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GOVERNMENT FUNDED INVENTIONS: THE BAYH-DOLE ACT AND THE HOPKINS V. CELLPRO MARCH-IN RIGHTS CONTROVERSY

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Table of Contents

I. Introduction

Before 1981, neither scientists nor universities owned the rights to any inventions created with the aid of federal money. This position reflected the belief, widely held by scientists from all disciplines, that publicly funded research belongs to the public. Federal policy echoed the belief that research must be publicized, rather ***212** than be kept secret until its commercial import is realized.[1] Therefore, government funded inventions were federally owned and rarely patented.

A generally hostile attitude toward the United States patent system also contributed to this state of affairs. The courts and many commentators were biased against granting a "monopoly" to a patent owner. Patents were considered to be a necessary evil that must be kept under tight control to prevent dangerous monopolies from stifling competition and hurting the American public.[2]

However, in 1982, with the creation of a special court[3] to handle patent appeals from the district courts, there came an increased judicial tolerance and respect for the patent system.[4] Moreover, some commentators hypothesized that the commercialization of certain technologies would never occur without the benefits of patent protection.[5] Further, no savvy company wanted to risk a large investment without some period of market protection to recoup its development costs.[6] Consequently, the public was deprived of the benefits of much potential research, especially biomedical research that can be very expensive to commercialize.[7]

***213** Over time these views evolved into a new belief: allowing private ownership of patents for inventions resulting from government sponsored research may benefit the public by stimulating the commercial development of important inventions. Congress recognized that many new discoveries are made in universities and federal laboratories but that commercial development of these innovations generally requires the action of business and labor.[8] With this awareness, Congress declared a policy of increasing cooperation between academia, federal laboratories, industry, and labor.[9] Ultimately, scientists began to realize that cooperation with commercial interests might prove beneficial, particularly as government funding dwindled.

This article explores policies and procedures of the Bayh-Dole University and Small Business Patent Procedures Act ("the Act" or "the Bayh-Dole Act"),[10] which allows for private ownership of inventions funded by the taxpayer. Government funding, while an important source of funding for research, is not without certain strings. Among some of the restrictions of the Bayh-Dole Act are march-in rights, a type of compulsory licensing; a requirement for substantial manufacture in the United States; and certain restrictions on the use of royalties. The controversy in *Hopkins v. CellPro* provided the circumstances for the first attempt, and failure, to employ the compulsory license provisions of the Bayh-Dole Act.

II. The Bayh-Dole University and Small Business Patent Procedures Act

This new attitude in Congress led to a legislative change in 1981 with the passing of the Bayh-Dole Act. The general purpose of the Act is to increase American innovation, and the specific objectives include encouraging the participation of small business firms and promoting the public availability of inventions, yet ensuring that the government obtains sufficient rights in federally supported inventions to meet the needs of the government and the public.[11]

*214 A. Applicability of the Act

In keeping with its stated objectives, the Act provides that inventors who receive federal funding may elect to retain rights in the invention. Although originally only inventors employed at small business firms and nonprofit organizations were subject to the Act,[12] in 1987 the coverage was expanded to include businesses of any size.[13] Today the Act benefits virtually everyone receiving federal funding for research.

The Act applies to "subject inventions," which are inventions "conceived or reduced to practice in the performance of work under a funding agreement."[14] Further, funding agreements must contain a number of provisions to effect certain requirements of the Act,[15] one of which is that any patent application must state that "the invention was made with government support and that the government has certain rights in the invention."[16]

The Act does not apply to closely related activities that fall outside the planned and committed activities of the government-funded project, as long as those activities do not detract from the performance of the funded activities. For example, an industry-sponsored application of basic, government funded research, would not be covered by the Act.[17] In

addition, the use of instruments purchased with government funds, a common occurrence in university laboratories, is not fatal to an inventor's ***215** claim of private ownership.[18] Finally, since 1982 the Act has specifically excluded scholarships, fellowships, training grants, and other funding given primarily for educational purposes.[19] Even with these exceptions, however, much biomedical research is covered by the Bayh-Dole Act because this research is largely supported by government funds.[20] This fact has profound implications for patent rights and licensing policies as demonstrated below.

B. Procedural Requirements of the Act

Funding agreements must contain provisions to effectuate certain requirements of the Act.[21] Researchers covered by the Act are called "contractors,"[22] and they must fulfill several requirements to comply with the law and retain property rights. After a contractor discloses the invention to administrative personnel responsible for patent matters, the contractor must also disclose the invention to the federal government within a reasonable period of time.[23] If the contractor fails to notify the federal government, title to the invention "may" pass to the government,[24] although the government rarely claims title.[25]

The contractor must also make a written election within two years after disclosure to the federal government, if the contractor wants to retain title to a subject invention.[26] However, if an event triggers a statutory bar period, the period for making this election will be shortened to not more than sixty days prior to the statutory bar date.[27] Further, the contractor must agree to file a patent application prior to any ***216** statutory bar dates,[28] and the application must include the statement that "the invention was made with government support and that the government has certain rights in the invention."[29]

Another implication for government sponsored research is that grant proposals for the research could be considered prior art. Under the Freedom of Information Act (FOIA),[30] the National Science Foundation (NSF) makes all government records, including awarded grant proposals, available to the public on request. This issue was addressed in *E.I. du Pont de Nemours & Co. v. Cetus Corp.*[31]

In *E.I. du Pont,* the plaintiff du Pont asserted a NSF grant proposal as prior art, seeking a declaration of invalidity of two patents owned by Cetus encompassing the process of polymerase chain reaction.[32] Cetus argued that this grant proposal was not sufficiently accessible to the interested public to constitute a "printed publication" under 35 U.S.C. § 102(b); Cetus contended that the grant proposal was not adequately stored and indexed and that the proposal had a vague title.[33] The court rejected this argument, noting that the submitter of the grant proposal was a preeminent researcher in the field of the invention, thereby alerting anyone interested in the field to publications under his name.[34] This researcher had also cited his NSF grant proposal in an article in *The Journal of Biological Chemistry.*[35] Thus, the court concluded that the grant proposal was accessible to the relevant public and constituted prior art within the meaning of section 102(b).[36]

Given the possibility of a grant proposal surfacing as damaging prior art, inventors must take precautionary steps to protect potentially important research. For example, researchers may designate grant proposals as relating to trade secrets or other ***217** confidential information,[37] thus preventing the disclosure of these portions of the proposal to the public without prior notice.[38] However, these designations must be made in good faith by appropriately marking the proposal, either at the time of submission or within a reasonable time thereafter.[39] As a result, researchers must be aware of and act on their aspirations of invention before such inventions are actually realized.

Although a contractor may elect to retain title in the invention,[40] the funding agency by law retains a nonexclusive, nontransferable, irrevocable, paid-up, worldwide license.[41] Thus, the government retains the right to use any invention it funds. In addition, the funding agreement itself may provide for additional federal rights.[42]

The Act also provides for "march-in rights,"[43] whereby the federal government can require the contractor to grant reasonable licenses to third parties under a specific set of circumstances. For example, when the patentee fails to take effective steps in a reasonable amount of time to achieve practical application of the invention, or the action is necessary for public health and safety reasons, or is required by public use ***218** regulations,[44] the federal government can require a contractor to grant a license or can even grant a license itself.[45]

In addition to march-in or compulsory licensing provisions, the Act requires that products that are produced by the use of the invention must be substantially manufactured in the United States.[46] The purpose of the U.S. manufacture and march-in provisions is to ensure that the American public and industry benefit from government-sponsored research.

The Act imposes additional requirements on nonprofit organizations. For example, any future assignment of patent rights must be approved by the funding agency, and a portion of any royalty fees must be paid to the inventor,[47] with the balance being used for scientific research or education.[48] Further, unless it is not feasible, licenses must be granted to small business firms.[49]

The Act also has exceptions that constrain the contractor's property rights. For research involving Department of Energy operations, national security, or foreign contractors, the federal government may restrict a contractor's right to retain title in the invention.[50] Election of title may also be restricted under "exceptional circumstances," where the restriction promotes the policies of the Act.[51] Examples of exceptional circumstances would be where the patentee's licensing policy is unreasonable or the patentee fails to utilize the invention.[52]

C. March-in Rights

One important policy consideration supporting the Bayh-Dole Act is the balancing of public versus private benefit.[53] Because inventions subject to the Act are made with public tax dollars, it is important to accommodate the public interest in these inventions. Thus, the Act provides for public interest measures such as substantial manufacture of patented inventions in the United States, preferences for ***219** small business firms, and compulsory licensing when necessary to protect the public welfare.[54] One mechanism for evaluating the success of the Bayh-Dole Act is to examine how successful the compulsory licensing or "march-in rights" have been in protecting the public welfare.

An opportunity to employ the march-in provisions under the Act occurred recently in *Johns Hopkins University v. CellPro.*[55] The *Hopkins v. CellPro* story is long and complicated, but can be summarized as follows. Scientists from Johns Hopkins University (Hopkins) invented a technology useful in the treatment of cancer. A second company, CellPro, began marketing a competing technology. Hopkins sued CellPro for patent infringement, and CellPro responded by applying to the federal government for a compulsory license to Hopkins' invention.

CellPro argued that it should be granted a compulsory license for three reasons: 1) the license terms offered by Hopkins were unreasonable; 2) contrary to the requirements of the Act, Hopkins failed to give preference to small businesses and instead licensed the invention to a large pharmaceutical company; and 3) CellPro had the only FDA-approved technology on the market. Therefore, if CellPro were enjoined from further manufacture, sale, or use of its technology, cancer patients using the technology would be deprived of its benefits. This harm to the public welfare could be prevented only if CellPro were granted a compulsory license on reasonable terms.

This capsule description of the CellPro march-in controversy inadequately elucidates the application of CellPro's arguments to the Bayh-Dole Act. Thus, the following sections discuss the technologies in question, the extensive litigation between the parties, the march-in petition itself, and the results of CellPro's petition. An additional section will describe the ultimate results of the six-year litigation and provide editorial comment about the positions of each party.

