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RESEARCH TOOL PATENTS – OPENING LOOPHOLES FOR OFFSHORE USE?

Several recent United States trial court holdings may create "loopholes" enabling research tool patents and compounds discovered through the use of such patents to be used for research purposes without infringement liability.

In *Bayer AG v. Housey Pharmaceuticals, Inc*., the Court held that liability for infringing imports and sales under 35 USC §271(g) applies only to products derived from patented manufacturing processes, and not to patented screening methods. The Housey patents generally relate to a method of determining whether a substance is an inhibitor or activator of a protein. However, under a plain reading of the statute, the Court found that §271(g) addresses only products derived from patented *manufacturing* processes, i.e., methods of actually making or creating a product, and not methods of gathering information about, or identifying a substance worthy of further development. According to the Court, the processes of identification claimed in the Housey patents were not steps in the manufacture of final drug products.

This decision complements recent policy statements by the US Patent Office on so-called "reach-through claims" to preclude claims to compounds identified by patentable assays without a direct description of such compounds. (See "USPTO Report on Comparative Study on Biotechnology Practices: Reach-Through Claims" available at www.uspto.gov). The Housey decision now makes it more difficult for the owner of an assay patent to sue a party for using an assay or a receptor to detect inhibitors outside the US. According to the Housey Court, the importation, use or sale of a manufactured final product is necessary to trigger infringement liability, and no remedy is available under §271(g).

In *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, BMS claimed that its use of RPR's patented intermediates for the preparation of taxol in an attempt to find taxol analogs fell within 35 USC §271(e)(1), which exempts from infringement liability the use of a patented invention solely for uses reasonably related to the development and submission of information to the FDA. The Court concluded that BMS' use of the intermediates as a starting point to identify taxol analogs was exempt under 35 USC §271(e)(1) because it was objectively reasonable for BMS to believe that there was a "decent prospect" that its use of the intermediates would have contributed to the generation of information that was likely to be relevant in the FDA review process.

In *Columbia University v. Roche Diagnostics*, Columbia sued Roche for its infringement of Columbia's patents directed to methods and products to produce genetically engineered erythropoietin (EPO). Because it concluded that infringement under 35 USC §271(a) must occur in the United States, the Court found that Roche did not directly infringe Columbia's patents for methods of genetically transforming cells to induce them to produce EPO, even if it obtained cell lines it used in Germany from its collaborator in the United States. The Court stated that mere ownership of products used to infringe abroad did not relocate the infringing activities of Roche to the United States. The Court also rejected Columbia's argument that importation of EPO, an unpatented by-product of Columbia's patented methods, should result in infringement under the so-called "fruit of the poisonous tree" doctrine. The Court concluded that Roche did not directly infringe the Columbia patents even if it subsequently imported EPO into the United States, because the EPO itself was not a patented invention under the statute.

As indicated from these cases, the nature of the research and collaborations in the biotechnology and pharmaceutical industries result in interesting factual scenarios relating to patent infringement under the US patent laws. While each situation must be evaluated on its own facts, courts have demonstrated that certain uses of patented products and methods do not result in infringement. It remains to be seen if the Appeals Courts agree with these trial court holdings, and how far future decisions broaden these rulings to other uses of patented research tools.

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WHEN IS A REACH-THROUGH LICENSE APPROPRIATE?

Many current biotechnology developments are research tools that enable a drug developer to discover a drug product. Examples of research tools include high throughput screening technologies and other assay methods, cell lines, monoclonal antibodies, reagents, animal models, clones and cloning tools, laboratory equipment and machines, databases and computer software.

Since the research tool's patents may not claim the products ultimately developed using the research tools, creative licensing structures are necessary to adequately compensate the creators of research tools. In many cases, the value of a research tool is not merely the cost that went into its development. Rather, it includes the value to the drug developer for access to the research tool that helps the drug developer identify and develop the pharmaceutical product. However, given the potential value of the products that may result from use of the research tool, up-front access fees or subscription licenses alone may not adequately compensate the research tool owner for permitting the licensee to use the research tool. Moreover, a development-stage biotechnology company may not have sufficient financial resources to pay up-front access fees, and pharmaceutical companies, despite adequate financial resources, may not wish to pay a large subscription fee for a tool that may or may not ultimately yield valuable future discoveries. Accordingly, licenses that create "reach-through" royalties are an alternative strategy for compensating research tool developers.

