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Natalie M. Derzko

# IN SEARCH OF A COMPROMISED SOLUTION TO THE PROBLEM ARISING FROM PATENTING BIOMEDICAL RESEARCH TOOLS

**Natalie M. Derzko†**

Patents are acknowledged to be of central importance in the area of biomedical research and development.[1] At the same time, however, many commentators have expressed concern about there being too much patenting in this area, particularly in the area of biomedical research tools.[2] The concern of these critics is that patents on research tools may block future biomedical research and development.[3] This paper argues that, while patenting of such tools is desirable and thus should not be obliterated, some legal limitations on the ability of patent owners to enforce their biomedical research tool patents should exist. That is, certain users and uses of research tools should be exempted from patent infringement and limits should be imposed on amounts and types of royalties that a patent owner can collect from their research tool patents.

Part I of this paper is devoted to defining the term 'biomedical research tool" and what it encompasses, as well as exploring how such tools might be used. In Part II, we develop an understanding of the problem associated with the patenting of biomedical research tools. In this context, we trace what essentially is the demise of the common law experimental use exception, and how this development has contributed to the urgency of the research tools problem. Part III considers the link between the statutory experimental use exception pursuant to 35 U.S.C. § 271(e)(1) and biomedical research tools. Section 271(e)(1) originally was intended to benefit generic

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† J.S.D. Candidate, Julius Silver Fellow in Law, Science and Technology, Columbia Law School; M.S. Biotechnology, Johns Hopkins University, 2001; LL.M., Harvard Law School, 1995; LL.B., Osgoode Hall Law School, York University, 1993; B.Sc. Human Biology, University of Toronto, 1991. Special thanks to Professors Harold Edgar, Richard Nelson and William Sage for their helpful comments on earlier drafts of this article. This article has been written in partial fulfillment of the requirements for the degree of Doctor of the Science of Law in the Faculty of Law, Columbia University.

1. *See infra* note 159.
2. *See, e.g., infra* note 21.
3. *Id.*

pharmaceutical companies who manufacture "copycat" drugs based on original, patented drugs. That is, this exception was intended to give these companies a safe harbor from infringing the original drug's patent while they conducted the necessary experiments to obtain FDA approval on their copycat drug.[4] However, both U.S. courts and the many players in the biomedical research community have interpreted the provision much more broadly. Recently, Judge Rader deviated sharply from this broad interpretive approach in *Integra Lifesciences I, Ltd. v. Merck KGaA*,[5] when he found that the experimental use exception in § 271(e)(1) cannot be extended to render non-infringing a company's otherwise infringing use of a patented research tool. Part III explores the effects of this decision on the patent problem relating to biomedical research tool patents. Finally, Part IV proposes a solution for addressing the problem arising from patents on biomedical research tools.

## I. WHAT ARE BIOMEDICAL RESEARCH TOOLS AND HOW MIGHT THEY BE USED

There are a broad range of materials that might be termed "research tools" because they can be used in the course of biomedical or biotechnological research. For example, research tools might include biochemicals, such as reagents, plasmids, antibodies and enzymes that are used to develop and test subsequent pharmaceutical end products.[6] Generally speaking, these products are used to test the efficacy or functionality of a pharmaceutical end product in a pre-clinical setting. It is conceivable that such research tools might also be used to produce or identify a pharmaceutical end product. Normally, such research tools would not become part of the final product, although it is possible that they may do so. Another type of research tool is a device that can be used and reused during the course of biomedical research, and often operates based on a particular methodology. Devices that run the Polymerase Chain Reaction (PCR), a technique widely used to amplify small amounts of DNA, are an example.[7] Other examples of such devices are protein and

4. *See infra* note 71.

5. 331 F.3d 860 (Fed. Cir. 2003). Judge Rader wrote the majority opinion for a three-judge panel, while Judge Newman wrote a dissent.

6. *See infra* note 12 and accompanying text.

7. *See, e.g.*, DONALD VOET & JUDITH G. VOET, BIOCHEMISTRY 904–05 (2d ed. 1995). PCR has been instrumental in revolutionizing biomedical research.

DNA sequencing instruments,[8] and microarrays[9] which allow a downstream researcher to study a great number of biological interactions at the same time, and knockout mice which provide a disease model.[10] As one can imagine, various combinations of research tools may be used when a new drug is researched, developed and tested.

In their report, the National Institutes of Health (NIH) Working Group on Research Tools used:

> the term "research tool" in its broadest sense to embrace the full range of resources that scientists use in the laboratory, while recognizing that from other perspectives the same resources may be viewed as "end products." For [the Working Group's] purposes, the term [included] cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry libraries, drugs and drug targets, clones and cloning tools (such as PCR), methods, laboratory equipment and machines, databases and computer software. . . .[11]

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8. Jürgen Drews, *Drug Discovery: A Historical Perspective*, 287 SCIENCE 1960, 1962 (2000).

9. Affymetrix is one company that manufactures microarrays. At their website, http://www.affymetrix.com/technology/tech_probe_content.html (last visited March 27, 2002), Affymetrix describes one of its microarray technologies as follows: "GeneChip® technology provides efficient access to genetic information using miniaturized, high-density arrays of oligonucleotide probes." Furthermore, they describe how their GeneChip® microarray works:

> Once fabricated, the GeneChip® probe arrays are ready for hybridization. The nucleic acid to be analyzed (the target) is isolated, amplified and labeled with a fluorescent reporter group. The labeled target is then incubated with the array and stained with fluorescent dye using the fluidics station and hybridization oven. After the hybridization reaction is complete, the array is inserted into the scanner, where patterns of hybridization are detected. The hybridization data are collected as light emitted from the fluorescent reporter groups already incorporated into the target, which is now bound to the probe array. Probes that most clearly match the target generally produce stronger signals than those that have mismatches. Since the sequences and position of each probe on the arrray are known, by complementarity, the identity of the target nucleic acid applied to the probe array can be determined.

10. For example,

> [t]he OncoMouse® transgenic animal technology relates to animal models that develop tumors as a consequence of containing recombinant activated oncogene sequences. First described by Dr. Philip Leder, its usefulness in basic medical research is widely recognized as these mice are key model systems for the study of cancer and in testing the effectiveness of novel cancer therapeutics.

Press Release, *NIH and E.I. Dupont Sign OncoMouse® Agreement* (Jan. 19, 2000), *available at* http://www.nih.gov/news/pr/jan2000/od-19.htm.

11. National Institutes of Health, *Report of the National Institutes of Health (NIH) Working Group on Research Tools* (June 4, 1998), *at* http://www.nih.gov/news/researchtools/index.htm.

Additionally, the NIH issued Guidelines[12] for recipients of NIH research grants and contracts regarding the dissemination of biomedical research tools. However, instead of the term "research tools," the Guidelines use the term "biomedical research resources" or "unique research resources," which the NIH defined as follows:

> The term "unique research resource" is used in its broadest sense to embrace the full range of tools that scientists use in the laboratory, including cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry and DNA libraries, clones and cloning tools (such as PCR), methods, laboratory equipment and machines. The terms "research tools" and "materials" are used . . . interchangeably with "unique research resources." Databases and materials subject to copyright, such as software, are also research tools in many contexts. Although the information provided here may be applicable to such resources, the NIH recognizes that databases and software present unique questions which [are not] fully explored in [the Guidelines].[13]

Therefore, the NIH Research Tools Working Group and the NIH Research Tools Guidelines use a similar definition for research tools; however, the Guidelines exclude databases and software from their definition. Also notably omitted from the Guidelines are "drugs and drug targets." No doubt, the inclusion of these two items in the NIH Working Group's definition of research tools is controversial since pharmaceutical companies see drugs and drug targets as being end products whose successful sale is key to their existence.

The Working Group elaborated on this tension when it described the difficulty of identifying something as a research tool, since what is a research tool in a user's hands might be an end product in the provider's hands:

> The very term "research tool" connotes a user perspective rather than a provider perspective. What a user sees as a research tool, a provider may see as a valuable end product for sale to customers. A striking example of this difference in perspective arises when a scientist in a university wants to use a candidate pharmaceutical compound in research. From the perspective of the university and the scientist, the compound is a mere research tool, potentially useful in making future discoveries. But from the perspective of the firm, the compound may be a very precious end product, the

12. Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources: Final Notice, 64 Fed. Reg. 72,090 (Dec. 23, 1999).

13. *Id.* at 72,092 n.1.

> payoff from significant investments of time and shareholder dollars in its own research.
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> The label "research tool" may apply less equivocally to the multitude of biological discoveries that precede the identification of new therapeutic compounds, including DNA sequences, databases, clones, cell lines, animal models, receptors and ligands involved in disease pathways, or laboratory techniques used to create or identify these discoveries. But even these "upstream" discoveries might seem like commercial end products to the institutions that discover them. Some of these materials might ultimately prove to be therapeutic or diagnostic products in their own right, marketable to consumers for use outside the laboratory. Others might have, or appear to have, sufficient commercial value as resources for use in the discovery of future products to motivate some firms to invest in their identification and development for sale or license to other firms for use in further research. What counts as a research tool and what counts as an end product thus varies from one institution to the next. Inevitably, each institution minimizes the value of the discoveries it borrows from others, while seeing great value in its own past and future discoveries.[14]

In the private firm context, research tools might be used to identify, develop, produce and test pharmaceutical end products for which marketing approval may be sought from the Food and Drug Administration (FDA). For example, as mentioned earlier, biochemicals, such as reagents, plasmids, antibodies and enzymes can be used to develop and test subsequent pharmaceutical end products (e.g., that might test the efficacy or functionality of a pharmaceutical end product in a pre-clinical setting). Many of these types of research tools can be purchased by a researcher from a company that is in the business of selling such tools to laboratories.[15] However, it is also conceivable that less readily available molecular targets, such as antibodies and receptors that are proprietary and not widely distributed, might also be used as research tools to produce or identify a pharmaceutical end product. If such targets are owned by the private firm doing the research, then there is no access problem. However, if such targets are owned by a third party, the private firm conducting the research may only be granted access under a license that may have onerous terms, and this could be problematic. As one can imagine, various combinations of research tools may be used

14. National Institutes of Health, *supra* note 11, at 5.

15. *See, e.g.*, the products available from Invitrogen at http://www.invitrogen.com (last visited Nov. 24, 2003).

when a new drug is researched, developed and tested. Interestingly, the tools used by private firms happen to be the same kinds of tools that public sector entities (e.g., such as universities) would use to conduct biomedical research. Consequently, it seems only appropriate to adopt one unified definition of "research tools" for all types of users.

This is so even though the Working Group has indicated that private firms find the term "research tool" to be problematic, particularly when it is defined broadly:

> From the perspective of private firms, the category "research tool" is itself problematic. Many individuals that we spoke to asked at the outset how we define research tools and took exception to a broad definition that included things such as therapeutic compounds that they regard as end products. Some people further noted that it is often hard to tell the difference between things that are used only in the laboratory and things that might potentially be sold to non-research consumers. For example, a DNA sequence that is currently of use only to researchers ultimately may prove to be a diagnostic marker or to encode a therapeutic protein. Moreover, even something that is used exclusively by researchers rather than by ordinary consumers may have considerable competitive value to a firm.[16]

While we must be mindful of private firms' concerns over broad research tool definitions, it would be imprudent at this stage of the analysis to exclude certain categories of patented inventions from the category of "research tool" identified by the Working Group. Consequently, in this paper, we adopt the Working Group's broad definition of research tools for all users. However, these concerns point to the fact that we should think of "research tools" under two categories, namely, "pure research tools" and "partial research tools." The term "pure research tools" would include tools that cannot be used in any manner other than for research. If a research tool provider is in the business of selling a research tool as a source of income, then the tool will more readily fall within the category of pure research tools. For example, research tools listed in a catalog (e.g., such as enzymes, cell lines, antibodies, reagents) and that might be sold to laboratories would fall under this category. Moreover, such items would be considered pure research items even if one university laboratory might have developed such a product non-commercially and might, out of courtesy, be willing to transfer such a tool to a user

16. National Institutes of Health, *supra* note 11, at 13.

who has requested a sample. The term "partial research tools," on the other hand, might include those tools that can be used during the course of research but also can be used in a non-research capacity, such as a drug product. Such distinctions are worth keeping in mind when identifying a possible solution to the patented research tools problem.[17]

In an era of ever-increasing patenting activity, the U.S. Patent and Trademark Office (PTO) has issued an increasing number of patents for inventions that might fall under the research tools category. Certainly, not all research tools are patentable. Only those tools that the PTO finds are new, useful and non-obvious and that are properly disclosed in the patent application can be protected.[18] In the next part of this paper, we will explore what concerns people have raised as to biomedical research tool patents. In the interim, we will build on the Working Group's comments about research tools and will systematically consider who are the providers and users of patented research tools and what types of uses each of these groups wishes to make of those research tools. The idea here is to create a relatively simple model of research activities involving the use of patented biomedical research tools so that we may better understand the problems that commentators have raised as to research tool patents, and to better evaluate possible solutions to those problems. The chart that follows describes this model, and provides a framework for the analysis in this article. This model will be referred to subsequently by reference to the alphanumerical designations used in this chart.

*PATENTED BIOMEDICAL RESEARCH TOOL ACTIVITY—USER/PROVIDER MODEL*

A. There are three types of research tool patent holders that might provide research tools to members of the public ("the providers"):

17. *See infra* part IV.

18. While not directly the subject of this article, some commentators argue that certain patents on research tools should not have been granted because such patents seek to patent what those commentators believe are naturally-occurring things, or should not have been allowed on such broad terms and based only on a research utility, and that this inappropriate patenting is exacerbating the research tools problem discussed, *infra*, Part II. *See, e.g.*, Richard Nelson, *The Market Economy, and the Scientific Commons* (Aug. 11, 2003) RES. POL'Y (manuscript accepted for publication and on file with the author). The assumption made in this article is that the research tool patents being considered have been properly issued by the PTO under U.S. patent law. If this is not the case then such patents should be invalidated. The reader, however, should be aware of this line of debate.

1. Entities in the private sector—for example, companies, and other profit-maximizing industry actors;
2. Entities in the public sector—for example, universities and research institutions, whether sponsored by government-procured public funds or private endowment; and
3. Individuals.

B. There are two types of uses that the providers might make of their research tool patents.
   1. Refusal to License: First, a provider may obtain a patent on a research tool but then refuse to licence it to any users because the provider sees a competitive advantage to being the exclusive user of the research tool without competition from someone else. One would expect that only a provider in the private sector might take this position. In fact, it seems inappropriate for a provider in the public sector, such as a university, to refuse to make a research tool available—even pursuant to a license, because a core academic value that all universities share is the dissemination of knowledge and to encourage scientific discovery.
   2. Licensing: Second, a provider may wish to make money from its patented research tool through a licensing program. Each of the three types of providers noted above could engage in this type of use of the research tool. If a private sector entity does this then one might consider it to be in the business of selling research tools.

C. There are three types of users amongst members of the public that might wish to use patented research tools ("the users"):
   1. Entities in the private sector—i.e., companies, and other profit-maximizing industry actors;
   2. Entities in the public sector—i.e., universities and research institutions, whether sponsored by government-procured public funds or private endowment; and
   3. Individuals.

D. There are four types of uses that the users might wish to make of patented research tools.
   1. New Product Development: First, a user might use a research tool in the course of research in order to develop a new product. Generally, this is a use that a private sector entity would most likely be involved in.

2. Design-Around Development: Second, a user might use a research tool to try to develop a commercially-viable design-around for it (i.e., a better or at least an alternative research tool). This is generally but not exclusively something that a private sector entity might do.
3. Research on the Tool Itself: Third, a user may wish to study the research tool itself, simply to better understand how it works but may have no interest in developing a commercially-viable design-around for it. A public sector entity is most likely to engage in this type of activity.
4. Using the Tool to Conduct Basic Research: Fourth, a user may just engage in a course of basic research that requires the use of a research tool. It is most likely a public sector entity that might want to use a research tool in this manner.

Although the model outlined above as to research tool patent providers and users is quite general, it will prove helpful in subsequent parts of this paper, as we explore the scope of the research tools problem, and possible ways to solve it. However, given that the concept of a research tool denotes a user perspective,[19] the focus in the forthcoming analysis will be on parts C and D of the model, namely the users of research tools and their potential uses of such tools. One nuance of the model that we will consider later is the situation where the public sector user acts in a commercially-driven manner. This phenomenon will factor into our analysis of a possible solution to the research tools patenting problem.