III. *Hopkins v. CellPro*

A. The Technology

The technology in *Hopkins v. CellPro* involved the discovery of antibodies specific for bone marrow stem cells (BMSC). BMSC are pluripotent cells[56] that can grow and differentiate into blood cells, including red blood cells, white blood cells, ***220** and a variety of specialized immune cells.[57] The discovery of antibodies specific for BMSC allows these rare cells to be purified from the other cells in the bone marrow.[58] Therefore, this technology makes it possible to purify a patient's BMSC, irradiate the patient to kill most of the patient's bone marrow and blood cells, including cancerous cells therein, and then replace the original stem cells with the purified BMSC, which repopulate the bone marrow and blood with healthy cells.[59]

Dr. Civens at Hopkins originally discovered a single antigen[60]--CD34 (or My10)--that is specifically expressed by BMSC.[61] Thus, when an antibody that specifically binds to CD34 is attached to a solid surface and cells are passed over the surface, BMSC bind to the antibody, which purifies these cells from all other cell types found in bone marrow. CellPro scientists discovered a different antibody that also binds to the CD34 antigen, which they called 12.8.[62] However, unlike the Hopkins' antibody, the 12.8 antibody binds to both biotin[63] and monkey stem cells.[64] These significant differences allowed CellPro to

quickly obtain FDA approval for a 12.8 antibody-based stem cell separator because the antibody binds to biotin, enabling CellPro to develop a device that could be tested on monkeys.[65] CellPro received FDA approval to market a stem cell purifying device called ""Ceprate SC" in December of 1996.[66]

***221 B. The Litigation**

Hopkins owns a series of four patents, called the Civens patents, pertaining to CD34 antibodies and their use.[67] Hopkins licensed these patents to Becton Dickinson (Becton), which then licensed certain aspects of the patents to Baxter Healthcare (Baxter). CellPro was aware of these patents and although it obtained non-infringement and invalidity opinions on these patents, CellPro was still concerned about possible infringement litigation.[68] Therefore, CellPro filed suit in the U.S. District Court for the Western District of Washington in April 1992 against Baxter and Becton, seeking a declaratory judgment of invalidity and non-infringement of three of the Civins patents.[69] In September 1993, the court dismissed CellPro's action on the ground that Hopkins was an indispensable party beyond the court's jurisdiction.

In March of 1994 Hopkins sued CellPro for willful infringement of the '204 patent, which claims monoclonal antibodies that bind the CD34 antigen on immature human bone marrow cells.[70] CellPro denied any infringement and counterclaimed for a declaratory judgment that all Civins patents were invalid, unenforceable, and not infringed. Hopkins denied invalidity and unenforceability of the patents in its answer and alleged that CellPro was infringing, contributorily infringing, and inducing infringement of all four Civens patents.[71]

The case was tried to a jury, which decided all issues in favor of CellPro. The jury held that all claims of the patents were invalid as obvious in view of the prior art and that most claims were invalid as not enabled.[72] Further, the jury found that CellPro was not liable for direct or contributory infringement, nor guilty of inducement.[73] In response to the jury decision, Hopkins moved for a judgment as a matter of law or alternatively for a new trial.[74] In reconsidering the case, the court decided that its initial construction of claim 1[75] of the '204 patent was flawed.[76] Although a thorough discussion of claim construction is outside the scope of this article, the court reinterpreted the claim as ***222** having a considerably broader scope, consequently trapping CellPro's Ceprate SC and 12.8 antibody in its net.[77]

CellPro then petitioned the Federal Circuit for a writ of mandamus requesting the court to direct the district court to vacate its order for a new trial and enter judgment based on the jury verdict.[78] However, the Federal Circuit denied CellPro's petition.[79] The district court subsequently granted judgment as a matter of law for Hopkins on the infringement of certain claims and a new trial on others, turning a complete CellPro victory in front of the jury into a total loss before the judge.[80] The court also prevented CellPro from introducing additional evidence pertaining to patent invalidity--evidence arguably required by the reinterpretation of the claims-- because the evidence had not been introduced during the first trial.[81]

Thereafter, a new jury found that CellPro had willfully infringed the Civens patents. The court trebled the damages because of the willful infringement, awarding Hopkins almost seven million dollars.[82] Further, the court ordered CellPro to repatriate cells that had been created before the patents issued and had been shipped to Canada after the patents issued.[83]

***223 C. CellPro March-in Petition**

Eight days before the second jury's verdict, CellPro petitioned the Secretary of the Department of Health and Human Services (DHHS) on March 3, 1997 to exercise "march-in" rights on behalf of CellPro and the public.[84] The petition was signed by former White House counsel Lloyd N. Cutler and former Senator Birch Bayh of Indiana, cosponsor of the Bayh-Dole Act. In the petition, CellPro argued that Hopkins, or its licensee Baxter, had "not taken … effective steps to achieve practical application of the subject invention."[85] CellPro repeatedly claimed that Baxter "sat on the sidelines" while CellPro developed the technology.[86] In fact, Baxter had not filed for PMA for its system until the week before trial--thirteen years after filing the patent application.[87] CellPro stated that it believed that Baxter and Becton had effectively abandoned the My-10 antibody and that Baxter might never gain FDA approval for its new antibody.[88] In contrast, CellPro's Ceprate SC system had already been approved by the FDA in December of 1996.[89]

CellPro emphasized that Ceprate SC was already used in over 200 medical facilities in the world[90] for the treatment of breast cancer, lymphoma, multiple myeloma, leukemia, and various other diseases.[91] Therefore, CellPro argued that removal of the system from the market "threatens a life-saving treatment option for thousands of children and adults … who will die unless

the … research is allowed to continue."[92] As a result, "action [is] necessary to alleviate health … needs."[93]

In addition, CellPro argued that Hopkins should have given a licensing preference to CellPro over Baxter under 35 U.S.C. § 202(c)(7)(D), because CellPro was a small business firm.[94] This statute provides that, "except where it proves ***224** infeasible after a reasonable inquiry, the licensing of subject inventions shall be given to small business firms."[95] It is unclear from the available record whether Hopkins ever addressed this issue or whether CellPro was willing and able to license the technology from Hopkins or Becton at the time of the initial license negotiations. However, this provision applies to licenses and sub-licenses of a patent.[96] Therefore, a plain reading of the statute suggests that Becton, as well as Hopkins, was required to give a licensing preference to CellPro.

Instead, Hopkins licensed its patents to Becton, which in turn granted Baxter an exclusive license in exchange for a $1,250,000 up-front payment and an 11% royalty on all sales of the CD34 antibodies.[97] Baxter subsequently offered CellPro and two other companies a non-exclusive license to the patents for a $750,000 up-front payment and a 16% royalty on all antibody sales.[98] The other two companies agreed to these terms, but CellPro repeatedly responded that it was unwilling to pay more money than Baxter for a non-exclusive license because a non-exclusive license was worth less than an exclusive license.[99]

CellPro neglected to consider, however, that Baxter was required to pay an 11% royalty to Becton for all antibody sales, whether directly made by Baxter or indirectly by CellPro. It was unreasonable for CellPro to expect Baxter to sub-license the invention at a loss. However, CellPro may have been reasonable in requesting a reduction of the up-front payment to $500,000,[100] since Baxter had already recovered its $1,250,000 payment to Becton from the other two sub-licensees. Thus, even with a reduced up-front payment, Baxter would not be sub-licensing at a loss.

After CellPro rejected Baxter's terms, Baxter insisted on obtaining an exclusive right to distribute CellPro products in Europe and Japan.[101] CellPro insisted in its petition that Baxter's terms were per se unreasonable.[102]

***225 D. Hopkins' Response**

Hopkins replied to CellPro's petition by pointing out that Baxter had made significant efforts in developing the antibody technology and had obtained regulatory approval to market its system in Europe.[103] Furthermore, Baxter had sub-licensed the technology to two other parties.[104] Hopkins stated that if the federal government exercised march-in rights in this instance, it would set a "chilling precedent" for future university-industry relationships.[105] Hopkins argued that such a precedent would allow companies to exploit patented technology with impunity under 35 U.S.C. § 271(e)[106] while obtaining FDA approval for their products.[107] Then, unless the patent owner grants a license with favorable terms, a company could petition the government for a march-in license based on the fact that it is the only company with a FDA approved product.[108] Hopkins asserted that this hypothetical was not a parade of horrors but a very plausible scenario.[109]

Hopkins also noted that CellPro continued to insist that it should only pay Baxter a 4% royalty, despite the fact that 4% is less than the royalty Baxter must pay to Becton, thus requiring that Baxter take a loss on every antibody sold by CellPro.[110] Most importantly, Hopkins argued that the public health was not threatened by the court's injunction against CellPro. Hopkins voluntarily agreed to modify the injunction to allow continued public use of CellPro's system until Baxter's own Isolex system was approved by the FDA,[111] which was expected by the end of 1997.[112] To ensure that ongoing ***226** clinical trials were not inconvenienced should CellPro stop supplying their system--a distinct possibility given the 50% royalty imposed on CellPro by the court--Baxter pledged to make its own system available to the trials free of charge and to provide equivalent support under the same contract terms as CellPro.[113] While Baxter did not clarify how it intended to gain FDA approval for a system switch to a non-approved device mid-trial, it later claimed that obtaining a swift response from the FDA should not be a problem.[114]

In addition, Hopkins argued that CellPro's public health arguments are not persuasive because CellPro's system has not been approved as a safe and effective treatment for the myriad of conditions described in CellPro's petition.[115] CellPro's system has only been approved for the processing of bone marrow, not peripheral blood cells, which is the approach more commonly used today.[116] Baxter negates the effectiveness of this argument, however, by claiming that its system shares the same benefits as the CellPro system.[117]

Finally, Hopkins argued that the Act's march-in rights are designed to protect against nonuse or unreasonable use by

patentees, allowing only responsible applicants to apply for march-in rights.[118] CellPro, a willful infringer, could hardly be viewed as responsible, asserted Hopkins.[119] Additionally, Hopkins claimed that the intent of the Act is to encourage "exclusive" licenses, and allowing march-in rights every time an ***227** infringer wins the race to FDA approval would undermine the intended exclusive rights.[120]

E. Both Sides Embellish Their Cases

Hopkins and CellPro embarked on a media blitzkrieg to win approval for their points of view, enlisting the aid of many senators and congresspersons on both sides.[121] CellPro employed a high-price publicity firm, Barston-Marstellar of New York, to spread heart-tugging tales of distress about the children who would die if the Ceprate system were removed from the market. CellPro also capitalized on the fact that the Ceprate system had even saved the life of the company's own president, Rick Murdock.[122]

Hopkins responded with an editorial describing CellPro's media campaign as a "new low in greed-driven manipulation of citizens at their most vulnerable."[123] In the same article, the author referred to march-in rights as a ""particular loophole," as well as a "sore subject for many businesses that have been reluctant to sign licenses to technology sponsored with government funds."[124] This claim seems tenuous given that no company had ever applied for march-in rights prior to CellPro's petition.[125] However, even senators joined the fray, describing CellPro's petition as "an effort to circumvent the ***228** court order," and claiming that "[t]here are important reasons not to let CellPro misuse the Bayh-Dole Act."[126]

