of the drug in animals. See § 312.23(a)(5); U. S. Dept. of Health and Human Services, Guidance for Industry, Good Clinical Practice: Consolidated Guidance 45 (Apr. 1996) ("The results of all relevant nonclinical pharmacology, toxicology, pharmacokinetic, and investigational product metabolism studies should be provided in summary form. This summary should address the methodology used, the results, and a discussion of the relevance of the findings to the investigated therapeutic and the possible unfavorable and unintended effects in humans"). The primary (and, in some cases, only) way in which a drugmaker may obtain such information is through preclinical *in vitro* and *in vivo* studies.

Moreover, the FDA does not evaluate the safety of proposed clinical experiments in a vacuum; rather, as the statute and regulations reflect, it asks whether the proposed clinical trial poses an "unreasonable risk." 21 U. S. C. § 355(i)(3)(B)(i); see also 21 CFR § 312.23(a)(8) (2005) (requiring applicants to include pharmacological and toxicological studies that serve as the basis of their conclusion that clinical

testing would be "reasonably safe"); § 56.111(a)(2) (2004) (providing that the Institutional Review Boards that oversee clinical trials must consider whether the "[r]isks to subjects are reasonable in relation to anticipated benefits"). This assessment involves a comparison of the risks and the benefits associated with the proposed clinical trials. As the Government's brief, filed on behalf of the FDA, explains, the "FDA might allow clinical testing of a drug that posed significant safety concerns if the drug had a sufficiently positive potential to address a serious disease, although the agency would not accept similar risks for a drug that was less likely to succeed or that would treat a less serious medical condition." Brief for United States as *Amicus Curiae* 10. Accordingly, the FDA directs that an IND must provide sufficient information for the investigator to "make his/her own unbiased risk-benefit assessment of the appropriateness of the proposed trial." Guidance for Industry, *supra,* at 43. Such information necessarily includes preclinical studies of a drug's efficacy in achieving particular results.

Respondents contend that, even accepting that the FDA is interested in preclinical research concerning drug characteristics other than safety, the experiments in question here are necessarily disqualified because they were not conducted in conformity with the FDA's good laboratory practices regulations. This argument fails for at least two reasons. First, the FDA's requirement that preclinical studies be conducted under "good laboratory practices" applies only to experiments on drugs "to determine their safety," 21 CFR § 58.3(d) (2004). See § 58.1(a); § 312.23(a)(8)(iii) (2005) (only "nonclinical laboratory study subject to the good laboratory practice regulations under part 58" must certify compliance with good laboratory practice regulations). The good laboratory practice regulations do not apply to preclinical studies of a drug's efficacy, mechanism of action, pharmacology, or pharmacokinetics. Second, FDA regulations do not provide that even safety-related experiments not conducted in compliance

with good laboratory practices regulations are not suitable for submission in an IND. Rather, such studies must include "a brief statement of the reason for the noncompliance." *Ibid.*

The Court of Appeals' conclusion that § 271(e)(1) did not protect petitioner's provision of the patented RGD peptides for research at Scripps appeared to rest on two somewhat related propositions. First, the court credited the fact that the "Scripps-Merck experiments did not supply information for submission to the [FDA], but instead identified the best drug candidate to subject to future clinical testing under the FDA processes." 331 F. 3d, at 865; see also *id.*, at 866 (similar). The court explained:

> "The FDA has no interest in the hunt for drugs that may or may not later undergo clinical testing for FDA approval. For instance, the FDA does not require information about drugs other than the compound featured in an [IND] application. Thus, the Scripps work sponsored by [petitioner] was not 'solely for uses reasonably related' to clinical testing for FDA." *Ibid.*

Second, the court concluded that the exemption "does not globally embrace all experimental activity that at some point, however attenuated, may lead to an FDA approval process." *Id.*, at 867.[7]

We do not quibble with the latter statement. Basic scientific research on a particular compound, performed without

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[7] The Court of Appeals also suggested that a limited construction of § 271(e)(1) is necessary to avoid depriving so-called "research tools" of the complete value of their patents. Respondents have never argued the RGD peptides were used at Scripps as research tools, and it is apparent from the record that they were not. See 331 F. 3d, at 878 (Newman, J., dissenting) ("Use of an existing tool in one's research is quite different from study of the tool itself"). We therefore need not—and do not—express a view about whether, or to what extent, § 271(e)(1) exempts from infringement the use of "research tools" in the development of information for the regulatory process.

the intent to develop a particular drug or a reasonable belief that the compound will cause the sort of physiological effect the researcher intends to induce, is surely not "reasonably related to the development and submission of information" to the FDA. It does not follow from this, however, that § 271(e)(1)'s exemption from infringement categorically excludes either (1) experimentation on drugs that are not ultimately the subject of an FDA submission or (2) use of patented compounds in experiments that are not ultimately submitted to the FDA. Under certain conditions, we think the exemption is sufficiently broad to protect the use of patented compounds in both situations.

