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Ms. Penny Dalziel
Association of University Technology Managers
49 East Avenue
Norwalk, CT 06851
Phone: (203) 845-9015
FAX: (203) 847-1304

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Volume VII **1995**

Editor's Preface

Volume VII of the *AUTM Journal* focuses on the importance of establishing a process for evaluating invention disclosures and licensing activities to make the most of potential benefits in the face of limited resources. This volume also brings a special treat to the reader through Niels Reimers' article telling how the emerging biotechnology industry was stimulated through an innovative and rewarding licensing strategy. An interesting piece from MIT proposes one model by which universities can examine the contributions of technology transfer to the economy. The *Journal* concludes with a caution to licensing managers to guard against increasing benefits at the expense of committing antitrust violations.

Julia Watson and Beth Fordham-Meier begin our discussion with their paper, "Invention Triage: Allocating Resources for Maximum Benefit," in which they identify criteria that can be used to help make the difficult "go/no go" decisions we all face in evaluating invention disclosures.

In his paper, "Appraising Inventions: The Key to Technology Management," John Perchorowicz uses a hypothetical case study to present a practical approach to technology appraisal, including a risk-adjusted valuation.

A highlight included in this *AUTM Journal* is "Tiger by the tail," by Niels Reimers. This paper, originally published by *CHEMTECH* in 1987, describes the elegance, magnitude, and importance of the Cohen-Boyer licensing program. It clearly illustrates how the realities encountered in valuing technology can be used to shape a licensing strategy that promotes the best outcome.

Using information specially gathered from MIT's licensees, Lori Pressman and her co-authors evaluate MIT's experience in stimulating investment through invention licensing. The authors set out to assess licensing in the context

of the objectives of the Bayh-Dole Act and to quantify the economic impact of active exclusive patent licenses. They and we hope that this paper will inspire other universities to employ models to examine investment induced by each university's licensing activities.

Kathleen Terry brings us up to the present with her paper, "Antitrust and Technology Licensing," in which she warns us that because of increased attention by the Department of Justice to intellectual property business arrangements, it is increasingly important to scrutinize our licenses for antitrust violations and patent misuse. This article assists the license drafter to recognize, analyze, and avoid potential problems.

On behalf of the AUTM Editorial Board, I extend our sincerest thanks and appreciation to Jean Mahoney, who has served as the Editor of the *AUTM Journal* since its inception six years ago. I also welcome our new members to the Editorial Board and look forward to their influence on the *Journal.*

The Editorial Board of the *AUTM Journal* is interested in receiving letters and comments from its readers concerning issues raised in published articles or on other matters of interest to our colleagues. Letters may be considered for the "Letters to the Editor" section or forwarded to the individual author for reply, at the discretion of the Editor.

We encourage our readers to submit original papers on topics of interest to professional technology managers. Those contemplating writing an article or a letter to the Editor are asked to contact the Managing Editor for content and review procedures.

Beatrice Bryan, Editor
September, 1995

Invention Triage: Allocating Resources for Maximum Benefit

Julie M. Watson*
Beth W. Fordham-Meier*

Technology transfer professionals managing offices that are overworked, understaffed, and undercapitalized are challenged to allocate scarce resources productively. A system in which resources are given only to those inventions that will derive the greatest benefit has been termed "invention triage."

At the Eastern Regional 1993 and Annual 1994 meetings of the Association of University Technology Managers (AUTM), workshops were conducted in which groups of technology transfer professionals considered sample inventions for application of the triage system. Participants were asked to first identify questions that are critical to determining an invention's potential value and then, based on their hypothetical answers to these questions, recommend the most productive course of action for each sample invention. Participants were urged to first consider the entire invention portfolio and then distribute available resources to realize maximum benefit. From the workshops, we hoped to learn the general criteria used by technology transfer professionals to assess an invention's

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* *Julie M. Watson is Assistant Dean for Research Administration at the Bowman Gray School of Medicine and Patent Administrator of Wake Forest University. Beth W. Fordham-Meier is Technology Transfer Specialist at Wake Forest University.*

potential, and the typical action plans derived from the application of such criteria.

The workshops allowed us to identify key factors used by technology transfer professionals in evaluating inventions. We also learned that, although technology transfer professionals more aggressively pursue those inventions that they think most promising, they seek to identify the minimum action necessary to keep *every* invention alive. The results of this strategy were predictably dismal -- participants were unable to complete their critical assessment of the entire invention portfolio, yet still managed to overspend their budget.

In this paper, we summarize the criteria identified by technology transfer professionals as most predictive of invention success and suggest a system for employing those criteria for invention triage. We argue that an applied system of invention triage, focused not on maximizing the potential of each invention but instead on maximizing the overall return, is an appropriate strategy when resources are scarce.

CRITERIA FOR INVENTION EVALUATION

The following criteria were identified by workshop participants as pivotal in assessing probability of success for sample inventions:

Intellectual Property Protection. Does the invention provide some proprietary angle? Is the invention protectable, whether by patent, trademark, copyright, or the possession of some tangible property?

The workshop participants heavily weighed the potential protectability of an invention to determine its value. In fact, participants were tempted to concentrate on the question of patentability as an end rather than a means to commercialization.

Urgency. Workshop participants promoted even mediocre inventions to the forefront if they faced a bar and thus a threat to protectability. Facing a deadline limited the participants' critical assessment of an invention; when there was a deadline, the participants opted to protect the invention and then considered their invention assessment complete.

Novelty. The degree of novelty and the assessment of competitive technologies were important to the workshop participants. Incremental improvements were considered less valuable than major advances; even the most embryonic inventions thought to have a high degree of novelty were considered more valuable and thus more worthy of resources than later-stage, but incremental, improvements.

Inventor. An inventor described as cooperative, enthusiastic, or eager to participate in the transfer process was thought to increase the probability of success in transferring an invention. Workshop participants were leery of pursuing inventions in which the inventor was described as being uncooperative. However, inventors who were recognized as international experts, even if difficult and unsupportive, were considered assets to the transfer process.

Market Size. Workshop participants were satisfied with determining market size and an invention's potential market impact based on qualitative assessments. Participants who believed that the market was "big enough" to warrant transfer attempts did not feel that they needed to obtain hard numbers or confirm the inventor's assessment before making a decision to pursue.

Expertise of Technology Transfer Professional. Although not explicitly applied, participants were biased toward inventions that fell within their areas of expertise or past experience. Participants readily recognized the value of even incremental improvements in their areas of expertise and identified creative applications of the technology that had not occurred to others.

APPLYING INVENTION TRIAGE

Workshop participants in both AUTM sessions sought to do something for *every* invention, whether or not an invention met the criteria they had defined for success. Technology transfer professionals are often reluctant to decline or release inventions and, as a result, shelve some inventions indefinitely. In a triage environment, scarce resources spread thinly across a large invention portfolio will not result in maximum payoff. Because it is impossible to allocate the time and money necessary to transfer every invention, we must be willing to decline or reject those inventions that are least deserving of our limited resources.

In order to successfully apply a triage system for invention management, we must critically consider whether it is more productive to work intensely on two projects rather than less intensely on four. We must be comfortable using others to help us transfer those inventions that fall outside our areas of expertise or require more resources than we can allocate. Finally, we must be willing to say no to inventions that are not worthy of our attention, and encourage their release through scientific publication. Abeyant and inactive categories should be the exception, not the rule.

Using Assessment Criteria in a Triage Environment

Invest Your Time at the Right Time. As soon as is practical after receiving a new invention disclosure, formulate the critical questions that are necessary to determine the invention's potential for success, and find a way to at least estimate answers to those critical questions. One technology transfer professional described her system of allocating an entire business day to evaluating and developing an appropriate transfer strategy for each new invention disclosure. She reasoned that if an invention warranted her time and money to effect its transfer, it surely warranted her time in initial critical assessment.

Although many technology transfer professionals are satisfied with qualitative assessments of an invention's potential market, it would be beneficial to obtain at least one hard number to provide some confirmation of your instinct and the inventor's view of the world. Developing some rudimentary understanding of market competition, size, and an invention's potential impact may help you better apply a system of invention triage.

Avoid Crisis Management. Bar dates for patenting an invention create situations that tempt us to act on projects that are urgent but may not be important or valuable. In addition, deadlines often inhibit our ability to carefully consider pertinent issues that help us determine the best course of action. Although we can't always control deadlines, we should avoid creating emergencies by considering inventions immediately after disclosure and allowing ourselves sufficient time for critical assessment.

Keep Your Objective in Focus. In a triage environment, it is critical to remain focused on your objective. If it is the successful transfer of an invention for the public benefit that drives your program, allocate your time and money only to those potentially beneficial inventions that require your specialized expertise to be transferred. Recognize that the public interest can sometimes be better served by disclosure of an invention through scientific publication. If the primary objective of your program is to return dollars to your institution, then don't spend time or money on inventions that, even if transferred, are unlikely to provide a big payoff. Finally, unless your program's objective is to enlarge your patent portfolio, remember that obtaining a patent is only a part of the transfer process and will not ensure that an invention can be successfully transferred. Whatever your program's mission, keep it firmly in focus as you make day-to-day decisions to allocate scarce resources.

When to Say Yes

To warrant allocation of your scarce resources, an invention should meet the following criteria:

Protectability. Protecting inventions provides incentive for companies to transform embryonic technologies into marketable products, and therefore should be the minimum requirement for you to pursue an invention. When assessing protectability, concentrate as much on enforceability as on patentability. If an invention is not protectable or you are unable to induce a company to give you something of value for it, you should not allocate scarce resources to effect its transfer.

Sufficient Novelty and Market Size. Determine if an invention's potential impact is sufficient to warrant the allocation of your time and money. This determination should not be based solely on instinct but on at least some rudimentary market research. If you determine that the market is small and that the invention will impact only a select few, encourage the inventor to release the invention directly to an interested company or by publication in scientific journals.

Consistent with Institutional Mission. Consider investing your scarce resources only in those inventions that may benefit the public in ways that further your institutional mission. For example, a technology transfer professional at a medical school should not allocate resources to transfer a novel electronic shooting range at the expense of inventions that may impact patient care. In addition to issues of novelty and marketability, think critically about the *subject* of an invention before allocating your time and money to effect its transfer.

When to Say No

Lack of Protectability. If an invention is not protectable, or if the available protection is unlikely to be enforceable, or if you are unable to conceive of a method to induce a licensee to

provide you with some value in exchange for the technology, decline or release it. Your time is too valuable to allocate precious resources in effecting transfer that could be accomplished through scientific publication.

Low Degree of Novelty and Small Market Impact. If your invention is only a minor improvement or will benefit only a select few, it does not merit your time and money. Recognize that it is appropriate for you to release technologies that may be inventive but won't provide a big enough "bang for the buck." Again, the suggestion is not to bury the discovery within your institution's walls, but to release the discovery to the public through scientific publication.

Not Consistent with Institutional Mission. If an invention has merit but is not consistent with your institutional mission, it does not deserve your time and money. Consider deputizing the inventor or using a technology licensing agent to transfer the invention, but do not allocate your scarce resources. Remember that, in a triage environment, your resources should be directed only toward those inventions that will provide the greatest benefit to the public and your institution.

When to Use Others to Transfer Technology

In a triage environment, certain inventions may have merit but do not meet all of the criteria for success. Other inventions that are less embryonic and more readily marketable, or that fall outside your areas of technical or licensing expertise, may not require your time and attention to be transferred. Rather than passively marketing or forever relegating these inventions to an abeyant category, consider whether they might be successfully transferred by others without diverting resources from those inventions that do need your particular expertise. Begin to think of yourself as a general practitioner that sometimes needs to refer certain inventions to a specialist or a paraprofessional. Options for using others to transfer technology include:

Deputizing the Inventor. Consider using the inventor to market his or her invention if he or she is enthusiastic, eager to participate directly in the transfer process, and understands how technology transfer furthers your institutional goals. Clearly, the inventor must keep you informed and recognize your authority on transfer issues, especially during the license negotiation stage. However, the inventor is the expert of his or her invention and can assist in the transfer process by effectively becoming an extension of your office.

Use a Technology Licensing Agent. Consider using a technology licensing agent if an invention requires a highly complicated license strategy that may be a significant drain on your scarce resources. If you are unable to allocate necessary resources to a worthy project, it is sometimes appropriate to seek the help of an agent. Likewise, an invention that falls outside your areas of expertise may be better exploited by an agent that understands and has contacts in the pertinent field. Technology licensing agents are also helpful if you have a conflict with your inventor -- an agent may be what is needed to form a more cohesive licensing team.

CONCLUSION

An invention triage system, conscientiously applied, should effectively reduce your workload and increase the productivity of your efforts. Critical assessment of each invention at the evaluation stage can minimize hours spent on unproductive or futile activity later in the process. Before adding an invention to your active portfolio, convince yourself that it provides some proprietary protection, is of sufficient novelty and market potential to warrant the hours and dollars you will invest, and fits within your institutional mission. If the invention doesn't meet these criteria, eliminate it sooner rather than later.

We are not always in a triage environment and often have conflicting objectives. Inventor satisfaction demands, portfolio development, and economic development activities can

intervene and influence resource allocation decisions. Even in these situations, though, strive to critically evaluate both the invention and your options, and understand the effect these decisions have on your overall program. Avoid simply asking yourself, "Can I do *something* with this invention?" The answer is too often yes, and striving to maximize the potential of every invention is a luxury your program may be unable to afford.

Appraising Inventions: The Key to Technology Management

John T. Perchorowicz, Ph.D.*

ABSTRACT

The process of developing a commercialization strategy for an invention begins with evaluation of its commercial potential at its current state of development. The evaluation includes assessments of technical feasibility, patentability, and marketability. Further appraisal of risk and time factors, costs, and estimated revenue yields a risk-adjusted present value. A hypothetical septic shock treatment provides a model of an appraisal that includes estimates of market demand and penetration, royalties and income.

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* *John T. Perchorowicz, Ph.D., is an Associate in the Institutional Relations Group of Research Corporation Technologies.*

INTRODUCTION

When an organization seeks to maximize the value of an invention through development or licensing, the commercialization process begins with an appraisal that includes analysis of technology, patentability, and marketability, as well as calculation of the expected value through the term of the patent. Technology managers allocate limited human and financial resources to inventions in their portfolios on the basis of rational assessments of factors such as anticipated risk, cost, time, and revenue.

The hypothetical case in this article presents a greatly simplified example of RCT's approach to technology appraisal.

TECHNICAL ASSESSMENT

The technical assessment defines the inventive concept, its theoretical basis and scope, as well as potential commercial applications and technical value.

A broad, objective review of fields in which the invention may have an impact requires unbiased research by an individual who understands the technology from a scientific perspective.

Resources available to the assessor include the inventors, their academic and industrial contacts, and searches of published technical articles and patents. Inventors often recognize their colleagues' technical publications but they rarely investigate patents. Often, industrial contacts provide useful information despite their biases and potential conflicts.

A vision of potential products results from an understanding of the invention's technical limitations. The assessor must identify other technologies required for commercialization, unprecedented products or markets, potential for circumvention of the patent, difficulty of detecting infringement, potential users of the technology and their motivations, and the costs and

benefits of adopting the technology in comparison to available or anticipated functional equivalents.

PATENTABILITY ASSESSMENT

An assessment of patentability provides a basis for formulation of patent strategy and an understanding of the strategy's strengths and weaknesses in relation to potential markets for defined products. An initial investigation reveals any bars to patent rights due to publications or failure to meet requirements for utility and enablement. Licensable claims must adequately cover the envisioned products.

