Patents Encroaching on Research Freedom

A tradition of disregarding patent infringement when it involves experimental use of an invention may be eroding for biologists

Some two dozen researchers at universities, companies, and government laboratories recently received letters from Johnson & Johnson warning them that the use in research of particular cells that produce monoclonal antibodies may infringe the company's patent rights. The letter raises the tricky question of the extent to which patent law can be used to restrict research uses of patented products and processes.

A similar issue was raised recently in a court decision concerning clinical testing of a patented drug. The U.S. Court of Appeals for the Federal Circuit, which now hears all patent appeals, ruled that Bolar Pharmaceutical, a generic drug manufacturer, broke the law by testing its version of a drug made by Roche Products before Roche's patent had expired. Some patent attorneys are concerned that, if the ruling is interpreted broadly, it could be used to restrict a variety of research activities.

Although Johnson & Johnson's warnings and the contest between Roche and Bolar are not directly related, they both address an area of patent law that is in a considerable state of flux. The statutes spell out in plain language how a patent grants a 17-year monopoly to an inventor, prohibiting others from making, using, or selling the invention. However, a tradition that began in the early 19th century has usually exempted experimental use of an invention from being construed as infringement. The issue at stake now is how to define when experimental use of patented technology becomes commercially threatening to an inventor and therefore no longer is entitled to that exemption. Some resolution of this ambiguity will be vital to the biotechnology industry, which is so heavily dependent on basic and near-basic research activities.

The contest between Roche and Bolar has been closely watched in the pharmaceutical industry. Early in 1983 Bolar began an effort to get federal approval to market flurazepam hydrochloride, the active ingredient in Roche's highly successful sleeping pill, whose trademark is Dalmane. Although the safety of this drug already was established, the Food and Drug Administration requires a generic drug manufacturer to prove it can meet the same standards. However, if the generic manufacturer is forced to wait until a drug's patent expires before such tests begin, the original manufacturer effectively gains a considerable extension on the patent's lifetime. [Legislation now being drafted by Representative Henry Waxman (D–Calif.) would resolve some of these problems (*Science*, 27 April, p. 369).]

Roche's patent for Dalmane expired on 17 January 1984, but Bolar began clinical trials long before that date. Roche brought a patent infringement suit against Bolar in July 1983. In October, the U.S. District Court in the Eastern District of New York ruled in Bolar's favor, but on 23 April 1984 that ruling was reversed on appeal. Bolar currently is planning to petition the Supreme Court to review the case, says attorney Robert Marrow, who represents the company.

The issue is how to define when experimental use is no longer entitled to an exemption from the patent laws.

"From the scientific point of view, the real threat [in the appeal court's decision] is it effectively prohibits any experiments with a patented product if it tends toward commercial development," Morrow says. "This is a far-reaching opinion that [could] negate the experimental use exception, unless it's for pure amusement."

Morrow's interpretation is something of a worst-case reading of the opinion handed down by Judge Philip Nichols, Jr. But other attorneys are also speculating about how far his opinion goes in this direction. "The experimental use exception is not gutted," says Jorge Goldstein, a patent attorney for a Washington, D.C., firm that represents a broad spectrum of corporate clients (but with no direct stake in the Roche-Bolar contest). "But for a company to argue that it's 'just doing research,' won't fly if it has a substantial commercial purpose."

The ruling "may not be a serious inroad" on the experimental exception to patents, says James Weseman, a patent attorney with a San Francisco law firm with biotechnology company clients. But certain passages in Judge Nichols' opinion where he uses "expansive language to define experimental use" are worrying, Weseman says.

For example, Nichols wrote: "Bolar's intended use is solely for business reasons and not for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry [and] is thus an infringement. . . . We cannot construe the experimental use rule so broadly as to allow a violation of the patent laws in the guise of 'scientific inquiry,' when that inquiry has definite, cognizable, and not insubstantial commercial purposes."

"The biotechnology industry is sensitive to anything that affects what they do best—research," Weseman continues. "If case law develops so that even in the earliest stages companies must avoid patent infringement, it will really restrict their abilities and stultify their research. There's plenty to worry about."

The recent actions by Johnson & Johnson could be another step toward restricting use of patents that is a cause for more worry. Johnson & Johnson patent attorney Geoffrey Dellenbaugh has been sending out letters to researchers warning against the use of particular monoclonal antibody–producing hybridomas, which the company has deposited with the American Type Culture Collection (ATCC) in the course of obtaining patents. "The fact that you have obtained samples of these hybridomas from the ATCC in no way grants you any right or license under our patents in the United States or other countries," one of the letters, sent to a researcher at the National Institutes of Health (NIH), says. "Your use of these hybridoma samples may constitute infringement of one or more of these patents, regardless of whether the thus-produced antibody is subsequently used or sold."