Moreover, both sides overstated their cases to NIH. CellPro repeatedly asserted that Hopkins, Becton, and Baxter did nothing to develop the invention until CellPro's device was approved by the FDA. However, Baxter's system was available in the same number of clinical sites as CellPro's device.[127] Even though Baxter did not file for PMA for U.S. approval of its products until one week before trial, Baxter obtained European approval of its system and made efforts to sub-license the technology.[128] Therefore, it is difficult to justify CellPro's argument that Hopkins and Baxter "sat on the sidelines" while CellPro exclusively developed the technology.[129]

To be fair, while Hopkins accused CellPro of "inflammatory rhetoric,"[130] Hopkins was equally guilty. Hopkins' accusation that CellPro was not "responsible" because CellPro willfully infringed Hopkins' patents ignores the fact that at the first trial the jury exonerated CellPro of all claims and further found all of Hopkins' patents invalid.[131] Furthermore, Hopkins asserted that the grant of a march-in license to CellPro would have a ""disastrous effect" on future technology transfer and could even have "a long term impact on the development of treatments for cancer and other diseases."[132]

Thus, both Hopkins and CellPro participated in rooster-strutting displays of bravado. Senator Ford of Kentucky put the conflict in perspective:

> I know that assurances have been given that this technology will continue to be made available. However, I believe a healthy amount of skepticism is certainly warranted when we are talking about human lives. These companies must be held accountable and must not deny patients access to life saving treatment.[133]

***229 F. NIH Decision**

After Hopkins voluntarily modified the injunction and pledged to provide Isolex devices free of charge to current clinical trials, the need for the government to exercise its march-in rights to protect the public became less clear. This factor, coupled with pending FDA approval of Baxter's system and Baxter's sub-licensing activities, led Dr. Harold Varmus, Director of NIH, to deny CellPro's petition. Dr. Varmus noted that Hopkins and Baxter had "taken effective steps to achieve a practical application" of the invention,[134] and that neither party had presented evidence that the separation of BMSC improved stem cell engraftment, disease free survival, or overall survival in patients. Thus, it was premature for either party to claim benefits other than those recognized in the FDA approval of CellPro's system, i.e., a decrease in infusional toxicities associated with the administration of bone marrow.[135]

Dr. Varmus asserted that it was equally inappropriate for NIH to substitute its judgment for that of clinicians and patients seeking to use the CellPro system. Dr. Varmus concluded that because CellPro can continue to make, use, and sell disposable products for the Ceprate system until such time as Baxter's alternative device is approved, there is no need for the

government to assert its march-in rights. The NIH review agreed "that patient needs [will] be met as long as one or the other cell separation device [is] available to people."

In response to CellPro's argument that Baxter will be unable to gain FDA approval to substitute its system for CellPro's system in ongoing clinical trials, Dr. Varmus stated that NIH will continue to monitor the situation and will initiate march-in proceedings without a new petition if the need arises.[136] Besides considering the public welfare, Dr. Varmus was concerned with the economic consequences of an exercise of march-in rights, remarking:

> [W]e are wary … of forced attempts to influence the marketplace for the benefit of a single company, particularly when such actions may have far reaching repercussions on many companies' and investors' future willingness to invest in federally funded technologies. … It would be inappropriate for the NIH, a public health agency, to exercise its authorities under the Bayh-Dole Act to procure for CellPro more favorable commercial terms than it can otherwise obtain from the court or from the patent owners.[137]

G. Aftermath

CellPro argued to NIH and the court that the 50% royalty imposed by the injunction would cause it serious financial strain, despite its cash reserve of 54 million ***230** dollars at the end of the first quarter of 1997.[138] The court responded that in the absence of a definitive statement by CellPro that it would cease operations because of financial strain, the injunction would stand as the lesser harm when compared to CellPro's willful infringement. The court, however, reduced the royalty from 100% of the incremental cost as requested by Hopkins to 60% of the incremental cost--about a 50% royalty.

Although it has only been a short time since NIH denied CellPro's petition, it is interesting to examine how the parties have fared since then. Initially, CellPro's financial status seemed robust. CellPro reported a net loss of $5.1 million for its first fiscal quarter ending June 30, 1997, compared with a net loss of $4.6 million the previous year. On June 30, 1997, the company's cash reserve totaled $47.8 million. At the end of the second quarter on October 29, 1997, CellPro reported a loss of $6.1 million, compared with $5.1 million the year before, and its cash reserve was down to $31 million. Yet, according to Hambrecht and Quist Research Excerpts, CellPro was still considered a "strong buy" in 1997, with revenues for the year up from $1.9 million to $2.5 million.[139]

Baxter, on the other hand, had some difficulties with its Isolex PMA in the year following its litigation victory. The FDA advisory panel withheld approval of Baxter's Isolex 300 stem cell separating device on July 25, 1997, because of ambiguous clinical data.[140] Despite Baxter's overwhelming success at trial and with NIH, Hambrecht and Quist suggested in 1997 that Baxter had "made little progress in the last 12 to 18 months. Recent information suggest[s] that [Baxter] could be scaling down [its] efforts or even exiting the field."[141]

In contrast, CellPro announced the submission of a peripheral blood PMA supplement to the FDA in October 1997.[142] Furthermore, pending Federal Circuit review of the case, CellPro won a partial stay of the injunction that required it to phase ***231** out manufacture of the Ceprate system.[143] CellPro seemed to have the advantage in the stem cell market.

Meanwhile, CellPro submitted a brief to the Federal Circuit arguing against the findings of the trial court.[144] In August of 1998, the Federal Circuit held that the district court's order for repatriation of cells from Canada was an abuse of discretion. The court noted that "[m]ere possession of a product which becomes covered by a subsequently issued patent does not constitute infringement until that product is used, sold, or offered for sale in the United States …."[145] The Federal Circuit also agreed that the district court should not have excluded newly relevant prior art as asserted by CellPro when the court reinterpreted the claims at the end of the first trial.[146]

However, the Federal Circuit did not find in CellPro's favor on the critical issues of claim interpretation, infringement, obviousness, and enablement.[147] The Federal Circuit upheld the district court's claim construction as to claim 1 of the '204 patent owned by Hopkins. Claim 1 originally read as follows:

> A monoclonal antibody which specifically binds to an antigen on non-malignant, immature human marrow cells, wherein said antigen is stage specific and not lineage dependent, and said antigen is also specifically bound by the antibody produced by the hydridoma deposited under ATCC Accession No. HB-8483.[148]

Deciding that the language after the wherein clause of claim 1 was the only language that attempted to describe the CD34

antigen, the court rewrote claim 1 to read, "Any monoclonal antibody that binds only to the CD34 antigen through an antigen-antibody interaction."[149]

This reconstruction of claim 1 hurt CellPro because although CellPro's antibody binds to monkey cells and arguably does not "specifically bind to … human marrow cells," the district court found that there was "no testimony, however, to establish that the antigen to which [the antibody] binds in primates is not CD34."[150] The court also found that the term "specifically binds" only meant a specific antigen-antibody ***232** binding and not an antibody that only binds to human cells.[151] Hence, by limiting the inquiry to the antigen-antibody interaction, the court held that CellPro's use of the antibody infringed upon claim 1 as rewritten.

Further, CellPro argued that its antibody does not "specifically bind to immature … human marrow cells" because of evidence that the antibody binds both to immature human marrow cells and to more mature cells."[152] The district court rejected this argument as well, citing CellPro's failure to provide testimony that the antibody is not binding to the CD34 antigen on the mature cells.[153]

CellPro did not pursue these two arguments on appeal to the Federal Circuit.[154] Instead, CellPro argued that construing the wherein clause of claim 1 to include any antibody that binds to CD34 was overly broad because CD34 is a cluster designation of cell surface markers and not all CD34 antigens are identical.[155] Thus, CellPro asserted, CD34 represents a genus of antigens, not a single antigen, and the test should be whether the antibody binds to My-10, not to CD34.[156]

The Federal Circuit rejected this argument, reasoning that CD34 is not a genus of antigens but rather a protein with at least three epitopes. To understand these esoteric distinctions, one must understand that "antigen" describes the entire molecule to which an antibody binds. However, antibodies do not typically bind to the entire antigen, but instead bind to small portions of the antigen called an "epitope."[157] Thus, epitope is a narrower term than antigen.

While CellPro erroneously asserted that CD34 was a genus of antigens, it is likely that CellPro meant to argue that the Hopkins' '204 patent only claims and/or enables antibodies to the particular epitope described as My-10 and does not describe antibodies directed to other possible epitopes of CD34. The issue thus framed is really one of claim scope and enablement--does the description of an antibody directed against a single epitope on an antigen enable every antibody directed against the same antigen?

***233** CellPro did not present this argument though, and the Federal Circuit held that the '204 patent sufficiently enabled[158] a broad reading of claim 1. Although the Federal Circuit noted that CellPro presented evidence that the two antibodies at issue do not bind to the same epitope, the court still affirmed the finding of infringement because the antibodies nevertheless bind to the same antigen.[159]

In light of CellPro's failure on appeal to the Federal Circuit, the Hambrecht and Quist predictions about CellPro's rosy future were premature. As of the writing of this article, CellPro has filed for Chapter 11 bankruptcy, and its stock has plunged from $35 to a few cents a share.[160] CellPro has agreed to pay 15.6 million dollars to settle this case, and in September of 1998, CellPro sold all of its assets to Nexell, a company partly owned by Baxter.[161] CellPro has laid-off ninety-three employees and its lab space is now leased to another biotech company.[162]

Baxter has agreed to continue distributing CellPro's CEPRATE kits for a limited time to ensure that patients and clinicians will continue to have access to cell selection technology until the FDA approves Baxter's Isolex Stem Cell Selection System. The Isolex system has not yet received premarket approval by the FDA, although this process is in the final stages.[163] After a six-year battle, Baxter still does not have its own stem cell separator on the market; however, it does have the exclusive right to market the remaining CellPro devices, and CellPro no longer exists.[164]

***234 IV. Other Measures of Bayh-Dole Success**

By most accounts, the Bayh-Dole Act has been a success,[165] at least in terms of stimulating technology transfer and patent applications. Although university research is still largely funded by the federal government, industry funding of this research has increased five-fold since Congress passed the Act.[166] In addition, the number of licenses granted by universities has

increased at least ten-fold.[167] Royalties paid to universities almost quadrupled from 1981 to 1992,[168] and more than doubled between 1991 and 1995.[169]

Although these numbers indicate the success of the Bayh-Dole Act, there is no appropriate control data available, and thus it is not clear how much of the growth is due to the Bayh-Dole Act and how much can be attributed to other factors. For example, the number of university-issued patents increased from 220 in 1979 to 1148 ***235** in 1989 to 3024 in 1998.[170] This represents more than a ten-fold increase in patents issued to universities since the enactment of the Bayh-Dole Act. In contrast, the number of patents issued to any "incorporated" entity--a substitute measure of industry totals--rose about three-fold over the same period of time.[171] This comparison suggests that the Bayh-Dole Act gave university technology a welcome boost.