A monopoly advantage enables the seller to induce and protect investments in product development. If a monopoly is unavailable, then a dominant patent position yields more value than a subservient position. The ability to either dominate follow-on technology or block current technology will provide value and leverage in licensing.

Geographic breadth of patents in countries where the invention will be practiced protects both licensee and licensor in their efforts to exclude competition for a time and maximize return.

Practicality and economic feasibility determine the capacity to enforce patents. Consider, for example, a new, unapproved use for a drug that is currently marketed for an approved use. Physicians could infringe patent claims for the new use by writing prescriptions for the unapproved use of the drug. Such infringements prove difficult to detect and costly to prosecute case by case.

Finally, infringements of patent claims to a process for making a product obtainable by other means may prove difficult to detect, unless the product bears traces of the claimed process. Alternatively, an unpatented process may circumvent the contemplated patent. Consideration of all these factors permits a determination of a patent's value to the licensee.

MARKET ASSESSMENT

The goals in market assessment include determination of the technology's expected value in marketable products, identification of potential licensees, and development of a commercialization strategy. After identification of optimum and secondary commercialization paths, the licensor can estimate appropriate royalty rates. While royalty rates bear directly on value, we need not repeat here the many published techniques for their determination. Rates and calculation theories vary among industries and technologies, based in part on their impact upon the final product's value.

Other factors that may require consideration include exclusivity, developmental investments, start-up companies, marketing costs and environment, competing technologies or products, and the target industry's receptivity to new ideas and willingness to invest in them.

FINANCIAL ANALYSIS

A financial analysis estimates the present value of a technology, an important value for planning decisions such as whether to allocate resources to commercializing the invention, and how to structure and value investments. While technical, market, and patentability factors impact analyses, true value determinations also consider risk factors, costs, time, and revenue.

A naive analysis would set the present value of an incremental improvement to a technology—say, a cure for a disease—based on the erroneous assumption that the market equals current expenditures for treatment of the disease.

The more sophisticated analysis modeled below values a product for the interdiction or treatment of septic shock. Septic shock results when patients with systemic bacterial infection experience circulatory collapse, a severe drop in blood pressure with its associated complications. This blood pressure drop

generally occurs rapidly, does not respond well to the usual pressor agents, and often leads to death within 24 hours. Each year in the United States and Europe, one million people develop sepsis and 35% die of the disease.

Rather than an intervention in the infectious cause of septic shock, this technology merely allows maintenance of blood pressure, prolonging the period during which the bacterial infection can be treated. The data in this example offer only an illustration rather than an exhaustive analysis.

The analysis begins with the patent's filing date, in this case of a GATT patent that will expire 20 years from that date. This determines the period of time during which revenue can accrue.

Next the appraiser determines the number of septic shock patients that could benefit from the treatment, how many will be treated, and how that number might change with time based on the expected date of product marketing and the percentage of market that would be captured if this were the sole available treatment. A treatment price provides the basis for an approximate calculation of sales and income, assuming a royalty rate reasonable to the industry.

Table 1 shows a financial analysis that employs these factors to calculate a present value for the royalty stream of about $23 million, calculated at a discount rate of 12%. Costs of patenting, development, and marketing are excluded in this table.

Table 1. Market for Septic Shock Treatment

Year	Patients (thousands)		Market	Treatment	Royalty at
	Sepsis	Shock	Penetration (%)	Market ($K)	5% ($K)
1995	1,000	500	0	0	0
1996	1,010	505	0	0	0
1997	1,020	510	0	0	0
1998	1,030	515	0	0	0
1999	1,041	520	0	0	0
2000	1,051	526	0	0	0
2001	1,062	531	30	47,768	2,388
2002	1,072	536	65	104,533	5,227
2003	1,083	541	80	129,943	6,497
2004	1,094	547	90	147,648	7,382
2005	1,105	552	90	149,124	7,456
2006	1,116	558	90	150,615	7,531
2007	1,127	563	90	152,121	7,606
2008	1,138	569	90	153,643	7,682
2009	1,149	575	90	155,179	7,759
2010	1,161	580	90	156,731	7,837
2011	1,173	586	90	158,298	7,915
2012	1,184	592	90	159,881	7,994
2013	1,196	598	90	161,480	8,074
2014	1,208	604	90	163,095	8,155
2015	1,220	610	90	164,726	8,236
				Present Value at 12%:	22,736

The model assumes that the invention occurred in 1994, no divulgation created a patent bar, and a provisional patent application was filed in 1995 to gain a year toward a formal filing and start of the clock toward patent expiration. For simplicity, this example assumes that one worldwide patent application was filed and that all patent actions occurred on the first day of the year. The patent therefore expires at the end of 2015, together with the right to collect royalties.

We also assume that one million people in regions covered by patents will contract sepsis in 1995. Estimating conservatively, the patient population increases 1% per year. Half will experience septic shock, including the symptoms of circulatory collapse described above for which the product is appropriate. Nearly all patients who experience shock will be treated. The cost of the treatment is set at $300.

The model further assumes that a product will achieve development, FDA approval, and marketing by 2001. During that first year of product life, the treatment will capture 30% of the potential market, ramping up to 90% over three years and maintaining that level for the life of the patent.

We can now calculate the market size and the royalty return based on a royalty rate of 5%. Calculating a present value at a discount rate of 12% yields $22.7 million.

The large present value of the royalty stream predicted by this best-case scenario seems to call for commercialization of the invention. However, this model does not account for the risks associated with developing the product and bringing it to market. The present value falls to $98,000 after adjustment for the risk factors summarized in Table 2.

Table 2. **Impact of Risk Factors on Present Value**

Risk Factor	Probability	Risk-Adjusted Present Value
Patent issues in strength and geographic breadth desired	80%	$18,189,000
Patent survives future legal challenges	90%	$16,370,000
Company licenses project in current state of development	10%	$1,637,000
Regulators grant final approval	1%	$164,000
Public accepts product	100%	$164,000
Public prefers product	60%	$98,000

Selection and quantification of appropriate risk factors results from extensive experience, research, and debate. These numbers, while inexact, provide a framework for rigorous critical analysis of a project's value, trackable over time as the probabilities of factors change.

At the time of most technology appraisals, the patent has not been filed. Additionally, despite the inventor's knowledge about his scientific competitors, the appraiser must conduct adequate industrial research to gain a sense of the anticipated patent's ability to dominate competing technologies. This perspective permits prospective licensees or investors to gauge potential returns.

The geographic breadth of patents also directly influences the ability to collect royalties. We could further assign a probability of patents issuing in each geographic region of importance and include a factor for each patent's strength. All of these risk factors change fluidly as additional information becomes available.

If we multiply the probability of obtaining a patent, set at 80%, by the probability of its surviving legal challenges, set at 90%, the overall probability of patent success falls to 72% at present. Because anticipated patents issue in all important areas, the

80% probability of issuance rises to 100% and ceases to negatively impact value, while the probability of surviving legal challenges may also change.

Similarly, each stage of technical development merits assignment of a degree of risk. University-derived technologies rarely permit easy assessment of the value of final products. Usually years of high-cost research precede product definition, development, and introduction.

The non-risk-adjusted value in the model assumed an existing product. Realistic risk factors include the project's attractiveness at its current state of development to a prospective licensee. This factor is influenced by performance of additional research to reduce the risk perceived by the licensee.

A more difficult assessment to control, the ability of a licensee to produce a marketable product, varies according to intensity of motivation, availability of capital, and influence of the product champion in driving the development process.

Recently, several products designed to interrupt the physiological progression in sepsis leading to circulatory collapse failed to gain regulatory approval following clinical trials. In light of this experience, we estimate the probability of licensing success for the product in its current state of development at only 10%. The potential licensee might view this as the probability of successfully obtaining regulatory approval. This probability would increase as additional data demonstrate the safety and efficacy of the treatment.

The likelihood of final regulatory approval might not exceed 1% based on industry experience with technologies at an equally early stage. If the compound proves effective in acute-care settings when administered for short time periods, long-term toxicity and safety issues may not arise. If these issues became significant, the estimate of probability of success would

decrease. The compound must complete pre-clinical trials and Phase I, II, and III clinical trials. In this case, investigators can easily measure the uncomplicated end points for clinical trials: blood pressure or mortality. We anticipate low toxicity based on available information. At any point in the regulatory process, failure will drive the probability of success to zero along with the present value of the technology. Conversely, this probability increases upon achievement of regulatory milestones.

Public acceptance generally follows approval by regulatory authorities. In this case we define the consumer as the prescribing physician. In Table 1, a market penetration of 90% represents knowledge of the need for intervention and recognition of a particular treatment. We assume a probability of acceptance by physicians of 100%. Note that this factor differs from market share as discussed below.

Patients could, of course, refuse treatment despite the advice of their physician. Recent products that encountered consumer resistance despite regulatory approval include genetically engineered tomatoes and milk produced using hormones.

Ability to differentiate the product relates to consumer preference. Although we have identified no competitors so far, some probably will appear eventually. The risk factor for competition depends on how users view this technology's differential utility, such as decreased side effects or increased benefits.

The model assumes that the product will reach the market first, capturing significant market share and recognition as an effective treatment. Assuming that competing products reduce this preference by 40%, we set the factor for product differentiation at 60%.

We calculate the probability of achieving success by multiplying together all of the assigned probabilities. For our example, this probability approximates 0.04% or 1 in 2,000. Based upon past

experience with technologies at a similar stage of development and risk profile, this probability proves sufficient to attract investment interest compared to most university-derived technologies.

Alternatively, to value an investment in the technology or to sell it outright, we could multiply the probability of achieving the present value derived in Table 1 by the probability of attaining successful introduction (the product of all of the probabilities in Table 2). This yields a value of about $100,000 for the invention at its present state of development.

This estimated value should achieve accuracy within an order of magnitude if it employs reasonably accurate risk factors. Frequently, errors arise from inclusion of the same risk in more than one factor or from over- or under-estimating requirements for commercializing the invention. Naturally the accuracy of estimates increases as a product approaches realization.

How can we apply these estimated values? In addition to the previously mentioned determination of selling price, the estimate permits allocation of constrained resources to maximize value. Valuing technologies allows prioritizing of development efforts.

Additionally, we can examine the impact of alternative actions on value. For example, the value added by experiments that the inventor might do to reduce risk can be estimated against the cost in dollars or equity ownership. Similarly, an investor who funds successful experiments may expect to receive an increased share of equity in return for the investment. Alternatively, the investor withholds funding if the cost of a particular step outweighs an increase in value.

Time rules the commercialization process, particularly revenue production. Although we can license a patent application, we could not enforce it against infringement prior to issuance. Thus we seek a licensee who will commercialize the invention as

quickly as possible to generate royalty income over the longest possible period until patent expiration. For our case study, royalties could reach $20,000 per day in the best-case scenario. Each day lost reduces income once the patent clock begins to run down.

An exclusive licensee will demonstrate high motivation to maximize return on investment by marketing a product as soon as possible, particularly if generic products promise to reduce market share and product price upon the expiration of the patent. Licensees of pharmaceuticals may experience difficulty in strengthening a monopoly position during the life of the original patent with new patentable material. Regardless, the licensor probably will not share in revenue derived from such additional patents.

Costs of developing and maintaining the technology also negatively impact the revenue stream in a number of ways. The licensor's cost of obtaining and defending patents is not included, because it probably will approximate the cost for similar pharmaceutical projects.

Likewise we excluded the licensee's development cost, which would figure into such revenue calculations as the amount of pre-royalty payments likely to be extracted. We included these costs indirectly in setting the probability of obtaining a license and gaining regulatory approval. A licensee performing this same exercise would balance its calculations of cost to license and develop product against expected profit. A licensor can take these into account when determining the type of licensee capable of affording the development of a technology.

This model, modified as needed over the life of a technology, guides allocation of resources, pricing of deals, and valuation of equity and investments. Much experience and research must inform the selection of the numbers entered into the simple spreadsheet and probabilities assigned to the risk profile. This effort affords a rational basis for making decisions about the

value of a technology and the factors affecting its commercialization.

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Tiger by the tail

When Stanford tried to license a recombinant DNA discovery, the legal implications and regulations of biotech were still untamed wilderness.

Niels Reimers*

It all began on a balmy evening in Hawaii at a Waikiki Beach delicatessen where Stanley Cohen of Stanford and Herbert Boyer of the University of California at San Francisco were excitedly engaged in a conversation. This conversation occurred in November 1972, at the time of a United States-Japan joint meeting on bacterial plasmids.

Herbert Boyer had been working on restriction enzymes, which "cleave" DNA at a particular site. Meanwhile, Stanley Cohen had been working in his laboratory on plasmid DNA. They contemplated that, with Boyer's restriction enzymes and Cohen's plasmid technology, it might be possible to insert foreign DNA into a plasmid, insert that plasmid into a living organism, and have that living organism replicate and produce expression products as directed by the foreign genetic information (Figure 1).

By March 1973, Cohen and Boyer achieved success in DNA cloning. They immediately perceived the importance of their discovery and began to prepare a publication, which appeared in November 1973. Prior to this publication, in June 1973,

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* *Niels Reimers, formerly the director of the Office of Technology Licensing at Stanford University, is now a principal at Intellect Partners in Palo Alto, California.* *This article is reprinted with permission from CHEMTECH, August 1987, 17 (8), pp. 464-471.*

Boyer attended a Gordon conference at which molecular biologists immediately recognized the incredible potential of the discovery. Some believed that Pandora's box had been opened and a possibility now existed that manmade organisms could escape from a laboratory and cause unknown diseases. One month after the Gordon conference, Maxine Singer and Heinrich Soll sent the National Academy of Sciences a thoughtful letter that initiated debate over the safety of recombinant DNA research. The letter was published in *Science* but aroused little public interest.

Figure 1

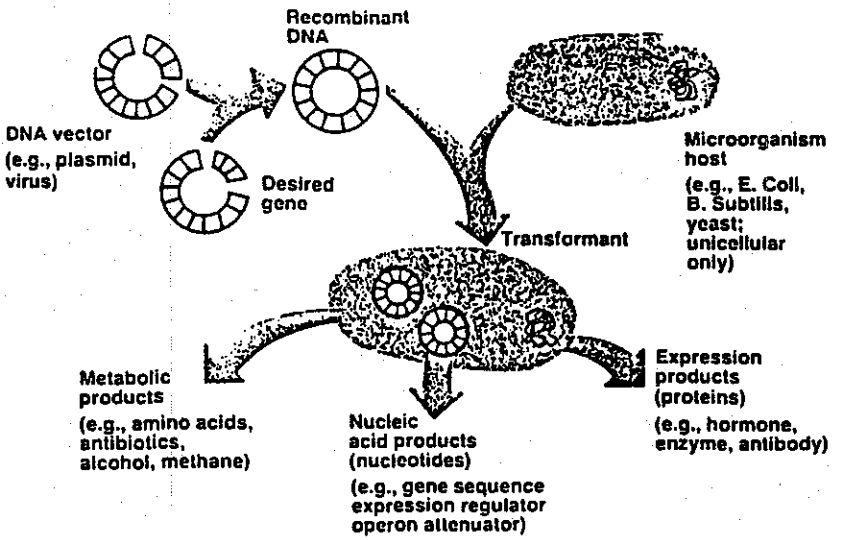

Figure 1. **Gene splicing procedure**

Another letter to *Science*, published in July 1974, did get the public's attention. This was by Nobel Laureate Paul Berg of Stanford and 10 other scientists (including Cohen and Boyer) who called for the National Institutes of Health (NIH) to establish safety guidelines for recombinant DNA research and asked scientists to observe a moratorium on certain DNA research of unknown biological hazard pending the issuing of those guidelines. We'll come back to the safety issue later.