About two dozen researchers from universities, companies, and government research institutions including NIH are involved so far. The letters were sent out because of the concern that "people might use the cells in a way that infringes the patent and deprives us of sales of antibodies," explains Dellenbaugh. The cells can be obtained from ATCC at a nominal cost, whereas Johnson & Johnson's subsidiary, Ortho Diagnostics, is marketing the antibodies (for research and diagnostic purposes) to make a profit. The company quite naturally would

like to protect its commercial interests and develop a market for its patented monoclonal antibodies. Researchers would like to use those antibodies (some of them are to T cells, which are part of the immune system). And scientists with the right know-how undoubtedly can make the antibodies—from the company's cell lines, obtained perfectly legally from ATCC—more cheaply than they can be bought.

"The reason we wrote those letters was to inform people of the possible legal consequences. We intend, in appropriate circumstances, to protect our rights," Dellenbaugh says. The question, as with the Roche versus Bolar ruling, is "How far does that extend?" he adds. "If

DOD Springs Surprise on Secrecy Rules

Pentagon officials have moved to resolve a major issue in their dispute with university scientists about government efforts to control militarily sensitive research. The Department of Defense (DOD) has decided to abandon its search for a formula to govern so-called gray areas of research—research which is not classified but is deemed militarily useful. Under the proposed policy, federally supported fundamental research would be treated on an either-or basis as classified or unclassified.

The immediate reaction from academic observers is that the decision has the merit of creating a clearly defined policy. Whether the new policy will satisfactorily resolve the controversial issue of prepublication review of nonclassified but sensitive research, however, is far from clear. The debate on scientific communication has caused divisions among policy-makers at the Pentagon and there is some skepticism about how fully the new policy has been accepted along the chain of command. A major issue is the working definition of fundamental research under the new policy and, therefore, what research will be covered. Some observers suggest that under the proposed policy, the Pentagon would put more and more types of research into the classified category.

For more than a year, DOD's effort to find forms of protection short of classification for gray-area research has been a major sticking point for Pentagon policy-makers and university officials debating the tightening of controls on scientific communication (*Science*, 3 June 1983, p. 1021). Recently there had been signs of a split in opinion within Pentagon ranks, with DOD under secretary for research and engineering Richard D. De Lauer identified as questioning the creation of a new category of controls on research (*Science*, 4 May, p. 471). But the decision caused surprise among outsiders.

In testimony at a House hearing on 24 May, deputy secretary for research and engineering Edith W. Martin said that DOD officials had decided "not to pursue the gray-area concept" because the option had proved to be "more complicated than it had seemed," and "the trade-offs unclear."

Martin's comments at the hearing were the first public mention of the decision. In a brief summary of the new policy, which did not appear in her prepared testimony, she described it as a "draft policy" that is still under discussion in DOD and in other federal agencies. To a question, however, she replied that she expected the policy to be accepted in substantially its present form and to apply to fundamental research sponsored by all federal agencies.

In response to a question of when and why the decision was made from Representative Doug Walgren (D–Penn.) who chaired the hearing, Martin said that the possibility of taking the "classification-nonclassification approach" had been considered from the beginning of DOD deliberations on the matter and, after discussions extending over more than a year, the conclusion evolved to adopt the classification alternative. This occurred 3 or 4 months ago, but was being enunciated publicly for the first time at the hearing.

The policy statement made available at the end of the hearing is as follows: It is the policy of this administration that the mechanism for control of fundamental research in science and engineering at universities and federal laboratories is classification. Each federal government agency is responsible for: a) determining whether classification is appropriate prior to the award of a research grant or contract and, if so, controlling the research results through standard classification procedures; b) periodically reviewing all research grants or contracts for potential classification. No restrictions may be placed upon the conduct or reporting of research that has not received national security classification.

The face-off between the universities and the Pentagon over gray-area research dates from the publication in 1982 of the Corson report, a National Academy of Sciences–sponsored study, "Scientific Communication and National Security," headed by Cornell University president emeritus Dale Corson. The study defined the research universities' concern about the problem. Corson appeared at the hearing and raised the issue of what he called "creeping grayness," noting that "There appears to be growing interest on the part of sponsoring agencies to extend the concept of grayness to ever more areas." But Corson and other university and industry witnesses by no means confined their criticism to the gray-area problem. By and large, they were most concerned with the application to research of legislation designed to control the export of militarily useful equipment and materials. In particular, they criticized the use of such legislation to restrict foreign nationals studying or working here.

Government witnesses were scheduled last at the hearings, but Martin did not deal directly with the criticisms by earlier witnesses. In effect, she trumped them with her announcement of the policy decision. There was no real exchange on the testimony since it came after a long session punctuated by intermissions for roll-call votes on the House floor and the Pentagon party had to depart for another engagement.

With details of the new policy unavailable, let alone information on interpretation and implementation, a wait-and-see attitude seems to dominate in the universities. But a snap reaction among knowledgeable observers is that the effect of the decision may be to return the debate on gray-area research to where it was before the Corson report.

—JOHN WALSH

someone made an improvement that used your patented invention and uses that for commercial purposes—whether they're in a university or not—that is infringement of your patent."