However, more than half of university-issued patents are in the field of life sciences or biotechnology,[172] a field exhibiting tremendous growth over the past two decades. Rather than compare the biotechnology field to industry as a whole, it is probably more instructive to compare the number of university-issued biotechnology patents to the number of such patents issued in other rapidly developing nascent fields such as the computer industry. A similar search of IBM-owned patents also shows an almost ten-fold increase in the number of patents issued over the same period.[173] Thus, patents issued for inventions in biotechnology and computer science have proceeded at a comparable pace. This growth may indicate the general increase in the importance of intellectual property combined with an actively growing field of technology rather than the effect of the Bayh-Dole Act.[174]

Additionally, although surveys have shown a great increase in royalties generated by university inventions, usually gross revenues are reported, rather than net royalties, and total profits are unavailable. Indeed, some commentators have ***236** suggested that after subtracting office space, salaries, benefits, and the like from net royalties, often no profit is recovered.[175]

Although industry partnerships benefit basic and applied research by supplementing a decrease in federal funding, some data indicate that industry affiliations have biased research. For example, a recent study shows that while 3% of the authors of calcium channel blocking papers revealed their financial interest in the outcome of the research, as many as 96% should have.[176] Further, at least two studies have shown that financial interests correlate strongly with favorable research conclusions.[177]

In addition, at least one research institution has stumbled along the perilous path towards commercial success. In 1992, Scripps Research Clinic, a well-known and respected research institution, came to an agreement with the foreign owned Sandoz Pharmaceutical Corporation. The agreement stipulated that Scripps receive some $300 million in funding over ten years in exchange for the right of first refusal to all of Scripps' research work.[178] Congress was appalled by the idea of wholesale ***237** exportation of federally funded inventions and quickly pressured Scripps into revising the deal.[179] The new deal limited Sandoz' access and control over Scripps' research and provided for additional licensing preferences and assistance to small businesses.

The Scripps' controversy also piqued Congressional interest in the reporting of federally funded inventions. A subsequent investigation revealed that Scripps had failed to acknowledge federal funding in forty-three patent applications.[180] This finding prompted the government to extend the investigation to other institutions, whereupon investigators concluded that federal funding of patented inventions is generally under-reported.[181] These results have prompted a general review of the ability of federal agencies to monitor the reporting requirements of the Bayh-Dole Act and may lead to the increased enforcement of these procedural requirements in the future.[182] This trend makes compliance with the procedural requirements of the Act even more important.

V. Conclusions

Although industry participation in basic research has increased in the last twenty years, most academic research is still funded by the federal government.[183] The Bayh- ***238** Dole Act allows the university or inventor to retain title to any inventions made with federal funding, as long as a number of procedural requirements are met. To retain title, the inventor must report the invention to the federal government and elect to retain title before a bar to patentability arises. In addition, the patent application must contain a statement that the invention was made with the aid of government funds.

Although the institution may elect to retain title, the federal government also retains a royalty free, non-exclusive worldwide

license to practice the invention. Additionally, the Act provides that the patentee should give small businesses a licensing preference, and all patented products must be substantially manufactured in the U.S. Further, the government may theoretically issue a compulsory license if a patentee fails to commercialize an important invention or if more reasonable licensing terms are required to protect the public welfare.

Another important consequence of federal funding is that grant proposals, which are made public once a grant is awarded (unless steps are taken to protect any confidential information in the grant), may be used as prior art against patentees. Therefore, the savvy inventor or patent attorney should take precautions in advance and include grant proposals by the inventor in the art submitted to the patent office. Likewise, accused infringers should not overlook this important source of potentially anticipatory prior art.

Although it is important for federally funded inventors to recognize and follow the Bayh-Dole Act's procedural requirements, to date no infringer has successfully escaped the consequences of infringement by alleging that the patentee failed to comply with these requirements. However, in at least one case, allegations by the infringer sufficiently peaked the funding agency's interest in a subject invention to begin an investigation of whether or not the government should take title to the invention. During the investigation, the cloud on the patent's title effectively precluded enforcement of the patent. Further, because evidence suggests that universities have been grossly under-reporting subject inventions to the government, it may become easier in the future to provoke a government investigation of a patent's title, thus effectively preventing enforcement of the patent during the investigation period.

It is unclear whether the Bayh-Dole Act crafts the appropriate balance between public and private interests or is enforced sufficiently to effect the theoretical balance created by the Act. The *Hopkins v. CellPro* controversy is not the best case to use for an evaluation of the Act's ability to balance private versus public sector needs. During this case, both parties exaggerated their positions. Moreover, Hopkins took the bite out of CellPro's public health argument by requesting that the injunction be delayed pending the approval of another product and by pledging to fill in the gap should onerous royalties inhibit CellPro's Ceprate sales or support activities. However, ***239** notwithstanding CellPro's failure to obtain a compulsory license, the government's response to the Scripps-Sandoz controversy effectively demonstrates that the government has not abandoned the public interest and that large corporations and institutions can be pressured into protecting the public interest even without the issuing of a compulsory license.

In conclusion, it is unclear how much, if any, the Bayh-Dole Act has contributed to the successful commercialization of government funded inventions. While the number of patent applications has increased dramatically, as have licensing and royalties, this growth parallels that seen in other growth industries that are generally independent of government funding. Further, there is evidence that industry partnerships may bias research results and that researchers underreport these conflicts of interest. Nonetheless, in spite of all these caveats, industry, universities, and patent lawyers alike all seem to favor the increase in university-industry partnerships created by the Act. The new industry of technology transfer was created by the Bayh-Dole Act and has provided positions for about 180,000 tech-transfer personnel.[184] In addition, the increase in the number of patent applications certainly benefits patent lawyers.

As for the general public, it is difficult to determine if the Bayh-Dole Act brings additional inventions to the market that would otherwise not have been commercialized. Even assuming that some inventions are commercialized that would not have been otherwise, the public pays the price for the short-term monopoly given to patentees. However, in the long run, it may be that the price is right.

Footnotes

[a1] Dr. Tamsen Valoir is an associate with the law firm of Jenkens & Gilchrist, P.C., Houston, Texas.

[1] Rochelle L. Stanfield, *Building a Better Mousetrap--Is the Government Getting in the Way?,* 11(35) THE NAT'L J. 1436 (1979) ("[T]raditional federal policy demands that such inventions belong to the public; no one should get exclusive rights to something developed with taxpayers' money.").

[2] *See, e.g.,* THE WRITINGS OF THOMAS JEFFERSON, 1788-1792, at 279 (Paul Leicester Ford ed. 1985) (providing an early

example). As a later example, see *Lear, Inc. v. Adkins,* 395 U.S. 653, 670, 162 U.S.P.Q. (BNA) 1, 8 (1968) (discussing protecting the public against "would-be monopolists").

[3] The United States Court of Appeals for the Federal Circuit was created by the Federal Courts Improvement Act of 1982, P.L. 97-164, codified at 28 U.S.C. § 44 *et seq*.

[4] Lawrence Schlam, *Compulsory Royalty-Free Licensing as an Antitrust Remedy for Patent Fraud: Law, Policy and the Patent-Antitrust Interface Revisited,* 7 CORNELL J. L. & PUB. POL'Y 467, 473 (1998) (arguing that "[t]he CAFC, however, has proven itself to be pro-patent. From 1982 through 1987 the CAFC upheld 89 percent of the district court decisions finding a patent valid and reversed 45 percent of the decisions rejecting a patent …. Pre-CAFC courts upheld only 30 to 40 percent of the decisions holding patents valid.").

[5] Rochelle L. Stanfield, *Building a Better Mousetrap--Is the Government Getting in the Way?,* 11(35) THE NAT'L J. 1436 (1979) (quoting one inventor who tried to avoid losing patent rights to the federal government by not inventing on government time: "We don't use federal money for any innovative development, only for basic research. If we can see an idea developing on a federal project, we don't pursue it. … You tend to hoard ideas you think will be productive until the day that you can finance them yourself."); Sunil R. Kulkarni, *All Professors Create Equally: Why Faculty Should Have Complete Control over the Intellectual Property Rights in Their Creations,* 47 HASTINGS L. J. 221, 237 (1995) (noting that "universities look upon patent royalties as a potential ""cash cow,"DDD' and that without patent protection the costly development needed to bring research to market would not occur).

[6] As an anecdotal example, see Rochelle L. Stanfield, *Building a Better Mousetrap--Is the Government Getting in the Way?,* 11(35) THE NAT'L J. 1436 (1979) ("Inventor Lonsdale was ready to test his process for removing metals from solution in uranium mining, but a number of large mining and chemical companies who had expressed an interest had shied away because the government owned the patent and would not grant Lonsdale exclusive rights to develop it. "No one wants non-exclusive rights.' said Lonsdale. However, a Japanese company was interested in developing the idea in Japan.").

[7] Duff McDonald et al., *Investing's New Frontier,* MONEY (Sept. 1998) (reporting that "it can cost [up to] $350 million to develop a [pharmaceutical] drug"); Patrick Flanagan, *Drug Prices: What's the Rationale?,* 82(7) MANAGEMENT REVIEW 10 (1993) ("The pharmaceutical industry cites a recent Tufts University study showing it costs $231 million over 12 years to bring the 'average' drug to the market. The same study reports the price tag was only $100 million for drugs that came to market 10 years ago. Factored into these costs are the so-called dry holes, or drugs that are researched but never sold commercially."), *cf.* Janice Marchiafava Hogan, *Revamping the Orphan Drug Act: Potential Impact on the World Pharmaceutical Market,* 26(2) LAW & POLICY IN INT'L BUSINESS 523 (1995) ("Sales of the Genentech [human growth hormone hGH] alone totaled $580 million in its first five years on the market, compared with only $45 million in development costs. Similarly, after spending $150 million on research and development of Erythropoietin (EPO), Amgen's sales of this drug totaled $893 million. Burroughs Wellcome's cumulative sales of AZT now exceed $1 billion.").

[8] 15 U.S.C. § 3701(3) (1994).

[9] *See id.*

[10] 35 U.S.C. §§ 202-212 (1994)

[11] 35 U.S.C. § 200 (1994) ("It is the policy and objective of the Congress to use the patent system to promote the utilization of inventions arising from federally supported research or development; to encourage maximum participation of small business firms in federally supported research and development efforts; to promote collaboration between commercial concerns and nonprofit organizations, including universities; to ensure that inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise; to promote the commercialization and public availability of inventions made in the United States by United States industry and labor; to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions; and to minimize the costs of administering policies in this area.").