In early April 1974, Vic McElheny, then a science writer for the *New York Times* and now a research associate at the Massachusetts Institute of Technology (MIT), noticed an article regarding the repressor gene. In pursuing this story, he learned two interesting facts. One was that there had been a meeting in Cambridge, Mass., to draft "the letter" by Paul Berg, *et.al.*, referred to above. The other fact was that there was a paper about to be published in the *Proceedings of the National Academy of Sciences* (*PNAS*), by Cohen, Boyer, and colleagues, entitled "Replication and Transcription of Eukaryotic DNA in *Escherichia coli*." Genetic information from a toad was successfully introduced into bacteria, crossing the species border. This work led McElheny back to the November 1973 *PNAS* article. McElheny's article in the *New York Times* on May 20, 1974, was forwarded to me that same day by Bob Byers, campus news director at Stanford University. This was my first knowledge of the work, and it looked like a promising licensing opportunity. Later that day, I received a news release from Stanford's Medical Center News Bureau, announcing the research results and their implications.

I called Stan Cohen to discuss the potential practical applications of this research. He acknowledged that the discovery was of great scientific significance, but he stressed that he did *not* want to have it patented and that, although there was great potential, significant commercial application might not occur for 20 years. After considerable discussion, he finally agreed that a patent application could be investigated. This investigation led me to Herb Boyer of the University of

California (UC) at San Francisco who, after some discussion, agreed to cooperate on the basis of Stan Cohen's willingness.

We contacted Josephine Olpaka, of the UC Patent Office, with the proposition that if the rights in the invention could be straightened out, assuming Cohen and Boyer were co-inventors, Stanford would manage the patenting and licensing of the technology, sharing net royalties 50-50 after deduction of 15% of gross income to Stanford for administrative costs and then deducting out-of-pocket patent and licensing expenses. Agreement was reached between the university and the inventors. But there was another hurdle.

In the storm of applications

Three research sponsors were involved in the discovery: the American Cancer Society, the National Science Foundation (NSF), and NIH. We were not aware of a precedent where the American Cancer Society had released any invention to any grantee. Eventually, the American Cancer Society, NSF, and NIH all agreed that the invention could be administered on behalf of the public under the terms of Stanford's "institutional patent agreement" with NIH. These administrative matters got straightened out just in time for us to file a patent application on Nov. 4, 1974--one week before the one-year U.S. patent bar was to occur on the basis of the November 1973 *PNAS* publication.

Remember, we learned about the discovery many months after publication; the delay precluded our chances of getting patent coverage in other countries. (*For more information on patenting biotechnology, see References 1 and 2.--Editor.*)

In the meantime, the informal moratorium on recombinant DNA research continued. In December 1974, scientists were invited to an international conference to review the progress, opportunities, potential dangers, and possible remedies associated with the construction and introduction of engineered

recombinant DNA molecules into living cells. The conference was held at the Asilomar Conference Center on California's Monterey Peninsula and was sponsored by NAS with funding provided by NIH and NSF.

Throughout this period and later, a patent application covering a 1972 work of Ananda Chakrabarty, a biologist working for the General Electric Company (GE), was making its way through the U.S. Patent Office. He had made a bacterium that could break down multiple components of crude oil. He did not engineer the bacterium through gene splicing and cloning; he used conventional genetic manipulation techniques. It appeared that this bacterium's appetite might have significant value for treatment of oil spills.

GE's patent application covered claims to the method of producing the bacteria, the bacteria combined with a carrier material, and the bacteria themselves. The patent examiner allowed the method and combination claims but rejected the claims for the bacteria *per se*, indicating that micro-organisms are products of nature and that as living things they are not patentable subject matter. GE appealed. We will come back to the progress of that case later in this chronology.

The meeting at Asilomar was well attended both by scientists and the media. In his article in *Rolling Stone*, entitled "The Pandora's Box Congress," Michael Rogers summarized the conference activities: "The conference--four intense, 12-hour days of deliberation on the ethics of genetic manipulation--should survive in texts yet to be written, as both landmark and watershed in the evolution of social conscience in the scientific community." He quoted a scientist as remarking, "Nature does not need to be legislated, but playing God does."

The moratorium was lifted, and recombinant DNA research was resumed, but under strict self-imposed laboratory safety guidelines. These became required of NIH grantees as a condition of research support. The guidelines involved levels of

physical and biological containment. An example of biological containment might be use of an organism that would not survive outside of the laboratory environment.

The media and public suddenly discovered recombinant DNA. One article about DNA cloning and its implications was titled, "Dr. Jekyll and Mr. Hyde and Mr. Hyde and Mr. Hyde." Other headlines included "Regulating Recombinant DNA Research: Pulling Back from the Apocalypse," "New Strains of Life--or Death," and "Playing God with DNA." Erwin Chargoff wrote in *Science* in June 1976, "Have we the right to counteract irreversibly, the evolutionary wisdom of millions of years, in order to satisfy the ambition and the curiosity of a few scientists?"

Into this atmosphere came the news that the basic recombinant DNA technique had been patented, although our case was still in the patent application stage at that time and had not yet been made public. This occurred during a meeting at MIT in June 1976. Patents meant corporate involvement to some who maintained that the profit motive clearly would drive recombinant DNA research into dangerous areas. More articles appeared: "Genetic Manipulation to Be Patented," and "Stanford, U. Calif. Seek Patent on Genetic Research Technique."

Getting mighty crowded

In May 1976, Stanford scientists and administrators met within Stanford to discuss the university's policy and practices with respect to patenting biotechnology discoveries, particularly the recombinant DNA patent. There were concerns that patents would interfere with scientific communication. There was also a concern about a perception by the public that Stanford would have a conflict of interest with respect to recombinant DNA safety issues if it were to hold a proprietary interest in recombinant DNA work. It was decided that the university would open these issues for review at a national public policy

level. Robert Rosenzweig, then Stanford Vice-President of Public Affairs, wrote NIH Director Donald Fredrickson, asking the government's views on the appropriateness of Stanford patenting and licensing recombinant DNA discoveries.

Meetings were held within the government. Norman Latker, then patent counsel for the Department of Health, Education, and Welfare, told me of a July 1976 meeting at NIH where he "walked into a den of scientists without a patent understanding." Over and over throughout this controversy, it was necessary to explain the patent system's role in encouraging innovation and being the antithesis of secrecy to scientists who had had no exposure to it. The government considered the following options:

- Abandon the patent
- Let the patent issue and require Stanford to dedicate it to the public
- Let Stanford license, but with government controls
- Review all licensing arrangements
- Review no licensing arrangements
- Require nonexclusive licensing only
- Impose no restrictions other than those already present in the terms of Stanford's institutional patent agreement
- Take title and handle any licensing

The patent issue was brought to the NIH Recombinant DNA Advisory Committee. Fredrickson wrote to the committee to raise the question of whether patents inhibit dissemination of research information. This stimulated me to write to Frederickson, conveying to him my experience: "I am not aware

of any economic, administrative, or physical force that will stop or delay a dedicated scientist at a university from promptly publishing his or her research findings, whenever he or she is ready to do so. From a pragmatic point of view, it would be fatal to the licensing program at this or any other university if an administrator delayed a scientist's publication in order to secure a patent position."

By September 1976, everyone was in the act, including Senator Edward Kennedy. After Fredrickson's prepared testimony about the safety issues at hearings held by Senator Kennedy, the senator asked, "Well, what about the patents?" Frederickson responded, noting Stanford's willingness to consider modification of its institutional patent agreement as it related to the recombinant DNA patent situation. He also advised that comment on patent issues was being requested not only from the NIH Recombinant DNA Advisory Committee but from those who participated in the public hearings on the recombinant DNA guidelines, as well as the public at large.

Fredrickson, in explaining the institutional patent agreement, added that through a licensing program, corporations could be encouraged to follow the recombinant DNA safety guidelines. At that time, the recombinant DNA safety guidelines could only be required of entities that accepted government research funds.

Two years after Rosenzweig's letter, the government, through a March 2, 1978, letter from Fredrickson, reaffirmed that it was appropriate that universities should, in general, patent and license recombinant DNA inventions provided that industry licensees comply with standards set forth in the NIH guidelines on research involving recombinant DNA molecules.

In the meantime, the public became aware of the GE patent application on "patenting of life." Recall, GE had appealed the rejection of the patent examiner on the patenting of micro-

organisms as products of nature. GE eventually appealed to the Supreme Court, which agreed to hear the case.

Many articles began to appear about the commercial potential of the technology. Genentech and other biotechnology companies were formed. The military aspects of DNA cloning were discussed. An article in the *Los Angeles Times* was headlined, "Russ Believed Plunging Into Gene Study--New Labs Could Lead to Development of Biological Weapons."

Finally eight years after the patent examiner's final rejection, on June 16, 1980, the Supreme Court held five to four that a living, manmade micro-organism is patentable subject matter. The Supreme Court based its decision on the fact that the Congress had used expansive terms in writing the patent laws, and therefore, they should be given wide scope. The Court cited the evidence that Congress intended statutory subject matter to "include anything under the sun that is made by man."

Supreme Court Chief Justice Warren Burger, writing for the majority, stated that "the patentee has produced a new bacterium with markedly different characteristics from any found in nature and one having potential for significant utility. His discovery is not nature's handiwork, but his own; accordingly, it is patentable subject matter under Section 101."

But let us return at this juncture to the Stanford and UC patent application and our licensing program. The application, originally filed on Nov. 4, 1974, covered both the process of making and the composition for biologically functional "chimeras." (A chimera is a mythical hybrid creature of two species, such as man and goat.) During the course of prosecution of the application, the patent examiner, Alvin Tanenholtz, indicated to our patent attorney, Bertram Rowland, that he was willing to allow process claims that described the basic methods for producing biological transformants, but that he was not willing to allow claims on the biological material *per*

se. The original patent application was then divided into "product" and "process" applications.

The process patent issued on Dec. 2, 1980 (Figure 2). Note that this occurred only six months after the Supreme Court's decision called by some as allowing "the patenting of life." Many perceived that issuance of the Cohen-Boyer process patent resulted from the Supreme Court decision. However, that decision related only to claims of our product application, which at that time was still pending prosecution in the Patent Office.

In the period between the Supreme Court's decision and our patent issuance, Genentech went public, experiencing a huge public demand for its stock.

Open house

We had tried something different in the prosecution of this patent. We reasoned that the patents, when issued, would underlie the entire field of genetic engineering. This clearly dictated, very early, a nonexclusive licensing strategy. And, given that we would seek to license the entire industry, challenges to the patents in the courts seemed certain. As a strategic move to enhance the validity of the patents, we determined to open the patent process to the public. (Normally, a patent application is held confidential by the Patent Office until its issue, when the entire prosecution history is made available for public review.)

Figure 2

United States Patent [19] [11] **4,237,224**
Cohen et al. [45] **Dec. 2, 1980**

[54] PROCESS FOR PRODUCING BIOLOGICALLY FUNCTIONAL MOLECULAR CHIMERAS

[75] Inventors: Stanley N. Cohen, Portola Valley; Herbert W. Boyer, Mill Valley, both of Calif.

[73] Assignee: Board of Trustees of the Leland Stanford Jr. University, Stanford, Calif.

[21] Appl. No.: 1,021

[22] Filed: Jan. 4, 1979

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 959,288, Nov. 9, 1978, which is a continuation-in-part of Ser. No. 687,430, May 17, 1976, abandoned, which is a continuation-in-part of Ser. No. 520,691, Nov. 4, 1974.

[51] Int. Cl.³ C12P 21/00

[52] U.S. Cl. ..... 435/68; 435/172; 435/231; 435/183; 435/317; 435/849; 435/820; 435/91; 435/207; 260/112.5 S; 260/27R; 435/212

[58] Field of Search ..... 195/1, 28 N, 28 R, 112, 195/78, 79; 435/68, 172, 231, 183

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Primary Examiner—Alvin E. Tanenholtz
Attorney, Agent, or Firm—Bertram I. Rowland

[57] ABSTRACT

Method and compositions are provided for replication and expression of exogenous genes in microorganisms. Plasmids or virus DNA are cleaved to provide linear DNA having ligatable termini to which is inserted a gene having complementary termini, to provide a biologically functional replicon with a desired phenotypical property. The replicon is inserted into a microorganism cell by transformation. Isolation of the transformants provides cells for replication and expression of the DNA molecules present in the modified plasmid. The method provides a convenient and efficient way to introduce genetic capability into microorganisms for the production of nucleic acids and proteins, such as medically or commercially useful enzymes, which may have direct usefulness, or may find expression in the production of drugs, such as hormones, antibiotics, or the like, fixation of nitrogen, fermentation, utilization of specific feedstocks, or the like.

14 Claims, No Drawings

Figure 2. **Process patent for making molecular chimeras**

We announced that anyone who was aware of factors that might affect the patent's validity was invited to make them known to the Patent Office. The patent file history was opened to anyone as we waived our right of secrecy. The demand for the file history was such that at one time more than 30 requestors were waiting to see it. Because that file then was not available to the examiner and prosecution of the patent might have been delayed, the Patent Office made additional copies for public review. Any company seeking to challenge the validity of the patents after their issue would have the burden of justifying why they had not raised those issues with the Patent Office during patent prosecution.

Additional factors were, indeed, brought to the Patent Office. In October 1981, a conference on "Patenting of Life Forms," organized by James T. Watson, was convened at Cold Springs Harbor Laboratories. In a postconference paper, an article by Albert Halluin, then of Exxon, brought perhaps the most significant new factors to the attention of the patent examiner.

We eventually closed the file in early 1983, largely because of the speculative articles in the media that accompanied every Patent Office action and every Stanford response. (In the prosecution of a patent application, a series of rejections by the patent examiner and responses by the patent attorney occur until the patent issues, or a final rejection occurs.) By then, the opening of the file had served its purpose. As a result of the open process, we believe the patents will have unusually strong presumptions of validity.

As I mentioned above, the original application was divided into a process patent (which issued Dec. 2, 1980) and a product patent application. The product application was again divided into an application covering prokaryotic hosts and another covering eukaryotic hosts. The prokaryotic product patent issued Aug. 28, 1984. The eukaryotic patent application is still before the Patent Office.

Recombinant DNA licensing

We had to consider a number of factors in devising a licensing strategy for an invention for which products had never been sold and which would apply not only to many diverse established industries, but in addition to the then newly emerging biotechnology industry. Our objectives were to develop a licensing program consistent with the public service ideals of the university, to encourage the application of genetic engineering technology for public use and benefit, to minimize the potential for biohazardous development, and finally, to provide a source of income for educational and research purposes.

Because the patents covered a basic process underlying many potential uses, any license would have to be suitable for a large number of applications, including not only companies specializing in biotechnology but existing companies in chemical, agricultural, pharmaceutical, mining, oil, and other industries. We could also anticipate that small as well as large companies and newly formed companies would utilize the technology.

It was also necessary to recognize that only U.S. patents were available because of prior publication. Because a patent covers the making, using, and selling of a technology, onerous earned royalty terms could drive a manufacturer to utilize the process offshore, paying royalties only on sales back to the United States.

