DOLLARS FOR GENES: REVENUE GENERATION BY THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

By Richard J. Gilbert[†]

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I. INTRODUCTION

Human embryonic stem cell research promises potential breakthrough therapies for diseases such as Alzheimer's and Parkinson's, spinal cord injuries, cancer, HIV/AIDS, multiple sclerosis, heart disease, and mental

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† Professor of Economics, University of California, Berkeley. The author is grateful to Galen Hancock, Roger Noll, Pamela Samuelson, and David Zilberman for helpful comments and discussions.

health disorders.[1] In November 2004 California voters passed Proposition 71. The initiative created the California Institute for Regenerative Medicine (CIRM) and authorized the state to issue up to $3 billion in general obligation bonds to fund human embryonic stem cell research and provide overhead for the Institute.[2] In addition to the potential for stem cell research to improve lives, some supporters of Proposition 71 also promised large royalty income from the licensing of new technologies that would result from CIRM-funded research.[3] A study prepared by Laurence Baker, Professor of Health Research and Policy at Stanford University, and Bruce Deal of Analysis Group ("Baker-Deal study") predicted that the state would earn from $537 million to $1.1 billion in royalties from research funded by Proposition 71.[4]

This Article derives a much lower estimate of likely licensing income from CIRM-funded research and development ("R&D"). My methodology refines the approach in the Baker-Deal study and also forecasts future licensing income based on an evaluation of historical licensing income from sponsored research at universities, hospitals, and research institutes. My best estimate of licensing income comprises only a few percent of expenditures on human embryonic stem cell research. California's share of this licensing income is likely to be less than one percent of R&D expenditures in current dollars. The allocation of these relatively small revenues is less important than the greater objective of disseminating CIRM-funded stem cell technology quickly and widely. While investments in stem cell research will generate some financial return for the state of California, the primary benefit from these investments will be progress toward improved

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1. *See* California Secretary of State, *Text of Proposed Laws – Proposition 71*, *in* CALIFORNIA OFFICIAL VOTER INFORMATION GUIDE 147 (2004), *available at* http://www.cirm.ca.gov/prop71/pdf/prop71.pdf [hereinafter *Proposition 71*]; Alliance for Stem Cell Research, Stem Cell Facts – Diseases and Injuries, http://www.allianceforstemcellresearch.org/page.php?id=126 (last visited June 14, 2006).

2. The bond authorization is subject to a $350 million annual limit. California Secretary of State, *Proposition 71 – Title and Summary*, *in* CALIFORNIA OFFICIAL VOTER INFORMATION GUIDE 68-73 (2004), *available at* http://www.ss.ca.gov/elections/bp_nov04/prop_71_entire.pdf.

3. Alan D. Cherrington, Carolyn Aldige & Joan Samuelson, *Argument in Favor of Proposition 71*, *in* CALIFORNIA OFFICIAL VOTER INFORMATION GUIDE 72 (2004), *available at* http://www.ss.ca.gov/elections/bp_nov04/prop_71_entire.pdf ("By making California a leader in stem cell research and giving our State an opportunity to share in royalties from the research, [Proposition] 71 will generate thousands of new jobs and millions in new state revenues.").

4. LAURENCE BAKER & BRUCE DEAL, ANALYSIS GROUP, INC., ECONOMIC IMPACT ANALYSIS: PROPOSITION 71, CALIFORNIA STEM CELL RESEARCH AND CURES INITIATIVE (2004).

therapies for the treatment of major chronic and acute diseases. To be more precise, if income generation were the sole justification for stem cell research funding (which of course it is not), the state would be better off investing in its own municipal bonds.