As to the first proposition, it disregards the reality that, even at late stages in the development of a new drug, scientific testing is a process of trial and error. In the vast majority of cases, neither the drugmaker nor its scientists have any way of knowing whether an initially promising candidate will prove successful over a battery of experiments. That is the reason they conduct the experiments. Thus, to construe § 271(e)(1), as the Court of Appeals did, not to protect research conducted on patented compounds for which an IND is not ultimately filed is effectively to limit assurance of exemption to the activities necessary to seek approval of a generic drug: One can know at the outset that a particular compound will be the subject of an eventual application to the FDA only if the active ingredient in the drug being tested is identical to that in a drug that has already been approved.

The statutory text does not require such a result. Congress did not limit § 271(e)(1)'s safe harbor to the development of information for inclusion in a submission to the FDA; nor did it create an exemption applicable only to the research relevant to filing an ANDA for approval of a generic drug. Rather, it exempted from infringement *all* uses of patented compounds "reasonably related" to the process of developing information for submission under *any* federal law regulating the manufacture, use, or distribution of drugs. See *Eli*

Lilly, 496 U. S., at 674. We decline to read the "reasonable relation" requirement so narrowly as to render § 271(e)(1)'s stated protection of activities leading to FDA approval for all drugs illusory. Properly construed, § 271(e)(1) leaves adequate space for experimentation and failure on the road to regulatory approval: At least where 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." § 271(e)(1).

For similar reasons, the use of a patented compound in experiments that are not themselves included in a "submission of information" to the FDA does not, standing alone, render the use infringing. The relationship of the use of a patented compound in a particular experiment to the "development and submission of information" to the FDA does not become more attenuated (or less reasonable) simply because the data from that experiment are left out of the submission that is ultimately passed along to the FDA. Moreover, many of the uncertainties that exist with respect to the selection of a specific drug exist as well with respect to the decision of what research to include in an IND or NDA. As a District Court has observed, "[I]t will not always be clear to parties setting out to seek FDA approval for their new product exactly which kinds of information, and in what quantities, it will take to win that agency's approval." *Intermedics, Inc.* v. *Ventritex, Inc.*, 775 F. Supp. 1269, 1280 (ND Cal. 1991), aff'd, 991 F. 2d 808 (CA Fed. 1993). This is especially true at the preclinical stage of drug approval. FDA regulations provide only that "[t]he amount of information on a particular drug that must be submitted in an IND . . . depends upon such factors as the novelty of the drug, the extent to which it has been studied previously, the known or

suspected risks, and the developmental phase of the drug." 21 CFR §312.22(b). We thus agree with the Government that the use of patented compounds in preclinical studies is protected under §271(e)(1) as long as there is a reasonable basis for believing that the experiments will produce "the types of information that are relevant to an IND or NDA." Brief for United States as *Amicus Curiae* 23 (emphasis deleted).

* * *

Before the Court of Appeals, petitioner challenged the sufficiency of the evidence supporting the jury's finding that it failed to show that "all of the accused activities are covered by [§271(e)(1)]." App. 62a. That court rejected the challenge on the basis of a construction of §271(e)(1) that was not consistent with the text of that provision or the relevant jury instruction.[8] Thus, the evidence presented at trial has yet to be reviewed under the standards set forth in the jury instruction, which we believe to be consistent with, if less detailed than, the construction of §271(e)(1) that we adopt today. We decline to undertake a review of the sufficiency of the evidence under a proper construction of §271(e)(1) for the first time here. Accordingly, we vacate the judgment of the Court of Appeals and remand the case for proceedings consistent with this opinion.

It is so ordered.

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[8] The relevant jury instruction provided only that there must be a "decent prospect that the accused activities would contribute, relatively directly, to the generation of the kinds of information that are likely to be relevant in the processes by which the FDA would decide whether to approve the product in question." App. 57a. It did not say that, to fall within §271(e)(1)'s exemption from infringement, the patented compound used in experimentation must be the subject of an eventual application to the FDA. And it expressly rejected the notion that the exemption only included experiments that produced information included in an IND or NDA. *Ibid.*