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## **Reach Through Royalties: The Scope of Research Tool Patents**

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Research tools are widely employed in the fields of industrial chemistry, biotechnology, informatics and development of pharmaceutical and diagnostic agents.

Research tools are of widely varying types, including computational hardware and software, models, techniques, informational libraries, assays, selection agents, qualification criteria, and other tangible or intangible tools that are employed in research and downstream development of products.

As specific examples, a particular screening methodology and reagent may be utilized in identifying candidates that may be effective drugs for medicinal purposes, a cell culturing methodology may be employed to produce a small peptide drug at high volume in a readily isolatable form, a method of chemical purification may be used to remove undesired stereospecific forms from a racemic mixture containing a molecule of interest, and a validation assay may be utilized for qualification of production equipment in order to manufacture a chemical compound or biological agent.

Simply stated, research tools can be thought of as technological tools in the tool kits of researchers and developers.

In commercially exploiting research tools, patent protection is frequently considered as the most practical means of securing rights that can be commercially licensed to others. Although a patent may be readily obtained on the specific research tool, the issue typically associated with license arrangements is the difficulty of capturing value that is appropriate to the ultimate result of the research tool usage. For example, if the research tool is a method of using a probe to screen potential therapeutic agents for identification, from a combinatorial population of hundreds of thousands of candidate molecules, the patented screening methodology may be used once, but may identify a therapeutic agent that passes through preclinical and clinical study to emerge as a multi-billion blockbuster drug.

If the research tool patent is licensed only on a per-use basis, the royalty may be grossly disproportionate to the end value realized by the licensed user of the research tool.

Patent owners have attempted to grapple with this issue by so-called reach-through license arrangements, in which the compensation paid for use of the research tool is predicated on the value of the end product that is identified or emerges as a downstream product of the user's implementation of the research tool.

At present, the law relating to the property of reach-through royalties or each-through patent infringement damages based on research tool patents is unsettled. In many instances where research tool patents are asserted in litigation, a countervailing attack is made by the accused infringer that the patent claims do not cover the product in question, but only an upstream technique or material whose usage has enabled the product to be identified or developed. Therefore, counterclaims of patent misuse are asserted, as well as attacks on the patent as lacking written description of the downstream product, or attacks based on the assertion that the product of the research tool usage is knowledge or information, that is inappropriate for imposing damages liability.

Quantitation of damages is problematic in a research tools context. Damages for patent infringement are typically based on reasonable royalty where it is not possible to prove lost profits with specificity (35 U.S. C. § 284). Lost profits typically are not a tenable basis for measuring damages of the research tool patent owner, since such approach requires a showing by the patent owner of ability to exploit demand for the patented product (*Panduit Corp. v. Stahl Brothers Fiber Works, Inc.*, 575 F.2d 1152, 1156 (6<sup>th</sup> Cir. 1978)), and the research tool (the patented product) is not the product of interest. The patent owner instead is focused on the downstream product of the use of the research tool as being the desired basis for damages.

In the realm of reasonable royalty determinations, there is potential recourse to other license transactions as a source of "going rate" royalties, but the problem faced by research tool patent licensors is that there is not at present a large established base of transactions from which to draw good correlations.

Further clarity may come to this area of the law in 2004, when the U.S. Court of Appeals for the Federal Circuit considers the litigation brought by the University of Rochester against G.D. Searle & Co., relating to a method of selectively inhibiting the Cox2 enzyme with a therapeutic agent identified by use of a screening technique.

More recently, however, in August 2003, the Court of Appeals for the Federal Circuit decided *Bayer Corporation v. Housey Pharmaceuticals, Inc.* (Fed. Cir. No 02-1598), in which the Court construed patents of Housey Pharmaceuticals on methods for screening inhibitors or activators of a protein that affects cultural or morphological characteristics of a cell that expresses the protein.

The patented method involved providing a first cell line producing the protein of interest, in which the cells exhibit a phenotypic response to such protein, and establishing a second cell line that produces the protein of interest at a lower or non-existent level, and exhibits a reduced or non-existent phenotypic response to the protein of interest. The

final steps of the patented method are incubation of a candidate substance with both cell lines (to determine whether it inhibits or activates the protein), and comparing the phenotypic response of the first cell line to the phenotypic response of the second cell line.

If the protein of interest is associated with a disease, the determination of activating or inhibiting effect then can be utilized in development of a therapeutic agent for the disease.

The product of the method of the Housey patents is information – specifically, the knowledge, or at minimum the suspicion, that a particular substance inhibits or activates a specific protein.

Housey based its patent infringement claim on the provisions of 35 U.S.C. § 271(g), which establishes infringement liability for unauthorized importation into the U.S., or sale, offer for sale or use within the U.S., of a product made by a process patented in a U.S. Patent. The statute excludes from protection products that are “materially changed by subsequent processes” or “that become a trivial or non-essential component of another product.”