A reach-through license generates royalties to the research tool developer on the sales of products that are discovered or developed through use of the research tool, even though the patented invention is not incorporated into the final product, *i.e.*, the manufacture, use and sale of the final product does not infringe any patents claiming the enabling tool. The recent proliferation of reach-through licenses has created controversy, with proponents arguing that reach-through licenses create incentives to further research tool development, while opponents claim that reach-through licenses extend the patent rights of the research tool owner, inhibiting dissemination, freedom of use and ultimately research and product development.

NEGOTIATING REACH-THROUGH ROYALTY PROVISIONS

When licensing a patented biomedical research tool, both the patent holder-licensor and tool user-licensee should consider the following:

Field of Use: Internal Research Purposes. A typical reach-through royalty license grant includes the right to practice the licensed patents to create, identify and/or develop compounds and pharmaceutical products comprising the compounds. In such case, the field of use is essentially limited to internal research for the purpose of discovering such pharmaceutical compounds, but the field of use usually does not include the right to use the tool for any other purposes or to sublicense it.

Therapeutic Uses of the Tool. Since some research tools may also have therapeutic or diagnostic uses (for example, monoclonal antibodies), the parties may agree to an expanded license grant or field of use that also permits the licensee to develop and commercialize the research tool itself. In either case, the license grant and fields of use must be thoughtfully drafted to reflect the parties' intent.

Definition of "Licensed Products." In a reach-through license, the definition of royalty bearing products generally covers all products that result from the use of the research tool (for example, "any pharmaceutical product that contains a compound that was identified by the use of the research tool").

Royalty Stacking. Consider flexible royalty payment schemes such as royalty stacking provisions and sliding-scale royalty rates, to avoid scenarios where the end products are subject to such prohibitive multiple royalty payments that the tool user has little or no incentive to further develop and commercialize the pharmaceutical product.

Royalty Term. In reach-through license arrangements, the compounds that are identified or developed by the practice of the patent rights claiming the research tool will comprise pharmaceutical products, which will take many years of clinical development before they are commercialized. In addition, the pharmaceutical product is likely to be covered by a number of other patents that have a longer life than the patent on the enabling technology. Accordingly, the parties may consider a fair and equitable royalty term that extends beyond the expiration of valid claims covering the research tools, while carefully considering the patent misuse doctrine and antitrust implications of such an extended royalty term.

Patent Misuse and Antitrust. Antitrust and patent misuse may be implicated whenever a patent owner seeks to expand the economic benefit beyond the scope of the patent grant. Accordingly, reach-through licenses must be structured to comply with antitrust and patent misuse prohibitions. Consult with counsel on the appropriate scope of reach-through rights necessary to overcome antitrust and patent misuse concerns. W&D

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Clients in the News

BioInvent AB (Malmö, Sweden) recently signed a three-year antibody collaboration with **Oxford GlycoSciences** (Cambridge, UK) for the identification, development, manufacture and commercialization of novel therapeutic antibodies targeting antigens provided by Oxford GlycoSciences.

Medivir AB (Huddinge, Sweden) announced the execution of a global development and marketing arrangement with **Reliant Pharmaceuticals** (Liberty Corner, NJ) for Medivir's anti-viral drug MIV-606 for the treatment of shingles.

Alexion Pharmaceuticals, Inc. (Cheshire, CT) recently signed a drug target discovery and validation agreement with **Curagen Corporation** (New Haven, CT) focused initially in oncology. In addition, Alexion Pharmaceuticals' announced the acquisition of exclusive worldwide commercial rights to newly discovered cell surface proteins and a research alliance with the **University Medical Center of Nijmegen** (Netherlands).