## II. WHAT ARE THE CONCERNS THAT EXIST AS TO BIOMEDICAL RESEARCH TOOL PATENTS?

Improved biomedical research tools facilitate research and development activities, and often make such research more predictive and efficient, even though there are costs associated with using such tools, particularly if the tools are patented and a user needs to obtain a license to use them. These costs must get factored into the overall cost of doing research. In recent years, commentators, such as Rebecca Eisenberg, have voiced increasing concern about the costs to society of patented research tools, and have written various articles on

19. National Institutes of Health, *supra* note 11 and accompanying text.

this point.[20] Eisenberg wrote one such article with Michael Heller in which the Abstract of the article described their message as follows:

> The "tragedy of the commons" metaphor helps explain why people overuse shared resources. However, the recent proliferation of intellectual property rights in biomedical research suggests a different tragedy, an "anticommons" in which people underuse scarce resources because too many owners can block each other. Privatization of biomedical research must be more carefully deployed to sustain both upstream research and downstream product development. Otherwise, more intellectual property rights may lead paradoxically to fewer useful products for improving human health.[21]

The research tools problem generated so much interest in the legal and scientific communities that the National Institutes of Health (NIH) established the Working Group referred to earlier "to look into problems encountered in the dissemination and use of proprietary research tools, the competing interests of intellectual property owners and research users underlying these problems, and possible NIH responses."[22] Additionally, a workshop was held on the topic at the National Academy of Sciences.[23]

Eisenberg and Heller mention several examples of "anticommons" that can arise in the context of biomedical research. First, they cite the notorious patent applications on expressed sequence tags (ESTs) that were filed by the NIH in 1991[24] as well as

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20. *See, e.g.*, Rebecca S. Eisenberg, *Technology Transfer and the Genome Project: Problems with Patenting Research Tools*, 5 RISK 163 (1994).

21. Michael A. Heller & Rebecca S. Eisenberg, Abstract, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698, 698 (1998).

22. *See* National Institutes of Health, *supra* note 11, as well as accompanying text; *see also* Principles and Guidelines for Research Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources, *supra* note 12 and accompanying text.

23. *See* INTELLECTUAL PROPERTY RIGHTS AND RESEARCH TOOLS IN MOLECULAR BIOLOGY: SUMMARY OF A WORKSHOP HELD AT THE NATIONAL ACADEMY OF SCIENCES, FEBRUARY 15–16, 1996 (National Research Council ed., 1997), *available at* http://books.nap.edu/books/0309057485/html/index.html [hereinafter RESEARCH TOOLS WORKSHOP SUMMARY].

24. In the RESEARCH TOOLS WORKSHOP SUMMARY, *supra* note 23, these events are described in more detail as follows:

> An expressed-sequence tag (EST) is part of a sequence from a cDNA clone that corresponds to an mRNA (Adams and others 1991). . . . In 1991 and 1992, NIH filed patent applications for 6,800 ESTs and for the rapid sequencing method developed by Craig Venter, who was a scientist at NIH. The PTO rejected NIH's application and when Harold Varmus became director of NIH, he decided not to appeal. But controversy caused by the initial patent application continued. In

similar types of applications filed by private firms since that time.[25] Second, they point out the more recent reach-through license agreements (RTLAs) that have been sought for using some patented research tools, such as, the patented OncoMouse® owned by DuPont Corporation.[26] The former scenario is said to be an example of "creating too many concurrent fragments of intellectual property rights in potential future products," whereas the latter scenario is said to be an example of "permitting too many upstream patent owners to stack licenses on top of the future discoveries of downstream users."[27]

Eisenberg and Heller describe RTLAs as follows:

> [A]n RTLA gives the owner of a patented invention, used in upstream stages of research, rights in subsequent downstream discoveries. Such rights may take the form of a royalty on sales that result from use of the upstream research tool, an exclusive or nonexclusive license on future discoveries, or an option to acquire such a license. In principle, RTLAs offer advantages to both patent holders and researchers. They permit researchers with limited funds to use patented research tools right away and defer payment until the research yields valuable results. Patent holders may also prefer a chance at larger payoffs from sales of downstream products rather than certain, but smaller, upfront fees.

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> 1992, Venter left NIH to form The Institute for Genome Research (TIGR), a nonprofit company, and William Haseltine joined the newly established private company, Human Genome Sciences (HGS), a for-profit company that initially provided almost all of TIGR's funding. The focus of the controversy then moved from the public to the private sector, and it changed from an issue about patenting research tools to an issue of access to unpatented research tools. Like many other research tools, ESTs fill different roles and some of the controversy has involved disputes of the relative importance of ESTs for uses other than research. *Id.* at 51.

As is discussed below, *infra* note 160, prevention in the form of a robust patent examining system is the best "solution" for the "anticommons" that might be created as a result of excessive patenting on upstream discoveries, such as ESTs. For example, the statutory requirements that a patent only be granted pertaining to inventions that are new, useful, non-obvious and properly described and enabled, help prevent an "anticommons" from being created in any technological area. *See infra* note 160.

25. Heller & Eisenberg, *supra* note 21, at 699.

26. *Id.* Since Heller and Eisenberg's seminal paper, *supra* note 21, the NIH and DuPont have signed an agreement based on terms set forth in a Memorandum of Understanding ("MOU") dated January 18, 2000. Pursuant to the MOU, "DuPont will continue to provide, at no cost, the OncoMouse® transgenic animal technology to academic laboratories for research uses and will allow unencumbered use and transfer of this technology among researchers at not-for-profit institutions. The MOU imposes no limitations on scientific publications or so-called 'reach-through' rights". *See* Press Release, *supra* note 10. *See also* the MOU *available at* http://ott.od.nih.gov/textonly/oncomouse.htm (last visited Aug. 16, 2003). Therefore, although NIH researchers and NIH grantees are not subject to RTLAs on the OncoMouse®, other groups of researchers may still be burdened by the RTLAs imposed by DuPont on this research tool.

27. Heller & Eisenberg, *supra* note 21, at 699.

> In practice, RTLAs may lead to an anticommons as upstream owners stack overlapping and inconsistent claims on potential downstream products. In effect, the use of RTLAs gives each upstream patent owner a continuing right to be present at the bargaining table as a research project moves downstream toward development.[28]

Interestingly, Cetus Corporation initially proposed RTLAs on any products developed using PCR.[29] However, this scheme was resisted by downstream users of the technology.[30] Since that time, Hoffman-LaRoche has acquired rights to PCR technology, and has offered licenses to use the technology without reach-through obligations. These licenses are initially more expensive but do not have any "strings attached."[31]

Given the costs of purchasing and licensing research tools, it is very likely that researchers and research entities would welcome a reduction in the costs of using research tools. The NIH Working Group on Research Tools, for example, found that: "virtually every firm that [they] spoke with believed that restricted access to research tools is impeding the rapid advance of research and that the problem is getting worse."[32] Consequently, many people likely agree with Eisenberg and Heller that there is a problem with the increasing number of patents issued to research tools, and would be pleased to find a solution to the problem.

One way to make research tools more readily available to some researchers is to create a research exemption by which certain users of research tools would be insulated from a charge of patent infringement even though they have no license to use the tool. The question is, how broad might such an exemption be? Some analysts believe that a research exemption should exist for public sector researchers and individuals conducting research on the tool itself to better understand how the tool works and also should exist for these same users when they engage in basic research with the tool. For example, Stephen Maebius and Harold Wegner have argued that "[u]niversity research uniquely needs a research exemption from

28. *Id.*
29. *Id.*
30. *Id.*
31. *Id.*
32. National Institutes of Health, *supra* note 11.

patent infringement to carry out its functions."[33] Such commentators would like to see such an exemption for the use of patented inventions generally and not only for biomedical research tool patents. Of course, many research tool providers (and at least private entity providers) likely would argue that it is irrelevant whether a public or private user is making use of a research tool for basic science research or drug development, since, if their tool is being used, then they should be compensated.[34]

To better appreciate the scope of such a research exemption, it is helpful to look to the model introduced previously which enumerated various types of research tool patent users (i.e., C1, C2 or C3) and various types of uses that a user might wish to make of a patented research tool (i.e., D1, D2, D3 or D4), and to create a matrix that shows the circumstances in which the research exemption might be available for a certain user engaging the research tool in a certain use. Such a matrix might look as follows:

| | C1 (private sector) | C2 (public sector) | C3 (individuals) |
|---|---|---|---|
| D1(new product development) | No – exception should not be available | No – exception should not be available | No – exception should not be available |
| D2(design-around development) | No – exception should not be available | No – exception should not be available | No – exception should not be available |
| D3(research on tool itself) | N/A – all activities likely business oriented | Yes – exception should be available | Yes – exception should be available |
| D4(tool in basic research) | N/A – all activities likely business oriented | Yes – exception should be available | Yes – exception should be available |

33. Stephen B. Maebius & Harold C. Wegner, *The Looming Crisis Over the Research Use Exception to Patent Infringement: What* Madey *Taught Duke University*, FINDLAW FOR LEGAL PROFESSIONALS, *available at* http://library.lp.findlaw.com/articles/file/00156/008583/title/Subject/topic/Education%20Law_Colleges/Universities/filename/educationlaw_1_145 (last visited June 28, 2003).

34. Anecdotal evidence as obtained from speaking with licensing negotiators of the University of Virginia, based on the extensive number of licensing requests made recently, post the *Madey v. Duke Univ.* decision discussed later. *See infra* note 40 and accompanying text.

The matrix reflects a series of value judgments in which commercial activities involving research tools would not be insulated from a patent infringement charge by a research exemption, but non-commercial activities involving research tools would be so protected. That is, all users engaging in new product development or design-around development with the tool (i.e., commercially-driven activities) would not be protected by such a research exemption. Moreover, the matrix reflects the view that it is unlikely that a private sector researcher could be said to engage in non-commercially driven research akin to public-sector research, since private-sector research is, by nature, commercial. This limited research exemption would not provide a complete solution to the research tools problem, since there are numerous legitimate research activities, albeit commercial in nature, that would remain exposed to research tool patents.[35]

Other commentators, such as Professor Janice Mueller, discuss an even broader research exemption that would extend into more commercial uses of patented inventions, and particularly of patented biomedical research tools.

> The public policies promoted by choosing to exempt "philosophical" research from liability while denying the benefits of the exemption to innovation having the slightest "commercial" flavor are suspect. Society benefits from new therapeutic and diagnostic products, whether or not they arose from a profit motive. Arguably, society may benefit more when profit motive drives innovation. This is because industry funding of university research tends to focus on short-term projects leading to marketable products rather than longer-term basic research. Thus, the "anti-commercialism" element of the experimental use doctrine as currently interpreted actually works against the prompt introduction of new drugs and therapies into the market place.
>
> Profit motive should no longer be held antithetical to the experimental use doctrine. A re-conceptualization of the experimental use doctrine must consider the commercial realities of the twenty-first century research and development process. The involvement of a for-profit firm in the use of patented research tools to develop new products should not be treated as per se outside the scope of the experimental use doctrine.[36]

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35. For example, in the chart, the research activities designated in the following boxes would remain exposed: C1-D1, C1-D2, C1-D3, C1-D4, C2-D1, C2-D2, C3-D1, and C3-D2. *See also infra* note 36 and accompanying text.

36. Janice M. Mueller, *No 'Dilettante Affair': Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 1, 36–37 (2001).

A matrix like the one provided above illustrating this broader viewpoint would, it seems, have every square marked as "yes—exception should be available." On a positive note, if this breadth of coverage were available in a general research exemption, then the research tools problem would not exist since all conceivable uses with a research tool would be exempt from patent infringement. Thus, research tools could be used freely. However, at the same time, patent protection for research tools would be effectively obliterated since research tool patents would not be enforceable against any users. Mueller acknowledges this fact and thus ultimately proposes a different approach discussed later.[37] Consequently, although society benefits tremendously from profit-driven research and perhaps benefits more from this type of research than from other research, such a broad notion of a research exemption is untenable. A more balanced view of such an exemption is the one advocated, for example, by Wegner and Maebius and discussed above. Such a view is fair since those companies engaging in commercial research should have the financial means to compensate research tool patent providers for the use of their tools, within reasonable parameters.

At one time, "it had been unquestioned that an experimental use exemption exists for purely scientific research to study and understand a patented invention, including [its] limited use to make *new* innovations that may or may not be outside the scope of the original patent."[38] These times no longer exist, as discussed below. Rather than at least offering a partial solution to the research tools problem by making, for example, a research exemption available to public sector researchers for non-commercial research, recent developments in patent law have only exacerbated the "anticommons" of research tools by making such a research exemption essentially unavailable, even to university or public sector researchers. The issues of a non-statutory experimental use exception and a *de minimis* exception to patent infringement recently were considered in *Embrex Inc. v. Service Engineering Corp.*,[39] and *Madey v. Duke University*[40]

The historical roots for the common law experimental use exception lie in a 19th century opinion by Justice Story in *Whittemore*

37. *See id.* at 39, 41. Mueller's ultimate approach is discussed *infra* note 167 and at the end of Part IV, and would allow for "non-consensual 'development use' of such tools. . .[but] in exchange for an ex post royalty payment." *Id.* at 41.

38. Maebius & Wegner, *supra* note 33, at 1.

39. 216 F.3d 1343 (Fed. Cir. 2000).

40. 307 F.3d 1351 (Fed. Cir. 2002).

*v. Cutter*.[41] While justifying a jury instruction given by a trial judge in a case involving patent infringement issues, Justice Story stated that "it could never have been the intention of the legislature to punish a man who constructed such a machine merely for philosophical experiments, or for the purpose of ascertaining the sufficiency of the machine to produce its described effects."[42] A few decades later, the law became "well-settled that an experiment with a patented article for the sole purpose of gratifying a philosophical taste, or curiosity, or for mere amusement is not an infringement of the rights of the patentee."[43] Its scope also was described in the leading nineteenth century Patents treatise as follows:

> An unauthorized sale of the invention is always [an infringing act]. But the manufacture or the use of the invention may be intended only for other purposes, and produce no pecuniary result. Thus where it is made or used as an experiment, whether for the gratification of scientific tastes, or for curiosity, or for amusement, the interests of the patentee are not antagonized, the sole effect being of an intellectual character in the promotion of the employer's knowledge or the relaxation afforded to his mind. But if the products of the experiment are sold, or used for the convenience of the experimentor, or if the experiments are conducted with a view to the adaptation of the invention to the experimentor's business, the acts of making or of use are violations of the rights of the inventor and infringements of his patent.[44]

More recently, the Federal Circuit held, in *Roche Products., Inc. v. Bolar Pharmaceutical Co.*,[45] that the common law experimental use exception was narrow and did not extend to experimental uses of a patented invention in the commercial sphere.[46] More specifically, the exception did not permit a generic company to carry out experimental activities with a patented drug that were necessary to obtain marketing approval.[47] Writing for the Federal Circuit, Judge Nichols

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41. 29 F. Cas. 1120 (C.C.D. Mass. 1813) (No. 17,600). Apparently, "Justice Story sought to justify a trial judge's instruction to a jury that an infringer must have an intent to use a patented invention for profit." Roche Prods., Inc. v. Bolar Pharm. Co., 733 F.2d 858, 862 (Fed. Cir. 1984).

42. *Whittemore*, 29 F. Cas. at 1121.

43. Peppenhausen v. Falke, 19 F. Cas. 1048 (C.C.S.D. N.Y. 1861) (No. 11,279). *See also* Roche Prods., Inc., 733 F.2d at 862.

44. William C. Robinson, THE LAW OF PATENTS FOR USEFUL INVENTIONS § 898 (1890).

45. 733 F.2d at 858.

46. *Id.* at 863.