[12] 35 U.S.C. § 201(c) (1994).

[13] Exec. Order No. 12,591, 562 FED. REG. 13,414 (1987). In order to promote the commercialization of the patentable results of federally funded research, the Order requires that all contractors, "regardless of size," be granted the titles to patents made in whole or part with federal funds, subject to a federal license.

[14] 35 U.S.C. § 201(e) (1994).

[15] 35 U.S.C. § 202(c) (1994). *See, e.g.,* Ciba-Geigy Corp. v. Alza Corp., 804 F. Supp. 614, 26 U.S.P.Q.2d (BNA) 1321 (D.N.J. 1992) for a discussion of the applicability of the Act to an invention. The court decided that the Act does not apply when research grants are used for related, but not identical research, and the granting contracts do not contain the provisions required by the Act, even if the Act is repeatedly referenced in a license agreement.

[16] 35 U.S.C. § 202(c)(6) (1994). Although section 202 provides certain procedural requirements, no private right of action to enforce the Act exists and a failure to include the statement of government rights will not benefit an alleged infringer. Gen-Probe, Inc. v. Center for Neurologic Study, 853 F. Supp. 1215, 30 U.S.P.Q.2d (BNA) 1077 (S.D. Cal. 1993). *Cf.* VDI Tech., Inc. v. Price, No. CIV. 90-341-M, 1994 U.S. Dist. LEXIS 12913 (D.N.H. Aug. 31, 1994) (denying enforcement of a patent under pre-Bayh-Dole law where a cloud on patent owner's title existed because the alleged infringer provided information about a federal grant that supported the activities of the patent owner. This information prompted the government agency to investigate the circumstances of the invention to determine if the patent owner actually owned a viable interest). Another ownership problem may arise when the inventor is a government employee. Per Executive Order 10096, the government obtains the entire right, title, and interest to and in all inventions of a government employee that bear a direct relation to or are in consequence of the official duties of the inventor. 15 FED. REG. 389 (1950), modified by Executive Order 10930, 26 FED. REG. 2583 (1961). *See, e.g., In re* Wynne, 229 U.S.P.Q. (BNA) 842 (Comm'r Pat. 1986) (holding that the Navy was entitled to the invention where the inventor applied for a patent shortly after leaving the Navy).

[17] 37 C.F.R. § 401.1(a)(1) (1999).

[18] 37 C.F.R. § 401.1 (a)(2) (1999).

[19] 35 U.S.C. § 212 (1999).

[20] Pat K. Chew, *Faculty-Generated Inventions: Who Owns the Golden Egg?,* 1992 WIS. L. REV. 259, 296-97 (1992) (stating that "[t]he federal government is the largest source of research funding. The National Institute of Health (NIH), National Science Foundation, and the Department of Defense provide about 80% of total federal funding of academic research, with NIH providing almost 50% of the total.") (citation omitted).

[21] 35 U.S.C. § 202(c) (1994).

[22] 35 U.S.C. § 201(c) (1994).

[23] 35 U.S.C. § 202(c)(1) (1994).

[24] *See id.*

[25] Pat K. Chew, *Faculty-Generated Inventions: Who Owns the Golden Egg?,* 1992 WIS. L. REV. 259, 296-97 (1992) (stating that the government claims title infrequently, citing telephone interviews with NIH employees as support). *Cf.* Southern Research Inst. v. Griffin Corp., 938 F.2d 1249, 1254-55, 19 U.S.P.Q.2d (BNA) 1761, 1766 (11th Cir. 1991) (in response to the USDA's claim that

the Bayh-Dole Act does not apply to its already licensed invention, the court concluded "that by 202(e) Congress has committed the refusal to assign or transfer patent rights to the discretion of the various federal agencies that acquire those rights in a manner putting such discretionary refusal beyond judicial review. In this case, the USDA declined to transfer its patent rights in 'A Method for the Control of Insects' to SRI, and we are without the statutory guidance to meaningfully assess that inaction, and thus without authority to review it.").

[26] 35 U.S.C. § 202(c)(2) (1994).

[27] *See id.*

[28] 35 U.S.C. § 202(c)(3) (1994). Presumably, this section refers only to statutory bar dates within the contractor's control, such as public disclosure, use, and offers for sale by the contractor, and does not refer to public use by third parties. Indeed, many of the federal regulations implementing this provision specifically refer to public use and sale by the contractor. *See, e.g.,* 10 C.F.R. § 784.12 (1999), 14 C.F.R. § 1274.912 (1999), 37 C.F.R. § 401.14 (1999), 45 C.F.R. § 650.4 (1999), 48 C.F.R. § 52.227-11 (1999). *Cf.* 43 C.F.R. § 6.2 (1999) (not limited to public use by the contractor).

[29] 35 U.S.C. § 202(c)(6) (1994).

[30] 5 U.S.C. § 552(a) (1994).

[31] E.I. du Pont de Nemours & Co. v. Cetus Corp., 19 U.S.P.Q.2d (BNA) 1174 (N.D. Cal. 1990).

[32] *Id.* at 1184.

[33] *Id. See In re* Hall, 781 F.2d 897, 900, 228 U.S.P.Q. (BNA) 453, 455 (Fed. Cir. 1986) (A printed publication is a publication that is ""sufficiently accessible" to members of the public who are interested in the art and exercise "reasonable diligence.")

[34] *E.I. du Pont de Nemours & Co.,* 19 U.S.P.Q.2d (BNA) at 1186.

[35] *Id.*

[36] *Id.*

[37] 45 C.F.R. § 612.8(a)(3) (1999).

[38] 45 C.F.R. § 612.6(d) (1999).

[39] 45 C.F.R. § 612.6(c) (1999).

[40] In the event that neither the contractor nor the federal government is interested in retaining rights to the invention, the Act also provides that the inventor may retain rights. 35 U.S.C. § 202(d) (1994).

[41] 35 U.S.C. § 202(c)(4) (1994) ("With respect to any invention in which the contractor elects rights, the Federal agency shall have a nonexclusive, nontransferable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States any subject invention throughout the world.").

[42] *See id.*

[43] 35 U.S.C. § 203 (1994) ("[T]he Federal agency … shall have the right, in accordance with such procedures as are provided in regulations promulgated hereunder to require the contractor, an assignee or exclusive licensee of a subject invention to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant or applicants, upon terms that are reasonable under the circumstances, and if the contractor, assignee, or exclusive licensee refuses such request, to grant such a license itself, if the Federal agency determines that such--
action is necessary because the contractor or assignee has not taken, or is not expected to take within a reasonable time, effective steps to achieve practical application of the subject invention in such field of use;
action is necessary to alleviate health or safety needs which are not reasonably satisfied by the contractor, assignee, or their licensees;
action is necessary to meet requirements for public use specified by Federal regulations and such requirements are not reasonably satisfied by the contractor, assignee, or licensees; or
action is necessary because the agreement required by section 204 has not been obtained or waived or because a licensee of the exclusive right to use or sell any subject invention in the United States is in breach of its agreement obtained pursuant to section 204.") [35 U.S.C. § 204 (1994) requires substantial manufacture in the U.S., *see infra* text accompanying note 46.]

[44] Although the Act and the federal regulations implementing the Act all refer to "public use regulations," this author is unable to locate an example of such public use requirements.

[45] 35 U.S.C. § 203 (1994).

[46] 35 U.S.C. § 204 (1994).

[47] 35 U.S.C. § 202 (c)(7)(B) (1994). However, a minimum royalty is not specified by the Act. *Cf.* 15 U.S.C. § 3710c(a)(1)(A)(I) (1998) (providing for a minimum 15% royalty for inventors in federal laboratories).

[48] 35 U.S.C. § 202 (c)(7)(C) (1994).

[49] 35 U.S.C. § 202 (c)(7)(D) (1994).

[50] 35 U.S.C. § 202(a) (1994).

[51] *Id.*

[52] 35 U.S.C. § 203(a) (1998).

[53] *See supra* note 11 and accompanying text.

[54] *See supra* Part II.B.

[55] 931 F. Supp. 303, 308 (D. Del. 1996) [hereinafter "*Hopkins III*"]. Prior to *Hopkins III,* this lawsuit proceeded through two introductory stages, reported at 160 F.R.D. 30, 34 U.S.P.Q. 2d 1276 (D.Del 1995) [hereinafter "*Hopkins I*"] and 894 F. Supp. 819 (D.Del. 1995) [[[[hereinafter "*Hopkins II*"].

[56] *See id.* at 308. Pluripotent or multipotent stem cells are capable of self-renewal, as well as differentiation into one or more subsets of mature, specialized cells. These cells can be used to treat many diseases and injuries.

[57] *See id.*

[58] *See id.* at 309.

[59] *See id.*

[60] An antibody binds to a specific site (on a particular cell) called an antigen. "Once an antibody attaches to an antigen on a cell, that cell is effectively flagged and scientists can use known techniques to separate the flagged cell from other cells." *Hopkins III,* 931 F. Supp. at 309.

[61] *See id.* at 309-10.

[62] *See id.* at 312.

[63] Binding to biotin, a B vitamin, allows the biotin-bound antibody to be purified by binding to yet another ligand called avidin--which is found in raw egg whites. Avidin binds very tightly to biotin, and can be easily conjugated to chromatography beads. Thus, avidin can be used to capture the biotin-antibody-BMSC complex from blood. This method greatly simplifies the purification of the cells. For a review of monoclonal antibodies and their use in treating cancer, see David M. Goldenberg, *New Developments in Monoclonal Antibodies for Cancer Detection and Therapy,* 44 CANCER 43 (1994).

[64] *Hopkins III,* 931 F. Supp. at 312. Binding to monkey cells facilitated FDA approval of the 12.8 antibody because preliminary tests could be conducted in monkeys.

[65] *See id.*

[66] CellPro's Ceprate SC system is approved for sale in Canada and 18 European countries, and received a pre-market approval (PMA) for use in the U.S. in December 1996. The approved use pertained to the processing of autologous bone marrow. 62(80) FED. REG. 20189 (April 25, 1997). *See also* http://www.cellpro.com/apv.html.

[67] The Civins patents are U.S. Patent Nos. 5,130,144, filed Mar. 22, 1991; 5,035,994, filed Sep. 7, 1990; 4,965,204, filed Jun. 1, 1987; and 4,714,680, filed Feb. 6, 1984.