In Part II, I describe two approaches to estimate potential CIRM royalty income, one based on expected future revenues and the other on extrapolation from actual licensing income earned from sponsored research at universities, hospitals, and research institutions. Taking the value of time into account, I show that both approaches predict present value licensing income that is a small fraction of the present value of CIRM R&D expenditures. I discuss different factors that limit the ability to generate licensing income in Part III, including uncertainty, distant payoffs, the need for additional investments, and unequal bargaining power. Part IV examines the revenue-generating potential for alternative licensing arrangements that rely on fixed fees, running royalties, and equity sharing. Historically, running royalties have been the main generator of license income for universities, hospitals, and research institutions, accounting for about eighty percent of total income. This Part describes why other arrangements, such as relying mainly on fixed fees, may appear attractive in theory yet under-perform relative to licenses that emphasize running royalties. This Part also considers equity participation by CIRM in licensee businesses. Equity sharing is a potentially rewarding path to commercialize CIRM technologies, and it should play a role in CIRM's overall technology transfer program. However, there is not much evidence that increased equity sharing would lead to significantly more licensing income than running royalties. Part V concludes.

II. ROYALTY INCOME

This Part reviews the estimate of future CIRM licensing income prepared by Laurence Baker and Bruce Deal and describes another approach based on actual past license revenues and R&D expenditures. Both approaches project that CIRM license income will be a small fraction of R&D expenditures after taking account of delays between expenditures and income and allowing for the time cost of money.

The Baker-Deal study uses a "prospective" approach to estimate royalty income from CIRM-funded research. This method estimates the likely number of major new therapies that will be introduced using technologies developed with CIRM research support and the expected revenues from these new therapies, and applies a royalty rate to estimate licensing income. An alternative approach is "retrospective," based on actual royalty

generation by research funded by universities, hospitals, and research institutes. Both approaches have merit as a means of estimating likely royalty income.[5] The time cost of revenues is a major issue, because it takes years to apply basic stem cell research to produce useful therapies and many more years for those therapies to wind their way through the U.S. Food and Drug Administration approval process. Nevertheless, CIRM may be able to generate some revenue over an earlier time frame by licensing technologies used as research tools to develop new therapies.[6] Another possible way for CIRM to accelerate income is to negotiate equity in companies that license its technologies and to profit from equity sales that capitalize the future value of stem cell research.

A. The Baker-Deal Methodology

The Baker-Deal study estimates that research funding by CIRM suffices to develop, in expected terms, 3.4 major new therapies, based on historical costs adjusted for inflation in the cost of health care R&D. The report projects $3 billion in revenues from a major biotechnology therapy.[7] In their base case the authors assume that the state will earn a royalty of two percent of sales of CIRM-funded therapies. This gives a nominal return of $60 million per major therapy and total royalty revenue of about $204 million for the estimated 3.4 therapies developed from CIRM-funded research. The authors assume a gap of ten years between the funding point and the start of royalties. The authors then inflate future royalty streams by an expected health care inflation rate of 4.2 percent to account for expected increases in the cost of drug therapies. Inflation increases the cumulative royalties to $537 million in their base case and $1.1 billion in their high estimate, which assumes a royalty rate of four percent of sales.

The obvious problem with this calculation is that a dollar of revenue earned ten years in the future does not have the same value to the state as a

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5. Neither approach is inherently superior. Future revenues in the prospective approach are speculative. Past performance in the retrospective approach need not be indicative of future returns.

6. The history of licensing revenues from the Cohen-Boyer patents suggests that the potential to earn revenues quickly is limited. Only about ten percent of the $254 million in revenues from Cohen-Boyer licenses was collected from up-front payments and R&D licenses. The remaining ninety percent came from product sales. *See* Maryann Feldman, Alessandra Colaianni & Kang Liu, *Commercializing Cohen-Boyer 1980-1997*, at 23 (DRUID Working Paper No. 05-21, 2005), *available at* http://www.druid.dk/wp/pdf_files/05-21.pdf.