47. *Id.*

offered the following comments about the common law experimental use exception:

> Bolar's intended "experimental" use is solely for business reasons and not for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry. Bolar's intended use of flurazepam hcl [sic] to derive FDA required test data is thus an infringement of the '053 patent. Bolar may intend to perform "experiments," but unlicensed experiments conducted with a view to the adaption of the patented invention to the experimentor's business is a violation of the rights of the patentee to exclude others from using his patented invention. It is obvious here that it is a misnomer to call the intended use *de minimis*. It is no trifle in its economic effect on the parties even if the quantity used is small. It is no dilettante affair such as Justice Story envisioned. 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.[48]

Knowing the background of the common law experimental use exception, we can now return to the twenty-first century, and consider the *Embrex* and *Madey* cases. In *Embrex*, the Federal Circuit affirmed the district court's finding of infringement where a defendant performed scientific experiments to improve (i.e., design around) a patent claiming a method for inoculating birds against disease by injecting vaccines into the egg before hatching.[49] The Court found that the doctors' tests could not be deemed experimental use or *de minimis* since the tests were "expressly for commercial purposes."[50] In a concurrence, Judge Rader explained that "the Patent Act leaves no room for any *de minimis* or experimental use excuses for infringement."[51] As to the *de minimis* defense, Judge Rader noted that "[d]amages for an extremely small infringing use may be *de minimis*, but infringement is not a question of degree."[52] Furthermore, as to experimental use, he noted that "neither the statute nor any past Supreme Court precedent gives any reason to excuse infringement because it was committed with a particular purpose or intent, such as for scientific experimentation or idle curiosity."[53] Judge Rader's disdain for broad exceptions to patent infringement has

48. *Id.*
49. Embrex, Inc. v. Serv. Eng'g Corp., 216 F.3d 1343, 1349 (Fed. Cir. 2000).
50. *Id.*
51. *Id.* at 1352.
52. *Id.* at 1353.
53. *Id.*

recently reappeared in the *Integra Lifesciences I, Ltd. v. Merck KGaA*[54] decision, as we will see later.[55]

To those seeking an expansive general research exemption, the *Embrex* case was discouraging since it signaled that commercially-driven design-around activities (e.g., such as those in the private sector, and referenced in the C1-D2 cross-section of the matrix provided above) [56] were not shielded from a finding of infringement under the common law experimental use exception. However, until recently, most observers expected that the common law experimental use exception should at least be operable in the public sector research context. However, the hopes of these observers were crushed when the Federal Circuit held in *Madey v. Duke University*[57] that the common law experimental use exception is exceedingly narrow and would not even extend to many (if not most) public sector research activities.

In *Madey*, the Federal Circuit reversed the district court's finding that Duke used a former professor's patented equipment for experimental purposes only and thus did not infringe his patents.[58] Judge Gajarsa reasoned that Duke, like other major research universities, funds research projects with no commercial application whatsoever; however, such projects "unmistakably further the institution's legitimate business objectives, including educating and enlightening students and faculty participating in these projects."[59] The Court then remanded the case to the district court to reconsider its decision in light of a significantly limited experimental use exception, holding:

> In short, regardless of whether a particular institution or entity is engaged in an endeavor for commercial gain, so long as the act is in furtherance of the alleged infringer's legitimate business and is not solely for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry, the act does not qualify for the very narrow and strictly limited experimental use defense. Moreover, the profit or non-profit status of the user is not determinative.[60]

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54. 331 F.3d 860 (Fed. Cir. 2003).
55. *See infra* discussion of this case in Part III.
56. *See* matrix in earlier discussion of Part II.
57. 307 F.3d 1351 (Fed. Cir. 2002).
58. *Id.*
59. *Id.* at 1362.
60. *Id.*

Although Judge Gajarsa in *Madey* did not go so far as to state that the experimental use exception does not exist, the Federal Circuit has made the exception so narrow that it seems only a garage tinkerer's (i.e., an individual's) use of a patented invention might be protected by the exception.

Not surprisingly, the Federal Circuit's ruling has led to profound discontent amongst universities and other public sector research entities.[61] Duke University appealed to the Supreme Court. Further, various parties, including the United States government and an association of universities whose faculties engage in scientific research, filed amicus curiae briefs.[62] The U.S. government took the position that the petition for certiorari should be denied because: (1) the *Madey v. Duke University* decision does not conflict with prior precedent; (2) the case stemmed from an interlocutory decision such that lower courts will be able to further explore the underlying facts in the case and then better develop the scope of the experimental use exception; and (3) the policy concerns addressed by Duke may be better resolved through the legislative process.[63] In their amici curiae brief, the association of universities wrote that "[b]y effectively eliminating the exemption for even noncommercial academic scientific research, the decision erects a significant roadblock to the advancement of science," and that, as such, "[t]he *amici curiae* are deeply disturbed by this ruling." [64] Moreover, the association pointed out that: "The decision below threatens to stifle [university research that has been crucial to scientific progress] and thereby endanger this nation's continued leadership in science and technology."[65] A particular concern of the universities was that they will need to expend considerable resources to pay for additional patent searches and infringement opinions. Additionally, they would have to engage in more licensing agreements and participate in more litigation, as a

61. *See infra* note 64 and accompanying text. *See also* anecdotal evidence discussed *supra* note 34.

62. *See* Duke University v. Madey, No. 02-1007 (Jan. 2, 2003) (petition for writ of certiorari filed), *available at* http://www.supremecourtus.gov/docket/02-1007.htm (last visited June 28, 2003).

63. Brief of Amicus Curiae United States at 1, Duke Univ. v. Madey, 307 F.3d 1351 (Fed. Cir. 2002), *cert. denied*, 123 S. Ct. 2639 (2003) (No. 02-1007).

64. Brief of Amicus Curiae Association of American Medical Colleges, et al. at 3–4, Duke Univ. v. Madey, 307 F.3d 1351 (Fed. Cir. 2002), *cert. denied*, 123 S. Ct. 2639 (2003) (No. 02-1007). The brief, in support of Petitioner, was filed in the Supreme Court of the United States on Jan. 29, 2003, *at* http://www.supremecourtus.gov/docket/02-1007.htm.

65. Association of American Medical Colleges' Brief, *supra* note 64, at 3–4.

result of the decision.[66] Yet, despite the alarming potential consequences of the *Madey* decision to future scientific progress as identified by universities, the Supreme Court denied review of this case.[67] The Court, it appears, was more convinced by the arguments made by Madey and the U.S. government than those made by Duke and the association of universities.

Therefore, the common law research exemption has been disemboweled and universities are left with having to turn to the legislators to clean up the mess. In the meantime, the research tools problem described by Eisenberg and Heller cannot be resolved either partially or fully by the common law experimental use exception.

## III. WHAT IS THE SCOPE OF THE STATUTORY EXPERIMENTAL USE EXCEPTION IN 35 U.S.C. § 271(E)(1) AND CAN IT SOLVE THE RESEARCH TOOLS PROBLEM?

The statutory experimental use exception found at 35 U.S.C. § 271(e)(1) was introduced by the Drug Price Competition and Patent Term Restoration Act of 1984, more colloquially known as the Hatch-Waxman Act, to statutorily overturn the Federal Circuit's decision in *Roche Products, Inc. v. Bolar Pharmaceutical Co.*[68] As suggested previously, in that decision, the Federal Circuit ruled that the common law experimental use doctrine was not broad enough to shield a generic pharmaceutical company's experimentation with a patented invention from a finding of patent infringement, even though the experimentation was undertaken to obtain the Food and Drug Administration's (FDA's) approval for a generic copy of the patented drug. Section 271(e)(1) states as follows:

> 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.[69]

By introducing § 271(e)(1), the legislators wanted to allow generic pharmaceutical companies to undertake those activities found

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66. *Id.* at 3.

67. Madey v. Duke Univ., 307 F.3d 1351 (Fed. Cir. 2002), *cert. denied*, 123 S. Ct. at 2639.

68. 733 F.2d 858 (Fed. Cir. 1984)

69. 35 U.S.C. § 271(e)(1) (2000).

to be infringing in *Roche v. Bolar* without liability.[70] However, since its inception, this statutory experimental use exception has been interpreted broadly by U.S. courts.[71] This broad interpretation has given companies seeking to make "copycat drugs" or, more generally, seeking to use a patented invention to make their own generic drug product, a complete endorsement to engage in almost any and all preparatory commercial and testing activities that might be necessary to be able to enter into competition with the innovative, patent-holding companies promptly after expiry of the relevant patent.[72]

In view of the broad interpretation afforded to the experimental use exception up until now, the increasingly vocal concerns of certain commentators about patenting research tools, and the exceedingly narrow scope of the common law experimental use exception, it should come as no surprise that various parties have recently tried to convince the courts that the statutory experimental use exception should encompass the free use of research tools in certain instances. We will explore these cases in a moment, once we analyze the wording of § 271(e)(1).

Although, as discussed above, the intention of § 271(e)(1) was to allow generic companies to use a patented invention to conduct the preparatory experimental work required to get FDA approval to market a drug, the wording of this provision is general enough to be applied more broadly. On its face, this provision exempts from patent infringement the unauthorized use of a patented invention, which arguably could be a patented research tool, if the use of that research tool is reasonably related to the development and submission of information under the Food, Drug and Cosmetic Act. Since the searching for, development and pre-clinical safety and efficacy testing of drugs for FDA approval could well require the use of one or more patented research tools, it is quite conceivable that § 271(e)(1) might be interpreted to exempt such use of patented research tools.

In *Intermedics, Inc. v. Ventritex, Inc.*,[73] an important case in the jurisprudential development of § 271(e)(1), Magistrate Judge Brazil

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70. *See* discussion *infra* Part III; *see also infra* note 71.

71. For an in-depth discussion on this topic, *see* Natalie M. Derzko, *A Local and comparative Analysis of the Experimental Use Exception—Is Harmonization Appropriate?* 44 IDEA 1 (2003).

72. *Id.*

73. 775 F. Supp. 1269 (N.D. Cal. 1991), *aff'd* 991 F.2d 808 (Fed. Cir.1993) in an unpublished disposition that is not to be employed or cited as precedent. This decision was cited with approval by the Federal Circuit in *Telectronics Pacing Systems, Inc. v. Ventritex, Inc.*, 982 F.2d 1520 (Fed. Cir. 1992).

established the following test to determine what activities might be acceptable under § 271(e)(1):

> [W]ould it have been reasonable, objectively, for a party in defendant's situation to believe that there was a decent prospect that the "use" in question would contribute (relatively directly) to the generation of kinds of information that was likely to be relevant in the processes by which the FDA would decide whether to approve the product?" [74]

When Magistrate Brazil asked that question, he found that the following activities of the defendant with Cadence, a generic copy of a patented medical device, fell within the scope of the provision: the manufacture of several hundred Cadences; sales of the Cadence to U.S. hospitals; sales of the Cadence to international distributors; testing of the Cadence, particularly in Germany; and demonstrations of the Cadence at trade shows. [75] Although this case focused on the allowable activities of a defendant manufacturing generic copies of a patented invention, the judge's question also can be posed in the context of the scenario that we are interested in here, namely, whether a defendant's use of a patented research tool might be protected by § 271(e)(1). It seems that the use of a patented research tool during the research and development of a drug product could fairly be said to contribute relatively directly to the generation of kinds of information that is likely to be relevant in the processes by which the FDA would decide whether to approve the product. Consequently, by this analysis, § 271(e)(1) should cover the use of research tools during the drug discovery process, since much of the data generated during this process is of interest to the FDA. In fact, generally speaking, the activities of a defendant with research tools are more closely related to the type of information of interest to the FDA than the activities of the defendant at issue in the *Intermedics, Inc. v. Ventritex, Inc.* case.

The FDA is interested in reviewing the information that forms the basis of any and all claims that are made in a pharmaceutical's labeling, known as the "package insert."[76] The FDA provides some direction regarding the content of the labeling in 21 C.F.R. § 201.56.[77]

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74. *Intermedics*, 775 F. Supp. at 1280.

75. *Id.* at 1282.

76. *See, e.g.*, STEVEN E. LINBERG, EXPEDITING DRUG AND BIOLOGICS DEVELOPMENT: A STRATEGIC APPROACH 53 (2d ed. 1999).

77. General Requirements on the Content and Format of Labeling for Human Prescription Drugs, 21 C.F.R. § 201.56 (2003):

In particular, the package insert should contain a summary of the essential scientific information needed for the safe and effective use of the product.[78] This would include pharmacological information, some of which may well be generated from experiments requiring the use of biomedical research tools.

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Prescription drug labeling described in § 201.100(d) shall contain the information in the format required by § 201.57 and shall meet the following general requirements:

(a) The labeling shall contain a summary of the essential scientific information needed for the safe and effective use of the drug.

(b) The labeling shall be informative and accurate and neither promotional in tone nor false or misleading in any particular.

(c) The labeling shall be based whenever possible on data derived from human experience. No implied claims or suggestions of drug use may be made if there is inadequate evidence of safety or a lack of substantial evidence of effectiveness. Conclusions based on animal data but necessary for safe and effective use of the drug in humans shall be identified as such and included with human data in the appropriate section of the labeling, headings for which are listed in paragraph (d) of this section.

(d)(1) The labeling shall contain specific information required under § 201.57 under the following section headings and in the following order:

Description.
Clinical Pharmacology.
Indications and Usage.
Contraindications.
Warnings.
Precautions.
Adverse Reactions.
Drug Abuse and Dependence.
Overdosage.
Dosage and Administration.
How Supplied.

(2) The labeling may contain the following additional section headings if appropriate and if in compliance with § 201.57 *(l)* and (m):

Animal Pharmacology and/or Animal Toxicology.
Clinical Studies.
References.

(3) The labeling may omit any section or subsection of the labeling format if clearly inapplicable.

(4) The labeling may contain a "Product Title" section preceding the "Description" section and containing only the information required by § 201.57(a)(1)(i), (ii), (iii), and (iv) and § 201.100(e). The information required by Sec. 201.57(a)(1)(i), (ii), (iii), and (iv) shall appear in the "Description"section of the labeling, whether or not it also appears in a "Product Title."

(e) The labeling shall contain the date of the most recent revision of the labeling, identified as such, placed prominently immediately after the last section of the labeling.

78. *Id.*

The notion that § 271(e)(1) should be broadly interpreted is supported by the Supreme Court's decision in *Eli Lilly & Co. v. Medtronic, Inc.*[79] In that case, the Court considered the meaning and scope of 35 U.S.C. § 271(e)(1).[80] In particular, the court considered whether, pursuant to 35 U.S.C. § 271(e)(1), activities which are undertaken for the purpose of developing and submitting to the FDA information necessary to obtain marketing approval for a *medical device* under § 515 of the Federal Food, Drug, and Cosmetic Act are exempt from patent infringement.[81] Since § 271(e)(1) did not specifically mention medical devices, Justice Scalia adopted a broad reading of the provision in order to include medical devices within the scope of the provision.

Yet, an argument also can be made that this Supreme Court decision would not support interpreting § 271(e)(1) to exempt the use of research tools during drug discovery. This was the view taken by Judge Crabb of the Western District of Wisconsin in *Infigen, Inc. v. Advanced Cell Technology, Inc.*,[82] an early case in which a court considered whether § 271(e)(1) might shield a defendant's use of a research tool from a finding of infringement. Judge Crabb relied on Justice Scalia's "perfect product fit" reasoning when determining the applicability of § 271(e)(1) to the facts before him.[83]

In the *Eli Lilly* decision, Justice Scalia spoke of the "perfect product fit" between § 271(e)(1) and § 156 dealing with patent term extensions.[84] Justice Scalia reasoned that, since medical devices, food additives, color additives, new drugs, antibiotic drugs and human biological products are all subject to premarket approval under various provisions of the Food, Drug and Cosmetic Act, and are all also eligible for a patent term extension, they should also be subject to the experimental use exception.[85] Justice Scalia contrasted these products with new animal drugs and veterinary products which were excluded from both provisions.[86] However, in a footnote to the discussion, Justice Scalia also revealed the weakness of his "perfect product fit" analysis on two fronts.[87] In 1986, "new infant formula"

79. 496 U.S. 661 (1990).
80. *Id.*
81. *Id.* at 663–64.
82. 65 F. Supp. 2d 967, 979–80 (W.D. Wis. 1999).
83. *Id.*
84. *Eli Lilly*, 496 U.S. at 672.
85. *Id.*
86. *Id.*
87. *Id.* at 672 n.6.

became subject to a premarket approval requirement, thereby making it fall within § 271(e)(1). However, it remained excluded from § 156.[88] Furthermore, in 1988, animal drugs and veterinary biological products were added to § 156 but deleted from § 271(e)(1).[89]

In the *Infigen* case, the defendants conceded that they used the method of the plaintiff's '720 patent and the culture media covered by the plaintiff's '822 patent.[90] The '720 patent was directed to a process for activating bovine oocytes (unfertilized eggs) for use in cloning, whereas the '822 patent was directed to a culture medium.[91] However, the defendants argued, with little support, that their use of the plainitff's patented method and culture media was not infringing in view of the protection afforded by § 271(e)(1), since they used the plaintiff's patented method and culture medium while working on the initial stages of a product that would later require FDA approval if it were commercially viable.[92] Judge Crabb was unconvinced, and reasoned, based on Justice Scalia's analysis in the *Eli Lilly* case, that § 271(e)(1) applied only to those patents covering products that were subject to a regulatory review period prior to their commercial marketing.[93] Since none of the plaintiff's patents covered a drug product, and no such patent was covered by § 156, the judge felt that § 271(e)(1) was not applicable.[94] Given the identified weakness with Justice Scalia's "perfect product fit" reasoning, Judge Crabb's analysis seems superficial and so is not very persuasive. Yet, for our purposes, the facts of the case and its outcome (namely that § 271(e)(1) was found not to exempt the use of patented research tools), are worth noting. As we will see, subsequent cases have grappled more directly with the question whether the use of a research tool in FDA-related research might be shielded by § 271(e)(1).