[68] *See* chronology of events in appendix, *infra.*

[69] CellPro alleged non-infringement and invalidity of U.S. Patent Nos. 4,714,680, 5,035,994 and 4,965,204, which encompass the use of CD34 antibodies for the purpose of identifying and selecting stem cells for stem cell transplantation in patients.

[70] U.S. Patent No. 4,965,204.

[71] *Hopkins III,* 931 F. Supp. at 306-07.

[72] *See id.* at 307.

[73] *See id.*

[74] *See id.*

[75] *See infra* notes 150-159 and accompanying text for additional discussion of the claims.

[76] *Hopkins III,* 931 F. Supp. at 313.

[77] *See infra* notes 148-159 and accompanying text.

[78] *In re* CellPro, Inc., Misc. No. 481, 99 F.3d 1159, 1996 US. App. LEXIS 27651 (Fed. Cir. Oct. 7, 1996) [hereinafter "*Hopkins IV*"].

[79] *See id.* at *5.

[80] *Hopkins III,* 931 F. Supp. at 319.

[81] *See id.* at 320.

[82] Johns Hopkins Univ. v. CellPro, 1997 U.S. Dist. LEXIS 14314 (D. Del. 1997) [hereinafter "*Hopkins V*"]. After the second trial of the case, Hopkins withdrew its claims on the '994 and '144 patents. *See id.* at *4. The court entered a judgment of willful infringement, and the second jury considered the question of willful infringement and damages. *See id.* at *5. The jury found that CellPro willfully infringed the Civens patents and awarded Hopkins damages of $2,320,493. *See id.* at *1. This value was based on a royalty of 10%, with an up front payment of $1,000,000. *See id.* at *14. Thereafter, Hopkins filed a motion requesting triple damages, as well as attorney's fees ($5,000,000) and costs ($1,500,000). *See id.* at *22, *28. The court awarded treble damages, noting such aggravating factors as i) deliberate copying (it is unclear to this author how the independent development of a stem cell antibody qualifies as copying), ii) unreasonable invalidity opinions and unreasonable reliance thereon, iii) setting aside three and later seven million dollars to fight the Hopkins' patents, iv) denying that the 12.8 antibody bound to CD34 while at the same time telling the FDA and the public that the antibody binds to CD34, v) counsel's inappropriate relationship with the courtroom deputy, vi) CellPro's ability to afford the 4.6 million dollars in damages because it had 60 million dollars available in cash and securities, and vii) because the case was not a close case (even though CellPro won the first jury trial). *See id.* at *28-*36. The court later ordered: "CellPro may continue to make, have made, use, and sell SC Systems and disposable products (including the 12.8 antibody) for use with SC Systems within the United States until such time as an alternative stem cell concentration device, manufactured under a license of the '204 and '689 patents, is approved for therapeutic use in the United States by the United States Food and Drug Administration and for a period of three months thereafter.'' *See id.*

[83] *See id.; see also* Johns Hopkins Univ. v. CellPro, Inc., 152 F.3d 1342, 1346, 47 U.S.P.Q.2d (BNA) 1705, 1706 (Fed. Cir. 1998) [hereinafter """"""*Hopkins VI*"].

[84] Letter from Lloyd N. Cutler and Birch Bayh to Donna Shalala, Secretary of the Department of Health and Human Services, dated March 3, 1997 [[[[hereinafter "Petition," on file with author].

[85] Petition at 13.

[86] Baxter "has not taken, [and] is not expected to take within a reasonable time, effective steps to achieve practical application of the patents." Petition, at 13. CellPro also claimed an "inordinate delay before Hopkins and its licensees attempted to develop a product for therapeutic uses." Letter and accompanying Memorandum from Lloyd N. Cutler and Birch Bayh to Robert Lanman, NIH Legal

Advisor, dated April 24, 1997 [hereinafter ""Memorandum," on file with author], at 7.

87 Baxter filed for PMA for its Isolex 300A on February 24, 1997, one week before trial began. Memorandum at 28, 31. Baxter stated that it intended to file for PMA for its 300I system later that year, but as of June 1999, no PMA has been filed. Letter from Gary Wilson, counsel for CellPro to Robert B. Lanman, Legal Advisor to NIH, dated May 8, 1997, [hereinafter "Wilson-Lanman Letter"], on file with author.

88 *See, e.g.,* Petition at 1; Memorandum at 27.

89 *See* note 66, *supra.*

90 Memorandum at 8.

91 Memorandum at 9.

92 Memorandum at 22.

93 Petition at 12 (citing 35 U.S.C. § 203 (requirements for march-in rights)).

94 Petition at 6.

95 35 U.S.C. § 202 (c)(7)(d) (1994).

96 35 U.S.C. § 203(a) (1994).

97 Petition at 7.

98 *See id.* at 8.

99 *See, e.g.,* Letter from Gary Wilson, counsel for CellPro, to Wendy Baldwin, Deputy Director of NIH, dated May 19, 1997 [hereinafter "Wilson-Baldwin Letter," on file with author]; Petition at 14-15. CellPro stated that it was only willing to pay a 4% royalty to Baxter. *See infra* note 110.

100 Petition at 8, 14.

101 Petition at 9. CellPro states that Baxter's demand for exclusive distribution rights of CellPro's products in foreign markets was an unlawful attempt to broaden the geographical effect of the Civins patents. However, an exclusive distributorship is not the same as a patent right because other parties can still market competing products (just not CellPro products) when no patent exists.

102 Petition at 14.

103 Letter from Hopkins to Wendy Baldwin, Deputy Director, Office of Extramural Research, NIH, dated June 2, 1997 [hereinafter "Supplemental Response," on file with author], at 2. Baxter's Isolex 300 magnetic cell-separator system received approval in Europe in January 1995. *Baxter International Inc.,* MED. AD. NEWS at 44, September 1996.

[104] Letter from Hopkins to Barber M. McCarey, Deputy Director, Office of Technology Transfer, NIH, dated July 29, 1997 [hereinafter "Surreply," on file with author], at 1.

[105] Surreply at 3.

[106] Section 271(e) provides an exception to infringement "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 …." 35 U.S.C. § 271(e) (1994).

[107] Surreply at 3.

[108] Surreply at 3. CellPro's argument is based on "the fortuity of having obtained FDA approval for [a system] that is no longer relevant to U.S. transplant center." Supplemental Response at 11.

[109] Surreply at 3.

[110] *See id.* However, according to CellPro a 4% royalty on the device would equate to a 16% royalty on the antibody itself. Wilson-Baldwin Letter at 12. There are several inconsistencies on royalty amounts claimed in the various letters to NIH, with the royalty rate Baxter must pay to Becton ranging from 11% to 5.5%. The different numbers may reflect different royalty bases, making it difficult for the reader to evaluate the "reasonableness" of the royalties required. It is clear, however, that the injunction against CellPro calls for a royalty of approximately 50% on the device. *See id.* at 4.

[111] The injunction was also modified in other ways. For example, when CellPro objected that the injunction required current clinical trials to purchase columns and antibodies at full price instead of for free as CellPro had been providing, Baxter and the court modified the injunction to allow these trials to continue receiving supplies free of charge. Memorandum at 4.

[112] Supplemental Response at 2. It is not clear to the author nor CellPro that this expectation is reasonable, given that Baxter filed its PMA in February 1997, because it generally requires at least 2 years for PMA approval by the FDA, and CellPro's own system had required 3 years for approval. Memorandum at 28-29.

[113] Press Release Issued Jointly by Johns Hopkins, Becton Dickinson, and Baxter Healthcare, at ‹http://hopkins.med.jhu.edu/NewsMedia/press/cellpro/joint_release.html› [on file with author].

[114] Surreply at 4. Hopkins asserts that clinicians familiar with both the Baxter and CellPro systems consider the Baxter product to be superior (Supplemental Response at 6) and that the FDA could allow the substitution of Baxter's device for CellPro's device in clinical trials already underway. Surreply at 4. In that regard, several bone marrow transplantation experts confirmed that both the CellPro and Baxter systems work well and are available in clinics. Eliot Marshal, *Varmus To Rule in Fight over Cell Sorting-Technology,* 276(5318) SCIENCE 1488 (1997). It is not clear to this author, however, that the expectation of substituting Baxter's system is reasonable considering that Baxter's device is not yet approved and that a switch mid-trial would require abandoning existing data. Malcolm Brenner of St. Judes Children's Research Hospital in Memphis states that the main advantage of the CellPro device is that it already has an FDA license, which means that any clinician can simply buy and use the device. In order to use the Baxter device, a clinician must first apply for an experimental-use permit. *Id.*

[115] Supplemental Response at 8.

[116] *Id.* Although the device was approved for autologous bone marrow transplantation, the procedure has largely been replaced by less invasive peripheral blood collection of stem cells. While the CellPro system may be legally used for this "off-label use," advertising this use is not legal. *See* Marshal, *supra* note 114. In fact, the FDA issued a warning to CellPro in January of 1997,

reprimanding CellPro for a misleading Christmas card that promoted the use of its device in parent-child peripheral blood transplants.

117 Supplemental Response at 2.

118 *See id.* at 4.

119 *See id.*

120 *See id.* This argument should not apply to Baxter since Baxter eliminated its exclusive rights by contracting with two sub-licensees.

121 For example, letters in support of Hopkins' position arrived from such luminaries as the President of the American Cancer Society, the President of Genentech, Presidents of Stanford University, Brigham Young University, University of Maryland at Baltimore, the Association of American Universities and the American Association of Medical Colleges, Vice President for Research from the University of Utah, thirty-five congresspersons, and four senators. *See* ‹http://www.hopkins.med.jhu.edu/NewsMedia/press/cellpro› for these letters [[[[also on file with author]. CellPro also enlisted the support of eleven senators and thirty-five congresspersons, including the cosponsor of the Bayh-Dole Act, Birch Bayh. Additionally, 26 doctors submitted declarations on behalf of CellPro, outlining the ways in which the injunction would adversely affect their work. Memorandum at 2.

122 William Plummer & Giovanna Breu, *Boss and Guinea Pig; Thanks to His Company, Rick Murdock Is Still Alive, The Boss Had a Cancer with No Known Cure,* PEOPLE 121 (June 16, 1997) ("[T]anned and fit, Rick Murdock, CEO of a small Seattle-area biotech company, radiates health as he strides down the hall of the University of Washington Medical Center, shaking hands with doctors and nurses who greet him as if he were a returning war hero--which in a way he is. But Murdock is disquieted. 'It's a strange feeling I get every time I walk in the front door of UW,' he says. 'There's a smell that takes me back: "Oh, God, here I go again. It's starting over."DDD' A little more than a year ago, Murdock, 50, discovered that he had an advanced case of mantle cell lymphoma, a rare form of cancer with no known cure. Doctors gave him 30 months to live. Murdock, however, had a weapon not available to others with the disease. At that very moment, his medical device company, CellPro, happened to be experimenting with a radical new approach to treating lymphomas. If any cancer patient can be said to be lucky, Rick Murdock was lucky, except for one potentially fatal flaw: CellPro's system, based on a means of purging lymphoma cells from blood, was still nine months away from completion, and Murdock needed it in two months. 'You've got to be kidding"DDD' said project head Nicole Provost of the new timetable. Incredulity gave way to urgency mixed with irony. 'We've got this guinea pig.' Provost recalls thinking, 'and he's my boss."DDD').