"We've had correspondence with J&J, but have not resolved the issue," says NIH patent attorney Thomas Ferris. "We don't consider it infringement [for researchers to use cell lines] as long as it is experimental." In letters to Dellenbaugh, NIH patent attorneys have said, "[W]e will cooperate in your attempt to enforce your patent rights while at the same time recognizing that the interests of the research programs of the [NIH] must be paramount, if it should prove to be more practicable to purchase hybridomas from ATCC for research purposes. We suggest that you promote your own sale of hybridomas by publicizing their availability to the NIH research community."

Dellenbaugh replied that each case should be considered individually, and that a determination should not rest "simply on whether the use is 'experimental.' . . . Since [there is] clear economic harm to Ortho, the rationale sometimes used for excepting experimental use from infringement should not apply."

NIH recently convened a meeting of its internal patent board, a group that includes patent attorneys and representatives from the various institutes, to consider the policy implications of the letters and has considered making recommendations on these issues to the Department of Health and Human Services. Currently, NIH is telling researchers "to go along the way they are."

Though Johnson & Johnson is not planning legal action to enforce its patent rights, according to Dellenbaugh, "If we decided an example needs to be made of an egregious infringement, we might do it." Hence, Ferris says, no matter what policy is laid down, such issues "ultimately can only be resolved in the courts."—**JEFFREY L. FOX**

Judge Curbs Use of Toxic Shock Data

In a legal victory for the Procter & Gamble Company, a federal judge in St. Louis last month ruled that the deposition of a researcher at the University of Wisconsin cannot be used in a suit against the company because his research was "preliminary." The researcher's findings are said to link Procter & Gamble's Rely tampon with the production of toxin associated with toxic shock syndrome.

The ruling is the latest development in a continuing legal battle over the data of microbiologist Merlin S. Bergdoll and its use in court. The controversy has raised questions about access to sensitive research findings during litigation (*Science*, 13 April, p. 132).

The court decision is contrary to an earlier decision by another federal judge, who allowed the data to be discussed in a trial. A Procter & Gamble spokeswoman characterized the St. Louis ruling as a "strong precedent," while the plaintiff's lead attorney, Tom Riley, remarked that the two decisions "send conflicting signals." The lawsuit was filed by Michael W. Rogers, whose wife allegedly died of toxic shock syndrome after using Rely tampons in 1980.

Bergdoll, with support from Procter & Gamble and other companies, has studied the production of toxic shock toxin in tampons since 1980. He has not released or published his data because he believes his findings are preliminary and inconclusive. But lawyers for toxic shock victims point out that Bergdoll has discussed his findings with the company and that the company has replicated his findings.

Although Bergdoll and Procter & Gamble have successfully fended off many attempts by lawyers to use the data in court, a U.S. District judge in Fort Worth ruled in 1983 that the data are admissible as evidence. During that trial, Bergdoll's data were revealed for the first time in detail by an expert witness for the plaintiffs, who reported that in laboratory tests Bergdoll found Rely tampons produced more toxic shock toxin than any other brand of tampon.

Bergdoll still contends that his research is incomplete and reiterated this point in a deposition in the Rogers case. U.S. District judge James Meredith agreed with Bergdoll and emphasized the need to protect preliminary research findings in general.

He wrote, "Dr. Bergdoll's research is preliminary in nature; . . . it would be misleading to the jury given the inconclusiveness of its nature. [T]o use [Bergdoll's] deposition in this trial would hinder his research efforts as well as other research efforts at universities throughout the country." Furthermore, "[A] release of incomplete data will harm Dr. Bergdoll's professional reputation and impair his ability to complete and publish the final results of his research efforts. Premature public disclosure of research is not harmful in this case alone, but will have an adverse affect [sic] on research into controversial areas conducted throughout the nation." Meredith ruled that Bergdoll's deposition and documents introduced at the deposition be placed under seal. The case was settled before trial.

Procter & Gamble spokeswoman, Sydney McHugh, said that the ruling was significant because, for the first time, a judge heard Bergdoll himself describe what conclusions could be drawn from his research.

Meredith said that Bergdoll "is not associated with defendants. . . . He denies that his research will assist the jury in this lawsuit. Under the circumstances, his testimony and data will be excluded." Riley, the plaintiff's attorney, contends, however, that because Bergdoll receives substantial support from Procter & Gamble, he "is not an impartial witness."

Michael Liethen, legal counsel for the University of Wisconsin, who along with Procter & Gamble represented Bergdoll, rejects any suggestion that Bergdoll has been improperly influenced by Procter & Gamble. Liethen says that company money is paid to the university and the university then allots the money to Bergdoll. The company "ought to be congratulated for funding toxic shock research. The federal government doesn't support it. If not for P&G funding, the research wouldn't be done."

Liethen says he is not sure what meaning the St. Louis ruling will have in other cases. "As a practical matter, each case has to be weighed on its own merits. In this case, there was extensive balancing of public and private interests." Given the hundreds of toxic shock lawsuits still pending, the issue of Bergdoll's data and its use in court is far from settled.—**MARJORIE SUN**