For example, *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*[95] involved a summary judgment motion on patent infringement in which the main issue before the Court was whether § 271(e)(1) rendered non-infringing Bristol-Myers Squibb's (BMS's) use of

88. *Id.*

89. *Id.* Now, however, a review of § 271(e)(1) reveals that certain animal drugs and veterinary biological products are included within the scope of § 271(e)(1).

90. Infigen, Inc. v. Advanced Cell Tech., Inc., 65 F. Supp. 2d 967, 979 (W.D. Wis. 1999).

91. *Id.* at 969.

92. *Id.* at 980.

93. *Id.*

94. *Id.*

95. Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc., No. 95 Civ. 8833 (RPP), 2001 U.S. Dist. LEXIS 19361 (S.D. N.Y. 2001).

Rhone-Poulenc Rorer's (RPR's) patented intermediates in its research and development program. Judge Patterson rejected the argument relied upon by the *Infigen* Court that the term "patented invention" in § 271(e)(1) is restricted in scope based on the products covered by § 156.[96] He pointed out that the Federal Circuit also declined to adopt such reasoning in *AbTox, Inc. v. Exitron Corp.*[97] and *Chartex International PLC v. M.D. Personal Products Corp.*[98] Thereafter, applying the *Intermedics* test identified above, Judge Patterson held that:

> A rational jury could only conclude based on these undisputed facts that it was reasonable, objectively, for a party in Bristol's position to believe that there was a "decent prospect" that its use of the RPR intermediates in Bristol's experiments "would contribute (relatively directly) to the generation of kinds of information that was likely to be relevant in the process by which the FDA would

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96. *Id.* at *6–*10 n.5.

97. *Id.* at *7–*10. The Federal Circuit declined to strictly follow Justice Scalia's "perfect product fit" analysis in *AbTox, Inc. v. Exitron Corp.*, 122 F.3d 1019 (Fed. Cir. 1997). At issue in that case was a patented class II medical device and method used in sterilizing medical instruments in plasma. Exitron was developing a plasma sterilizer of its own and hired MDT to undertake certain testing on the device that was consistent with the type of testing that would have to be undertaken to obtain FDA approval for a class II medical device. However, at the time of the litigation, Exitron had not yet filed an FDA application or marketed the device. Accordingly, AbTox, the plaintiff, alleged that the actual purpose of the testing was to interest potential customers and induce MDT to purchase the rights to the device. Rader J., writing for the panel, held that Exitron's activities were shielded by the experimental use exception since the statute "does not look to the underlying purposes or attendant consequences of the activity . . . , as long as the use is reasonably related to FDA approval." *Id.* at 1030. One of the issues that Judge Rader had to resolve in this case was whether the experimental use exception should extend to class II medical devices. The dilemma arose because a strict reading of Justice Scalia's opinion in *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 674 (1990), suggests that there has to be a "perfect product fit" between those products whose use can be subject to an experimental use exception, and those for which a patent term can also be extended pursuant to § 156. Class I and II medical devices only need to undergo an abbreviated premarket approval process, unlike class III medical devices which undergo a much more rigorous approval process. Furthermore, unlike class III medical devices, class II medical devices are not eligible for patent term extensions. Therefore, a "perfect product fit" approach would lead to the decision that class II medical devices are not a "patented invention" pursuant to § 271(e)(1). Nonetheless, Judge Rader decided that the court must adopt the Supreme Court's broader holding (rather than the "perfect product fit" approach) since § 271(e)(1) was not expressly limited to class III medical devices.

98. Bristol-Myers Squibb Co., 2001 U.S. Dist LEXIS 19361, at *8–*10. In *Chartex International PLC v. M.D. Personal Products Corp.*, 1993 U.S. App. LEXIS 20560 (Fed. Cir.1993) (unpublished), the patent owner alleged that the defendant's female condom, which was either a Class I or II medical device, was not within the scope of § 271(e)(1) because neither a Class I nor a Class II device is eligible for a patent extension under § 156. *Id.* at *5 n.2. The Federal Circuit rejected this argument, noting that possible limitations from one section should not be read into the other. *Id.*

> decide whether to approve the product." *Intermedics*, 775 F. Supp. at 1280. Accordingly, Bristol's experiments with the RPR patented intermediates are entitled to the exemption Congress provided in 35 U.S.C. § 271(e)(1) as "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 . . . ."[99] (Footnotes omitted).

Consequently, Judge Patterson found that § 271(e)(1) protected BMS' experimental uses of RPR's patented intermediates:

> (1) even where each such use does not directly result in an FDA application being filed, so long as the use was made in order to determine whether or not an application for approval would be sought; and (2) even though each such use of the patented intermediates may not directly yield information that could be submitted to the FDA, but relates to a preliminary activity that may facilitate or be useful in generating information that could be submitted to the FDA.[100]

Given Judge Patterson's solid reasoning and reference to precedent, one might have thought that the Federal Circuit would take the same position when faced with the question whether § 271(e)(1) exempts the use of a patented research tool from infringement if it is used solely for uses reasonably related to the development and submission of information to the FDA. However, this is not what occurred. In line with the trend of narrowing the scope of exceptions to patent infringement started with *Embrex* and *Madey*, the Federal Circuit recently held in *Integra Lifesciences I, Ltd. v. Merck KgaA*,[101]

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99. Bristol-Myers Squibb Co., 2001 U.S. Dist. LEXIS at *19–*21.

100. *Id.* at *24. In taking this position, Judge Patterson was influenced by the U.S. District Court of Massachusetts' reasoning in *Amgen v. Hoechst Marion Roussel, Inc.*, that post hoc analyses of the coverage of § 271(e)(1) are not appropriate:

> Amgen's post hoc analysis misses the mark. The Defendants are protected by the statute if the production of the three batches of GA-EPO was objectively likely to generate useful information, even if the results were later discarded or abandoned for reasons unrelated to FDA approval. The exemption is not so ephemeral that it will be lost as a result of conduct which post dates the making, using or selling of the patented product.

Bristol-Myers Squibb Co., 2001 U.S. Dist LEXIS 19361, at *22 (quoting Amgen v. Hoechst Marion Roussel, Inc., 3 F. Supp. 2d 104, 109 [D. Mass. 1998]).

101. 331 F.3d 860, 872 (Fed. Cir. 2003). This panel was comprised of Judges Rader and Prost in the majority, and Judge Newman in dissent. At the time of writing, a clerk in the Federal Circuit Clerk's Office reported telephonically that an *amicus curiae* had filed a Petition for Rehearing of this case on July 28, 2003. However, the Federal Circuit had not yet ruled on

that § 271(e)(1) cannot be so extended. In doing so, the court affirmed the lower court's ruling as to § 271(e)(1).[102] However, the majority did call into question the $15 million reasonable royalty awarded by the jury since the factual record did not appear to support such an award, and remanded the case back to the district court for further consideration of this issue.[103]

The *Integra v. Merck* case involved five patents belonging to Integra and its co-plaintiffs relating to a short tri-peptide segment of fibronectin known as the "RGD peptide."[104] This peptide promotes cell adhesion by interacting with $\alpha_v\beta_3$ receptors. Good cell adhesion is important for wound healing, biocompatibility of prosthetic devices and angiogenesis (i.e., new blood vessel growth).[105] A defendant scientist, Dr. Cheresh, working at The Scripps Institute (also a defendant), discovered that blocking $\alpha_v\beta_3$ receptors inhibits angiogenesis, and that inhibiting angiogenesis can be a way to halt tumor growth as well as treat other conditions (e.g. diabetic retinopathy, rheumatoid arthritis, psoriasis, and inflammatory bowel disease).[106] Merck found Dr. Cheresh's work promising and consequently hired him and Scripps to investigate potential drug targets involving this mechanism.[107]

Thereafter, several potential drug candidates were identified and Merck and Scripps pursued further research under an agreement to fund "the necessary experiments to satisfy the biological bases and regulatory (FDA) requirements for the implementation of clinical trials" [108] for such drug candidates. After discovering the existence of this agreement, Integra offered a license to Merck since it believed that Dr. Cheresh's angiogenesis research was a commercial endeavor that infringed its patents. (In her dissenting opinion, Judge Newman indicated that Dr. Cheresh had synthesized and studied cyclic RGD peptides of various structures, which presumably were the subject of Integra's patents.)[109] However, Merck refused such a license, taking the position that its activities were protected by 35 U.S.C. § 271(e)(1),

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the Petition. *See* Federal Rules of Appellate Procedure 35 and 40 for rules describing this Petition process.

102. *Integra Lifesciences I*, 331 F.3d at 868, 872.

103. *Id.*

104. *Id.* at 862.

105. *Id.*

106. *Id.* at 863.

107. *Id.*

108. *Integra Lifesciences I*, 331 F.3d at 863.

109. *Id.* at 873–74.

as well as arguing that the Integra patents were invalid.[110] The district court held that the statutory experimental use exception did not exempt Merck's activities, and found Merck liable for infringing Integra's patents.[111]

In the majority's analysis, Judge Rader first examined previous court pronouncements and legislative reports describing § 271(e)(1) as a limited exception allowing generic companies to conduct the necessary testing, namely bioequivalency testing, to get drug approval on a generic substitute drug.[112] For example, Judge Rader pointed to *Hoechst-Roussel Pharmaceuticals, Inc. v. Lehman*[113] in which the Federal Circuit noted that "[s]ection 271(e) permits premarket approval activity conducted for the sole purposes of sales after patent expiration."[114] Consequently, in these first paragraphs of the decision, Judge Rader was essentially informing the reader of his view that § 271(e)(1) should be seen as a narrow exception, just like the common law experimental use exception. He then characterized the issue before the Court as follows:

> This court has not considered the question arising in this case, namely, whether the pre-clinical research conducted under the Scripps-Merck agreement is exempt from liability for infringement of Integra's patents under § 271(e)(1). The Scripps-Merck experiments did not supply information for submission to the United States Food and Drug Administration (FDA), but instead identified the best drug candidate to subject to future clinical testing under the FDA processes. Thus, this court must determine whether the § 271(e)(1) safe harbor reaches back down the chain of experimentation to embrace development and identification of new drugs that will, in turn, be subject to FDA approval.[115]

Next, Judge Rader focused on the language of § 271(e)(1), placing particular emphasis on the term "solely," which had essentially been written out of the statute in previous court decisions.[116] He concluded that Merck's activities were not protected

110. *Id.* at 863.

111. *Id.*

112. *Id.* at 865–66.

113. 109 F.3d 756 (Fed. Cir. 1997).

114. *Integra Lifesciences I*, 331 F.3d at 865 (quoting Hoechst-Roussel Pharms., Inc. v. Lehman, 109 F.3d at 763).

115. *Integra Lifesciences I*, 331 F.3d at 865–66.

116. *See* Derzko, *supra* note 71, particularly the discussion of the Federal Circuit's decision in *Telectronics Pacing Systems, Inc. v. Ventritex, Inc.*, 982 F.2d 1520 (Fed. Cir. 1992).

by § 271(e)(1), because such activities were not sufficiently related to the development and submission of information to the FDA:

> The 1984 Act further specifies the subject of the reasonable relationship test. The exemption covers uses "reasonably related to the development and submission of information" to the FDA. Thus, to qualify at all for the exemption, an otherwise infringing activity must reasonably relate to the development and submission of information for FDA's safety and effectiveness approval processes. The focus of the entire exemption is the provision of information to the FDA. Activities that do not directly produce information for the FDA are already straining the relationship to the central purpose of the safe harbor. The term "reasonably" permits some activities that are not themselves the experiments that produce FDA information to qualify as "solely for uses reasonably related" to clinical tests for the FDA. Again, however, the statutory language limits the reach of that relationship test.
>
> In this case, the Scripps work sponsored by Merck was not clinical testing to supply information to the FDA, but only general biomedical research to identify new pharmaceutical compounds. The FDA has no interest in the hunt for drugs that may or may not later undergo clinical testing for FDA approval. For instance, the FDA does not require information about drugs other than the compound featured in an Investigational New Drug application. Thus, the Scripps work sponsored by Merck was not "solely for uses reasonably related" to clinical testing for FDA.[117]

Later, after approving the *Intermedics* test applied by the District Court, Judge Rader then noted that "§ 271(e)(1) simply does not globally embrace all experimental activity that at some point, however attenuated, may lead to an FDA approval process."[118] Moreover, "[t]he safe harbor does not reach any exploratory research that may rationally form a predicate for future FDA clinical tests."[119]

At the end of his opinion, Judge Rader revealed what may well have been his greatest motivation for not wanting to extend the scope of § 271(e)(1) to cover Merck's experimental activities which involved the use of Integra's patented RGD peptides:

> [S]uch an extension would not confine the scope of § 271(e)(1) to *de minimis* encroachment on the rights of the patentee. For example, expansion of § 271(e)(1) to include the Scripps-Merck

117. *Integra Lifesciences I*, 331 F.3d at 866.

118. *Id.* at 867.

119. *Id.*

> activities would effectively vitiate the exclusive rights of patentees owning biotechnology tool patents. After all, patented tools often facilitate general research to identify candidate drugs, as well as downstream safety-related experiments on those new drugs. Because the downstream clinical testing for FDA approval falls within the safe harbor, these patented tools would only supply some commercial benefit to the inventor when applied to general research. Thus, exaggerating § 271(e)(1) out of context would swallow the whole benefit of the Patent Act for some categories of biotechnological inventions. Needless to say, the 1984 Act was meant to reverse the effects of *Roche* under limited circumstances, not to deprive entire categories of inventions of patent protection.[120]

Judge Rader is correct that Merck's reliance on § 271(e)(1) does not fall within that section's historic and legislatively anticipated framework, which stems from the needs of generic companies seeking to make copycat drugs. Yet, at the same time, the Federal Circuit has not followed its previously laid out broad analytical approach as to the scope of § 271(e)(1), as driven primarily by the test set forth in the *Intermedics* decision.[121] In this regard, one might criticize the *Integra v. Merck* decision as not properly following the broad interpretive approach generally laid down by Federal Circuit and Supreme Court precedent.[122] As suggested earlier, the activities with a research tool, as in the *Integra v. Merck* case, are much more closely related to the development and submission of information to the FDA than the activities that were exempted in the *Intermedics v. Ventritex* case.[123]

Moreover, Judge Rader's reasoning is problematic since he suggests that the FDA is only interested in the results from clinical trial testing and not in information that is yielded about a drug at the much more preliminary "drug hunting" stage.[124] As noted earlier, the

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120. *Id.*

121. For an extensive discussion of this broad reasoning, *see* Derzko, *supra* note 71 and accompanying text.

122. Although Judge Rader reached the same ultimate decision as Judge Crabb in *Infigen, Inc. v. Advanced Cell Tech., Inc.*, 65 F. Supp. 2d 967 (W.D. Wis. 1999), about § 271(e)(1) not exempting an entity's use of a research tool, he did not adopt the same reasoning as Judge Crabb, namely, that there must be a "perfect product fit" between those patented inventions covered by § 271(e)(1) and those that are subject to patent term extensions pursuant to § 156. This aspect of Judge Rader's decision at least is in accordance with the Federal Circuit's previous reasoning as to § 271(e)(1) in *AbTox, Inc. v. Exitron Corp.*, 122 F.3d 1019 (Fed. Cir. 1997), discussed *supra* note 97, and *Chartex International PLC v. M.D. Personal Products Corp.*, 5 F.3d 1505 (Fed. Cir. 1993), discussed *supra* note 98.

123. *See supra* note 73 and accompanying text.

124. *Integra Lifesciences I*, 331 F.3d at 866.

content of a drug's product insert defines those aspects of a drug for which the FDA will want to see experimental data.[125] This information includes a description of a drug and its pharmacology and toxicity.[126] Some of the information relevant to these subject areas could be generated at very early stages in a drug product's development in what might be termed the "drug hunting" stage, and well before clinical testing for a drug begins. Therefore, this characterization of the scope of § 271(e)(1) coverage seems incorrect.