Housey’s infringement claim was based on Bayer’s importation of information generated by the patented process, and Bayer’s importation of a pharmaceutical composition identified by the patented process.

Concerning the imported information, the CAFC held that the infringing products contemplated by the statute were physical goods, and that information was not covered by the statute.

Concerning the Bayer pharmaceutical composition that Housey contended had been identified by the patented process, the Court looked at the relationship between the “process patented in the United States” as specified in the statute, and the resulting product, as to whether the drug was a “product which [was] *made* by [that] process.”

The Court held that the Bayer drug was not an infringing product, since the “process of identification and generation of data are not steps in the manufacture of a final drug product” and that “the [patented] process must be used directly in the manufacture of the product, and not merely as a predicate process to identify the product to be manufactured.” Accordingly, Housey’s claim of infringement was denied.

In its analysis, the Court differentiated its decision in *Bio-Technology General Corp. v. Genentech, Inc.*, 80 F.3d 1553 (Fed. Cir. 1996), where it held that a protein made by a host organism expressing an inserted plasmid was a product “made by” the patented process for creating the plasmid itself.

Specifically, the CAFC held that Bio-Technology's human growth hormone (hGH) was a product made by the Genentech patented method for constructing a plasmid, despite the fact that the plasmid and hGH were separate and distinct products.

Genentech's patent was directed to a method for constructing a replicable cloning vehicle (e.g., a plasmid) capable in a microorganism of expressing a polypeptide (e.g., human growth hormone).

The Court, in holding that Bio-Technology's human growth hormone produced by a recombinant plasmid-based method in Israel was an infringing product "made by" the Genentech patented process under 35 U.S.C. § 271(g), looked to the legislative history of the Process Patents Amendment Act of 1988, Pub. L. No. 100-418, § 9006(a), 102 Stat. 1107, 1567 (1988), the legislation that enacted § 271 (g). In the legislative history, a Senate Report noted that:

"The patented process may be for the process of preparing a DNA molecule comprising a specific genetic sequence. A foreign manufacturer uses the patented process to prepare the DNA molecule which is the product of the patented process. The foreign manufacturer inserts the DNA molecule into a plasmid or other vector [which is] inserted into a host organism; for example, a bacterium. The plasmid-containing host organism still containing the specific genetic sequence undergoes expression to produce the desired polypeptide. Even if a different organism was created by this biotech procedure, if it would not have been possible or commercially viable to make the different organism and product expressed therefrom but for the patented process, the product will be considered to have been made by the patented process."

The Court also pointed to the legislative history and the statement in the Senate Report that "[T]he Committee expects the courts to exercise careful judgement in distinguishing those products *that are too far removed from the patented process*" (emphasis added).

On such basis, the Court held that as a matter of law, it could not be said that the production of hGH "is too remote from the claimed process of making a replicable cloning vehicle," and on such basis the Court held that Bio-Technology's hGH was a product "made by" the Genentech patented process.

Taking all of the foregoing into account, some useful approaches suggest themselves for addressing § 271(g) issues in situations that are not within the scope of the legislative history of § 271(g), i.e., do not involve expression-competent biological material.

First, it is desirable in drafting patent claims covering the research tool to encompass all steps of the research tool usage or technique, to order to provide a broad scope of coverage that maximizes the likelihood that the end commercial product will be covered by the claims.

Rather than simply claiming a research tool method in narrow and specific steps, it may be desirable to claim such method as a constituent part of a broader specified methodology for producing the end product. For example, instead of claiming "[A}

method of determining” as was done in the Bayer case, , in which the product of the method was information derived from the last “comparing” step in the recited methodology, it may be preferable to draft the claim to recite a method for producing an inhibitor or activator substance, as a therapeutic agent for modulating activity of the protein of interest. Such a claim would include the steps of the Housey patents, and the additional step of “synthesizing said inhibitor or activator substance as a therapeutic agent for *in vivo* modulation of said protein, for therapeutic intervention in treatment of a disease state or condition associated with said protein.” This sort of claim on its face should not be objectionable under PTO practice or judicial criteria, and in effect embodies a chimeric approach of combining the claiming of downstream product production with conventional research tool claiming.

Second, attention should be paid to filing of research tool patent applications in foreign countries, to obviate issues under the importation provision of § 271(g).

Third, in view of the legislative history of § 271(g) with its emphasis on “products that too far removed from the patented process,” it is well to include in the specification of the research tool patent application a discussion of the straightforward and direct progression from the use of the research product to a downstream product. Such discussion may beneficially focus on the standard and routine character of converting the results of the research tool usage to the downstream product, with respect of the time, complexity and commercially demonstrated character of the steps involved. This will provide appropriate support for claims of the type mentioned above, as well as providing a basis for the position and subsequent argument that the products in question are not “too far removed from the patented process” and therefore warrant protection under the provision of § 271(g).