7. The revenue figure is based on a forecast of the revenue potential for eighteen biotechnology therapy approvals in 2004, adjusted for inflation. BAKER & DEAL, *supra* note 4, at 81.

dollar of revenue earned in the present. The study accounts for inflation in health care costs, but does not discount future revenue flows. In their defense, the authors report only projected revenue flows, not the value of these revenues. A correct value calculation should discount future revenue flows by the time value of money. While reasonable people may disagree over the appropriate choice of a discount rate, a number at the low end of the range is the rate of interest paid by ten-year treasury bonds. Treasury bonds are exempt from state taxes, but not federal tax. Investments by a state should count federal taxes as a cost, but not state taxes, as they are returned to the state coffers. The interest rate for treasuries, also called the yield, is consistent with these financial flows.[8]

In June 2006, the ten-year treasury bond yielded about 5.0 percent.[9] Discounting the estimated royalty flows in the Baker-Deal study base case by this rate reduces the value of these royalties from $537 million to about $189 million in current dollars, or about thirty-five percent of the royalty revenue reported in the study. The study's high estimate assumes that the state would earn a royalty of four percent of sales, which corresponds to a present value royalty income of about $379 million from the state's $3 billion research investment. Taking into account the value of time, the study's estimated royalty income does not come close to paying back the state's investment in R&D, let alone earn a positive return on that R&D.[10]

Applying the interest rate on treasury bonds reduces the estimated royalties in the Baker-Deal study by about sixty-five percent. A higher discount rate, which is arguably appropriate to account for the high risk of stem cell R&D, would result in still lower present value royalty income. The state's actual payout of licensing income would be less than the discounted numbers indicate, because CIRM plans to assign a share of royalty income to grantee organizations and inventors. The grantee organiza-

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8. One could make an argument for discounting future revenues using the much higher rate of return on private investment, which is the opportunity cost of using state funds. There is a large literature on the appropriate discount rate. *See, e.g.*, Peter G. Warr & Brian D. Wright, *The Isolation Paradox and the Discount Rate for Benefit-Cost Analysis*, 96 Q.J. ECON. 129 (1981).

9. Bankrate.com, Treasury Bill Interest Rates and Treasury Note Interest Rates, http://www.bankrate.com/brm/ratewatch/treasury.asp (last visited June 21, 2006) (indicating that the yield for ten-year constant maturity treasury bonds was 5.05% on June 21, 2006).

10. Discounting the expected flow of CIRM R&D expenditures does not change the conclusion that the expected present value of CIRM royalty income is a small fraction of the present value of R&D expenditures, even assuming the study's high estimate for expected royalties. The present value of R&D expenditures is about $2.4 billion assuming annual expenditures of $300 million per year and a five percent discount rate.

tions' normal policies for externally funded R&D govern how much inventors may accumulate. This is a sensible policy. It ensures that inventors have the same financial incentives to work on CIRM-funded research projects as they do for other projects and does not unduly discourage research entities from accepting CIRM grants.[11] The current CIRM intellectual property policy requires no payment of licensing revenues to the state of California unless total royalties earned by grantee organizations, net of payments to inventors, exceed a threshold of $500,000, adjusted for inflation. For royalties that exceed the threshold, the policy specifies that the grantee organization pay twenty-five percent of its share remaining after payments to inventors to the state of California.[12] As an example, the University of California's current policy permits inventors to retain thirty-five percent of net licensing income from their discoveries.[13] For royalties from inventions funded by CIRM, twenty-five percent of the remainder, or about one-sixth of total revenues, would go to the state. If other funding sources were used in the creation of a CIRM-funded patented invention, the state's return would be proportionate to the share of research support provided by CIRM. The CIRM sharing rule (one quarter to the state after deducting thirty-five percent for the inventor's share, assuming the therapies predicted in the Baker-Deal study exceed the CIRM threshold) would reduce the state's share of estimated royalty income to about $31 million in the Baker-Deal study base case and $62 million in the study's high estimate.

These estimates of royalty income to the state are only a few percent of the total investment in stem cell research that will be funded by CIRM. Under these scenarios, the state's financial return from royalty income for research funded by CIRM will be extremely modest. The state of California will not earn a profit from royalties on stem cell technologies funded

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11. *See* Roger G. Noll, *The Painful Implementation of California's Stem Cell Research Program*, STANFORD INST. FOR ECON. POL'Y RES. POL'Y BRIEF, October 2005; Roger G. Noll, *The Politics and Economics of Implementing State-Sponsored Embryonic Stem-Cell Research* 36-37 (Stanford Inst. for Econ. Pol'y Res. Discussion Paper 04-28, June 2005).