In addition, Judge Rader's comment that the FDA is not interested in the "hunt for drugs" nor about drugs other than the compound for which an Investigational New Drug (IND) application is submitted to the FDA[127] is problematic because it seems to suggest the § 271(e)(1) may offer a greater scope of protection for drugs once they become the subject of such an application to the FDA. This leads to a highly uncertain situation for drug developers who simply do not know until very late in the drug development stage whether a drug's data will get submitted to the FDA for consideration in the context of an IND application. A drug developer would want to know at the outset of undertaking certain activities with a patented invention whether or not they will be considered infringing activities.[128]

On the other hand, the Court reached a valid position from a policy perspective, if one examines what would have been the consequences of exempting from infringement under § 271(e)(1) the use of research tools to conduct FDA-required research. On this level, it is important to recognize that when § 271(e)(1) is relied on by generic pharmaceutical companies to conduct experiments with its generic copy of a patented drug for FDA approval, the exclusive patent rights on the "patented invention" or drug that is sought to be copied are not entirely abrogated. That is, even if the experimental use exception allows the generic company to undertake certain activities with the patented invention/drug prior to patent expiration without liability for infringement, the generic company will not be able to sell the generic copy until after the patent expires and after it obtains FDA approval for the copy. In the meantime, the owner of the patented drug retains the exclusive right to sell the drug and reap

125. *See supra* notes 76 & 77 and accompanying text.

126. 21 C.F.R. § 201.56 (2003).

127. *Integra Lifesciences I*, 331 F.3d at 866.

128. It should be noted that Judge Newman explained in her dissent that one of the compounds tested by Merck did, in fact, become the subject of an IND application in 1998. *Id.* at 874. Given Judge Rader's reasoning, it is unclear whether he factored this fact into his analysis of Merck's activities.

profits from it while the patent remains in force. This is a much different scenario from how the experimental use exception would impact owners of patented research tools.

If the provision were to allow research entities conducting biomedical research for FDA approval purposes to use the research tools for free and be exempted from a charge of infringement under § 271(e)(1), then the patented research tool provider would not be able to financially benefit from its patent monopoly vis-à-vis these entities.[129] So, in actual fact, the experimental use exception would abrogate the patentee's rights entirely vis-à-vis a patentee's large customer group, namely, biomedical companies in the business of drug development, including the right to sell or license its patented research tool to such companies, as alluded to by Judge Rader.[130] This is rather different from just limiting the right to control one aspect of the patented invention's many possible uses during the patent term, where that use does not generally affect the company's ability to earn revenue from that patented invention's (i.e., the drug's) sales to consumers (i.e., patients). It is true, however, that any other uses of research tools not within the context of research undertaken for FDA approval would still be subject to the full brunt of the patent's force, and would not be exempt from a charge of infringement.[131] Depending on the percentage of potentially exempt versus non-exempt uses as to a patented research tool, a patent's exclusivity could be encroached upon to a greater or lesser degree.

Judge Newman's dissent included a consideration of the common law research exemption, which the majority pointed out was not an issue before the Court.[132] Consequently, Judge Newman's comments, particularly her comment that "today the court disapproves and essentially eliminates the common law research

129. For example, in footnote 4 of the Judge Rader's opinion in the *Integra* case, he refers to a National Institutes of Health (NIH) definition of research tools as "tools that scientists use in the laboratory, including cell lines, monoclonal antibodies, reagents, animal models, growth factors, combinatorial chemistry and DNA libraries, clones and cloning tools (such as PCR), methods, laboratory equipment and machines." *Integra Lifesciences I*, 331 F.3d at 872 n.4 (quoting Sharing Biomedical Research Resources: Principles and Guidelines for Recipients of NIH Research Grants and Contracts, 64 Fed. Reg. 72,090, 72,092 n.1 [Dec. 23, 1999]).

130. *Integra Lifesciences I*, 331 F.3d at 867.

131. *Id.*

132. *Id.* at 864 n.2. While the majority was strictly correct in noting that the common law research exemption issue was not before the Court, Judge Newman explained that the matter was before the District Court but that, at the Federal Circuit's oral hearing for this case, counsel explained that the matter was not being addressed on appeal partially because of a recently decided case, *id.* at 878, which we can assume to have been *Madey* discussed above, *supra* note 40 and accompanying text, and discussed in part II of this article.

exemption"[133] are not entirely appropriate. On the other hand, given our discussion in this paper, her comments are relevant and worth examining.

Judge Newman argues that Merck's drug development activities[134] are embraced either by the common law research exemption or by the statutory exception at § 271(e)(1).[135] More specifically, Judge Newman writes that Merck's initial basic research was shielded by the common law research exemption and Merck's subsequent development activities were shielded by § 271(e)(1).[136]

As to the common law research exemption, Judge Newman contends that:

> The subject matter of patents may be studied in order to understand it, or to improve upon it, or to find a new use for it, or to modify or "design around" it. Were such research subject to prohibition by the patentee the advancement of technology would stop, for the first patentee in the field could bar not only patent-protected competition, but all research that might lead to such competition, as well as barring improvement or challenge or avoidance of patented technology. Today's accelerated technological advance is based in large part on knowledge of the details of patented inventions and how they are made and used. Prohibition of

133. *Integra Lifesciences I*, 331 F.3d at 873.

134. Although the majority never described Merck's relevant research activities involving Integra's patented RGD peptides, Judge Newman included the following helpful description of such activities:

> The record describes modifications in the structure of RGD-containing peptides and investigations of their properties in the Scripps/Merck collaboration, including: receptor binding assays to investigate the efficacy and specificity of structural change; angiogenesis/chick CAM assays for inhibition of blood vessel formation in chick embryos when vessel growth is artificially induced, to study the mechanism of action, pharmacokinetics, and other properties; angio-matrigel experiments to investigate inhibition of artificially induced vascularization in mice; cell adhesion assays by spectrophotometric measurement of inhibition of cell attachment to protein, to provide information about mechanisms, efficacy, and other properties; chemotaxis studies to determine the effect of various peptides on cell migration over extracellular matrix fibers; use of chick embryos to obtain pharmacokinetic data; fluorescent-activated cell sorting to study the effect on the receptor-ligand binding reaction, to aid in understanding mechanisms of activity; vascularization of the retina and induced arthritis of the joints, studied with mice and rabbits; chick CAM assays to study angiogenesis associated with tumor transplantation and growth in chick embryos; and tumor growth in SCID-mice or nude mice, including studies of mechanism, pharmacology, and pharmacokinetics.

*Id.* at 874.

135. *Id.*

136. *Id.* at 878.

> research into such knowledge cannot be squared with the framework of patent law.[137]

Furthermore, Judge Newman states that although she does not intend her decision to set the "boundaries of the research exemption for all purposes and all activities,"[138] she does observe that "there is a generally recognized distinction between 'research' and 'development,' as a matter of scale, creativity, resource allocation, and often the level of scientific/engineering skill needed for the project,"[139] and notes that "this distinction may serve as a useful divider" to decide what might be covered by the exemption.[140] At the end of her discussion about the common law research exemption, Judge Newman finds that:

> [A]n ultimate goal or hope of profit from successful research should not eliminate the exemption. The better rule is to recognize the exemption for research conducted in order to understand or improve upon or modify the patented subject matter, whatever the ultimate goal. That is how the patent system has always worked: the patent is infringed by and bars activity associated with development and commercialization of infringing subject matter, but the research itself is not prohibited, nor is comparison of the patented subject matter with improved technology or with designs whose purpose is to avoid the patent.[141]

Judge Newman's views on the common law research exemption are similar to the broad notions of such an exemption delineated in Janice Mueller's writing discussed earlier.[142] However, Judge Newman adds the additional nuance that the applicability of the research exemption should be dictated by whether an activity can be denoted as a "research" or a "development" activity.[143] In practice, defining the line between these two activities could prove difficult. Consequently, the delineation between coverage of a research exemption based on commercial versus non-commercial activities seems to be a more practical approach. The amount of damages could be used to reflect that the infringing party merely used a patented

137. *Id.* at 875.
138. *Id.* at 876.
139. *Integra Lifesciences I*, 331 F.3d at 876.
140. *Id.*
141. *Id.*
142. *See supra* note 36 and accompanying text.
143. *Integra Lifesciences I*, 331 F.3d at 876.

invention in research, for example, while seeking to develop a better, new product, and thus should not have to pay a high damage award.[144]

After stating her views about the common law experimental use exception, Judge Newman turned to a discussion of her view of the scope of the "safe harbor" (or experimental use exception) in § 271(e)(1). Unlike the majority, she interpreted § 271(e)(1) to be broader than simply applying to the activities of generic companies seeking to develop copycat drugs. In addition, Judge Newman expressed her further dissent from the majority's views on § 271(e)(1) as follows:

> The majority also holds that none of the research by Scripps/Merck qualifies for § 271(e)(1) immunity because the research was directed to "discovery," not to federal registration. I agree that "the § 271(e)(1) safe harbor [does not] reach back down the chain of experimentation to embrace development and identification of new drugs." . . . However, the territory that the Scripps/Merck research traversed, from laboratory experimentation to development of data for submission to the FDA, was either exempt exploratory research, or was immunized by § 271(e)(1). It would be strange to create an intervening kind of limbo, between exploratory research subject to exemption, and the FDA statutory immunity, where the patent is infringed and the activity can be prohibited. That would defeat the purposes of both exemptions; the law does not favor such an illogical outcome.[145]

Judge Newman's argument is convincing, namely that an "intervening limbo" between the coverage of infringement exemptions should not exist.[146] However, it is premised on her view of how broad the common law experimental use exception should be. For reasons noted earlier,[147] her view of this exception may be too broad.

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144. Judge Rader mentioned *de minimis* damage awards for small infringing uses in *Embrex Inc. v. Service Engineering Corp.*, 216 F.3d 1343 (Fed. Cir. 2000), which might be appropriate in such an instance. Interestingly, if we look to the matrix of exempted user activities that should be available in a research exemption, *see supra* part II of this article, Judge Newman's position can be illustrated as additionally exempting activities that are marked in the matrix as C1-D3 and C1-D4, and likely also C1-D2 and C2-D2. Nonetheless, Judge Newman's view appears to be slightly narrower than Professor Mueller's view on the question of what the scope of a research exemption should be, since earlier we found that Professor Mueller's notion of a research exemption would encompass a "yes" in all squares in the matrix. *See supra* notes 37 & 38 and accompanying text.

145. *Integra Lifesciences I*, 331 F.3d at 877.

146. *Id.*

147. *See* discussion accompanying *supra* notes 142 & 143, and discussion in part II of this article, text accompanying *supra* notes 36 & 37.

At the end of her reasons, Judge Newman explained that, in her view, the RGD-containing peptides claimed in the Integra patents were not research tools but rather "new compositions having certain biological properties."[148] In her mind,

> A research tool is a product or method whose purpose is use in the conduct of research, whether the tool is an analytical balance, an assay kit, a laser device (as in *Madey v. Duke University*), or a biochemical method such as the PCR (polymerase chain reaction). It is as subject to the patent right as is any other device or method, whether it is used to conduct research or for any other purpose. Use of an existing tool in one's research is quite different from study of the tool itself.[149]

Thus, Judge Newman's definition of a research tool is what was termed in Part I of this paper as a pure research tool. However, as discussed in Part I, both pure and partial research tools exist and should be considered as we study and attempt to solve the research tools problem. Moreover, Judge Newman's viewpoint that Integra's RGD peptides are not research tools does not coincide with the facts. A likely utility of the RGD peptides was, either in part or entirely, for use in the conduct of research. Consequently, only Judge Rader has recognized the research tool nature of Integra's RGD peptides.

Yet Judge Newman speaks persuasively about the need to have appropriate infringement exemptions in place to support and facilitate research and development activities in our technology-based economy. This is the case even though Judge Newman believes that a broad common law research exemption should exist to protect commercially-driven research activities. This is a broader view than the one advocated in Part II of this paper. However, Judge Newman's comments as to what a research tool might be, and the refusal to see the RGD peptide as a research tool reflect much weaker reasoning. Judge Newman's narrow views of what constitutes a research tool (which are narrower, for example, than the NIH's views) reflect an indifference on Judge Newman's part as to the consequences to patent holders of establishing broad infringement exemptions. As such, her comments provide no guidance as to how to actually strike the right balance in the area of patented research tools between respecting patent rights and providing appropriate research exemptions to properly encourage innovation. Accordingly, what follows in the last

148. *Integra Lifesciences I*, 331 F.3d at 878.

149. *Id.*

section of this paper is a proposal on how to set the various legal levers available in patent law to strike such a balance.

Given the weighty issues addressed in the *Integra* case, it will be interesting to see whether the Federal Circuit will decide to reconsider this case en banc.[150] Although Judge Rader's decision has failed to follow the extremely broad interpretation previously afforded to the exempting coverage of § 271(e)(1), his position is based on a sound policy concern of not entirely abrogating the patent rights of research tool patent holders.[151] In this regard the *Integra* case could be interpreted more broadly to mean that a statute setting forth an exemption to a right cannot be so broadly interpreted that it entirely removes the benefit of that right. At the same time, however, Judge Newman raises equally weighty policy concerns on the opposite side of the spectrum. What is clear from the *Integra* case at this stage is that the Federal Circuit is not currently willing to endorse a broad reading of § 271(e)(1) that would help address the patented research tools problem. Of course, the *Integra* case may not be the end of this line of cases. A different set of facts involving the use of a research tool "higher up the chain" of drug research and closer to the point of an investigational new drug (IND) submission may well lead to a subsequent court decision (even under Judge Rader's analysis in *Integra*) that § 271(e)(1) exempts the use of such a research tool.

One way to prevent the spread of the § 271(e)(1) exemption into exempting the use of research tools might be by legislative amendment. Some guidance on how § 271(e)(1) could be amended can be obtained by looking at German jurisprudence interpreting its experimental use exception, which is called an "experimentation privilege" and is found at section 11 No. 2 of the German Patent Act. The *Klinische Versuche (Clinical Trials) II*[152] decision discusses the

150. *See* comments in *supra* note 101 as to the status and background of this situation.

151. *Integra Lifesciences I*, 331 F.3d at 867.

152. Klinische Versuche (Clinical Trials) II (Case X ZR 68/94), Federal Supreme Court of Germany, BGHZ 135, 217, [1998] R.P.C. 423 *translated in* 1998 WL 1043174 (BGH[Ger]) (1998). In *Clinical Trials II*, the patent in suit claimed erythropoietin as a polypeptide having a defined amino acid sequence obtained by means of genetic engineering. The defendant relied on the German experimentation privilege and conducted clinical trials with samples containing as the active agent a recombinant human erythropoietin extracted from the kidney cells of baby hamsters. The clinical trials were intended to confirm the animal test results, and to supply the necessary data to obtain official pharmaceutical permission to market the product. In particular, the defendant sought to identify the relevant clinical differences in the effectiveness and digestibility between its product and another product on the market. On appeal to the Federal Supreme Court of Germany, the Court concluded that the defendant's activities were protected by the experimentation privilege.

German experimentation privilege. In the course of its reasoning, the Federal Supreme Court of Germany noted the following as regards section 11 No. 2 of the German Patent Act:

> In order to limit the rather wide scope of the concept of experiment, section 11 No. 2 of the Patent Act requires as the scope of the exemption the determining operating fact that the experiment must be related to the object of the patented invention. It follows from this that *the object of the invention must itself be the object of the experimental activities for the purpose of obtaining results.*[153] (Emphasis added).

If the U.S. experimental use exception in § 271(e)(1) were similarly limited so that the object of the patented invention itself had to be the object of the experimental activities, then the provision could not be interpreted in such a way as to cover the use of patented research tools in drug research and development, since the drug candidate submitted to the FDA for approval and not the patented research tool would generally be the object of the experimental activities.

To some, an endorsement from the Federal Circuit in the *Integra* case that § 271(e)(1) shields a biomedical company's use of research tools in the course of research generating data for submission to the FDA would have been a positive development. This would have been particularly the case for smaller biomedical companies who are more heavily financially burdened by the licensing costs that they must pay to use the research tools that are needed in their research and development activities. Larger innovative pharmaceutical companies could also have greatly benefited financially from such a decision even though they may be feeling somewhat less of a financial burden than small biomedical companies from all of the licensing costs on the patented research tools that they use to conduct their research. And the costs of using a patented research tool, such as Integra's RGD peptides is not insubstantial.[154] For example, although the *Integra* case was remanded to the District Court for a reevaluation of the damages issues, the initial damages award against Merck that was established by a jury was $15 million to compensate Integra for its loss of a reasonable royalty![155]

On the other hand, as suggested earlier while examining Judge Rader's decision, such an outcome in the *Integra* case would have been highly problematic for the many biotechnology companies that

153. *Id.* at *431.

154. *Integra Lifesciences I*, 331 F.3d at 871.

