Litigation Alert: *Integra LifeSciences I, Ltd. v. Merck KGaA* – Applying the Supreme Court's Broad Interpretation of the FDA Exemption for Patent Infringement

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On July 27, the Federal Circuit in *Integra LifeSciences v. Merck* ruled on the Supreme Court's broad interpretation of the patent infringement exemption set forth in 35 U.S.C. § 271(e)(1), for "uses reasonably related to the development and submission of information" to the Food and Drug Administration (FDA). The Federal Circuit reversed the district court's judgment of infringement, finding that all of the uses at issue qualified under the safe harbor provision of 35 U.S.C. § 271(e)(1) because they were "reasonably related to research that, if successful, would be appropriate to include in a submission to the FDA," even though not all of the experiments ultimately resulted in information submitted to the FDA.

Integra LifeSciences owns patents related to the peptide sequence of amino acids arginine (R), glycine (G) and aspartic acid (D), known as the "RGD peptide." Scripps Research Institute found RGD peptides to be effective in inhibiting angiogenesis – the development of blood vessels – which is a factor in some serious diseases, such as solid tumor cancers, diabetic retinopathy and rheumatoid arthritis. As a result, Scripps entered into a collaborative agreement with Merck to develop a drug based on these findings, and specifically to evaluate the "efficacy, pharmacology, pharmacokinetics, and mechanism of action" of several RGD peptides toward the goal of obtaining permission to conduct clinical trials through an Investigational New Drug (IND) application to the FDA. Integra claimed that the early experiments conducted by Scripps, as well as the subsequent studies conducted jointly by Merck and Scripps, infringed Integra's patents on RGD peptides. Merck and Scripps argued that their experiments fell under the safe harbor provision set forth at 35 U.S.C. § 271(e)(1), which exempts from infringement uses of patented inventions that are "reasonably related" to obtaining information for submission to the FDA.

The relevant portion of the safe harbor provision states: "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 . . . 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 or veterinary biological products." 35 U.S.C. § 271(e)(1).

The majority opinion noted that the FDA exemption is not applicable to "basic scientific research unrelated to development of a particular drug." However, since all of the experiments at issue were conducted "after discovery of the anti-angiogenesis property of the experimental RGD peptide," they did not fall under the ambit of "basic scientific research."

The majority opinion further explained that whether the uses in question are "reasonably related to the development of information for submission to the FDA" is established *at the time of the experiment*, and "does not depend on the success or failure of the experimentation or actual submission of the experimental results." Therefore the Court held that the entire series of experiments qualified for the FDA exemption because all were conducted for "the purposes of determining the optimum candidate angiogenesis inhibitor" for commercial development, even though only one particular RGD peptide, EMD 121974, was selected as the candidate for the IND application. The court further found that the FDA

exemption is not restricted to studies that follow the FDA's Good Laboratory Practices regulations for clinical studies, and rejected Integra's proposal to exclude from the FDA exemption any experiments that were "entirely routine."

In dissent, Judge Rader argued that the majority opinion expands the exemption even beyond the Supreme Court's already broad interpretation. He notes that two of the patents-in-suit are research tool patents that have no application outside of the laboratory, and criticizes the majority for failing to distinguish the research tool patents from the others (*i.e.*, patents directed at the compounds themselves). The majority opinion explained that it did not address the research tool patents because Integra declined to argue on appeal that Merck and Scripps used the RGD peptides as research tools, and thus "the issue is not present."

Judge Rader asserts that patents for research tools are "beyond the scope of the 'patented compounds' that the Supreme Court placed within the statutory exemption," citing legislative history discussing the primary purpose of the statute to permit generic manufacturers to establish the bioequivalence of a generic substitute for FDA approval and the intended "de minimus" impact on the rights of patent holders. The Supreme Court's June 13, 2005, decision in *Merck v. Integra LifeSciences*, 545 U.S. 193 (2005), focused on "patented compounds" because Integra did not assert that Merck's and Scripps' experiments used the RGD peptides as research tools. Although Judge Rader looks to the Supreme Court's opinion for support, the Supreme Court did not limit the exemption to patented compounds, but rather explicitly declined to express any view as to whether use of patented research tools qualified for the exemption. Also, despite the legislative history, the language of the statute does not restrict the exemption to patented compounds or otherwise exclude research tool patents.

Although the majority opinion declined to address the issue of research tool patents specifically, its holding that the FDA exemption includes any research that "if successful, would be appropriate to include in a submission to the FDA" arguably encompasses research tool patents, and certainly will be cited by future patent litigation defendants as such. As Judge Rader points out, if research tool patents indeed are subject to the FDA exemption, the value of such patents will be greatly impacted.

The opinion is available at http://www.fedcir.gov/opinions/02-1052c.pdf.

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