12. CIRM, INTELLECTUAL PROPERTY POLICIES FOR NON-PROFIT ORGANIZATIONS 19 (2006), *available at* http://www.cirm.ca.gov/policies/pdf/IPPNPO.pdf [hereinafter IPPNPO].

13. OFFICE OF THE PRESIDENT, UNIVERSITY OF CALIFORNIA TECHNOLOGY TRANSFER PROGRAM, ANNUAL REPORT, FISCAL YEAR 2004 13 (2004) [hereinafter U.C. TECHNOLOGY TRANSFER ANNUAL REPORT 2004]. License revenue sharing policies vary substantially among universities. Part of the variation is the result of an accounting artifact; revenues may be assigned to a laboratory, yet be under the control of the inventor. *See* Saul Lach & Mark Schankerman, *Incentives and Invention in Universities* 6 (Nat'l Bureau of Econ. Research, Working Paper No. 9727, 2003).

by CIRM, nor will royalties return a significant fraction of CIRM expenditures to the state.

B. A Retrospective Approach

An alternative approach to estimate likely royalty income from CIRM investments requires one to extrapolate from royalties actually earned by universities, hospitals, and research institutes on their past R&D investments. This estimate is retrospective because it is based on returns to historical R&D expenditures rather than likely future returns to expenditures by CIRM. Most CIRM grantees will be associated with universities, hospitals, and research institutes. Hence, licensing revenues from these organizations, particularly hospitals and health-related research institutes, provide an appropriate baseline to estimate revenues from CIRM licenses.[14]

As a reference point, Table 1 shows licensing income from sponsored research at universities and research institutes surveyed by the Association of University Technology Managers (AUTM) for fiscal years 2003 and 2004. For fiscal year 2003, AUTM reported net licensing income of $867 million and total research expenditures of $34.8 billion. Net licensing income equals gross license income less license income paid to others and legal fees expended, plus legal fees reimbursed. The corresponding figures for fiscal year 2004 are net licensing income of $925 million and total research expenditures of $37.2 billion. For both fiscal years, licensing income averaged about 2.5 percent of research expenditures.[15]

Licensing income earned by U.S. hospitals and research institutes surveyed by AUTM was a considerably larger fraction of sponsored research expenditures in FY 2003 and 2004. In fiscal year 2003, these hospitals and research institutes earned licensing income of about $292 million and had total research expenditures of about $3.7 billion. For fiscal year 2004 the corresponding figures are licensing income of $314 million and revenues of about $4.1 billion. Licensing income was 7.9% of sponsored research expenditures at hospitals and research institutes surveyed by AUTM in FY 2003 and 7.7% of sponsored research expenditures in FY 2004.

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14. California universities, hospitals, and non-profit research institutes received the first round of CIRM grants. Press Release, CIRM, ICOC approves first stem cell grants in California (Sept. 9, 2005), *available at* http://www.cirm.ca.gov/pressreleases/2005/09/09-09-05_ii.asp.

15. AUTM, AUTM LICENSING SURVEY: FISCAL YEAR 2003 50 (2003); AUTM, AUTM U.S. LICENSING SURVEY: FISCAL YEAR 2004 56 (2004).

Table 1
AUTM Licensing Survey: FY 2003 and 2004

	U.S. Universities		U.S. Hospitals and Research Institutes	
	FY 2003	FY 2004	FY 2003	FY 2004
Sponsored Research Expenditures ($ millions)	34,827	37,162	3,699	4,082
Net Licensing Income ($ millions)	867	925	292	314
Net Licensing Income as Percent of Research Expenditures	2.5%	2.5%	7.9%	7.7%

The licensing income reported in Table 1 is net of legal fees, but not of other administrative costs associated with running a technology transfer program. Data on overhead costs are available for the University of California's technology transfer program. For fiscal years 2000 through 2004, the University of California system-wide Office of Technology Transfer incurred operating expenses, other than legal and other direct expenses, equal to about fifteen percent of total licensing revenues.[16] Deducting fifteen percent for operating expenses reduces the net licensing income in Table 1 to about 2.1% of research expenditures for all university research and 6.6% of research expenditures for U.S. hospitals and research institutes.