At the time we began our licensing effort, only the process patent had issued. Hence a company could make the product overseas using the patented process and sell that product in the United States without infringing the process patent, having utilized the process in a country where we did not have patent protection. We decided to investigate the International Trade Commission (ITC) as a means of addressing this potential problem. The ITC enforces Section 337 of the Tariff Act of

1930, which prohibits certain unfair methods of competition and unfair acts in the importation of articles into the United States. Of particular interest to us were remedies available to a U.S. manufacturer whose method patent is subject to an unlicensed competitor who practices the patented *method* abroad and sells the noninfringing *product* in the United States. A favorable decision could involve exclusion orders, or cease-and-desist orders, directed to preventing the importation of the goods involved.

We obtained a favorable written opinion from a law firm experienced in ITC dealings suggesting that the ITC could stop products made overseas with recombinant DNA technology at the U.S. border. We distributed this opinion freely to foreign companies.

We also needed to consider that a patent grant is limited to 17 years. Because the development, testing, and regulatory approvals could take up to 10 years or more, there was a possibility that the patent could expire before royalty-bearing products would reach the marketplace. We had filed a "terminal disclaimer" with the Patent Office in 1980, when the first process patent application issued. The terminal disclaimer meant that regardless of how long the divisional patent applications were prosecuted before the Patent Office, those patents, once issued, would expire on Dec. 2, 1997, the same date of expiration as the 1980 patent. The Patent Office often requires terminal disclaimers to prevent an applicant seeking to extend patent life from filing continuation applications.

For us, these factors argued for initiating a licensing program as soon as possible. This was also considered desirable from the standpoint of many companies, desiring some certainty both that a license could be obtained and knowing the royalty terms that would be factored into their financial decisions. High earned royalties in certain cases could preclude substitution of recombinant DNA-made products over existing products.

In early August 1981, we announced the availability of licenses. This was a significant news item, and broad media coverage occurred. But to be even more certain that companies intending to use recombinant DNA technology would be advised of the license's availability, we placed paid announcements in *Science* and *Nature*. Terms of the license announced in August were only guaranteed for those companies signing up before Dec. 15, 1981. Hence, if a company desired certainty, it might choose to take a license before Dec. 15 because possible future changes to the license agreement were not divulged. However, the general perception was that royalty terms would increase.

In designing terms of the license, we held discussions with companies known to be practicing the technology to learn of any "deal-breaking" terms. One license clause that took considerable discussion related to application of the recombinant DNA safety guidelines. Because we had neither the desire, capability, nor the charge to become a regulatory agency for enforcement of the guidelines, an early draft clause provided that the NIH be involved in this role. However, the NIH also did not wish to become a regulatory agency. The clause that emerged from discussions with NIH and companies required the licensee to follow the intent of the recombinant DNA safety guidelines. It should be noted that by this time the biotechnology industry voluntarily had agreed to follow the guidelines.

A $10,000 minimum annual advance on royalties was determined as reasonable even for small companies intending to practice in the biotechnology marketplace. As a further encouragement for licensees to sign up before Dec. 15, 1981, a five-times credit on the $10,000 minimum annual advance on royalties was offered in the original license agreement--that is, for each $10,000 payment, the licensee would receive a $50,000 credit against future earned royalties. A company could accrue this credit for five years or until the first calendar year in which over $1 million of end product was sold. Because there was a $10,000 signing fee that also received the five-times credit,

licensees could accumulate a credit as much as $300,000. And most have, as a relatively small number of companies to date have had annual recombinant DNA product sales over $1 million.

Fixing a price tag

Determining the royalty structure took a great deal of thought. It was necessary to consider all forms of the technology's utilization. This included determination of classes of royalty bases against which an earned royalty could be applied. (An earned royalty is that royalty applied against the sale of an item using the licensed technology.) We ended up with four categories of royalty base:

- Basic genetic product
- Process improvement product
- Bulk product
- End product

The royalty rates ranged from 10% for the basic genetic product to 1/2% for the end product.

Basic genetic products include DNA chimeras (transformants) and vectors. For example, the transformed organism that makes insulin is a basic genetic product with a royalty of 10%.

Bulk products are products that will be processed further by a manufacturer and not used or consumed by the end user. An example of a bulk product is the disaccharide sweetener that will be used in soft drinks and diet foods. Based on annual sales volume, the royalty ranges from 3% down to 1%.

End product is a product for use by what we called the "ultimate consumer," such as an insulin injection, vaccine, or pharmaceutical. The royalty ranges from 1% to 1/2% based on annual sales volume.

Process improvement product is a material developed for or by a manufacturer to improve an existing process. An example is an enzyme that catalyzes a reaction. If an enzyme is genetically engineered and improves an existing process, the royalty is 10% of the costs savings or other economic benefit.

We specified that if a licensee sells to another licensee, the two parties could agree among themselves as to which would pay the royalty. Generally, the end-product producer pays. We had determined that the relatively short sales period from August to December would be optimum to develop interest and maintain momentum. But this also required us to actively and vigorously promote the license. We contacted companies throughout the free world and, that fall, visited companies in the United States, Europe, and Japan. We prepared exhibits (Figures 3, 4, and 5, for examples) to explain the technology and the license structure. At this time, many of the companies who intended to use the promising new technology did not fully understand the technology itself and how they would implement it.

To reduce incentives for overseas manufacture, the license provides for a flat royalty of 1/2% on end product made in the United States but sold outside the United States.

To reduce tinkering and to emphasize to potential licensees that our terms were standard, the license agreement was printed.

As licenses were signed, the signing was publicized. For many companies, this served to notify stockholders and the public of a company's entrance into the field of genetic engineering. As we approached December, relatively few licensees had sent in signed agreements. But in the final two weeks, the arrival rate of signed license agreements increased sharply. By midnight on Dec. 15, 1981, 73 licensees had signed up.

Figure 3

	End products	Bulk products	Basic genetic products	Process improvement products
Brief description	Goods sold in a form for utilization by the ultimate consumer	A material intended for further formulation, processing, or chemical transformation	Products sold for further processing or genetic manipulation and/or neither end, bulk, or process improvement products	Products developed and used by Licensee in its manufacturing processes to enhance production efficiency
Examples	Final dosage form pharmaceuticals Animal vaccines Microorganisms used for animal or human food biodegradation, and mineral leaching Industrial process enzymes	Antibody or hormone sold to pharmaceutical company Dipeptide sold to beverage company as sweetener Amino acid sold in bulk to a health-care firm Chemical intermediates produced by microorganisms and sold in bulk	Plasmid Unicellular organism transformants Nucleic acid segments	Enzymes or antibodies for chemical manufacturing Microorganisms for production of pharmaceuticals or chemicals Nitrogen-fixing microorganisms used by agricultural company to reduce fertilizer consumption
Earned royalty rates by net sales volume				
Up to $5 million	1.00%	3%	10%	10% of cost savings and economic benefit
$5–$10 million	0.75%	2%	10%	
More than $10 million	0.50%	1%	10%	

Figure 3. **Licensed product classification and royalties**

Figures 4 and 5

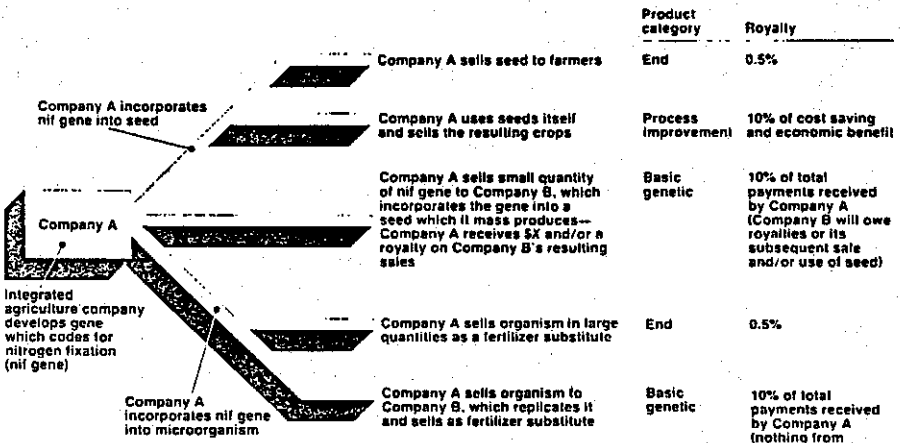

Figure 4. Agricultural example

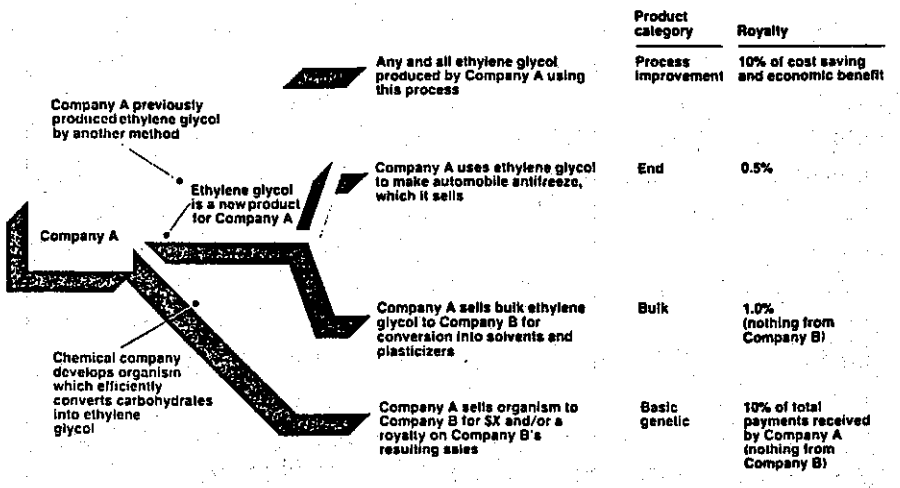

Figure 5. Commodity chemical example

An article in *Business Week*, entitled "Universities Hold Fall Sale," had a cartoon showing a carnival barker on a platform with about 5-foot lengths of helical DNA stacked up behind him and an audience of men in business suits either waving money at the barker or walking off with the DNA helixes with smiles on their faces.

After Dec. 15, 1981, licenses continued to be available but with a single-times credit rather than the five-times credit on the $10,000 minimum annual royalty. Ninety-three licenses have been signed to date (April 1987). However, because of acquisitions by one licensee of another and some terminations by companies determining not to utilize recombinant DNA technology, the number of current licensees is 81, as of April 1987. Since the end of September 1986, the new license end-product royalty rate has been a flat 1% based on sales volume.

Products based on recombinant DNA technology are beginning to enter the marketplace with increasing frequency. The first commercial recombinant DNA product, human insulin, was engineered by Genentech and is being marketed by Eli Lilly under the trade name of Humulin. Human growth hormone, engineered and marketed by Genentech, was approved for public sale in the fall 1985. And quite recently, the hepatitis B vaccine engineered by Chiron and distributed by Merck was approved for public sale. Tissue plasminogen activator (TPA), which is anticipated to replace urokinase and streptokinase in the treatment of blood clots, is expected to be approved for public sale within the next few months. We estimate the first-year sales of TPA at $450 million. By 1997, when our patents expire, it has been estimated that over $30 billion of sales of genetically engineered products will have occurred.

Stanford and UC believe that the licensing program has met its goals. The net royalties received by the universities are being used for educational and research purposes which, in a self-regenerative manner, may yet produce other discoveries for public use and benefit.

GLOSSARY

Chimeric DNA	DNA composed of two or more sequences derived from different origin such as *E. coli* and toads.
Eukaryotes	Cells that contain a membrane-enclosed nucleus (e.g., yeast, plant, and animal cells.)
Expression	Process of making proteins from information stored in genes.
mRNA	Messenger RNA; used to transfer information from one or more genes on DNA to the ribosomes for subsequent translation.
Operon	Series of genes of related function that are transcribed into a single mRNA molecule.
Plasmid	Extrachromosomal, covalently closed circular DNA molecule.
Prokaryotes	Cells that do not contain a nucleus (e.g., bacteria).
Transformants	Organisms containing foreign genetic information.
Vector	The agent used to carry foreign DNA into a cell (e.g., a plasmid or virus).

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(2) Simmons, Edlyn S. CHEMTECH, March 1987, p. 144.

CHRONOLOGY

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March 1973	Cohen and Boyer achieve first successful DNA splicing
September 1973	Publication of letter alluding to dangers of DNA splicing by Singer and Soll in *Science*
November 1973	Publication of paper on DNA splicing by Cohen, Chang, Boyer, and Helling in *Proc. Natl. Acad. Sci. USA*
July 1974	Publication of letter calling for NIH guidelines for DNA splicing by Berg, *et.al.*, in *Science*
May 1974	Publication of paper by Cohen and Boyer, *et.al.*, on transfer of animal DNA fragment into *E. coli* plasmid in *Proc. Natl. Acad. Sci. USA*
May 1974	Announcement concerning transfer of animal DNA fragment into *E. coli* by Stanford News Bureau
Nov. 4, 1974	Patent application filed by Stanford University
December 1974	Asilomar Conference
June 1976	Publication of Chargaff letter, warning about DNA splicing, in *Science*

1976	Negotiations between Stanford and NIH patenting; Congress gets involved
1976	NIH safety guidelines are published
1978	NIH affirms patenting of recombinant DNA inventions by universities
1980	Chakrabarty's bacterium held patentable by Supreme Court
Dec. 2, 1980	Process patent for making molecular chimeras issued to Stanford
August 1981	Availability of licenses for use of DNA technology announced by Stanford
October 1981	Conference at Cold Spring Harbor on patenting life forms
August 1984	Product patent for prokaryote DNA issued to Stanford

UPDATE

Editor's Note: The reader is reminded that this article was originally published in 1987 and that changes have been made since that time. For example, royalty rates have increased, the eukaryotic patent issued April 26, 1988, and persons mentioned may no longer be employed at the same location.

As of August 18, 1995, Stanford had 316 corporate licensees. The three Cohen-Boyer patents generated $27 million in royalty revenue in Fiscal Year 94/95, and Stanford continues to sign on new licensees.

Floyd Grolle, Ph.D.
Manager, License Administration
Stanford University
Office of Technology Licensing

Pre-Production Investment and Jobs Induced by MIT Exclusive Patent Licenses: A Preliminary Model to Measure the Economic Impact of University Licensing

Lori Pressman, Sonia K. Guterman, Irene Abrams, David E. Geist, and Lita L. Nelsen*

ABSTRACT

This paper examines the effectiveness of invention licensing at the Massachusetts Institute of Technology (MIT) Technology Licensing Office (TLO) in achieving one of the major objectives in the Bayh-Dole act: to induce investment by the commercial sector in the development of inventions arising from government-funded research at universities, and by doing so, to enhance economic development. Data on investment and jobs created were obtained directly from the licensees. Conservatively, we estimate that just under a billion dollars have been invested by the commercial sector toward the development and early commercialization of licensed inventions from MIT alone, and that over two thousand jobs have been created and/or sustained as a direct result of these licenses. The term *pre-production investment* is used here to refer to money spent developing new products and efficient ways to produce and market these products. It excludes the costs of

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* *Lori Pressman, Sonia K. Guterman, Ph.D., Irene Abrams, and David E. Geist, are professional staff members of the Technology Licensing Office at the Massachusetts Institute of Technology. Lita L. Nelsen is Director of this program.*

producing (or investment required to produce) mature products. This sum does not include investment and jobs generated by non-exclusive patent license agreements, or by no longer active exclusive patent license agreements, or by any type of copyright license agreement. Approximately 77% of the investment in MIT technology and 70% of the jobs in this study are associated with start-up companies, which account for only 35% of the total number of licensees (see Table 4). A preliminary extrapolation to all university licenses, based on the MIT data and on the results of the Association of University Technology Managers (AUTM) surveys (1,2), suggests that total pre-product introduction development investment nationwide in university-based technology is in the range of at least $2 to $5 billion per year.