155. *Id.*

are mainly or exclusively in the business of developing, manufacturing and selling research tools and thus rely on patent protection to secure their investment and make their existence feasible. By threatening such companies' abilities to enforce their patent rights against commercial research tool patent users conducting FDA-related research, an entire industry sector could be destroyed. This, in turn, could lead to a drought as to new research tool innovations. In the longer run, the lack of new research tool innovations could negatively affect those biomedical companies conducting pharmaceutical research that rely on such new tools to conduct cutting-edge biomedical research. Such companies could be prevented in the future from conducting such research in an efficient manner because they are lacking the necessary research tools. This would slow our progress in exploring new research frontiers, and discovering new drugs.[156]

Consequently, contrary to Eisenberg's and Heller's views that the "upstream" patenting of research tools is necessarily a bad thing because such "upstream" patenting can block subsequent research, a strong argument can be made that the existence of such patent protection may actually encourage further technological development by constantly providing researchers with new and better research tools that can lead researchers to the new frontiers in research. Without patent incentives, there likely would not be any extensive development of new research tools. It would be useful if an empirical study could be conducted to examine whether allowing patenting of research tools actually encourages subsequent innovation because the better quality research tools that are produced allow subsequent research to be undertaken with greater rapidity and accuracy. Two examples of patented high quality research tools are the PCR reaction and microarray technology, both of which have revolutionized biomedical research. Knockout mice also have introduced a useful model by which to study disease and the effectiveness of a drug as a treatment for a particular disease.[157]

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156. "The biotech industry is establishing itself as the discovery arm of the pharmaceutical industry." Jürgen Drews, *Drug Discovery: A Historical Perspective*, 287 SCIENCE 1960, 1960 (2000). *See also* Kelly Longo of Global Strategic Alliances, Pfizer Global Research and Development, Address at the Virginia Biotechnology Summit (Oct. 14, 2003), where the link between these industries also was noted. *See* The 2003 Virginia Biotechnology Summit (Oct. 13–15, 2003), *available at* http://www.vabio.org/2003/summit_schedule_03.htm (last visited Nov. 25, 2003).

157. Knockout mice, in particular, have been shown to have tremendous predictive power in identifying which drugs and drug targets will be successful:

In any event, it is important to keep in context the extent to which § 271(e)(1) could even offer a solution to the research tools problem. In the second part of this paper, we considered a matrix of patented research tool users and the uses for such tools that illustrates in what categories of user and use the policy arguments are in favor of finding a research exemption. This matrix is reproduced below.

| | C1 (private sector) | C2 (public sector) | C3 (individuals) |
|---|---|---|---|
| D1(new product development) | No – exception should not be available | No – exception should not be available | No – exception should not be available |
| D2(design-around development) | No – exception should not be available | No – exception should not be available | No – exception should not be available |
| D3(research on tool itself) | N/A – all activities likely business oriented | Yes – exception should be available | Yes – exception should be available |
| D4(tool in basic research) | N/A – all activities likely business oriented | Yes – exception should be available | Yes – exception should be available |

As noted earlier, this matrix reflects the position that users engaging in new product development or design-around development with the tool (i.e., commercially-driven activities) should not be

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> After a decade of using mouse knockouts, the data on their predictive power in drug discovery is irrefutable. The top 100 selling drugs in 2001 are directed only to 29 drug targets, many with multiple agents addressing the same target. Of these 29 targets, 23 have been knocked out and in every case the knockout mouse was highly predictive as to the on-target effects and side effects of the associated drugs.

Arthur T. Sands, *Industrializing Breakthrough Discovery*, CURRENT DRUG DISCOVERY, Aug. 2002, at 21. Sands indicates that this success will lead to a more efficient and cost-controlled way to discover new drugs:

> Since knockout mice have been shown to model drug activity, they provide an unprecedented level of predictive power over the drug discovery process and can be extremely valuable to the pharmaceutical and biotechnology industries. With the effective use of mouse knockout technology, expensive drug discovery activities such as high-throughput screening, medicinal chemistry, preclinical research and clinical trials can be focused on the drug targets that are most likely to lead to breakthrough therapeutics.

*Id.* at 23.

protected by a research exemption, but non-commercial activities involving research tools should be so protected.

Yet, given such a model for the scope of a research exemption, § 271(e)(1) would not be effective in providing such scope to the exemption, even if the *Integra* case were decided in favor of Merck. The coverage of § 271(e)(1) would only extend to the use of a research tool in drug development (i.e., the C1-D1 box), where the user most likely is from the private sector (since public sector entities do not tend to be in the business of seeking FDA drug approval). Consequently, § 271(e)(1) could address only a small subset of all of the valid uses for research tools that one might think of, namely, one out of twelve such possible uses. Section 271(e)(1) could not, for example, offer a solution in a *Madey*-type problem (assuming it to be in a biomedical context) where a public sector institution wishes to engage in research on the tool itself to understand better how it works or wishes to use the tool to conduct basic research. Therefore, even if Rader found research tool use in the course of FDA-related research to be exempt from patent infringement in *Integra*, under § 271(e)(1), this could not offer a "complete" solution to the research tool problem.

## IV. A PROPOSED SOLUTION FOR ADDRESSING THE PROBLEMS ARISING FROM PATENTS ON BIOMEDICAL RESEARCH TOOLS.

The "anticommons" problem with research tools is a serious science policy issue that warrants attention and a solution that will optimize innovation incentives. This part provides a proposal on how to set the various legal levers available in patent law to achieve such a solution. Optimizing innovation incentives is the key to improving a society's well-being by allowing society to access new and better products, particularly in the biomedical or drug development area.[158] Given the acknowledged importance of patents as innovation incentives for members of the biotechnology industry[159] who are at

158. *See, e.g.*, Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 878 (1990).

159. For example, in an essay by Rebecca Henderson, Luigi Orsenigo, and Gary P. Pisano, it is noted "that the lack of adequate patent protection was a major obstacle to the development of the biotechnology industry in Europe." Rebecca Henderson et al., *The Pharmaceutical Industry and the Revolution in Molecular Biology: Interactions Among Scientific, Institutional, and Organizational Change*, *in* SOURCES OF INDUSTRIAL LEADERSHIP: STUDIES OF SEVEN INDUSTRIES 267, 302 (D.C. Mowery & R.R. Nelson eds., 1999). This is an empirical indication that patents provide important innovation incentives in the biotechnology industry. Moreover:

> In the fields of chemical products and pharmaceuticals, intellectual property rights have tended to be strong since the turn of the 20th century, and this has

the root of biomedical research tool development, any solution that optimizes innovation incentives should respect the rights of research tool patent holders (i.e., research tool providers).[160] This includes making sure that research tool providers are sufficiently compensated for their research and development efforts on research tools, and are able to earn a reasonable amount from the tools that they have created and patented. After all, if we as a society want our biomedical researchers to be able to continue to discover new and better drug products, then such researchers will need new and better research tools to assist them, and someone will need to pay research tool providers for the research and development costs of such tools. However, at the same time, it is important to have in place some kind of a research exemption that will not completely abrogate the rights of research tool providers but will nonetheless allow certain worthy research projects involving research tools to be undertaken without the research tool user having to pay royalties or face the threat of a patent infringement suit. Finally, for those research and development activities that do not end up being covered by a research exemption, it is important to have some way to control the size of royalty payments that are paid out for licences to use research tools such that the financial burden imposed by license fees does not get so oppressive that valuable research and development projects are halted or their progress slowed down.

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> enhanced the ability of firms to capture the returns to their R&D. However, these industries tend to be unusual in the extent to which they depend on intellectual property rights in order to profit from their innovations . . . .

David C. Mowery & Richard R. Nelson, *Explaining Industrial Leadership*, *in* SOURCES OF INDUSTRIAL LEADERSHIP: STUDIES OF SEVEN INDUSTRIES 359, 380 (D.C. Mowery & R.R. Nelson eds., 1999). As well, Merges and Nelson describe the same phenomenon within the chemical industry, a subset of which is the pharmaceutical industry. Merges & Nelson, *supra* note 159, at 897–98. These industries are related to the biotechnology industry.

160. In this paper, the assumption is that the research tool patents that exist are validly issued by the U.S. Patent and Trademark Office. This, of course, is the first line of defense in preventing "anticommons" problems from developing (i.e., preventing upstream patent rights from blocking downstream research and development activities). For example, one of the examples that Eisenberg and Heller turned to when describing their "anticommons" concept were expressed sequence tags (ESTs). The U.S. Patent and Trademark Office (PTO) has taken steps to clarify what type of scrutiny should be afforded to patent claims on gene fragments by adopting both written description guidelines, United States Patent and Trademark Office, *Revised Interim Written Description Guidelines Training Materials & Revised Interim Utility Guidelines Training Materials*, *at* http://www.uspto.gov (last visited Aug. 11, 2003). By granting patents only on those inventions involving gene fragments that are new, useful, non-obvious, and appropriately defined and described, there should be less concern that an "anticommons" of inappropriate patents might get created in an area.

A legislative solution is urgently needed to address situations in which defined users may use patented research tools pursuant to a research exemption. The matrix provides those categories for which such a legislative solution should be available.[161] Essentially, public sector research entities (e.g., universities) and individuals should be protected by such a legislatively-established research exemption when they wish to study a research tool to better understand how it works, and also when using a research tool in the course of basic research. Both pure and partial research tools (as defined in part I) should be covered by this limited exception. A legislatively-established solution should be provided in such circumstances because little money is available amongst the noted user groups to pay for licensing fees, and yet these non-profit research activities should be encouraged. In other words, the situation contemplated in *Madey* (albeit in the biomedical context) should be protected by a research exemption.

This research exemption, however, should not necessarily be so broad as to allow public sector research tool users to be able to get research tools from research tool providers for free. If users wish to have such tools in a ready-made format (as seen, for example, in research tool catalogs available from research tool providers), then such users should still be expected pay a fee for such tools, so long as the price is reasonable. Thus, we need to take into consideration the non-profit status of the user. On the other hand, if the public sector user decides to make the patented research tool on its own for use in its own research activities, then it should not face a patent infringement lawsuit.

The harder question is which, if any, commercially-driven activities using patented research tools should be protected. Prof. Mueller has suggested that a research exemption should be available to even cover commercially-oriented activities where the research entity is trying to develop a design-around of a patented invention (e.g., such as a research tool) or is using a research tool in the course of trying to develop a new product.[162] While such activities are perhaps worthy of being protected by a research exemption, since they are likely to yield another useful commercial product, it seems only fair that the commercial user of the tool pay a reasonable price for using it. This price should not be excessive (i.e., it should be *de minimis*), and it should reflect only the amount of use that the user

161. *See supra* Part II.

162. *See supra* text accompanying note 36.

engaged in to develop the new product or design around. In any event, given the previously-identified competing policy concerns that a broad research exemption might completely destroy the value of research tool patents, it is appropriate to draw the line between exempted and non-exempted activities based on what are commercial and non-commercial activities.

An additional wrinkle in this problem is when a public sector entity, such as a university, ends up acting like a commercial entity, for example, by seeking to enforce biomedical patent rights that it might have, or by partnering with a private sector entity in developing a new commercial product or a commercial design-around to an existing research tool (i.e., thus falling within the C2-D1 and C2-D2 boxes of the research exemption matrix discussed previously). This is by no means an uncommon occurrence ever since the Bayh-Dole Act was passed in 1980:

> As publicly-supported institutions of higher learning, universities have a longstanding mission to foster research and the dissemination of new knowledge. Since 1980, the Bayh-Dole Act has directed universities to take on the further mission of promoting commercial development of the discoveries that they make with federal funds. In furtherance of this new mission, federal law encourages universities to patent their discoveries and to license them to firms in the private sector. Many universities have established technology transfer offices to market the discoveries of their scientists in accordance with the Bayh-Dole Act.[163]

Because of the Bayh-Dole Act, the bright lines between commercial and non-commercial research are blurred.[164] Whereas the Bayh-Dole Act does not make it more likely that a private sector entity (e.g., a company) would be engaged in non-commercial research, it does make it more likely that a public sector entity (e.g., a university) would be engaged in commercial research.

In view of the Bayh-Dole Act, if a university undertakes the use of a research tool in a project with commercial overtones, the legislatively established research exemption should not be available.

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163. National Institutes of Health, *supra* note 12. For more information on the Bayh-Dole Act, 35 U.S.C. § 207(a) (2000), *see* Rebecca S. Eisenberg, *Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research*, 82 VA. L. REV. 1663 (1996). *See also* David C. Mowery, et al., *The Growth of Patenting and Licensing by U.S. Universities: An Assessment of the Effects of the Bayh-Dole Act of 1980* (unpublished manuscript, on file with the author).

164. *See generally* National Institutes of Health, *supra* note 11.

An example of a commercial motive by the university would be if the university used a research tool in the course of research which led to a patent directed to a design-around of the research tool or a new product. It seems only fair that if a university is seeking patent rights and trying to gain revenue from the existence of the patent in a certain subject area, then that university must also be willing to respect research tool patents, and thus pay a reasonable amount for using such patented inventions.[165]

As noted at the beginning of this part, the research tools problem must be addressed by respecting research tool patents and establishing a limited legislative research exemption. Further, it is important to have some way to control the size of royalty payments that are paid out for licenses to use research tools, in the context of those research and development activities that do not end up being covered by such a research exemption. This last feature of a proposed solution to the research tools problem should be done ideally by eliminating reach-through license agreements (RTLAs) and ensuring that the royalties that are otherwise charged by patented research tool providers are not unreasonable.[166]

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165. Richard Nelson presents a proposal of Rochelle Dreyfus for a research exemption in slightly modified form that similarly limits the exemptions' applicability:

> Of the several proposals for a research exemption that have circulated recently, I find one of the most interesting to be that put forth by Rochelle Dreyfuss (2002). In what follows, I amend slightly. Under the proposal a university or non-profit research organization (under one version of her proposal, any research organization) would be immune from prosecution for using patented materials in research if 1) those materials were not available on reasonable terms (this is my amendment), and 2) if the university or other research organization agreed not to patent anything that came out of the research, (or if they did patent to allow use on a nonexclusive royalty free basis—my amendment).

Richard Nelson, *The Market Economy, and the Scientific Commons* (Aug. 11, 2003) RES. POL'Y (manuscript accepted for publication and on file with the author).

166. Interestingly, in her article, Professor Mueller proposes a different approach to solving the research tools problem which relies on the use of reach-through royalty schemes rather than eliminating them. Mueller, *supra* note 36, at 59. In taking this position, she finds support in the writing of John Barton who argues that reach-through royalties are not *per se* improper. *Id.* at 59 n.290. Mueller summarizes her solution in her conclusion as follows:

> A potential solution is a "liability rule" model that permits the non-consensual "development use" of research tools not readily available for licensing or purchase, while providing an ex post royalty payment to the patent owner that would be correlated to the commercial value of the new product developed from the non-consensual use. This "reach-through" royalty approach provides the best approximation of the true worth of the research tool to its user. It ensures a royalty award of sufficient amount to maintain incentives for the development and patenting of new research tools, yet alleviates the access restrictions and up-front costs currently associated with acquisition and use of many proprietary research tools.

The RTLA is problematic because it imposes a tax of unknown magnitude on future biomedical research products such as pharmaceuticals.[167] Consequently, it would be helpful to be able to develop a legal basis upon which to find that RTLAs on research tool patents are unenforceable. One route might be to find that RTLAs constitute patent misuse.

The doctrine of patent misuse arose from the Supreme Court's decision in *Morton Salt Co. v. G.S. Suppiger Co.*,[168] where the Court found that "respondent [was] making use of its patent monopoly to restrain competition in the marketing of unpatented articles, salt tablets, for use with the patented machines, and [was] aiding in the creation of a limited monopoly in the tablets not within that granted by the patent."[169] Accordingly, the Court found that "a patent affords no immunity for a monopoly not within the grant . . . . [A]nd the use of it to suppress competition in the sale of an unpatented article may deprive the patentee of the aid of a court of equity to restrain an alleged infringement by one who is a competitor."[170] Thus, to determine whether an RTLA on a research tool might constitute patent misuse, we must ask whether an RTLA on a patented research tool is a means by which the patent owner of the research tool improperly extends the scope of the patent monopoly on the tool. A clear answer to this question is not available since the existing case law on patent misuse is not right on point.

One place to look for guidance is *Mallinckcrodt, Inc. v. Medipart, Inc.*[171] which examined the doctrine of patent misuse in the context of the doctrine of patent exhaustion, also known as the first sale doctrine. Generally, the patent exhaustion doctrine states that

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*Id.* at 66. However, if one were to adopt Professor Mueller's approach, this would not solve the problem of research tools. While the approach may facilitate immediate access to research tools by biomedical researchers, stacking royalty obligations on the products of the research will still exist, and what is worse, such royalties will have to be paid at an unknown later date and in unknown amounts. An excessive amount of such future payment obligations could quickly discourage a biomedical company's investors from continuing to invest in it even if the drug products that the company was anticipated to develop appeared promising. This, in turn, could lead to abandoned biomedical research projects which would only exacerbate the research tools problem. Moreover, Mueller's approach is akin to a compulsory licensing scheme which is contrary to traditional U.S. patent law principles. *See infra* notes 226–229 and accompanying text.

