Keywords: **Section 271(e)(1) exemption, preclinical research, reasonably related, common law research exemption.**

Summary: **Preclinical research that is not included in an FDA submission can be exempt from patent infringement under 35 U.S.C. § 271(e)(1) if the drug maker has a reasonable basis for believing that the research, if successful, would be appropriate to include in an FDA submission.**

Merck v. Integra Lifesciences
available at http://a257.g.akamaitech.net/7/257/2422/13jun20051230 / www.supremecourtus.gov/opinions/04pdf/03-1237.pdf
Decided June 13, 2005

I. Facts

Integra Lifesciences sued Merck, the Scripps Research Institute, and Dr. David Cheresh for patent infringement in the Southern District of California. Integra owns five patents related to a tripeptide sequence known as the "RGD peptide." The RGD peptide "promotes cell adhesion by attaching to $\alpha_V\beta_3$ integrins, [which are] receptors commonly located on the outer surface of certain endothelial cells."

Beginning in 1988, Dr. Cheresh, a researcher with Scripps participating in a joint venture with Merck, began researching techniques to fight cancer and other diseases by blocking the formation of new blood vessels from existing vessels. In 1994, Dr. Cheresh succeeded in reversing tumor growth in chicken embryos using an RGD peptide provided by Merck. In November 1996, Merck initiated the formal FDA review process so that it could eventually begin human trials on one version of Dr. Cheresh's tumor fighting RGD peptide.

Earlier in 1996, however, Integra charged that Merck, Scripps, and Dr. Cheresh had willfully infringed their patents by using the RGD peptide in Dr. Cheresh's cancer treatment experiments. Merck, Scripps, and Dr. Cheresh responded that their actions did not infringe Integra's patents, and that even if they did, they were protected by the common law research exemption before 1995 and by 35 U.S.C. § 271(e)(1) from 1995 onward.

At the conclusion of the trial, the district court held that Merck's pre-1995 actions were protected by the common law research exemption but left the question regarding the Section 271(e)(1) exemption to the jury. The relevant jury instruction read in part that "[t]o prevail on this defense [Merck must prove] that it would be objectively reasonable for a party in [Merck'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 process by which the FDA would decide whether to approve the product in question."

The jury found that Merck, Scripps, and Dr. Cheresh had infringed Integra's patents and awarded damages of $15 million. In post-trial motions, however, the district court dismissed Integra's suit against Dr. Cheresh and Scripps, denied Merck's motion for a judgment as a matter of law ("JMOL"), and affirmed the jury's damage award.

Merck appealed to the Court of Appeals for the Federal Circuit. The Federal Circuit affirmed the district court's denial of Merck's JMOL motion, holding that the experimentation "was not clinical testing to supply information to the FDA, but only general biomedical research." And, as such, Dr. Cheresh's research was not *solely* for uses reasonably related to an FDA submission, as required by Section 271(e)(1).

Merck appealed to the Supreme Court, which granted certiorari to review the Court of Appeals' construction of Section 271(e)(1).

II. Issue

Is the use of a patented invention in preclinical research that is not included in a subsequent FDA submission exempted from patent infringement under 35 U.S.C. § 271(e)(1)?

III. Discussion

Yes - as long as the research is "reasonably related" to the development and submission of information to the FDA. The unanimous Supreme Court held that Section 271(e)(1) exempts from infringement *all uses* that are "reasonably related" to the process of developing information for submission. More particularly, the Court held that "where a drug maker has a reasonable basis for believing that a patented compound may work…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,'" and exempted under 271(e)(1).

35 U.S.C. § 271(e)(1) states that "[i]t 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…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."

The Supreme Court began its analysis by interpreting the plain meaning of Section 271(e)(1). The Court held that the plain language of the statute provides an exemption to "all uses of patented inventions that are reasonably related to the development and submission of *any* information under the FDCA" (Emphasis added). From this, the Supreme Court determined that the exemption necessarily included preclinical studies that are appropriate for submission to the FDA and, thus, could apply to any phase of research, including preclinical research.

Next, the Court addressed Integra's argument that only research pertaining to a drug's safety for humans should qualify for the 271(e)(1) exemption. The Court rejected this assertion and noted that the FDA, in fact, requires Applicants to submit research related not only to humans, but also to animals. In particular, the Court noted that to obtain permission from the FDA to conduct human trials, drug manufacturers are virtually always required to submit evidence from previous animal trials.

Next, the Court addressed the Court of Appeals' holding. The Court noted that the Federal Circuit opinion had been based on two somewhat-related grounds. First, that the Section 271(e)(1) exemption only applied to that research that eventually becomes part of the FDA submission, and second, that the Scripps-Merck research was too far attenuated from the FDA submission to qualify under 271(e)(1). As to first point, the Supreme Court held that notwithstanding the "solely" language, the 271(e)(1) exemption can apply to experimentation on drugs that are not ultimately subject of an FDA submission or to the use of patented compounds in experiments that are not ultimately submitted to the FDA. Specifically, the Court noted that drugmakers and scientists typically have no way of predicting which experiments will ultimately lead to an FDA filing, and that those experiments that seem most promising at the onset may lead nowhere and vice-versa. As such, limiting the 271(e)(1) exemption to only those drugs or compounds that will eventually be part of an FDA application, as the Federal Circuit proposed, would defeat the

statute's purpose to encourage research and experimentation. As for the Federal Circuit's attenuation argument, the Court agreed in theory but held that research does not become more attenuated (i.e., less reasonably related) just because the research did not ultimately become part of an FDA submission.

For the reasons stated above, the Supreme Court vacated the judgment of the Federal Circuit and remanded the case back to the Federal Circuit to determine whether the evidence presented at trial was sufficient to support the jury's verdict in light of the new construction of Section 271(e)(1).