BACKGROUND

Previous studies of the economic impact of university licensing have focused on the economic impact after product introduction (1,2). For example, the AUTM's Economic Impact Committee is in the process of refining its estimates of job creation from licenses that have matured into product sales. Based on 1993 royalty income of $350 million (U.S. institutions reporting), the current estimate of the committee is $17 billion of product sales and 137,000 jobs (3). This measure of commercial success, while important, underestimates the total economic impact of university licensing because it omits the economic impact of university licensing *before* first sales of licensed products. University technology is typically very forward-looking, and requires very large investments to bring products to market. Investment levels in development remain high even after the first sales of licensed products. An economic impact analysis based on product sales alone reveals only a fraction of the total effect of university licensing on the U.S. economy. This paper offers a complementary approach to studying the early impact of a technology program by focusing on pre-production investment.

Most university licenses are only recently consummated. The average university license is probably no more than three years old. An earlier paper has shown that the university licenses that do succeed in bringing a product to market take an average of eight years to do so (4). Since the passage of the Bayh-Dole Act, the pace of patenting and licensing in universities has grown at an exponential rate (4). Thus, one can expect a considerable increase in the next ten years in both product sales (and concomitant manufacturing job creation) and in investment in development arising from new licenses.

INTRODUCTION

The primary goal of this paper is to create a model to examine licensing activity at the Massachusetts Institute of Technology (MIT) in the context of certain objectives outlined in the Bayh-Dole Act, with the emphasis on quantifying licensee investment in product development and, therefore, jobs created in product development. A case study of university licensing is presented in this paper by MIT, describing certain activities and impacts derived therefrom. From there we make a preliminary extrapolation to the economic impact of product development investment resulting from university licensing nationwide.

The Bayh-Dole Act, named after its senate co-sponsors, (PL 96-517, enacted in 1980) allowed universities to elect to retain title to inventions arising from their federally funded research and to grant licenses to patents deriving from these inventions. The preamble, reproduced below, describes the objectives of the new law.

35 U.S.C. § 200. Policy and objective

> *"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 the nonuse or unreasonable use of inventions; and to minimize the costs of administering policies in this area."*

Measuring how well an organization has met some of the objectives in the preamble to Bayh-Dole is fairly straightforward; measuring performance against other objectives is not so straightforward. What is the measure to indicate whether a university has "promote(d) the commercialization and public availability of its inventions"?

University inventions are "embryonic." At the time a university is ready to hand its inventions off to industry, most have not even reached the prototype state, much less demonstrated manufacturability and practicality in the market. These inventions will require substantial investment in product and market development, and many may never succeed. Thus the task of the university in licensing these inventions is to find industrial licensees willing to make the high-risk investment.

The Bayh-Dole Act, allowing the university to grant exclusive licenses, enables the university to make that high-risk investment more attractive to industry: if the company makes the investment and succeeds in developing the product, *exclusive*

patent protection will reduce its market risk. Thus one important measure of a university's success in carrying out the objectives of Bayh-Dole is the level of product development investment the university has "induced" through its licensing efforts.

DEFINITIONS

The definitions used during this study are defined throughout this paper and provided here as an easy reference for the reader.

Biotechnology Licenses: Licenses for human therapeutics and diagnostics, and for chemicals produced by living organisms.

"Classic" Start-up: A company where the MIT licensed technology is the enabling technology in the formation of the company and either (i) the company has raised at least half a million dollars in investment capital or (ii) it is selling product and is paying earned royalties.

Induced Investment: Pre-Production Investment outside the licensor that is directly traceable to license agreements.

Induced Investment Rate: Induced Investment per License per Year.

Induced Investment Ratio: Induced Investment/Revenue to MIT.

Investment Outlier: A license inducing more investment than most of the other licenses.

Large Entity: A company employing more than 500 people.

Pre-Production Investment: Money spent developing new products and efficient ways to produce and market these

products. It excludes the costs of producing (or investment required to produce) mature products.

Physical-Science Licenses: Licenses for lasers, semiconductor components, novel materials, novel manufacturing processes, computer architectures, control systems, and medical devices.

Revenue Outlier: A license generating more revenue than most of the other licenses.

Revenue to MIT: License issue fees, reimbursed patent costs, license maintenance fees, and earned royalties.

Small Entity: A company employing fewer than 500 people.

METHOD

At the time the data were assembled (early 1995), the MIT TLO had 205 *active, exclusive, patent* license agreements: 104 licenses to 89 separate companies for biotechnology products, and 101 licenses to 99 separate companies outside the biotech area. These licenses cover over 700 issued patents and patent applications, the majority of which were federally funded, and thus attributable to Bayh-Dole objectives.

Biotechnology licenses include licenses for human therapeutics and diagnostics, and for chemicals produced by living organisms. Licenses outside the biotech area include licenses for lasers, semiconductor components, novel materials, novel manufacturing processes, computer architectures, control systems, and medical devices and will be referred to as physical-science licenses.

The 104 exclusive, active biotechnology licenses cover 388 issued patents and patent applications, 246 of which (63%) were funded by the U.S. Government. The biotechnology licenses represent a total of 524 active license years, or an average

duration of 5.04 years per license. The 101 active, exclusive physical-science licenses cover 314 issued patents and patent applications, 241 of which (77%) were funded by the U.S. Government. The 101 active, exclusive physical-science licenses represent a total of 426 active license years, or an average duration of 4.22 years per license.

Seventy-one of the licenses were granted to "classic" start-up companies (see Definitions for "classic" start-up). Ninety-seven of the licenses are to other small entities (using the Federal Government definition of a small entity as a company employing fewer than 500 people). Thirty-seven of the licenses are to large entities. Eighty-nine, or 44%, of the licenses are to companies located in Massachusetts, reflecting the impact on the local economy.

Several complementary methods were used to gather the induced investment data, but in all cases the licensee itself provided the figures on investment and employment. Sources of the self-reported data include:

1. Letters from CEO's or project managers to the MIT TLO stating the total dollars invested toward the commercialization of licensed products, and stating the number and type of employees working on the project. Such letters were written at the request of a TLO staff member. The licensees were assured that the data would be presented only in aggregate form and the confidentiality of the individual respondents would be strictly maintained.

2. Business plans showing the amount of money, the number and kind of personnel, and the time budgeted for each phase of development of the licensed products. Submission of such business plans and business plan updates are required in the diligence section of MIT exclusive license agreements. Follow-up phone

conversations were made to the companies to confirm that the allocated money had been spent according to the schedule in the business plan. If the company's plans had changed since submission of the written plan, the updated numbers were used.

3. Balance statements from start-up companies. These audited statements, required by the MIT TLO in the reports and records section of its license agreements, show the total sum raised by start-up companies. If the technology that started the company included other non-MIT technology, the company was contacted to help pro rate the investment appropriately.

4. Questionnaires filled out by licensees that asked for the amount of investment brought into their company as a result of the license, and how that investment had been allocated between research and development and production and marketing efforts. The questionnaire also asked how many full-time equivalent employees were working on the licensed products, how many of those were in research and development, and how many were in production and marketing.

5. Follow-up phone conversations. This was an important part of the data clarification and verification process.

It would not have been possible to gather this privileged data without the ongoing business relationship that exists between the MIT TLO and its licensees. We doubt that a request for such information from an entity other than the licensor would have elicited such a helpful response, and we suggest that other offices interested in gathering similar information do so in the context of their ongoing relationship with their licensees.

Detailed data were gathered by the above method for a sample of biotechnology licenses and for a sample of physical-science

licenses. The physical-science sample is comprised of all the exclusive, active, patent licenses of one of the authors (Pressman), and the average license is 3.79 years old, somewhat younger than the 4.22 year average for all MIT licenses in the physical sciences. The main methods for gathering the data on the eighteen licenses in the physical-science sample were: requesting a personal letter from the CEO or project manager; verifying the numbers on business plans already in the licensing office files; and reviewing balance statements from the start-up companies. A questionnaire was used to supplement this information and to gather additional information on employment associated with the license. One company in the physical-science sample had a mature product line and had made significant investment in setting up production facilities. This company had also made very significant investment in research and development. For the purpose of this study, which is focusing on pre-product introduction high risk investment, the R&D number only was used.

The data for the biotechnology sample was generated by sending the questionnaire described in point 4 above to every third licensee in an alphabetized list of the exclusive, active, biotechnology patent licensees. In the biotechnology sample, the average license is 4.3 years old, younger than the 5.04 year average for all biotech licenses. Unfortunately, our experience with the biotech samples pointed out a weakness of the questionnaire method versus the personal interview method. Investment data from large entity biotech licensees was frequently not available. This produced significant distortion, particularly for one pharmaceutical product now on the market where investment was undoubtedly of the order of magnitude of $50 to $150 million, but no self-reported data on investment were given.

RESULTS

Tables 1P and 1B below, representing the physical-science sample ("1P") and the biotech sample ("1B"), respectively, illustrate the primary role played by start-up companies in investment and employment generation:

Table 1P:

	THE PHYSICAL-SCIENCE SAMPLE			
	Total	**Start-ups**	**Other Small Entities**	**Large Entities**
Number of Licenses	18	9	5	4
Avg. Age of License in Years	3.8	4.9	2.7	2.6
Induced Investment in $M	$ 66	$ 58	$ 2	$ 6
Full-Time Equivalent ("FTE") Employees	215	173	20	22

Table 1B:

	THE BIOTECH SAMPLE			
	Total	**Start-ups**	**Other Small Entities**	**Large Entities**
Number of Licenses	19	7	9	3
Avg. Age of License in Years	4.3	5.4	3.6	3.8
Induced Investment in $M	$ 139	$ 119	$ 19	$ >>.4[b]
Full-Time Equivalent ("FTE") Employees	255	186	59	10[b]

[b] See Method section for a discussion of the difficulty of obtaining informative data from the biotech large entities licensees. The actual number is much higher, but difficult to quantify.

The total self-reported investment for both samples is $205 million, and the total self-reported number of full-time equivalent employees is 470. In both samples, a large fraction of the investment is made by start-up companies, accounting for a large fraction of the jobs. In the physical-science sample, over eighty-five percent of the investment is associated with start-up companies, and over eighty percent of the jobs are associated with start-up companies. In the biotech sample, over eighty-five percent of the reported investment is associated with start-up companies, and seventy percent of the jobs are associated with start-up companies. This result is biased by the differential response of the start-ups and by the difficulty of the large-entity, biotech licensees in accurately identifying investment directly attributable to efforts to commercialize licensed products. (Two-thirds of the start-ups and small entities answered the questionnaire while only half of the large entities did so.)

It is interesting to point out the internal consistency of the self-reported investment and jobs data. A well-accepted estimate of money needed to support one high-tech job is $125,000 (7). Therefore, $205 million could be expected to support 1,640 job years. If all 470 jobs existed over all 4.05 years (average for all licenses in samples), then there would be 1,904 job years. Intuitively, it is more likely that there were fewer employees in the earlier years of the license. Thus, it is easy to create a very plausible scenario where 1,640 job years would be spread over 4 years, with the companies employing progressively more employees every year: for example, 350 employees the first year, 390 the second, 430 the third, and 470 the fourth (350 + 390 + 430 + 470= 1,640).

It is also significant to compare the revenue derived by MIT from licenses, with the far larger investment made by these companies developing the technology outside of MIT. Table 2 summarizes the revenue to the university from these licenses. Line 1 of the table shows patent costs incurred before the effective date of the license for the cases that are the basis of

the samples in this study: $552 thousand for physical-science inventions, $874 thousand for biotech inventions. Line 2 shows the license contract-associated revenue for these cases, defined here as the sum of license issue fees, patent cost reimbursement paid by licensees, license maintenance fees, and earned royalties on sales. The difference between the first and second lines is the net revenue to MIT associated with the licensing contract itself, shown in Line 3: $524 thousand for physical-science inventions, and $1.3 million for biotech. Line 4 lists sponsored research dollars to MIT associated with the license, and Line 5 in the table gives the sum of the preceding lines.

Table 2:

COSTS AND PAYMENTS TO MIT FOR PHYSICAL-SCIENCE AND BIOTECH CASES

	Physical-Science Sample[a]	Biotech Sample[b]
1. Out-of-pocket patent costs, before license is signed.	$ (552) K	$ (874) K
2. License revenue: license issue fee, reimbursed patent costs, license maintenance fees, and earned royalties on sales.	$ 1,076 K	$ 2,189 K
3. Net Licensing Revenue	$ 524 K	$ 1,315 K
4. Sponsored Research Funding	$ 1,761 K	$ 2,359 K
5. Net Revenue to University	$ 2,285 K	$ 3,674 K

[a] 17 companies, 18 licenses

[b] 19 companies, 19 licenses

The revenue received by the university is modest when compared with the over two hundred million dollars of investment by the commercial sector toward the development

of businesses based on these inventions (see Tables 1P and 1B). This is consistent with the spirit of the Bayh-Dole act and MIT's policies of licensing. The primary goal of the MIT TLO is to encourage, induce, and attract commercial investment to MIT inventions and to further product development and economic development. Revenue generation is only a secondary goal (5).

Based on this philosophy of licensing (and blessed with a small but continuing licensing income stream that makes this possible), the MIT Technology Licensing Office invests in patenting all inventions that it believes to have a "reasonable chance" of breaking even on licensing. This procedure is in contrast with a return-maximization strategy practiced by commercial entities who license university inventions and invest only in those inventions likely to be "big winners." MIT invests in about 40% of the invention disclosures it receives, in contrast to the commercial entities who invest in "fewer than 10%" of the invention disclosures they receive. (Private communication from several such companies and the authors' own data indicate that this number is substantially lower than 10%.)

Tables 3P and 3B below were generated by an extrapolation of the data in Tables 1P and 1B. As to the full MIT portfolio of active, exclusive licenses, the average investment per start-up was extrapolated to all start-ups, and the average investment per other small entities was extrapolated to all other small entities, etc. Because the results varied greatly between start-up licenses, other small entity licenses, and large entity licenses, the extrapolations were made separately for each category and then summed. The extrapolations of investment were made on the basis of license-years (see Appendix A). The extrapolations for jobs were made simply on the basis of number of licenses (see Appendix B).

Table 3P:

	101 EXCLUSIVE, ACTIVE, PATENT PHYSICAL-SCIENCE LICENSES[a]			
	Total	**Start-ups**	**Other Small Entities**	**Large Entities**
Number of Licenses	101	41	41	19
Avg. Age of License in Years	4.2	4.0	4.5	4.3
Induced Investment in $M	$ 288	$ 214	$ 25	$ 49
Full-Time Equivalent ("FTE") Employees	1,055	786	164	105

[a] Data extrapolated from start-ups in sample to all start-ups, from small entities in sample to all small entities, and from large entities in sample to all large entities. One investment outlier was included in the initial data sample from which the extrapolation was made. (See Discussion section for discussion of outliers.)