167. For a discussion of RTLAs, *see supra* notes 26–31 and accompanying text. The notion of a tax is developed *infra*.

168. 314 U.S. 488 (1942).

169. *Id.* at 491.

170. *Id.*

171. 976 F.2d 700 (Fed. Cir. 1992).

"one who buys patented article[s] of manufacture from one authorized to sell them becomes possessed of an absolute property in such articles, unrestricted in time or place."[172] Perhaps a more helpful statement of this doctrine is as follows:

> [A]s between the owner of a patent, on the one side, and a purchaser of an article made under the patent, on the other, the payment of a royalty once, or, what is the same thing, the purchase of the article from one authorized by the patentee to sell it, emancipates such article from any further subjection to the patent throughout the entire life of the patent, even if the latter should be by law subsequently extended beyond the term existing at the time of the sale, and that, in respect of the time of enjoyment, by those decisions the right of the purchaser, his assigns or legal representatives, is clearly established to be entirely free from any further claim of the patentee or any assignee . . . .[173]

This description of the doctrine of patent exhaustion suggests that, if there is a sale for a fee of a patented research tool, then the holder of the research tool patent cannot, for example, seek an additional payment from the purchaser of a final research product that either contains the patented research tool or is manufactured based on information obtained from a research tool. However, what if the patented research tool was not sold outright but rather its use was licensed?

*Mallinckrodt, Inc. v. Medipart, Inc.*[174] may provide some guidance on this point also. This was a patent infringement and inducement to infringe case which related to the use of a patented medical device in violation of a "single use only" notice that accompanied the sale of the device.[175] Medipart argued, based on the doctrine of patent exhaustion, that the "single use only" notice was a restriction that constituted patent misuse since "*no* restriction is enforceable under patent law upon a purchaser of a sold article."[176] In the decision, the Federal Circuit discussed certain early cases dealing with domestic patent exhaustion.[177] In deciding whether or not Mallinckrodt's actions constituted patent misuse, the Court reasoned that "[t]he appropriate criterion is whether Mallinckrodt's restriction is reasonably within the patent grant, or whether the patentee has

172. Keeler v. Standard Folding Bed Co., 157 U.S. 659, 666 (1895).

173. *Id.*

174. *Mallinckrodt*, 976 F.2d at 700.

175. *Id.*

176. *Id.* at 703 (emphasis in original).

177. *Id.* at 704–08.

ventured beyond the patent grant and into behavior having an anticompetitive effect not justifiable under the rule of reason."[178] The Federal Circuit held that restrictions on the sale of a patented item may be acceptable even if it was the first sale since it was a sale with notice of the restriction that the device was for "Single Use Only."[179] Accordingly, "[t]he restriction here at issue [did] not *per se* violate the doctrine of patent misuse or the antitrust law."[180]

The Federal Circuit conveniently summarized its important *Mallinckrodt* holding in *B. Braun Medical, Inc. v. Abbott Laboratories*:

> [In *Mallinckrodt*], we canvassed precedent concerning the legality of restrictions placed upon the post-sale use of patented goods. As a general matter, we explained that an unconditional sale of a patented device exhausts the patentee's right to control the purchaser's use of the device thereafter . . . . The theory behind this rule is that in such a transaction, the patentee has bargained for, and received, an amount equal to the full value of the goods (citations omitted). This exhaustion doctrine, however, does not apply to an expressly conditional sale or license. In such a transaction, it is more reasonable to infer that the parties negotiated a price that reflects only the value of the "use" rights conferred by the patentee. As a result, express conditions accompanying the sale or license of a patented product are generally upheld . . . . Such express conditions, however, are contractual in nature and are subject to antitrust, patent, contract, and any other applicable law, as well as equitable considerations such as patent misuse . . . . Accordingly, conditions that violate some law or equitable consideration are unenforceable. On the other hand, violation of valid conditions entitles the patentee to a remedy for either patent infringement or breach of contract . . . . This, then, is the general framework.
>
> In *Mallinckrodt*, we also outlined the framework for evaluating whether an express condition on the post-sale use of a patented product constitutes patent misuse. The patent misuse doctrine, born from the equitable doctrine of unclean hands, is a method of limiting abuse of patent rights separate from the antitrust laws. The key inquiry under this fact-intensive doctrine is whether, by imposing the condition, the patentee has "impermissibly broadened the 'physical or temporal scope' of the patent grant with

178. *Id.* at 708.

179. *Id.* at 702, 709.

180. *Mallinckrodt*, 976 F.2d at 701.

> anticompetitive effect," (citation omitted).... Two common examples of such impermissible broadening are using a patent which enjoys market power in the relevant market, see 35 U.S.C. § 271(d)(5) (1994), to restrain competition in an unpatented product or employing the patent beyond its 17-year term. In contrast, field of use restrictions ... are generally upheld, (citation omitted), and any anticompetitive effects they may cause are reviewed in accordance with the rule of reason (citation omitted).[181]

The case of RTLAs is not directly analogous to the situation contemplated by *Mallinckrodt* and the patent exhaustion doctrine (also known as the first sale doctrine). *Mallinckrodt* teaches us that it is acceptable to license the use of a research tool for a fee and with express conditions. However, can the license be granted on the condition that a postponed fee will have to be paid based on potential future sales of a research product generated using the tool, rather than only having to pay a fee for the use of the tool *per se*? One might argue that a logical extension of the first sale doctrine is that it is only fair to charge the user of a patented technology a royalty based on the number of times that the user uses the technology, rather than on an extraneous and unknown factor, such as the sales of a downstream research product that results from using the upstream research tool. An exclusive or nonexclusive license on future discoveries as a payment for the use of the research tool would be similarly inappropriate by this analysis. The problem with charging deferred royalties based on the sales of a downstream research product is that the purchasers of the downstream research product become directly saddled with the costs of the research tool since each unit of research product sold likely will be priced with these future royalties in mind. Thus, this cost is akin to a tax on the final research product that the purchaser of the product effectively pays. One of the problems with this analysis is that, arguably, *Mallinckrodt* suggests that the first sale doctrine is not applicable since the user of the research tool had notice of the reach-through royalty scheme. While this may be true, the research tool user likely would not have known the magnitude of the total royalty payment since the downstream research product would not have been created at the time that the RTLA was negotiated.

Another argument that RTLAs constitute patent misuse might stem from an analogy based on *Brulotte v. Thys Co.*,[182] a case in

181. 124 F.3d 1419, 1426 (Fed. Cir. 1997).

182. 379 U.S. 29 (1964). Although the *Brulotte* precedent finding post-expiration royalties to be *per se* unenforceable has recently been challenged by Judge Posner in *Scheiber v. Dolby Laboratories, Inc.*, 293 F.3d 1014 (7th Cir. 2002), *cert. denied*, 537 U.S. 1109 (2003), the

which the Supreme Court considered whether the respondent misused its hop-picking machine patents by extending the term of its patent licenses beyond the expiration dates of the patents. The Court concluded "that the use by a patentee of royalty agreements that project beyond the expiration date of the patent is unlawful *per se*."[183] Speaking for the Court, Justice Douglas reasoned that:

> A patent empowers the owner to exact royalties as high as he can negotiate with the leverage of that monopoly. But to use that leverage to project those royalty payments beyond the life of the patent is analogous to an effort to enlarge the monopoly of the patent by tieing the sale or use of the patented article to the purchase or use of unpatented ones.[184]

A relevant fact underpinning the Court's decision in *Brulotte* was that the licenses in question did not differentiate between royalties to be paid during the pre- and post-patent expiration periods. In *Aronson v. Quick Point Pencil Co.*,[185] the applicant set up a license agreement with the respondent for the keyholders on which the applicant had filed a patent application.[186] The respondent agreed to pay a royalty rate of 5% for the exclusive right to make and sell the keyholders, with the stipulation that if the applicant's patent application was not allowed within five years, the royalty would be reduced to 2.5% for as long as respondent continued to sell the keyholders.[187] The Court held that the royalty agreement here was lawful and enforceable since, unlike *Brulotte*, this was not a situation where a patent monopoly was misused by negotiating with the leverage of that monopoly.[188] The Supreme Court stated: "Here the reduced royalty which is challenged, far from being negotiated 'with the leverage' of a patent, rested on the contingency that no patent would issue within five years."[189]

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Supreme Court of the United States declined to grant certiorari in the *Scheiber* case in order to reconsider its ruling in *Brulotte*. Accordingly, *Brulotte* remains the governing law on the question of post-expiration royalties. For a discussion of this issue, *see* Michael P. Sandonato & Howard D. Shatz, *Will Supreme Court Accept Invitation on Post-Expiration Royalties?*, N.Y.L.J., Dec. 2, 2002, at 4; *and* Daniel L. Reisner & David K. Barr, *High Court Declines to Reassess 'Brulotte,'* N.Y.L.J., Feb. 3, 2003, at 4.

183. Brulotte v. Thys Co., 379 U.S. at 32.

184. *Id.* at 33.

185. 440 U.S. 257 (1979).

186. *Id.* at 259.

187. *Id.* at 260.

188. *Id.* at 265.

189. *Id.*

Based on *Brulotte*, it might be argued that RTLAs unlawfully extend the period during which royalties must be paid beyond the term of the patents as to which user rights are being licensed. Such an extension could occur if the patent to which the RTLA pertains expires before the sales of a downstream research product occur and royalties become due. This might occur in situations where royalties end up being imposed on downstream research products more than twenty years from the date of filing the patent. If the RTLA has the same royalty rates before and after patent expiration, then *Aronson* would not be applicable. However, a court might find that it is not appropriate to analogize to *Brulotte* and *Aronson* if the postponed royalty payments are the only consideration provided by the licensee for the right to use the research tool protected by the RTLA.

None of the patent misuse cases discussed here lead us directly to the conclusion that RTLAs are a form of patent misuse. And yet, since the concept of an RTLA seems to inappropriately expand the monopoly rights on a patented research tool beyond the scope of the patent itself, it seems reasonable to argue that RTLAs can be a form of patent misuse. Ultimately, since patent misuse is a "fact-intensive doctrine,"[190] courts will end up considering each RTLA on a case-by-case basis to determine whether it is fair and equitable.[191]

Even if the patent misuse doctrine fails to provide the basis upon which to find RTLAs unenforceable, a research tool user might argue that a RTLA involving the research tool is unenforceable because the RTLA charges an unreasonable royalty. In fact, this argument also could be made in the context of regular royalty payments on patented research tools that might be excessive. A benchmark case that elucidates various factors that should be considered in evaluating what is a reasonable royalty is *Georgia-Pacific Corp. v. U.S. Plywood-Champion Papers Inc.*[192] The Court in that case contemplated a hypothetical license negotiation framework for determining a reasonable royalty to be imposed on a defendant/patent

190. *See supra* text accompanying note 181.

191. While a case-by-case approach to determining the enforceability of RTLAs might be acceptable for large, private sector research tool users who can afford litigation, it is problematic for smaller research tool users who cannot afford such litigation. For such a smaller research tool user, a legislative solution that deems RTLAs unenforceable may be most helpful.

192. 318 F. Supp. 1116 (S.D. N.Y. 1970). This case has been cited extensively as the case that enumerates the factors to be considered to determine what is a reasonable royalty. *See, e.g.*, SmithKline Diagnostics, Inc. v. Helena Labs. Corp., 926 F.2d 1161, 1168 (Fed. Cir. 1991).

infringer.[193] In this hypothetical negotiation framework, the court indicated that a reasonable royalty is:

> The amount that a licensor (such as the patentee) and a licensee (such as the infringer) would have agreed upon (at the time the infringement began) if both had been reasonably and voluntarily trying to reach an agreement; that is, the amount which a prudent licensee—who desired, as a business proposition, to obtain a license to manufacture and sell a particular article embodying the patented invention—would have been willing to pay as a royalty and *yet be able to make reasonable profit* and which amount would have been acceptable by a prudent patentee who was willing to grant a license.[194] (Emphasis added.)

This framework contemplates that a reasonable royalty is one that the licensee could pay and still be able to make a reasonable profit.[195] Therefore, this test could be applied to scrutinize any type of royalty payment being made on a research tool. However, it is important to consider that a research tool user might need to be able to make a reasonable profit after having used several research tools and paid several such royalties. Additionally, in determining what amounts to a reasonable royalty, the fact that a research tool provider should be able to earn a reasonable profit from the royalties in order to cover the provider's research and development costs also should be factored into this analysis.

Moreover, a strong argument can be made that an RTLA that imposes royalty payment obligations not based on the actual use of a research tool but rather based on the sales of a future product is unreasonable, since there is uncertainty as to the magnitude of the royalty and further uncertainty as to whether the royalty will allow the research tool user to make a reasonable future profit on the sale of the future product. One way to eliminate RTLAs from the biomedical research tool patent domain is by legislative amendment. For example, 35 U.S.C. § 284, which defines what constitutes a reasonable royalty, might be amended to indicate that royalty payments made pursuant to RTLAs are unreasonable.[196]

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193. *Georgia-Pacific Corp.*, 318 F. Supp. at 1121.

194. *Id.* at 1120.

195. *Id.*

196. The relevant portion of 35 U.S.C. § 284 (2000) states: "Upon finding for the claimant the court shall award the claimant damages adequate to compensate for the infringement, but in no event less than a reasonable royalty for the use made of the invention by the infringer, together with interest and costs as fixed by the court."

Yet even if a legislative amendment to the meaning of what constitutes a reasonable royalty is not passed, it should be possible to convince a court to render unenforceable a RTLA granting authorization to use a patented research tool in return for a payment of unknown magnitude based on the sales of an unknown future product that may be developed. Judicial skepticism toward "use" royalties on end products is evident. For example, in *Foster v. American Machine & Foundry Co.*,[197] the patentee, Foster, had a patent directed to a welding improvement, and the defendant manufactured welding machinery that included this improvement.[198] The defendant then sold or leased its welding machinery to mill producers who produced longitudinally welded tubes and pipes.[199] The defendant was found to infringe Foster's patent, and the district court awarded a reasonable royalty "for a license to [the defendant] to continue its manufacture and sale of the equipment and for a license to [the defendant's] customers to use the equipment."[200] However, the patentee felt that it was owed a royalty based on the "extent of use of [the Foster] 'welding system' by the *mill operators* who leased the welding equipment containing the infringing [component] from [defendants]."[201] The Court rejected this notion, finding no "history evidencing willingness by the mill operators to pay a running, or throughput royalty, based on their production, for rights to the welding process."[202] This case is not directly analogous to the one that generally might exist with RTLAs on biomedical research tools, since, in the research tools situation, both the user of the patented research tool in research and the seller of the ultimate product developed with help from the research tool might be one and the same person. In the *Foster* case, the defendant who made the infringing welding machine, and the mill operator who used the machine to make the final product (i.e., welded tubes and pipes) were two separate entities.[203] On the other hand, the *Foster* case indicates reluctance on the part of a court to impose a reasonable royalty based on the sales of a product (i.e., the welded tubes and pipes) developed by using a machine that incorporates the patented product. In the research tool scenario, the final product might be a drug that is

197. 492 F.2d 1317 (2nd Cir. 1974).
198. *Id.* at 1319.
199. *Id.* at 1320.
200. *Id.*
201. *Id.*
202. *Id.* at 1321.
203. *Foster*, 492 F.2d at 1320.

developed as a result of an extensive research protocol that includes the use of the patented research tool.

