

PRESENTATION:

**RESEARCH TOOLS
IN THE BIOTECHNOLOGY INDUSTRY
AND THE HATCH-WAXMAN ACT**

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I would like to discuss research tools, the biotechnology industry, the Hatch-Waxman Act,¹ and other issues regarding research, use, infringement and exemption. I am trying to think about what side I am on. I work part-time at Chiron and part-time at U.C. Berkeley. Although I am not sure, Chiron probably both buys and sells research tool technology. I think we are a net buyer, but I am not sure.

Currently, there is a political debate in the United States regarding research tool patents and whether or not they are actually inhibiting research and slowing down innovation. It may help to quickly define research tools in biotechnology. These are typically patents that cover genomic type inventions or high throughput assay technologies and other methods of discovering drugs that go into clinical trials and combinatorial chemistry libraries. There is not enough time to explain all of this to you, if you do not already know about this technology; but the impact on drugs and pharmaceuticals is amazing. It has changed the research process of pharmaceutical discovery from one of controlled serendipity to one of extremely high probability of serendipity. Basically you can do so much more, so much more quickly.

For example, one of the first licenses we did with a large pharmaceutical partner in this area had to do with combinatorial chemistry and high throughput screening. That company had looked for a decade and a half for a lead compound to put into development against a particular disease. They had a couple of leads, I think three in total, but they all actually died very quickly. Within three weeks of signing the deal with them, we delivered to them twelve lead compounds. That is how powerful this technology is.

The problem with this technology is that it is used literally in research, in experiments; it is not technology that covers the final product or drug that is sold in the marketplace. We have a patent system that is superbly designed to cover the product that is sold in the marketplace, but not the process of innovation itself. A number of legal scholars, including

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¹ Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 1984 Stat. 1538 (codified as amended in scattered sections of 21 & 35 U.S.C.).

Micky Eisenberg at University of Michigan, raise the possibility that this type of technology and patents thereon are actually inhibiting research. They believe there are too many patents on too many steps in the innovative process, resulting in a marketplace with inefficient licensing or in which licensing will be unavailable, and that there is a net negative in the public bargain of a patent in exchange for disclosure of the invention.

This issue has caused quite a bit of concern. I am on a committee with the National Academies that is studying whether or not there is, in fact, a problem with research tool patents. Our preliminary results so far have turned up nothing. We have been unable to obtain quantitative data on whether or not there has actually been any slowing down of innovation. We cannot find any.

In my own experience at Chiron, we annually review every research program and decide whether or not to continue it. Part of that review involves a competitive analysis to see what other products are in development for the same indication, and at what stages. It occurred to me that during this annual process I've looked at hundreds of products going forward in development, which have all been products of research tool technology. I am very skeptical that there is actually a significant public issue or threat to the innovative process – in fact, quite the opposite. I would suggest that one of the real threats to innovation in the pharmaceutical field is the Hatch-Waxman Act, because of the broadly worded language of the exemption, and interpretations of that exemption, as discussed by Judge Rader.

Research tools are usually used in very early stages of research, for example, to identify a promising chemical entity, a promising structure which itself is usually derived later on by clinical chemists to adjust properties of solubility, bioavailability, toxicity, etc. Again, it is practiced generally quite early in the process. There are large pharmaceutical companies that are claiming that the Hatch-Waxman Act exempts them from infringement in using these research tools. But I have been advised by German colleagues that the research use exemption in Germany probably would not extend to biotechnology tools, because it is not research on the tool; it is the use of the tool for its intended commercial purpose. The decision in *Intermedics*² makes one wonder whether a U.S. court would read Hatch-Waxman in the same way, such that these are not uses of the tool that are reasonably related to an FDA filing. These uses may be five-to-ten years remote in time from a filing with regulatory agencies. In fact, generally they do not actually involve the entity that is eventually filed on, with perhaps the exception of antibody-type inventions. This is one of a number of clouds hanging over research tool technology.

Another is the six-year statute of limitations. During a ten-year process of development, which is often done in secret, it is quite likely that one will not find out that their research tool patent has been violated until a product is approved, and maybe not even then.

² *Intermedics, Inc. v. Ventritex, Inc.*, 152 F.R.D. 188 (N.D. Cal. 1991), *aff'd.*, 991 F.2d 808 (Fed. Cir. 1993) (non-precedential decision).

Another problem is the measure of damages. As my question to Judge Rader brought up, I was really thankful that this conference got me to read *Roche v. Bolar*³ again. I read it in 1984; it got overturned and then I set it aside, thinking it was a dead case, but it is not. It has amazing language on injunctions and damages. One of the issues regarding research tools or pharmaceuticals involves the scenario, spun out in the horror stories of academics, in which somebody gets a patent on a general approach or a particular gene that can be used therapeutically for a number of indications, they develop it for indication X, and then an infringer develops it for indication Y. They prove infringement and they are going to get an injunction – they will get an injunction. Although they may not get a preliminary injunction, at the end of the trial, if they prove their case, they are entitled to a permanent injunction. I believe there is only one case, called *Activated Sludge*,⁴ where a permanent injunction was not awarded by the court. Basically, the city of Milwaukee would have been poisoned if the injunction had been put into place. As a result, people said “gee, you cannot count on equitable relief anymore.”

Judge Nichols opinion in *Roche v. Bolar* cites patent statute Section 283, which by its own wording is discretionary. It uses the word “may” and cites a Supreme Court case, the *Hecht*⁵ case, which had to do with price controls during World War II. That case involved a statute with mandatory injunction language; the Supreme Court refused to grant an injunction, based on equitable principles, even in the face of the mandatory injunction statute. The *Bolar* case goes on to say, in effect, “if Congress wants us to give up our normal principles of equity in applying injunctions, they are going to have to be pretty damn explicit in their statute and tell us that, otherwise we are going to do it.” The Judge suggested that when the case is remanded the research that was done to approve clinical trials should be looked at. The patentee was seeking an injunction to have this research destroyed, so it could never be relied upon for getting an FDA approval. The Judge pointed out all the equitable principles that should be considered, including the good faith of the actor, etc. I think this opens up tremendous possibilities, when there is a public need that is not being met by a patentee, as to whether or not you are entitled to an injunction at the end of the day. Additionally, the Judge commented on damages; in particular, whether they are properly measured by the amount of infringement or its economic impact on the licensee.

Today we have one case in the area of research tools, *Sibia v. Cadus*.⁶ On appeal the patent was found invalid. At the district court level, it involved a patent on a screening method that had been offered for license on what it called “research through royalties,” another controversial area. The jury made the damage calculation by assuming the probability of success of the screening method, by assuming a probable market size, probable market penetration and a probable price. The assumed figures were used to calculate value over the life of the patent and then discount to present net value, which came out to be \$19

³ *Roche Prod. Inc. v. Bolar Pharm. Co.*, 733 F.2d 858 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 856 (1984).

⁴ *Activated Sludge v. Sanitary Dist. of Chicago*, 64 F. Supp. 25 (N.D. Ill. 1946).

⁵ *Hecht Co. v. Bowles*, 321 U.S. 321 (1944).

⁶ *SIBIA Neurosciences, Inc. v. Cadus Pharm. Corp.*, 225 F.3d 1349 (2000)

million. That was a significant award, particularly for a defendant unsuccessful in its screening program.

There are a number of areas of real significance in biotechnology regarding the research exemption. These areas include the Hatch-Waxman Act, damages and injunctive relief, and the statute of limitations.

Thank you.