Table 3B:

	104 EXCLUSIVE, ACTIVE, PATENT BIOTECH LICENSES[b]			
	Total	**Start-ups**	**Other Small Entities**	**Large Entities**
Number of Licenses	104	30	56	18
Avg. Age of License in Years	5.0	5.3	4.5	6.4
Induced Investment in $M	$ 634	$ 498	$ 132	$ >> 4[c]
Full-Time Equivalent ("FTE") Employees	1,241	822	363	>> 56[c]

[b] Data extrapolated from start-ups in sample to all start-ups, from small entities in sample to all small entities, and from large entities in sample to all large entities. Two investment outliers were in the initial data sample from which the extrapolation was made. (See Discussion section for a discussion of outliers.)

[c] See Method section for a discussion of the difficulty of obtaining informative data from the biotech large-entities licensees. This number is higher, but difficult to determine.

Table 4 below is the sum of the values in Tables 3P and 3B, and represents the total induced investment and total jobs associated with 205 MIT active, exclusive patent licenses.

Table 4:

	TOTAL EXCLUSIVE, ACTIVE, PATENT LICENSES			
	Total	**Start-ups**	**Other Small Entities**	**Large Entities**
Number of Licenses	205	71	97	37
Avg. Age of License in Years	4.6	4.6	4.5	5.3
Induced Investment in $M	$ 922	$ 712	$ 157	$ >> 53[a]
Full-Time Equivalent ("FTE") Employees	2,296	1,608	527	>> 161[a]

[a] See Method section for a discussion of the difficulty of obtaining informative data from the biotech large-entities licensees. This number is higher, but difficult to determine.

DISCUSSION

The issue, as in all sampling surveys, is how representative are the data, and therefore how reliable and accurate are the extrapolations.

The biggest problem in extrapolation of the data to the entire MIT portfolio is the statistically infrequent revenue and investment outliers. Revenue outliers are defined as those licenses that generate more revenue to MIT than most other licenses. Investment outliers are defined as those licenses that induce more investment than most other licenses. Investment outliers may be attributed to a successful public or private stock offering, or may be associated with a very large development commitment within an existing company to take a product to market, e.g. a human medical therapeutic. (There is one such drug product in the biotech sample, but the large entity licensee

did not reveal the data.) The problem with both revenue and investment outliers is that their inclusion or non-inclusion in small samples can bias the resulting extrapolations.

To further illustrate the concept of "revenue outliers," consider the current portfolio of MIT exclusive patent licenses. Only two (of 205 total exclusive patent licenses) yield more than $500 thousand per year in running royalties, and together these comprise 27% of the total yearly income. In addition, in a typical year, MIT TLO may receive no more than two or three other payments greater than $250 thousand from "one-time" payments such as license issue fees, major sublicense fees, and/or liquidation of stock received from past start-up licenses. In all, while 6 of the current active, exclusive licenses have yielded more than $1 million in revenue, fewer than 31 have yielded more than $200 thousand.

Table 5A illustrates the degree to which the average license revenue of the samples in the study were biased by "outliers" by comparing three subdivisions of the data: average for all licenses in the portfolio; average revenue for the entire portfolio when the "outliers" were omitted; and average revenue for the sampled licenses. In general, the sampled licenses were closer to the full portfolio *minus* the outliers, indicating that the sample understated the impact of the outlier licenses.

Table 5A:

	AVERAGE REVENUE/LICENSE		
	All Licenses: (101 licenses for Physical Sciences, 104 for Biotech)	**All Licenses minus Licenses with lifetime revenue greater than $1M**	**Samples: (18 licenses for Physical Sciences, 19 for Biotech)**
Physical Science	$ 159 K	$ 67 K	$ 75 K
Biotech	$ 209 K	$ 93 K	$ 115 K
All	$ 185 K	$ 81 K	Not Applicable

Investment outliers, like revenue outliers are infrequent, and would stand out clearly and intuitively from within a complete set of data on induced investment. Unfortunately a complete set of data on induced investment for all 71 start-up licenses is not available to analyze. A disproportionate number of investment outliers included in the respondent sample, (either too many or too few), could seriously distort the extrapolations to the entire MIT sample. Forty-one percent of the investment in the physical-science sample was from one investment outlier, and seventy-two percent of the investment in the biotech sample was from two investment outliers.

In addition to the issues of revenue outliers and investment outliers, there are other issues related to the representativeness of the samples. The biotech data were based on a questionnaire, which itself polled only a fraction of the total exclusive, biotech licenses in the MIT portfolio (30 out of a total of 104). The randomness of the sampling (every third company, alphabetically) enhances representativeness, aside from the outlier problem. A major issue, however, is bias based on non-responsiveness. Table 5B shows a comparison of respondents and non-respondents.

Table 5B:

LICENSE INCOME FROM RESPONDING AND NON-RESPONDING BIOTECH LICENSES

	Total	Average per Company
Responding (19) (7 start-ups plus 12 non start-ups)	$ 1,981 K	$ 104 K
Non-Responding (11) (2 start-ups plus 9 non start-ups)	$ 4,551 K	$ 414 K

A higher fraction of start-ups responded, most likely reflecting the closer relationship the MIT TLO naturally has with start-up licensees. The larger "license income per licensee" figure for the non-respondents reflects one large-company license yielding substantial running royalty streams (one of the "revenue outliers" discussed above).

In the physical-science sample, the issue is not one of responsiveness. The entire population was queried, and with repeated follow-up efforts through phone calls and letters, all licensees responded. The technology of the physical-science sample, however, was narrower than that of the TLO's non-biotech licenses as a whole: it included lasers, semiconductor components, and medical devices, but omitted materials science, computer science, mechanical and manufacturing engineering. Some indication of the fact that the physical-science sample is indeed representative of all the licenses in the physical sciences is the similarity of the average revenue received from the 18 licenses in the physical-science group—$75K/license—with that of the total physical-science portfolio, controlled for revenue outliers—98 licenses yielding an average of $67K/license.

Age of the licenses is also a very significant factor in assessing representativeness of the samples. Age is significant in analyzing both the "total" development investment made (which will increase with age at least until product introduction) and the rate of development investment (that is, investment per year, which is a clearer measure of jobs created in a given year). Rate of development investment usually also increases with age of license until product introduction or, in the case of biomedical licenses, until submission to the FDA for marketing approval. Thus, if the data are based on "young" licenses, they will tend to significantly underestimate both the total investment and the rate of investment. Table 5C below analyzes the degree to which the age of the licenses in the samples was representative of the age of all the exclusive patent licenses in MIT's portfolio.

Table 5C:

	AVERAGE AGE IN YEARS/LICENSE		
	All Licenses: (101 licenses for Physical Sciences, 104 for Biotech)	Samples: (18 licenses for Physical Sciences, 19 for Biotech)	No Earned Royalty Licenses: (16 licenses for Physical Sciences, 15 for Biotech)
Physical Science	4.22	3.79	3.17
Biotech	5.04	4.30	3.95
All	4.63	4.05	3.55

Table 5C illustrates that the average license is 4.63 years old for the portfolio as a whole, while all licenses in the samples are an average of 4.05 years old. The age of sample licenses on which there were no earned royalties on product sales was even less, as expected: an average of 3.55 years. Because it has been estimated that the typical university license requires eight years of development investment before products reach market (3), the MIT licenses can be seen as only half way through their development cycle. The fact that the sample licenses were somewhat younger than all licenses that formed the basis of the extrapolation would tend to produce an underestimate of induced investment.

With this discussion on the issues of representativeness in mind, it is interesting to further consider the implications of the data. Table 6 compares the total license revenue received by the university with the total reported investment in the technology. The fluctuations in the ratio of induced investment to licensing revenue are due to the fluctuations introduced by revenue and investment outliers. The ratio of induced investment to licensing revenue for the entire group of 205 licenses, keeping in mind that the licensing revenue *is not* extrapolated, and that the induced investment number *is* extrapolated, is 24 to 1.

Table 6:

INDUCED INVESTMENT COMPARED WITH LICENSING REVENUE					
	Physical-Science Sample (18)	Biotech Sample (19)	Physical Sciences All (101)	Biotech All (104)	All (205)
License Revenue to MIT (license issue fees, license maintenance fees, patent reimbursements, running royalties) (A)	$1.1M[a]	$2.2M[a]	$16.1M[a]	$21.8M[a]	$37.9M[a]
Induced Investment (B)	$66M[a]	$139M[a]	$288M[e]	$634M[e]	$922M[e]
(B)/(A)	60	63	18	29	24

[a] Actual data

[e] Extrapolated data

Note that the extrapolated investment-to-licensing revenue ratios for the full portfolio are smaller than the sample ratios. Refer to Table 5A, which illustrates that the average revenue per license in both the physical-science and biotech samples is less than the average revenue for all licenses in the physical sciences, and for all biotech licenses, respectively. This is an important reminder that a high induced investment ratio can be both an indicator that a license induced a lot of investment, or that it has earned very little royalties. As university license portfolios mature, the induced investment ratio may ultimately equilibrate to a ratio lower than the 24 to 1 measured here, yet the total induced investment may have increased. It will be interesting to examine this ratio again in about five years.

Table 7 below shows induced investment for the different categories of licenses: start-ups, other small entities, and large entities, whose respective ratios of investment-to-license revenue were 41:1, 14:1, and 6:l. The authors doubt the validity of the 6:1 ratio, which is seriously distorted by the difficulty of the biotech large entities with many projects and products directly attributing a fraction of their investment specifically to the licensed technology. This estimate is probably very conservative.

Table 7:

INDUCED INVESTMENT COMPARED WITH LICENSING REVENUE BY COMPANY TYPE

	Physical Sciences All Licenses (101)			Biotech All Licenses (104)			Total Licenses (205)		
	Start-ups	Small Entities	Large Entities	Start-ups	Small Entities	Large Entities	Start -ups	Small Entities	Large Entities
License Revenue to MIT (A)	10.4M[a]	2.3M[a]	3.4M[a]	7.0M[a]	9.3M[a]	5.5M[a]	17.4M[a]	11.6M[a]	8.9M[a]
Induced Investment (B)	214M[e]	25M[e]	49M[e]	498M[e]	132M[e]	4.1M[e]	712M[e]	157M[e]	53.1M[e]
(B) / (A)	20.6	10.9	14.4	71.1	14.2	0.75	40.9	13.5	6.0

[a] Actual data

[e] Extrapolated data

Thus, a license portfolio with a different mix of these entities could result in a different investment ratio. (Again, a caveat: as the samples are subdivided, the number of datapoints decrease, and the effect of statistical fluctuations on the accuracy of the conclusions is enhanced.)

Anticipating that there will be significant interest in extrapolating these numbers to the portfolio of university licenses, we present Table 8 below, which could form the basis of a weighted extrapolation for licensing portfolios where the number of active license years of the various types of licenses are known. Table 8 gives induced investment, in dollars per license per year, for various categories of license: physical-science start-up, small entity, and large entity; and biotech start-up, small entity, and large entity. Note again that we believe the biotech large-entity number to be unreliable.

Table 8:

INDUCED INVESTMENT PER YEAR FOR ALL LICENSES IN BOTH SAMPLES

	Physical Sciences All Licenses (18)			Biotech All Licenses (19)			Total Licenses (37)		
	Start-ups	Small Entities	Large Entities	Start-ups	Small Entities	Large Entities	Start-ups	Small Entities	Large Entities
Number of License Years (A)	44.1	13.6	10.5	37.9	34.1	9.8	82.0	47.7	20.3
Induced Investment (B)	58.2M[e]	1.9[e]	6.4M[e]	119.7M[e]	17.1M[e]	0.4M[e]	177.9M	18.9M	8.4M
(B) / (A)	$1.3M	$0.14M	$0.61M	$3.2M	$0.50M	$0.04M	$2.2M	$0.40M	$0.41M

[e] Extrapolated data

IMPLICATIONS

The extrapolated data based on the reported data are impressive: an estimated $0.92 billion in technology development investment from 205 current, exclusive MIT patent licenses (see Table 4). It can be anticipated that both the rate of investment and the total investment for these 205 licenses will increase substantially over time as the products of these relatively young licenses (average about four and a half years old) move from the research stage through development and into manufacturing. (Though, some, of course, will terminate because of either product failure or market failure.)

Extrapolating from MIT licenses to university licenses as a whole is a large leap, but worth considering. Two proposed methods will be discussed. One method would use information of the type presented in Table 8, on induced investment per license per year; another method would use information of the type presented in Table 7, on induced investment compared with licensing revenue to the university. Two sample extrapolations will be performed using the MIT extrapolated data, and the published data from the AUTM surveys (1,2).

On the issue of representativeness of the MIT data to the university community, the authors note that the MIT licenses may differ from AUTM licenses in the following ways:

- A different proportion of exclusive versus non-exclusive licenses.
- A different proportion of patent versus copyright licenses
- A different proportion of start-ups, or different types of start-ups.
- A different proportion of licenses in the physical sciences versus licenses in the biological sciences.

Concerning the first two points, the AUTM Licensing Survey lists 8,354 (see (1), p. 155) active licenses and options to U.S. Universities, U.S. Hospitals and Research Institutes, and Patent Management Firms, but does not give information on what fraction of the 8,354 licenses were exclusive patent licenses. A first order of magnitude estimate might start based on the MIT experience, that 10% of the MIT agreements are option agreements and 90% are license agreements, and that half of the license agreements are exclusive patent license agreements. Thus, for the purpose of making a preliminary estimate, assume that forty-five percent, or 3,759 of the 8,354 active license and option agreements are exclusive patent licenses. Although only a third of the product-producing licenses in the AUTM Public Benefits Survey were exclusive, we do not believe that this percentage is generalizable to all licenses, including those not yet associated with products. In our experience, large entities are more likely to have product in the market faster, indeed are more likely to license a university patent just in time to introduce a product that would otherwise infringe on that patent, and are much more likely to take nonexclusive licenses.

On the third point, that MIT may have more start-ups than general, the AUTM Licensing Survey does list what fraction of licenses involved equity. For the purposes of this estimate, those licenses will be assumed to be start-ups. To estimate the number of start-ups, note that the AUTM Licensing Survey reported 459 (see (1), p.7) licenses with equity to U.S. Universities, U.S. Hospitals and Research Institutes, and Patent Management Firms. Thus, 459 of the 3,759 estimated active exclusive patent licenses, or 12.2%, were to start-ups.

On the fourth point, that the proportion of licenses in the physical sciences and biotechnology is not known in the AUTM Licensing Survey, it is known in the AUTM Public Benefits Survey. The authors categorized the products in that survey as physics-related, chemistry-related, software, medical devices, and then biological and agricultural products. 60% of the

products are biological and agricultural, and the remaining 40% are physics-related, chemistry-related, software, and medical devices. The same 60-40 biotech/physical-science estimate can be obtained another way. First, note that in the AUTM Licensing Survey, 252 of the 2050, or 12.3% (see (1), p. 160) of the licenses and options to U.S. Universities, U.S. Hospitals and Research Institutes, and Patent Management Firms in 1993 were to U.S. Hospitals and Research Institutes, and therefore are virtually entirely biotechnology. Second, of the remaining 1,798 licenses and option agreements, 1,277 or 71% were to U.S. Universities with medical schools (see (1) pp. 64-68). Scanning pages 64-68 of the AUTM Licensing Survey reveals that having a medical school is highly correlated with having a large number of licenses. Of the 25 schools reporting the most licenses, only 6 *do not have* a medical school. Of the 25 schools reporting the fewest licenses, only 7 *do have* medical schools. Therefore, the authors surmise that well over half of the university licenses reported in the survey are in the biological sciences. Therefore, conservatively assigning 50% of the university licenses to biotechnology, and adding in the 12.2% from the U.S. Hospitals and Research Institutes, also results in a 60-40 estimate for biotechnology and physical sciences, respectively.