*Stickle v. Heublein, Inc.*[204] is another case that illustrates the judiciary's skepticism toward "use" royalties on end products, and is more analogous to the situation that exists with RTLAs on biomedical research tools. In that case, the patentee had a number of patents directed to methods and machines for making taco shells, which the defendant used to make taco shells.[205] The district court awarded damages in the amount of $1.485 million based on a "reasonable royalty" of 4.2% on the defendant's sales price for taco shells.[206] The Federal Circuit held that this damage award was clearly erroneous and should have been based on a lump-sum for each machine rather on the defendant's production of tacos.[207] In reaching this conclusion, the Court noted that:

> Since there is no evidence that users in the food industry upon purchase of food processing equipment also expect to pay a use royalty (whether based on a separate method patent or on the right to control use of patented machines), a willing licensor could not have reasonably expected to secure a use royalty from either the maker or user.[208]

Of course, if a user of a patented research tool that was subject to an RTLA sought to rely on the *Stickle* case, a patented research tool provider might argue that the case is distinguishable because there is evidence (for example, the presence of an industry practice) that RTLAs are entered into for the use of biomedical research tools. However, if such an argument were made, challenging evidence could be provided of the general discontent in the industry with such RTLAs, and efforts to resist such RTLAs. For example, as noted earlier, the biomedical research industry was successful in resisting a RTLA on patented PCR technology that Cetus Corporation had tried to impose.[209] Moreover, the NIH Research Tools Guidelines expressly indicate that it is inappropriate for recipients of NIH

204. 716 F.2d 1550 (Fed. Cir. 1983).
205. *Id.* at 1553.
206. *Id.*
207. *Id.* at 1563.
208. *Id.* at 1562.
209. *See* discussion *supra* Part I.

research grants and contracts to enter into RTLAs when they seek licenses to use biomedical research tools.[210]

If we could eradicate reach-through licence agreements from the research tools landscape, then a major cause of the "anticommons" in the biotechnological research tools industry would be eliminated. However, as Heller and Eisenberg noted, "too many concurrent fragments of intellectual property rights in potential future products" can also create an anticommons in this area.[211] While Heller and Eisenberg mentioned patent applications on expressed sequence tags (ESTs) as an example of this problem (which we considered earlier in this section),[212] any large bundle of research tools for which licenses might be required to be obtained to conduct biomedical research could also lead to the same problem. Consequently, even if RTLAs were eliminated, the biomedical research community may still carry a substantial licensing "tax" on its future research and development endeavors. It would be helpful if there were some way in which a biomedical research entity could amass the necessary research tools licenses at a lesser cost to be able to pursue a desired course of research.

A solution to the problem would be to create a patent pool that might encompass the necessary patents to conduct biomedical research and could be licensed to a research entity. Carl Shapiro examines how these business arrangements might operate—mostly in the computer software and electronics industries—to dissolve the "anticommons" in those areas.[213] However, creating business arrangements of this kind that do not run afoul of the antitrust laws is not easy. Patent pools are acceptable, from an antitrust perspective, if "blocking" or "essential" patents are placed in the pool but unacceptable if "substitute" or "rival" patents are in the pool.[214] "Blocking" is described as follows in the "Antitrust Guidelines for the Licensing of Intellectual Property:"

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210. Principles and Guidelines for Recipients of NIH Research and Grants on Obtaining and Disseminating Biomedical Research Resources: Final Notice, 64 Fed. Reg. 72,090, 72,094 (Dec. 23, 1999).

211. Heller & Eisenberg, *supra* note 21, at 700.

212. *See supra* notes 24, 159 and accompanying text.

213. Carl Shapiro, *Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard-Setting* (Mar. 2001) (unpublished manuscript, on file with University of California, Berkeley), *available at* http://repositories.cdlib.org/iber/cpc/CPC00-011. Shapiro speaks of a "patent thicket" to describe the "anticommons" problem.

214. *Id.* at 17.

> Sometimes the use of one item of intellectual property requires access to another. An item of intellectual property "blocks" another when the second cannot be practiced without using the first. For example, an improvement on a patented machine can be blocked by the patent on the machine. Licensing may promote the coordinated development of technologies that are in a blocking relationship.[215]

These Guidelines also make the following comment on pooling arrangements:

> Pooling arrangements generally need not be open to all who would like to join. However, exclusion from cross-licensing and pooling arrangements among parties that collectively possess market power may, under some circumstances, harm competition .... In general, exclusion from a pooling or cross-licensing arrangement among competing technologies is unlikely to have anticompetitive effects unless (1) excluded firms cannot effectively compete in the relevant market for the good incorporating the licensed technologies and (2) the pool participants collectively possess market power in the relevant market. If these circumstances exist, the Agencies will evaluate whether the arrangement's limitations on participation are reasonably related to the efficient development and exploitation of the pooled technologies and will assess the net effect of those limitations in the relevant market ....
>
> Another possible anticompetitive effect of pooling arrangements may occur if the arrangement deters or discourages participants from engaging in research and development, thus retarding innovation. For example, a pooling arrangement that requires members to grant licenses to each other for current and future technology at minimal cost may reduce the incentives of its members to engage in research and development because members of the pool have to share their successful research and development and each of the members can free ride on the accomplishments of other pool members .... However, such an arrangement can have procompetitive benefits, for example, by exploiting economies of scale and integrating complementary capabilities of the pool members, (including the clearing of blocking positions), and is likely to cause competitive problems only when the arrangement includes a large fraction of the potential research and development in an innovation market.[216]

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215. U.S. Dept. of Justice & U.S. Fed. Trade Comm'n, *Antitrust Guidelines for the Licensing of Intellectual Property* § 2.3 (Apr. 6, 1995), *available at* http://www.usdoj.gov/atr/public/guidelines/ipguide.htm.

216. *Id.* § 5.5, at 28–29.

Consequently, if the biomedical community were able to organize a number of blocking research tool patents into a patent pool which could be freely licensed to any interested research entity, then this may be an approach for overcoming the research tools problem that also would be acceptable to the antitrust authorities. Such a patent pool could be organized through a trade organization. Of course, the challenge would be to identify blocking research tool patents and get the owners of such patents to agree to license them in a pool. Perhaps if other options for commercializing their inventions were blocked because they were found to be unlawful (e.g., if RTLAs were found to constitute patent misuse), then this would fuel sufficient interest among research tool patent holders to come together and create a patent pool.

However, Heller and Eisenberg have suggested in their article that "a patent anticommons could prove more intractable in biomedical research than in other settings"[217] because cooperation, for example in the form of a patent pool, among members of the research tools industry may be difficult. They argue that this may be the case "[b]ecause patents matter more to the pharmaceutical and biotechnology industries than to other industries."[218] While it may be true that each individual pharmaceutical or biotechnology patent is more valuable, generally speaking, than individual patents in other industries, no doubt a combination of patents, for example in the computer software or electronics industries, also could be valuable.[219] Nonetheless, members in such industries have successfully created patent pools encompassing such patents.[220] It also is worth noting that the pooling of intellectual property rights is very common in the copyright area, where this is done, for example, with the rights of copyright owners to written works or music.[221] Such arrangements

217. Heller & Eisenberg, *supra* note 21, at 700.

218. *Id.*

219. This is certainly the case, for example, with the commercially important laser patents. *See* Karl Jorda, *The Thirty-Year Laser Patent War*, 43 IDEA 545, 545 (2003).

220. *See, e.g.* Shaprio, *supra* note 213, at 17–18. For example, Shapiro mentions the Department of Justice-approved patent pool on MPEG-2 video compression technology which encompasses patents from Fujitsu, General Instrument, Lucent, Matsushita, Philips, Scientific-Atlantis, Sony and Columbia University. *Id.* Another approved patent pool that Shapiro mentions is the patent pool covering digital versatile disk (i.e., DVD) technology that encompasses patents of Philips, Sony and Pioneer. *Id.* Apparently, Philips, Sony and Pioneer jointly license their patents that are necessary to make discs and players that comply with the DVD-Video and DVD-ROM standards. *Id.*

221. The American Society of Composers, Authors and Publishers (ASCAP) and Broadcast Music Incorporate (BMI) are two collective rights organizations that fulfill this role. For more information on these organizations, *see* Robert P. Merges, *Contracting into Liability*

can provide guidance as to how to efficiently administer and enforce a patent pool of research tool patents.[222] Thus, it should not be taken as a foregone conclusion that an anticommons in the biomedical research tools area will prove intractable as Heller and Eisenberg suggest.

If a particular patented research tool were of central importance to the biomedical industry but was being licensed at an exorbitant royalty rate or by way of a RTLA, or not at all, one way that such a research tool might be made accessible at a reasonable price to those seeking to use it in subsequent innovation efforts would be by a government patent buyout mechanism. For example, the patents for PCR technology would be attractive selections for a government buyout because PCR technology is of central importance to the biomedical community. Another such technology is the knockout mouse.[223] Michael Kremer describes his notion of a government patent buyout as follows:

> Under the mechanism, the market value of patents would be determined through a sealed-bid second-price auction, and the government would then offer to buy patents at this private value times some constant markup which would reflect the typical ratio of social to private value. Most of the patents that the government bought would be placed in the public domain. However, in order to give auction participants an incentive to reveal their true valuations, a small proportion of patents, chosen randomly, would be sold to the high bidder. Patent holders would have the right to accept or reject the government's offer.[224]

Once the government obtained control of the patent, the invention could be made widely available at a reasonable price. The National Institutes of Health (NIH) or a different governmental/public entity might be charged with the task of getting the invention into the public forum. Establishing such a patent buyout mechanism likely will entail some costs. However, these costs may well be worth incurring to forego the costs that may be associated with RTLAs, including the royalty costs as well as opportunity costs of research and development projects that did not proceed due to the inability to

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*Rules: Intellectual Property Rights and Collective Rights Organizations*, 84 CAL. L. REV. 1293, 1328 (1996).

222. *Id.*

223. *See supra* note 157 for more information regarding the importance of knockout mice to current and future drug discovery methodologies.

224. Michael Kremer, *Patent Buyouts: A Mechanism for Encouraging Innovation*, 113 Q.J. ECON. 1137, 1146 (1998).

pay such royalties. If a patent buyout mechanism were used to solve the research tools problem, it would be important that any non-government "high bidder" that obtains the patent be obligated to make the patented research tool available to the public on reasonable terms prior to the auction taking place. A neutral trade organization or the auction participants themselves might be called upon to define what constitutes "reasonable terms" for the licensing of a patented technology. The rule, however, would be that the royalty rate would have to be lower than what the patentee offers, perhaps in return for a tax break, and the non-government "high bidder" that obtains the patent would not be allowed to enter into any RTLAs involving the patented research tool.

The multi-faceted solution discussed here stems from the user/provider model of patented biomedical research tool activity that was introduced in Part I of this paper. However, the focus of that model to date has been on parts C and D of the model, namely the users of research tools and their potential uses of those tools. Underlying this focus is an assumption that we are dealing generally with research tool providers denoted in the B.2 category, namely those that seek to license and make money directly from their research tools, since these are the providers that would be willing to provide research tools to users. However, those research tool providers that refuse to license their research tools because they see this position as being advantageous (i.e., in the B.1 category) should also be considered. As to this second group of providers, and the research tools that they have developed, those users whose research with research tools ends up being protected by a research exemption, as proposed in Part IV of this article, would be able to make and use such research tools freely for the limited purposes described. However, other research tool users who might wish to use such research tools would have little recourse under existing U.S. patent law which does not have a doctrine of compulsory licensing that might require the providers to license their patented research tools.

While this may seem unfair, two things should be noted. First, the user who wishes to use such a tool could create a design-around and use a different and perhaps better tool in his or her own subsequent research. As discussed previously,[225] such a use of the patented research tool to create the design-around would amount to an infringement; however, a court should only impose minimal damages on the user given the circumstances. Moreover, once having

225. *See, e.g.*, Judge Rader's comments to this effect, *supra* note 52.

developed a design-around, the user may then have greater leverage to negotiate a license, (e.g., in the form of a cross-license) to allow use of the provider's patented research tool. Second, the user will eventually be able to use the invention once the patent on the research tool expires. In some ways, this may be a better situation than the user would have been in had the provider decided to maintain the research tool invention as a trade secret, since such a monopoly on an idea is not limited in time so long as it is kept secret. (On the other hand, in the trade secret scenario, a user who independently develops the research tool would be able to use it freely, unlike in the patent scenario.)

Ultimately, from a society's perspective, if there is truly a situation where a provider does not wish to license a research tool, it is likely because the provider is anticipating developing a better invention with the tool (e.g., a new drug or a better research tool) that the provider does intend to share with society by selling or licensing it. The provider may have calculated that maintaining exclusivity over the tool is critical to providing sufficient incentives to move ahead with research as to the better invention. Consequently, society will benefit from the tool's existence, albeit indirectly. Moreover, if such an invention is not forthcoming, simple economic thinking suggests that a profit-maximizing actor (as all research tool providers might be expected to be) would be willing to license their patented research tool if there was a demand for the tool. This then would bring the originally "refusing" research tool provider back into the fold of the mainstream analysis in this article.

An outstanding consideration, however, is whether U.S. patent law should be amended to require compulsory licensing of biomedical research tools to resolve the situation discussed in which a research tool provider refuses to license his tools or only at an exorbitant price. The argument in favor of imposing a compulsory licensing scheme on biomedical research tool inventions is that society will benefit more from the patented biomedical research tool if it were licensed to numerous users who might all then use it in their research and compete in the search for a drug. For example, Mueller proposes what is essentially a compulsory licensing scheme, i.e., a "liability rule" model that would permit the non-consensual 'development use' of patented research tools that are not readily available for licensing or purchase, while providing an ex post royalty payment to the owner of the patented research tool of sufficient amount to maintain adequate

incentive for innovation in new tools."[226] Such a system, Mueller suggests, would be particularly helpful "where significant transaction costs are associated with accessing the patented research tools necessary to develop downstream application products such as new drugs, therapies, and diagnostics."[227] A quantitative analysis would be beneficial to evaluate the extent to which "refusing research tool providers" exist, and to evaluate whether compulsory licensing actually fosters greater innovation."[228] Robert Merges, for example, has engaged in an analysis that "counsels against compulsory licensing as a way to reduce transaction costs" and advocates "that privately established Collective Rights Organizations (e.g., patent pools as mentioned in this article) will often emerge to break the transactional bottleneck."[229] Ultimately, any compulsory licensing scheme should be adopted with caution since the notion of compulsory licensing runs counter to traditional principles underlying U.S. patent law, and may end up having a negative effect on the licensing of biomedical research tool patents in the long run and the future development of such tools.[230]

## V. CONCLUSION

In this paper, we first developed an understanding of what a research tool might be. To better conceptualize the research tools problem and propose a solution for it, we developed a simple model of patented research tool activity. Second, we examined the research tools problem, namely, that patenting of research tools may be creating an "anticommons" that may be hindering subsequent innovation because undertaking such innovation is too costly. In this context, we traced the demise of the common law experimental use exception to understand the negative impact of these developments on the research tools problem. Third, we considered how the experimental use exception found at 35 U.S.C. § 271(e)(1), on its face, might shield from infringement a researcher's use of a patented research tool during a course of research undertaken to produce a pharmaceutical end product that will require FDA approval.

226. Mueller, *supra* note 36, at 54–55.

227. *Id.* at 9.

228. Merges, *supra* note 221, at 1295.

229. *Id.*

230. For more information on compulsory licensing generally, *see* M.J. ADELMAN ET AL., CASES AND MATERIALS ON PATENT LAW 1235–36 (1998); ROBERT PATRICK MERGES, PATENT LAW AND POLICY: CASES AND MATERIALS 993 (2d ed. 1992). *See also* Merges, *supra* note 221, at 1296–97.

Additionally, we discussed the *Merck* case, in which the Federal Circuit decided that § 271(e)(1) did not extend this far.

Although many players in the biomedical community would welcome the ability to use research tools for free in the course of research under some form of infringement exemption, research tool manufacturers might suffer a potentially fatal blow if such exemptions became too widespread, irrespective of whether the exemption were to be pursuant to § 271(e)(1) or otherwise. Moreover, a weakened research tool manufacturing industry could have a long-term negative impact on future biomedical innovation since the stream of improved research tools may cease. This is because improved research tools are often what allow biomedical researchers to learn more about biological systems and thus push the innovation frontier outward.

In the last section, this paper proposes a compromising, innovation-optimizing solution to the research tools problem. This solution includes a limited research exemption for public sector (e.g., university), non-commercial research in which a researcher engages in research with a tool or seeks to better understand how the tool itself works. Beyond this, since RTLAs can create a potentially large financial burden of unknown magnitude on downstream research products, it would be best to eliminate RTLAs from the research tools landscape, either by legislative amendment or by finding a legal doctrine by which RTLAs might be found to be unenforceable. For example, one might argue that RTLAs lead to unreasonable royalties. The patent misuse doctrine might also be relied upon in this instance. Principles of what constitutes a reasonable royalty also should be kept in mind to keep non-RTLA-type royalties under control as well. Finally, to reduce the costs of using needed research tools in biomedical research, we consider the possibilities by which the biomedical industry might organize itself to create patent pools that contain some of the essential research tool patents for licensing to research entities. If a handful of patents is particularly crucial to future biomedical research, the government might be able to purchase such patents in a patent buyout auction and make the patents available to research entities under reasonable terms. All of these steps should be taken before resorting to a compulsory licensing scheme to render patented research tools, that are hard to access due to high transaction costs associated with such access or due to a provider's unwillingness to license, more accessible. Compulsory licensing schemes are contrary to transactional principles underlying U.S. patent law and may provide less effective outcomes in the long run. Of course, the

first line of defense against creating an anticommons caused by a proliferation of research tool patents is to ensure that the PTO is granting valid patents on research tools only after carefully scrutinizing the claims sought to be patented.