123 ‹http://www.hopkins.med.jhu.edu/NewsMedia/press/cellpro/odza.html›.

124 *Id.*

125 The author of the editorial goes even further stating that this is just the first step in "nationalizing our healthcare system." ‹http://www.hopkins.med.jhu.edu/NewsMedia/press/cellpro/odza.html›.

126 Letter to DHHS by Senator Barbara Mikulski of Maryland, dated May 6, 1997 [on file with author]. *See also* ‹http://www.hopkins.med.jhu.edu/NewsMedia/press/cellpro/mikulski.html›.

127 Supplemental Response at 2.

128 Baxter filed its PMA for its Isolex 300A on February 24, 1997, one week before trial began. Memorandum at 28, 31. Baxter intends to file for PMA for its 300I system later this year, but this has not yet occurred as of June 1999. *See* Wilson-Lanman Letter and note 87, *supra.*

[129] Memorandum at 27. However, Baxter's counsel stated that "development efforts didn't get under way until the latter part of '91 or the early part of '92." Memorandum at 27, n. 25.

[130] *See, e.g.,* Memorandum at 5 (describing the "consequences in terms of the untold suffering if not death of thousands of children and adults cannot be justified as a way to ensure that there will be a market for Baxter's own product, if and when FDA approval can be obtained."

[131] Supplemental Response at 4.

[132] Supplemental Response at 3, 5. *See also* Hopkins' accusation that CellPro "shamelessly exploits the fears of those patients and their families." *Id.* at 1.

[133] Letter to DHHS by Wendell Ford, U.S. Senator of Kentucky, at ‹ http://www.hopkins.med.jhu.edu/NewsMedia/press/cellpro/ford.html›.

[134] Determination in the case of *Petition of CellPro, Inc.,* by Dr. Harold Varmus, Director of NIH, dated August 1, 1997, at ‹http:// www.nih.gov/news/pr/aug97/niha-01.html› [hereinafter "Determination," on file with author].

[135] *Id.*

[136] *Id.*

[137] *Id.*

[138] Wilson-Baldwin Letter at 8.

[139] ‹http://www.hamquist.com/research/excerpts/cpro_961113.html›.

[140] Baxter's Isolex in Limbo After Panel Ambivalence, Medical Industry Today, July 25, 1997.

[141] ‹http://www.hamquist.com/research/excerpts/cpro_961113.html›.

[142] *CellPro Announces Submission of Their Peripheral Blood Supplement to FDA,* BUSINESS WIRE (October 9, 1997); *CellPro Applies for Second Indication for Ceprate SC System,* MEDICAL INDUSTRY TODAY (October 10, 1997) (reporting that "CELLPRO INC. (Bothell, WA) is seeking another indication for peripheral blood stem cells for its Ceprate SC Stem Cell Concentration system and has filed a premarket approval (PMA) application supplement to the FDA. To back up its attempt for a second indication, CellPro presented the FDA with data from a 134-patient Phase III clinical trial that it completed in June. The company's PMA supplement proposes to change the product's labeling to state that the Ceprate SC System is indicated for peripheral blood stem cells and that selection of peripheral blood stem cells results in more than a 100-fold reduction in the number of tumor cells present in the autograft, according to CellPro. The company said its open-label, randomized clinical trial began in Jan., 1995 at 15 North American sites.").

[143] *CellPro Wins Partial Stay of Injunction,* INTELLECTUAL PROPERTY TODAY 15 (March, 1998) ("The United States Court of Appeals for the Federal Circuit has granted its motion to stay enforcement of certain provisions of the Permanent Injunction entered against it. … Under the terms of the Permanent Injunction, CellPro had been required to phase down sales of disposable

products sold for use with the CEPRATE (R) SC Stem Cell Concentration System outside the U.S. by 25% per quarter based on sales during the last quarter of 1996. The Court of Appeals ruling stays the phase-down requirement pending review of the case on appeal.").

144 The brief is reported in 1(23) MEALEY'S LITIGATION REPORT: BIOTECHNOLOGY A1 (1997).

145 *Hopkins VI,* 152 F.3d 1342, 1366, 47 U.S.P.Q.2d (BNA) 1705, 1723 (Fed. Cir. 1998).

146 *See id.* at 1357, 47 U.S.P.Q.2d at 1715-16.

147 *See id.* at 1357-68, 47 U.S.P.Q.2d at 1716-25.

148 *Hopkins II,* 819 F. Supp. 819, 832 (D. Del. 1995).

149 *Hopkins III,* 931 F. Supp. 303, 316 (D. Del. 1996).

150 *Id.*

151 *See id.* at 315.

152 *Id.* at 314.

153 *See id.* at 316-17.

154 The first argument may have been dropped because an antibody that specifically binds human marrow cells might nonetheless bind to monkey cells if the monkey cell also expresses a CD34 antigen or very similar equivalent. The second argument regarding the 12.8 antibody binding to mature cells may have been abandoned due to poor data.

155 *Hopkins VI,* 152 F.3d 1342, 1351-52, 47 U.S.P.Q.2d (BNA) 1705, 1716-17 (Fed. Cir. 1998).

156 *See id.*

157 *Hopkins III,* 931 F. Supp. at 308 ("antibodies sometimes connect with only a portion of the antigen, known as an epitope").

158 CellPro also presented non-enablement arguments, but they were not directed to this aspect of the claims.

159 *Hopkins VI,* 152 F.3d at 1357-59, 47 U.S.P.Q. 2d at 1717. (The Federal Circuit considered additional issues in its opinion, which are not discussed in this article.)

160 Douglas Gantenbein, *Are You Courting Disaster?,* SUCCESS 3(46): 64 (1999) ("CellPro's stock, once traded at as high as $35 a share, has nose-dived to just three to four cents a share.").

[161] *Nexell Therapeutics To Acquire Certain CellPro Assets,* BUSINESS WIRE (September 28, 1998); *CellPro Files for Bankruptcy, Sells Assets, Lawsuit Settled,* MARKETLETTER (October 5, 1998) ("U.S. biotechnology firm CellPro is filing for bankruptcy, its chief executive Rick Murdock has resigned, a number of jobs have been lost, it has sold off its assets and has settled a patent infringement lawsuit. CellPro has agreed to pay Baxter Healthcare Corp, John Hopkins University and Becton Dickson approximately $15.6 million after a U.S. appeals court ruled that the company infringed patents when developing its Ceprate SC hematological transplant system. As a result, the firm is to discontinue operations other than backup functions necessary to support a limited number of Ceprate kits for which Baxter will act as worldwide distributor. CellPro is also planning to sell nearly all its intangible assets and intellectual property to Nexell Therapeutics, a subsidiary of VIMRx Pharmaceuticals, in exchange for $3 million in VIMRx securities. Baxter also holds a minority stake in Nexell. CellPro says that the situation has forced it to file a bankruptcy plan of reorganization which will lead to the discontinuation of its European operations and the loss of 93 jobs worldwide.").

[162] Keith Ervin, *Media Focus Stays Fixed on Eastside,* THE SEATTLE TIMES (February 17, 1999) ("CellPro, a once-bright light of Bothell's biotechnology industry, is gone. But there's new life for 90,000 square feet of its former lab space in Canyon Park East. Another biotech luminary, Icos, has leased the space to gear up for expanded clinical trials of several promising drugs ….").

[163] *Definitive Agreement Signed to Restructure Nexell Therapeutics,* BUSINESS WIRE (February 23, 1999) ("Nexell's lead product, the Isolex (R) Cell Selection System, is marketed in a number of countries and is currently under final review by the FDA in the United States.").

[164] Seth Shulman, *Cashing In on Medical Knowledge,* 2(101) TECHNOLOGY REVIEW 38 (March 13, 1998) ("Andrew Yeager, director of bone-marrow transplant programs at Emory University, where physicians have been using the CellPro treatment with some success as a last-ditch effort to save lives of children suffering from acute leukemia, lamented to the Seattle Times: 'It's unfortunate that these sorts of things in corporate America can threaten therapeutic clinical trials and potentially life-saving therapies."DDD').

[165] *See, e.g.,* Rebecca S. Eisenberg, *SYMPOSIUM ON REGULATING MEDICAL INNOVATION: Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research,* 82 Va. L. Rev. 1663, 1708 (1996) ("Since its passage in 1980 the Bayh-Dole Act has been consistently hailed as an unqualified success in stimulating the commercial development of discoveries emerging from government-sponsored research in universities.").

[166] Kenneth Sutherlin Dueker, *Biobusiness on Campus: Commercialization of University-Developed Biomedical Technologies,* 52 FOOD DRUG L.J. 453, 466 (1997) ("Industrial support of university research increased from four percent of total funding in 1980 to seven percent of total funding in 1990."); *Money + Science = Ethics Problems on Campus; Corporations Supporting Research Brings Up Ethical Issues,* 11(268) THE NATION 11 (1999) ("In 1997 US companies spent an extraordinary $1.7 billion on university-based science and engineering research, a fivefold increase from 1977.").

[167] Dueker, *supra* note 166, at 465-66 ("The efficacy of the Bayh-Dole Act can be seen through a number of data. From 1974 through 1984, just over 1000 licenses were granted by universities; from 1989 through 1990, 10,510 licenses were granted.").

[168] G. Kenneth Smith, *Faculty and Graduate Student Generated Inventions: Is University Ownership a Legal Certainty?* 1 VA. J.L. & TECH. 4 ("A survey conducted by the Association of University Technology Managers (AUTM) in which 130 U.S. and Canadian schools responded determined that in the fiscal year 1992 academic institutions received 7604 invention disclosures, filed 3251 patent applications, were granted 1731 patent and received $260 million in gross royalties. In 1981 only $7 million was received in royalties.").