As MIT does not have a medical school, it is likely that it has a disproportionately large share of licenses in the physical sciences relative to the university licensing community: 50-50 versus 40-60. Therefore, noting that, in MIT's experience, licenses in the physical sciences consistently induce significantly less investment than licenses in the biological sciences, estimating that 60% of the AUTM licenses are in biotech is a conservative estimate.

Therefore, a rough extrapolation, based on the induced investment per license per year method, to the AUTM data could be made with this equation:

(S-U bio x $3.2M/lic/year (see Table 8)) + (S-U phys x $1.3M/lic/year (see Table 8)) + ((other licenses) x $.4M/lic/year (see Table 8))

Where "S-U bio" = estimated number of biotech start-ups = .6 x 459 = 275

and "S-U phys" = estimated number of physical science start-ups = .4 x 459 = 184

and "(other licenses)" = estimated number of other licenses = 3,300

This method, which makes *no attempt to correct for the fact that the induced investment in large entity biotech licensees is surely not zero*, results in an estimate of $2.5 billion of pre-production investment associated with universities' licenses every year.

Another approach to a preliminary extrapolation of induced investment would be to use the ratio of investment outside the university to revenue to the university. Referring to Table 7, note that start-ups appear to induce approximately 40 times the investment outside of the university as revenue to the university. Assume an induced investment ratio of 10.9:1 for other types of licenses. This is the smallest of the three reliable data points: small entities in the physical sciences, large entities in the physical sciences, and small entities in biotechnology, and ignores the unreliable number for the large entity biotech licenses.

Assume that 12.2% of the licenses were to start-ups; then a preliminary induced investment ratio for the AUTM licenses would be:

$$40 \times 0.12 + 10.9 \times 0.88 = 14.4$$

Based on $350 million of "royalty" payments in 1993 (3), this estimates the total induced investment nationwide at $5 billion in 1993. Note that the definition of "royalty" in the AUTM Licensing Survey (see (1), p. 4) does not include patent reimbursement costs, which were in the denominator of the MIT "induced investment" ratio (see Definitions section for "Revenue to MIT"). Removing patent reimbursement costs from the denominator in the induced investment ratio would make it larger, and thus would *increase* the estimate for the university licensing community.

The authors hope that these rough but dramatic estimates, based on what we believe to be very conservative assumptions, will inspire our colleagues to do similar studies at their own institutions. It appears that while the cumulative effect within MIT is of the order of magnitude of several hundred million dollars per year, the cumulative effect outside of our institution is of the order of magnitude of several billion dollars per year, even before first sales of licensed products. More detailed data nationwide on the types of licenses, exclusive versus non-exclusive, patent versus copyright, start-up, small entity, and large entity will permit more accurate, and the authors believe, higher estimates of the economic impact of university-based licensing. Such information would be very valuable to the entire licensing community, and we urge our colleagues to provide this information at the time of the next AUTM Licensing Survey.

SUMMARY AND CONCLUSIONS

Almost one billion dollars and over two thousand jobs are associated with 205 MIT active, exclusive, patent licenses (see Table 4). The $0.92 billion of pre-production investment does not include investment catalyzed by licensees who use the profits from licensed products to invest in and produce other technologies. This direct investment occurred over a total of 950 active license years, for an average investment of approximately $1.0 million invested per license per year. Assuming an average

cost per employee of $125,000/year (7), this works out to approximately 8 employees per license per year or a total of 7,400 job-years created by MIT licensing.

Licensing revenue to MIT is small compared to the amount of investment induced in the commercial sector. The ratio of 24 to 1 is consistent with the university's goal to move the technology to the private sector, and to focus on revenue generation for MIT only as a secondary goal. Under this policy, many inventions are patented and licensed, not only those deemed to be most likely to provide a large return.

On the matter of the data collection, we emphasize that it is the special relationship between university and licensee that makes gathering such information possible. We recommend that gathering the induced investment and employment data become a standard part of the licensing process, and that it be tracked much as universities track earned royalties. On the questions of study design, sampling, and extrapolation, we recommend that time be spent investigating the investment and jobs associated with both revenue and investment outliers, as they likely have a disproportionate contribution to total economic impact.

A disproportionate share of the induced investment and employment is associated with start-up companies, though at least some of this bias may be attributable to the challenge of obtaining meaningful data from large entities by the questionnaire method alone. Start-up companies in our study population comprised only 35% of the total number of licenses, yet accounted for 77% of the induced investment and 70% of the employment (see Table 4).

As university technology is typically very forward-looking and requires very large investments to bring products to market, an economic impact analysis based on product sales alone reveals only a fraction of the total effect of university licensing on the U.S. economy. Therefore, we recommend that the university

licensing community report induced investment and employment data as well as data on license revenue to the university in the form of license issue fees and earned royalties. The extrapolated data for the MIT exclusive, active, patent licenses reflect $0.92 billion of investment toward the commercialization of licensed products, and estimate that over two thousand people are presently employed in business efforts to bring these licensed products to market.

Two methods for extrapolating to the university licensing community were suggested. Based on certain assumptions about the distribution of licenses in the AUTM survey, one method employed the induced investment rate calculated from the MIT case study, and estimated at least $2.5 billion per year in pre-production investment associated with university licenses. The second method, based on the same assumptions, employed the induced investment ratio calculated in the MIT case study, and estimated $5 billion in pre-production investment for 1993. Assuming that $125,000 supports one job (7), this level of investment contributes between 20,000 and 40,000 jobs to the U.S. economy even before sales of licensed products.

The concept of self-reported induced investment reveals the economic impact directly traceable to licensing activity. There is also a well-known indirect "catalytic" effect of such high technology development and product sales (6) associated with business activities related to the licenses. Companies originally formed from university technology go on to invest in and manufacture other products, which in turn produce income and expenditures that promote economic development at large in the surrounding community.

Induced investment is a powerful outcome of university licensing and is an important way that a university may demonstrate the degree to which its efforts "promote the commercialization and public availability of inventions" under the Bayh-Dole act.

Acknowledgments

The information reported in this paper is a result of hard work performed by the entire staff of the MIT Technology Licensing Office. Thanks are extended to the administrative and financial staff for building and maintaining the office database; to all the licensing officers, including Christina Jansen, Alex Laats, John Preston, Jack Turner, and Jean Weidemier, for reviewing lists of licensees and answering many questions that all started: "Do you remember...?"; to our inventors for the inventions that make this all possible; and to our licensees for all their hard work. Special thanks to those who graciously helped us gather the information presented in this paper.

NOTES

1. *AUTM Licensing Survey Fiscal Years 1993, 1992, 1991*, conducted by Diane C. Hoffman, Inc., 23 Perrine Path Cranbury, NJ 08512, Copyright 1994, The Association of University Technology Managers, Inc.

2. *AUTM Public Benefits Survey*, conducted by Diane C. Hoffman, Inc., 23 Perrine Path, Cranbury NJ 08512, Copyright 1994, The Association of University Technology Managers, Inc.

3. Ashley Stevens, Chair AUTM Economic Development Committee, presentation entitled "Measuring Economic Impact," AUTM Advanced Licensing Course held in Arizona, December, 1994.

4. Ditzel, Roger G., "Public Law 96-517 and Risk Capital: The Laboratory-Market Connection," *Jour. Assoc. Univ. Technol. Managers*, Vol. III, 1991.

5. Vest, Charles M., "University-Government-Industry Research Cooperation," presented as the MITRE Corporation Distinguished Lecturer Program, April 7, 1993:6

6. Bank of Boston, Economics Dept., "MIT: Growing Businesses for the Future," June 1, 1989.

7. U.S. Bureau of the Census, *Statistical Abstract of the United States: 1994* (114th Edition), Washington, D.C., 1994, p. 613, No. 977.

APPENDIX A

Sample investment extrapolation for the physical-science licenses based on the data in the samples and on the number of license-years in each of the subcategories:

II phys = (II rate phys S-U) x (# lic-years phys S-U)
+ (II rate phys SE) x (# lic-years phys SE)
+ (II rate phys LE) x (# lic-years phys LE)

Where II phys = Extrapolated Induced Investment for the 101 physical-science licenses

and II rate phys S-U = Induced Investment Rate for the physical-science start-up licenses
= $1.3M/lic/year

and II rate phys SE = Induced Investment Rate for the physical-science small entity licenses
= $.14M/lic/year

and IIrate phys LE = Induced Investment Rate for the physical-science large entity licenses
= $.61M/lic/year

and # lic-years phys S-U = number of license years of the physical-science start-up licenses
= 164 (see Table 3P: 41 x 4)

and # lic-years phys SE = number of license years of the physical-science small entity licenses
= 184.5 (see Table 3P: 41 x 4.5)

and # lic-years phys LE = number of license years of the physical-science large entity licenses
= 81.7 (see Table 3P: 19 x 4.3)

Formula for Extrapolation = (($1.3M/Lic/Year) x 164)
+ (($0.14M/lic/year) x 184.5)
+ (($0.61M/lic/year) x 81.7
= $288M

APPENDIX B

Sample jobs extrapolation for the physical-science licenses based on the data in the samples and on the number of licenses in each of the subcategories:

Jobs phys = ((Jobs phys S-U)/(sample # lic phys S-U))
x (tot # lic phys S-U)
+ ((Jobs phys SE)/ (sample # lic phys SE))
x (tot # lic phys SE)
+ ((Jobs phys LE)/ (sample # lic phys LE))
x (tot # lic phys LE)

Where Jobs phys = Extrapolated jobs for the 101 physical-science licenses

and Jobs phys S-U = Jobs reported by start-up licensees in physical-science sample = 173

and Jobs phys SE = Jobs reported by small entity licensees in physical-science sample = 20

and Jobs phys LE = Jobs reported by large entity licensees in physical-science sample = 22

and sample # lic phys S-U = number of physical-science start-up licenses in sample = 9

and sample # lic phys SE = number of physical-science small entity licenses in sample = 5

and sample # lic phys LE = number of physical-science large entity licenses in sample = 4

and tot # lic phys S-U = total number of physical-science start-up licenses = 41

and tot # lic phys SE = number of physical-science small entity licenses = 41

and tot # lic phys LE = number of physical-science large entity licenses in sample = 19

Formula for Extrapolation = ((173/9) x 41) + ((20/5) x 41)
+ ((22/4) x 19) = 1,056

Antitrust and Technology Licensing

Kathleen R. Terry*

Antitrust in patent related matters has been dead for the last fifteen years. As surely as we now have a Democratic president, the eyes of the Antitrust Division of the Department of Justice (DOJ) are again on not only mergers and acquisitions, but also on business arrangements involving all types of intellectual property. That includes university patent, trademark, and copyright licenses.

Our field is new and expanding. Most of us were not working in technology management back in the days of the "Nine No-No's," when the DOJ attempted to have certain licensing practices declared *per se* illegal. We have fallen out of the habit of scrutinizing our license terms for antitrust violation and its companion, patent misuse. The purpose of this article is to assist the university license drafter in how to recognize, analyze and avoid potential problems.

I. ANTITRUST VIOLATIONS

A company, practicing its patent internally, is free to use the patent in nearly any way it chooses. It may shelve the patent. It may improve the patented product until it is outside the scope of claims. It may package any number of patents into one product. It may continue to derive income long after the patent expires. When a patent

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* *Kathleen R. Terry is Campus Director of Technology Transfer Services at the State University of New York at Buffalo.*

goes outside the company via a license agreement, each of the above activities may raise questions under the Sherman Antitrust Act.

The Sherman Antitrust Act of 1890, 15 United States Code §§ 1-7, was intended to halt monopolies, conspiracies, and agreements that have the effect of restraining or suppressing the operation of a free market in setting prices for goods and services, resulting in higher prices or limited availability to consumers. Whether an activity imposes an unreasonable restraint is analyzed under the "rule of reason." The analysis begins by determining whether the company has market power: that is, the ability profitably to maintain prices above, or output below, competitive levels for a significant period of time. Then the nature of the restraint is analyzed for anticompetitive effect. Finally, any justification for the restraint is balanced against the anticompetitive effect. For example, a new industry has considerable leeway in controlling its market to ensure quality. If it did not, the entire market might never develop. A few activities have been found repeatedly to be so unreasonable that courts have declared them to be *per se* illegal--that is, the occurrence of the practice is sufficient to find a company guilty of antitrust, and no balancing need be done. The best example of a *per se* antitrust violation is price fixing among competitors.

Examples of the effect of the Sherman Act crop up in everyday life. For instance, in the 1980's, the DOJ caused AT&T to be dismantled into local and long distance carriers, which allowed other carriers to compete more effectively in the field. With the flux of technological and business changes, DOJ is now considering amending the settlement decree to allow the local companies to expand into long distance service. More recently, the giant chip maker, Intel, withdrew its bid to acquire Intuit, for fear of disallowance of the

merger. It is clear that antitrust has "teeth" and should be considered.

Before speculating about where today's trends may lead, it may be useful to take a look at the recent past. During the heyday of antitrust in 1968, the Assistant Attorney General, heading the Antitrust Division of the Department of Justice, announced a list of "Nine No-Nos" of patent licensing, which it considered *per se* antitrust violations. They were:

- requiring a patent licensee to purchase an unpatented material from the licensor;
- grantback of title to the licensor of the licensee's improvements to the patented technology;
- attempting to impose restrictions after sale of the patented product;
- tie-in and tie-out: tying of products or services outside the scope of the patent claims, or restricting the licensee's freedom to deal with other suppliers;
- an agreement outside the license not to grant other licenses (that is, concealing the exclusive nature of the agreement);
- mandatory package licenses;
- any broadening of the royalty base;

- restriction on sale of products made with the patented process;

- price fixing.

Fortunately for university patent licensing, DOJ never succeeded in persuading a court to declare these practices *per se* illegal antitrust violations. In 1981, recognizing that licensing activity is too complex in its nature for blanket prohibitions, DOJ repudiated its *per se* position, leaving instances of the "Nine No-Nos" to be analyzed under the rule of reason. There have been few patent-related cases brought by the Division since the early 1980's. Antitrust climate changes. Assistant Attorney General Anne K. Bingaman, in a talk at a meeting commemorating the 60th anniversary of the Antitrust Division on January 10, 1994, announced that DOJ would again be scrutinizing practices involving intellectual property, and planned to revise the Division's 1988 International Guidelines (36 Patent, Trademark and Copyright Journal 170, 181). She said:

> "The core rights of owners of intellectual property are reasonably clear, but beyond that core, matters are a good deal less settled. Whether the holder of a patent may, for instance, tie unpatented supplies to the packaged products; engage in compulsory grantbacks; or place post sale restrictions on resale by purchasers are just a few of the host of issues that have been debated and litigated in the patent/antitrust field for several decades....I want to be clear today that we are in the process of reviewing and revising the International Guidelines for re-issuance shortly. Given my strong belief in competition, I think courts should be hesitant to read the statutory grant of provisions

> expansively, but should recognize the anticompetitive potential of restrictive practices at or beyond the borders of the clearly conveyed statutory rights." (47 Patent, Trademark and Copyright Journal 253).

On May 26, 1994, in connection with an antitrust action against a British company, Pilkington, plc, Robert E. Litan, Deputy Assistant Attorney General in the Antitrust Division, further stated: "The Division strongly supports intellectual property rights. Those rights can provide important incentives to innovate. We will not, however, turn a blind eye toward abusive intellectual property arrangements that reduce incentives to innovate." (48 Patent, Trademark and Copyright Journal 156).

