Merck KG aA v. Integra Lifesciences I, Ltd., et al., 545 U.S. 193 (2005)

Supreme Court of the United States, June 13, 2005

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Summary

The Court held that:

1. The use of patented compounds in preclinical studies is exempted from patent infringement under the regulatory review exemption as long as there is a reasonable basis to believe that the compound tested could be the subject of a submission to the Food and Drug Authority (FDA) and the experiments will produce the types of information relevant for such submissions;
2. Additionally, the exemption covers the use of patented compounds in preclinical research, even when the patented compounds do not themselves become the subject of an FDA submission;
3. 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.

The Facts

Integra Lifesciences and other claimants held five patents on genomic peptide sequences. During the terms of the patent protection, Merck KG aA supplied the patented peptides to its contract researchers for use in preclinical studies from 1995 to 1998. The studies were conducted to evaluate the suitability of each of the peptides as potential drug candidates and once a primary candidate for clinical testing was in the pipeline, to perform the toxicology tests necessary for FDA approval to proceed to clinical trials. Integra, *et al*., filed a patent infringement suit, claiming, *inter alia*, that Merck had willfully infringed their patents by supplying their peptides to its contract researchers for use in preclinical studies. Merck argued its actions were permitted by the regulatory review exemption provided under the Drug Price Competition and Patent Term Restoration Act of 1984, (35 U. S. C. §271(e)(1), which provides:

> "It shall not be an act of infringement to make, use, or sell a patented invention (other than a new animal drug or veterinary biological product) … 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 'regulatory review exemption' or 'the exemption' hereinafter).

Under the Federal Food, Drug, and Cosmetic Act of 1938 (FDCA) a drug maker must submit research data to the FDA in an investigational new drug application (IND) – i.e., when seeking authorization to conduct human clinical trials, and in a new drug application (NDA) – when seeking authorization to market a new drug.

The jury found in favor of Integra *et al*., and awarded damages, which was later affirmed by a District Court. The Court of Appeals for the Federal Circuit (CAFC) rejected Merck's appeal, on the ground that the regulatory review exemption did not apply because the research work sponsored by Merck was not clinical testing to supply information to the FDA, but only general biomedical research to identify new pharmaceutical compounds. The CAFC also held that the FDA has no interest in the hunt for drugs that may or may not later undergo clinical testing for FDA approval. The Supreme Court disagreed with the CAFC's findings.

The legal issues

In the Courts' view, the CAFC's findings appeared to rest on two related propositions.[1] First, it credited the fact that the experiments did not supply information for submission to the FDA, but instead identified the best drug candidate to subject to future clinical testing. Second, the CAFC concluded that the safe harbor does not globally embrace all experiments that at some point, however attenuated, may lead to an FDA approval process.

In the view of the Supreme Court, the text of regulatory review exemption makes clear that it provides a wide berth for the use of patented drugs in activities related to the federal regulatory process. The 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. 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.

The Court went on to say that basic scientific research on a particular compound, performed without the intent to develop a particular drug, is surely not reasonably related to the development and submission of information to the FDA. However, it does not follow from this that the regulatory review exemption 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.

The Supreme Court held that under certain conditions, the exemption is sufficiently broad to protect the use of patented compounds in both situations.

1. Drug makers undertake experimentation, because they do not have any way of knowing whether an initially promising candidate will prove successful in the end. Congress did not limit the regulatory review exemption 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 seeking for marketing 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. Properly construed, the regulatory review exemption leaves

[1] See pp. 11/12 of the opinion.

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 to the FDA;

2. 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, it 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. This is especially true at the preclinical stage of drug approval.

Points of Significance

1. On remand, the CAFC reversed the finding of infringement and held that all experimental activities under dispute fell under the exemption because they were conducted to determine the optimal candidate peptides and to comply with requirements of the drug approval process (*Integra Lifescience I, Ltd. v. Merck KG aA (Merck II)* 496 F.3d 1334, 1340 (Fed. Cir. 2007)[2];

2. The Supreme Court's opinion brings the focus on the terms of "reasonably related to" in defining the contours of the safe harbour. No infringement can be claimed in as far as the reasonable relatedness of the use of patented products with the development and submission of information to the FDA can be satisfied. The interpretation rejects the understanding that only experiments ultimately necessary for submission of information (for example, to show bioequivalence) could be subject to the exemption;

3. The wide interpretation applied by the Supreme Court in the case at hand provides an appropriate balance to the narrow construction of another important patent exception - i.e. the research/experimental use exception - by the United States Federal Circuit in *Madey v. Duke University*, 207 F.3d 1351 (Fed. Cir. 2002).[3] Against this background the interpretation of the regulatory review exemption under §271(e)(1) provides a safe harbor for research on patented products, in as far as the use is reasonably related to the development and submission of data to FDA. In a footnote to the decision, the Supreme Court stated that it did not need

[2] See the summary in this database.
[3] See the summary in this database.

to and did not express a view about whether, or to what extent, the regulatory review exemption shields from infringement the use of research tools. Similarly, on remand the CAFC declined to comment on the issue as not being before the court.[4]

Key words: regulatory review exemption.

Available at: https://www.supremecourt.gov/opinions/04pdf/03-1237.pdf

[4] But see the dissenting opinion by Judge Rader of the CAFC as analyzed in the case summary of the *Merck II* decision in this database.