[169] Frederic P. Zotos, *Unlocking the Potential of Innovation,* INTELLECTUAL PROPERTY TODAY (February, 1998) ("One measure of success is the size of the royalties paid to the universities by their commercial partners. By this measure, universities have been quite successful. Royalties rose from $186 MM in 1991 to $424 MM in 1995."); *Money + Science = Ethics Problems on Campus; Corporations Supporting Research Brings Up Ethical Issues,* 11(268) THE NATION 11 (1999) ("According to the Association of University Technology Managers, a boosterish pro-alliance trade group, corporate licensing of university inventions now accounts for $21 billion in annual revenue, which in turn supports 180,000 jobs."); *cf.* Kenneth Sutherlin Dueker, *Biobusiness on Campus: Commercialization of University-Developed Biomedical Technologies,* 52 FOOD DRUG L.J. 453, 465-66 (1997) ("Such successes are the exceptions that make the rules. According to Lita Nelsen, Director of MIT's Technology Licensing Office

(TLO), most schools with 'successful' licensing programs receive between 0.5% and 2% of their total research budget from licensing royalty revenues and only plan to see 5% from licensing long term. Nelsen explains that 'with one or two exceptions, even the most successful university licensing offices receive licensing revenue equal to 1 or 2% of their universities' total research budgets. Most of these universities, and especially the exceptions with slightly higher percentages, rely on single "blockbuster" patents for the majority of their revenue."DDD').

170 Data generated by searching LEXIS: LEXPAT: UTIL for the following searches:
assignee(university) and date = 1979 [result 220 patents];
assignee(university) and date = 1989 [result 1,148 patents];
assignee(university) and date = 1998 [result 3,024 patents];
assignee(inc!) and date = 1979 [result 10,207 patents];
assignee(inc!) and date = 1989 [result 19,503 patents];
assignee(inc!) and date = 1998 [result 33,098 patents].

171 *See id.*

172 As determined by the search: assignee (university) and date = 1998 and (DNA or RNA or gene or protein or virus or bacteria) [result 1784 patents] 1784/3024= 59%. The field of biotechnology was born with the pivotal recombinant DNA technology work by Cohen and Boyer, in 1979. *See, e.g.,* U.S. Patent No. 4,237,224, issued Dec. 2, 1980, filed Jan. 4, 1979.

173 A similar search of IBM electronic patents, reflecting a field that is expanding as actively as biotechnology, showed an increase of 326 to 615 to 2660 patents over the same time period. Thus, electronic patents also grew almost ten-fold over the same period.

174 Thomas A. Massaro, M.D., *Symposium on Regulating Medical Innovation: Innovation, Technology Transfer, and Patent Policy: The University Contribution,* 82 VA. L. REV. 1729 (suggesting that the increase in university technology transfer may be due to factors in addition to the Bayh-Dole Act); Rebecca S. Eisenberg, *SYMPOSIUM ON REGULATING MEDICAL INNOVATION: Public Research and Private Development: Patents and Technology Transfer in Government-Sponsored Research,* 82 Va. L. Rev. 1663 (1996) (questioning the value of the Bayh-Dole Act).

175 *Id.*

176 David Shenk, *Money + Science = Ethics Problems on Campus; Corporations Supporting Research Brings Up Ethical Issues,* 11(268) THE NATION 11 (1999) ("It turned out that while just 3 percent of the calcium channel authors surveyed had publicly disclosed potential conflicts of interest, the percentage of those who should have--that is, the percentage of those who publicly favored the drug and had a financial relationship with the manufacturers--was a bit higher: 96[%]"); *Id.* (questioning, "[W]hat are we to make of a recent study published in JAMA suggesting that an astounding 43 percent of women and 31 percent of men suffer from 'sexual dysfunction'--once we also discover that two of the study's authors served as paid consultants to Pfizer, which manufactures Viagra? (The relationships were not disclosed in JAMA)"); Krimsky S. et al., *Scientific Journals and Their Authors' Financial Interests: A Pilot Study,* 67(4-5) PSYCHOTHER. PSYCHOSOM. 194-201 (1998) ("One of every three articles in our sample has at least one Massachusetts-based author with a financial interest.").

177 Deborah E. Barnes & Lisa A. Bero, *Why Review Articles on the Health Effects of Passive Smoking Reach Different Conclusions,* 279(19) JAMA 1566-70 (1998) (summarizing in the abstract that "[a] total of 106 reviews were identified. Overall, 37% (39/106) of reviews concluded that passive smoking is not harmful to health; 74% (29/39) of these were written by authors with tobacco industry affiliations. In multiple logistic regression analyses controlling for article quality, peer review status, article topic, and year of publication, the only factor associated with concluding that passive smoking is not harmful was whether an author was affiliated with the tobacco industry (odds ratio, 88.4; 95% confidence interval, 16.4-476.5; P<.001). CONCLUSIONS: The conclusions of review articles are strongly associated with the affiliations of their authors."); Henry T. Stelfox et al., *Conflict of Interest in the Debate over Calcium-Channel Antagonists,* 3381(2) N. ENGL. J. MED. 101-06 (1998) (summarizing in the abstract that "[a]uthors who supported the use of calcium-channel antagonists were significantly more likely than neutral or critical authors to have financial relationships with manufacturers of calcium-channel antagonists (96 percent, vs. 60 percent and 37 percent, respectively; P<0.001). Supportive authors were also more likely than neutral or critical authors to have financial relationships with any pharmaceutical manufacturer, irrespective of the product (100 percent, vs. 67 percent and 43 percent, respectively; P< 0.001). CONCLUSIONS: Our results demonstrate a strong association between authors' published positions on the safety of

calcium-channel antagonists and their financial relationships with pharmaceutical manufacturers.").

178 Christopher Anderson, *Agencies Set Rules on Financial Disclosure; Research-Funding Agencies,* 265(5169) SCIENCE 179 (1994) ("The new agreement, signed this week, ends a furor that erupted in December 1992 when Sandoz announced its intention to invest $300 million over ten years in return for right of first refusal to nearly all research at Scripps. Members of Congress and officials at the National Institutes of Health (NIH), which awards Scripps about $70 million a year in research grants, also questioned provisions that appeared to give Sandoz unusual control in shaping Scripps research and imposing restrictions on researchers.").

179 *Id.* ("One of the more controversial partnerships in biomedicine is back on track, now that the two parties--[Switzerland-based] Sandoz Pharmaceutical Corp. and the Scripps Research Institute of La Jolla, California--have bowed to political pressure and agreed to limit Sandoz's investment in and access to discoveries at the federally funded institution.") *Id.* (continuing "[Representative Ron Wyden (D-OR),] is particularly pleased with a promise by Scripps to help small businesses, such as start-up biotech companies, in licensing technology that Sandoz passes over. Scripps intends to give small businesses 6 months to claim such research, as well as to open an office to assist them and to reinvest some of its Sandoz royalty income to improve ties with such companies.").

180 *Id.* ("The Scripps Research Institute is back in the congressional doghouse. The La Jolla California, institute took a beating last year for a deal with the Sandoz Pharmaceutical Corp. that would have given the [foreign] company the first fruits of its federally funded research; now it stands accused of failing to disclose that the research behind 43 patent applications was partially funded by the government.").

181 Teresa Riordan, *Patents Keeping Track of Federally Aided Technology is the Subject of a Congressional Hearing Today,* THE NEW YORK TIMES, Late Ed., Section D; Page 2; Column 4 (July 11, 1994) ("The Inspector General's office focused on the Scripps Research Institute in La Jolla, Calif., finding that Scripps had acknowledged Government financing in 51 of 121 patents reviewed. Investigators considered that a suspiciously low number given that Scripps, the largest nonprofit biomedical research institution in the United States, gets $70 million of its annual $120 million budget from N.I.H. and other Government sources … 'Scripps is a microcosm,' Mr. Wyden said in a telephone interview last week. A number of institutions spot-checked by the Inspector General, he said, 'appear to have a rather dramatic under-reporting of Federal involvement in technology that is later patented."DDD').

182 *Prepared Statement of the Honorable June Gibbs Brown Inspector General, Department of Health and Human Services Before the Subcommittee on Labor, HHS and Education Committee on Appropriations U.S. House of Representatives,* FEDERAL NEWS SERVICE (January 12, 1995) (testifying that "[i]n one case, involving oversight of extramural research inventions, we found that: the National Institutes of Health (NIH) have limited its oversight of grantees by not requiring documentation for some Federal requirements; lacks a systematic process for ensuring that grantees submit all required invention information; and does not fully utilize its invention database to monitor grantee compliance.").

183 Pat K. Chew, *Faculty-Generated Inventions: Who Owns the Golden Egg?,* 1992 WIS. L. REV. 259, 296-97 (1992) ("The federal government is the largest source of research funding. The National Institutes of Health (NIH), National Science Foundation, and the Department of Defense provide about 80% of total federal funding of academic research, with NIH providing almost 50% of the total.").

184 David Shenk, *Money + Science = Ethics Problems on Campus; Corporations Supporting Research Brings Up Ethical Issues,* 11(268) THE NATION 11 (1999) ("According to the Association of University Technology Managers, a boosterish pro-alliance trade group, corporate licensing of university inventions now accounts for $21 billion in annual revenue, which in turn supports 180,000 jobs.").

*240 APPENDIX

Chronology of Events

• Baxter takes an exclusive license from Becton for $1,250,000 and an 11% royalty in August 1990.

• Baxter sub-licenses the invention again for $750,000 and a 16% royalty in December 1992.

• Baxter offers CellPro a sub-license for $750,000 plus a 16% royalty in early 1992.

• CellPro counteroffers $500,000 to be credited against future 16% royalties.

• Baxter files for an exclusive distribution license in Europe and Japan and nonexclusive license in the U.S.

• CellPro files DJ action in Washington in April 1992.

• Sales of CellPro's Ceprate SC begin in Europe.

• CellPro's DJ action is dismissed in September 1993.

• Baxter sub-licenses again for $750,000 and a 16% royalty in November 1993.

• Baxter obtains European approval for the Isolex 300A.

• CellPro seeks to accept Baxter's original $750,000 and 16% royalty offer in March 1994 and Baxter responds that a greater royalty is now required.

• A jury finds for CellPro on virtually all issues in August 1995.

• Court finds for Hopkins on JMOL on some issues and orders a new trial on others in June 1995.

• Federal Circuit denies CellPro's petition for mandamus in October 1996.

• CellPro obtains FDA approval for Ceprate SC in December 1996.

• Baxter submits PMA for Isolex 300I in February 1997.

• CellPro files a petition for march-in rights in March 1997.

• Court orders CellPro to pay treble damages of $7 million in July 1997; the injunction is partially stayed until Baxter's system obtains FDA approval.

• CellPro's petition is denied by NIH.

• CellPro loses claim interpretation, enablement, and obviousness appeal to the Federal Circuit in August 1998. CellPro wins on the issues of repatriation and introduction of prior art.