The new Guidelines, published on August 8, 1994, pounded the last nail in the coffin of the "Nine No-Nos" as *per se* illegalities. The general principles are clearly pro-patent licensing:

> (a) for the purpose of antitrust analysis, the Agencies [DOJ and the Federal Trade Commission] regard intellectual property as being essentially comparable to any other form of property; (b) the Agencies do not presume that intellectual property creates market power in the antitrust context [in contrast to the earlier presumption that a patent *always* conferred market power on the owner]; and (c) the Agencies recognize that intellectual property licensing allows firms to combine complementary factors of production and is generally procompetitive. (49 Patent, Trademark and Copyright Journal 714.)

The Guidelines discuss and give examples of licensing situations formerly covered by the "No-Nos," but in a positive and pro-licensing manner. For example: "[f]ield-of-use, territorial, and other limitations on intellectual property licenses may serve procompetitive ends by allowing the licensor to exploit its property as efficiently and effectively as possible." And, "[t]he Agencies will not require the owner of intellectual property to create competition in its own technology."

A potentially troublesome new area has been added to antitrust scrutiny: that of anticompetitive arrangements in research and development, the "innovation market," consisting of the research and development directed to particular new or improved goods or processes, and the close substitutes for that research and development. Exactly how this analysis will be done is difficult to predict at this time.

Be warned, that although the effort to establish *per se* violations has been abandoned, some practices are still very suspect. For instance, price fixing has been declared illegal in so many contexts, (including the practice of coordinating scholarship offers to prospective students), that it is difficult to imagine a situation where price fixing would be considered acceptable, even in a vertical relationship. Some other practices have been considered by high courts and must be avoided, as discussed below.

II. PATENT MISUSE

Antitrust actions by the federal government are not the only trap awaiting the unwary licensor. Patent misuse is related to antitrust, but is broader in scope and effect, and strikes at the validity of a patent in question. Patent misuse is an equitable, judicially-created defense to patent infringement or royalties due under a license. A patentee who seeks to extend the exclusive patent rights

beyond the scope and term of the patent claims comes into court with "unclean hands," and the court will not allow such a party to enforce the patent.

Patent misuse and avoiding antitrust violations are the province of the license drafter, who should work closely with patent counsel to attempt to avoid problems as much as possible by careful drafting of the patent application and claims.

III. AVOIDING SUSPECT PRACTICES

In attempting to maximize the value of university technology, there are certain practices (temptations) that arise frequently. Because the rule of reason is a balancing act, it is necessary to look at all possible procompetitive and anticompetitive factors. Because patent misuse is an equitable defense, these factors should be looked at in light of general principles of fairness.

Some problems can be cured long before they arise during patent prosecution by good communication between the technology manager and the patent attorney.

A. Mandatory Package Licenses

Why would a licensor seek to require a licensee to take a package of patents? There are valid, economically sound reasons. A license agreement is generally negotiated early in the life of an invention, when neither licensor nor licensee is completely sure of the path of product development. In a complicated device, there could be as many as forty patents covering the parts, and it may be impossible to determine at the time the license is executed

whether, absent licensed rights, the licensee would infringe one or forty patents. Product lines change, and the licensee may later wish to add a patented component that was not specifically included in the patent license. The licensee may want access to improvements that are not available or not yet invented at the time of execution, and the licensor may be willing to help the licensee stay competitive. Finally, the essence of the license often is a simple promise not to sue, and a licensee wants the assurance of not being sued by the licensor for infringement of a non-included patent. There are bad reasons, too: the royalty rate may go up with the number of patents included, and if the licensee has need of a vital patent, he has no choice but to pay for unwanted patents. Some of the patents may expire later than others, prolonging the royalty period. These are the sort of procompetitive and anticompetitive factors to be balanced under a rule of reason. Congress agreed that balance is needed:

> **35 USC 271 (d) (5):** ... no patent owner otherwise entitled to relief for infringement of a patent shall be denied relief or deemed guilty of misuse or illegal extension of patent rights [because] he: ... (5) conditioned the license of any rights to the patent or the sale of the patented product on the acquisition of a license to rights in another patent or purchase of a separate product, unless, in view of the circumstances, the patent owner has market power in the relevant market for the patent or patented product on which the license or sale is conditioned.

B. Post Expiration Royalties

An important measure of a patent is temporal. Under *Brulotte Co. v. Thys* (379 U.S. 29, 85 S.Ct. 176, 143 USPQ 264 (1964) *rehearing denied* 379 U.S. 985 (1968)), it is clearly illegal to extend an obligation to pay royalties beyond the expiration of a patent even when negotiated at arm's length by willing parties. Unfortunately, those last years of a patent's life are almost always the most valuable: development and regulatory hurdles have been cleared; the market has been developed; the product has built up a following; there is clamor for more; competitors are waiting eagerly to enter the market. Then the patent expires.

During the days of the "submarine" patent, it was possible to keep a patent pending for thirty or forty years. Now, with the term of a patent measured from its filing date, and with continuing applications taking the same expiration date as the parent, any patent pending more than twenty years will expire before it can be enforced! There are few techniques available now to extend the term of a patent. One thing that is important is to prosecute as swiftly as possible, with no extensions of time beyond three months for response. Because time on appeal will be restored, it may be better to go on appeal rather than refile an application. An important--and difficult or impossible--goal is to wrap the technology in discrete packages that can be filed independently, not as continuations-in-part (c-i-p), so that each c-i-p takes its own term of twenty years from filing, rather than the term of the very first in the chain. Examples of this point in existing patent files: any c-i-p that was not subject to a terminal disclaimer would have qualified for separate filing.

C. The Trade Secret/Best Mode Problem

What if the university is transferring know-how along with patent rights? Trade secrets can be included in a license with patents and can legally draw royalties indefinitely, depending on the bargaining power of the licensing parties and the nature of the technology (*Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470, 94 S.Ct. 1879, 182 USPQ 763 (1974)). It does not violate the Brulotte rule when the trade secret is not illusory to extend the *trade secret* royalties past the term of the patent. With due regard to the commercial power of a patent, the *patent* royalties should be presumed to be at least as valuable as the trade secret royalties. That is, the royalty rate should be cut at least in half after the patent rights are not enforceable, because no patent issued, the patent expired, or the patent was declared invalid.

A mere recitation that the license also covers know-how is not sufficient to save the agreement. In the recent case *Litton Sys. v. Honeywell, Inc.*, 1995 WL 366468 (C.D.Cal.), a $1.2 billion jury verdict was reversed by the judge because, the patent being declared invalid, the license agreement became unenforceable because "there is a total absence of evidence that Louderback ever actually used any Litton trade secret in manufacturing a mirror for Honeywell.... The mere existence of an agreement not to use plaintiff's trade secrets does not relieve plaintiff of the burden to prove that the defendant accused of appropriating the trade secrets did in fact make use of them, and that the use was prohibited by the agreement."

Can trade secrets be kept while still satisfying the requirement of enabling the best mode of making

and using the invention? *Christianson v. Colt Industries Operating Corp.*, 798 F.2d 1051, 230 USPQ 840 (7th Cir. 1986), *transferred* 822 F.2d 1544, 3 USPQ 2d 1241 (Fed. Cir. 1987) *vacated on other grounds*, 486 U.S. 800, 108 S. Ct. 2166, 7 USPQ 2d 1109 (1988) provides some teachings. Colt made the M16 rifle for the United States Army under several patents. When the patents expired, Christianson sought to enter the market. Unfortunately, Christianson was never able to make a rifle that the Army would buy, because the detailed manufacturing specifications that made the rifle parts interchangeable were not disclosed in the patent specification and, presumably, Christianson's engineering staff was not able to duplicate the manufacturing specifications satisfactorily. Christianson brought suit against Colt for antitrust violations, alleging that Colt's patents were invalid *ab initio* for failure to satisfy the disclosure, enablement, and best mode requirements of Section 112. Christianson claimed that because the claimed parts could best be used for incorporation into the standard M16 rifle, Colt should have disclosed the crucial interchangeability in the patent specifications. The District Court held for Christianson, but on appeal the Federal Circuit reversed, holding that while Section 112 requires the patent to enable one of ordinary skill to practice the claimed invention, it has never required the patentee to disclose data on how to mass produce the claimed invention. There was no showing that Christianson could not make the claimed parts according to the patent specification; he simply wasn't able to assemble the parts into an M16 rifle. The question of whether the patents enable one to mass produce the parts and "to incorporate them in a particular manner desired by a particular customer is simply and totally irrelevant." The patentee is not

obliged to make a free gift of production data to competing manufacturers. As to the claim that Colt should have disclosed assembly into the M16 rifle, because that was the best mode of using the parts, the Court pointed out that a limitation on interchangeability or use in the M16 rifle appears nowhere in the claims. Because the best mode requirement relates only to practicing the claimed invention, it only necessitates disclosure in the patent specification as to the use of individual claimed parts in *a* rifle.

D. Trademark/Patent Licenses

Like trade secrets, trademarks are potentially eternal. Like trade secrets, trademarks can be included within a patent license with great care. It is necessary to avoid tying: that is, to make the use of the trademark a freely bargained for, separate grant with separate royalty stream, justified by a non-illusory statement of value. There is one important point to remember: a patent, and all that it contains, is freely available to the public on expiration of the patent. If the name that the patentee wishes to claim as its trademark is included in the patent, it cannot be registered and cannot be enforced as a trademark when the patent expires. This unfortunate situation arises most often in plant patents: the name on the patent "Morning Glow Petunia" cannot be claimed as a trademark. Pharmaceutical companies have long been aware of this problem. The generic name that is imposed on a proprietary drug is long, unpronounceable, and unrememberable while the trade name, which is theirs forever, is short, evocative, and easy to remember.

E. Scope of Claims

It is hazardous to go outside the scope of the claims in establishing a royalty base: that is, the accounting item on which the percentage royalty is calculated. The scope of the claims can be broadened during drafting and prosecution by including all categories of subject matter: composition of matter, process of making, methods of using, device for using. An illustrative example is United States Patent Number 5,048,532. This inventor made a special kind of disposable esophageal catheter and assembled existing electronic equipment to collect data. He analyzed peaks and minima from the resulting curves to determine several important physiological measurements. He never made a black box to collect, analyze, and display results. The company licensing the patent is developing such a monitor, which may or may not be patentable. The catheters and monitors are separate items, priced and sold separately. It could be an illegal extension of patent scope to include the monitors in the royalty base, *except that* the patent claims the method of collecting, analyzing, and displaying results. Because the device is made specifically to practice the method claims, it is within the scope of the patent. By collecting royalties on monitors as well as catheters, another temptation is avoided: that of attempting to fix the catheter price so that the licensee cannot use the disposables as a loss leader for the sale of monitors.

An analogous case in the biotechnology art did not involve a license, but is a valuable lesson in how the courts are sticking to the clear meaning of the words of a claim. *Amgen Inc. v. United States International Trade Commission*, 902 F.2d 1532, 14 USPQ 2d 1734 (Fed. Cir. 1990) involved erythropoietin (EPO), the

most valuable biotechnology product to date. The case arose when Amgen attempted to block the importation of EPO by Chugai Pharmaceutical Company, under Section 337 (a) of the Tariff Act of 1930, 19 USC §§ 1337 and 1337(a), which made unlawful the importation into the United States of articles that "are made, produced, processed, or mined under, or by means of, a process covered by the claims of a valid and enforceable United States patent." Amgen had a patent with claims directed to recombinant DNA sequences coding for EPO, vectors carrying those sequences and host cells expressing those vectors to produce a good yield of recombinant EPO. At this time, Amgen had no claims to the rEPO itself or to a process of using the host cell to make rEPO. Chugai used the same or equivalent host cell in Japan and imported the rEPO into the United States. The ITC dismissed this case for lack of subject matter jurisdiction, and Amgen appealed to the Federal Circuit. The issue on appeal was interpretation of the language "process covered by the claims" of Section 337 (a). Amgen's position was that the section did not require a "traditional process claim." Not so, said Judge Rich. Although the host cell could be considered a machine because it produced rEPO, the host cell claim did not cover a process any more than a claim to a machine would cover the process performed by the machine. There was nothing nontraditional about host cell claims that should call for revision of longstanding claim interpretation. Finally, Judge Rich held that "cover" had a plain meaning in the language and among the patent attorneys at whom the statute was directed, and concluded that "cover" could only mean a patent having at least one claim defining a process. The Court affirmed the ITC dismissal of the complaint.

One section of the "Boucher Bill" now in Congress would amend 35 U.S.C. § 271 to make the importing, selling, or using products made using a "biotechnological material" an act of infringement. Many patent attorneys are against the bill, the principal arguments being that the amendments are unnecessary because competent attorneys have learned how to draft appropriate claim language, and that technology-specific legislation may violate NAFTA/GATT provisions requiring patents to be available without discrimination as to field of technology. A good biotech patent attorney knows how to write a claim that will give protection under §271 (g) which makes it an act of infringement to import a product made by a patented process: not "I claim hybridoma 101" but "I claim a process for detecting X disease using hybridoma 101." Use good patent attorneys!

IV. MISCELLANEOUS

The new Guidelines clearly recognize that such licensing practices as field of use, cross-licensing, and joint development are likely to be procompetitive. However, outside the simple, direct licensing of a simple, direct patent, other problems unrelated to antitrust or misuse may arise that can interfere with the smooth progress to a successful license, and lead to license cancellation or litigation.

A license is usually the basis for a long-term, ongoing relationship between the parties, and all means by which the relationship can be kept amicable should be considered. Business people are not usually patent attorneys and may have difficulty in understanding the patent that is the core of the agreement. The most common error is thinking that everything disclosed in the specification may be freely practiced by the patentee, his

assignees, or licensees, while actually there may be other patents in existence that cover some of the technology disclosed in the specification. Make sure the patent attorney keeps the language as clear and simple as possible. A good attorney will be very clear on exactly what the claims cover and will sound an early alert to any dominant patent, owned by a third party, that will prevent the patentee from practicing the patent.

Broad patents are frequently licensed in exclusive fields of use. It is desirable, but not always possible, to define a field of use within one independent claim. Granting rights to "Claims 4, 5, and 6, but to no other Claims" can be helpful in keeping a licensee from inadvertently straying outside his fence.

As patent prosecution goes along, claims are amended or dropped. As product development goes along, features are added or changed or dropped. A client will, more often than not, never pay close attention to an application after it is filed. The patent issues and both client and attorney are shocked to find it doesn't cover the product. It is the technology manager's job to keep the attorney informed as product development goes along. Sometimes, economy can be achieved by canceling claims that have turned out to be worthless.

Beware the joint invention. If the inventor has made a truly seminal discovery and has applied for broad coverage that will dominate all uses, it is probable that other entities will seek to work in cooperation with the first inventor, with resulting joint inventions. This is a more common situation in universities than in industry. The problem is twofold. First, the joint owner may have cross-licensing agreements with unknown third parties. Secondly, the joint owner may use the joint rights as a back door to using the dominant patent without paying royalties.

V. CONCLUSION

The fifteen year lull in patent antitrust actions by the Antitrust Division of the Department of Justice may be over. The patent misuse defense is on the rise. The technology manager should avoid the temptation of licensing outside the scope of the patent by obtaining as long a patent term as possible, broadening the scope of claims, claiming all appropriate subject matter, and coordinating patent prosecution with product development. Other problems unrelated to antitrust or misuse also can most easily be avoided if recognized early.

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