Licensing income earned by U.S. hospitals and research institutes, rather than income earned by universities, arguably better represents the income that the California Institute of Regenerative Medicine will earn. Independent survey research by Castillo, Parker, and Zilberman provides more evidence that medical product and process licenses are likely to command higher royalty percentages than other licenses. Respondents to a survey of thirty-six universities reported royalties of 6.3 to 9.4 percent of sales for medical products, compared to an average royalty of 3.9 percent

16. U.C. TECHNOLOGY TRANSFER ANNUAL REPORT 2004, *supra* note 13, at 16 (showing in exhibit 26 that total licensing revenues include a one-time $200 million legal settlement related to its human growth hormone invention and that including this amount reduces the share of operating expenses to about ten percent of total licensing revenues).

of sales for agricultural products and 6.3 percent for engineering products.[17]

The higher royalties earned on health care technologies reflect the large share of research and development expenses in the medical products sector. In 2001, R&D expenses were 7.8 percent of net sales for pharmaceuticals and medicines and at least 9.0 percent of net sales for medical equipment and supplies,[18] compared to an average for all industry of 4.1 percent.[19] The greater importance of R&D in these industries allows a licensor of new technology to bargain for a larger fraction of net sales relative to royalty percentages in many other industries. The value of a technology to a potential licensee is the amount that the technology saves in product development costs or the additional value that the technology allows the licensee to offer its customers. If R&D costs average only four percent of product revenues, a potential licensee in a competitive market will not be willing to pay a royalty of more than four percent to license an R&D technology unless the technology offers an increase in value that the licensee can capture with a higher price. Competition caps the royalty that the licensee can offer. A licensee could offer more in a market where it has more pricing discretion, although it would not pay a royalty that exceeds its own cost of investing in R&D to develop an alternative technology or the cost of licensing an alternative technology from another source.

The numbers in Table 1 compare *current* royalty income to *current* research expenditures. However, current royalty income is the payoff for research expenditures that occurred many years in the past. Research discoveries take years to evolve into potentially useful products. Regulatory approval adds several more years before companies can market potentially useful drugs and therapeutics. A more accurate estimate of the benefits of R&D would compare R&D investments to expected future payoffs adjusted for the time value of money. Detailed estimates depend on a number of assumptions, including the lag between R&D investment and the launch of commercial products, assumed rates of inflation in health care costs and prices, real discount rates, and the time profile of royalty revenues and licensing expenses.

A partial correction for the temporal effects of R&D and the receipt of royalty income uses the royalty income in Table 1, adjusted for operating

17. Federico Castillo, Doug Parker & David Zilberman, The Performance of Offices of Technology Transfer (1999) (unpublished manuscript, on file with Department of Agricultural and Resource Economics, University of California, Berkeley).

18. NATIONAL SCIENCE FOUNDATION, SCIENCE & ENGINEERING INDICATORS 2004, tbl. A-20 (2004) (omitting federal funding for R&D in this figure).

19. *Id.* at tbl. A-19.

expenses, as a proxy for royalties that will occur in the future as a result of the R&D expenditures shown in the table. This calls for discounting royalties by a real, inflation-adjusted discount rate to account for both increases in health care costs and the time value of money. Assuming a lag of eight years between R&D expenditures and the receipt of income and a real discount rate of five percent, the ratio of royalty income to R&D falls to about 4.5 percent.

The state's actual licensing income will comprise a much smaller fraction of its R&D expenditures. Following the revenue sharing policies currently adopted by CIRM and assuming the University of California policy that assigns thirty-five percent of license revenues to the inventor, the state will receive about one-sixth of total royalty revenues (twenty-five percent of revenues remaining after deducting an inventor share of thirty-five percent). These policies reduce my estimate of the state's licensing revenues to less than one percent of CIRM-funded expenditures on stem cell R&D, one sixth of the estimate of total rate of return on research investment, which is 4.5 percent.

This estimated return implicitly assumes that all CIRM-funded R&D projects will exceed the CIRM threshold for paying royalties to the state. In fact, few technologies generate revenues that exceed the CIRM threshold, although those that do account for a high share of total licensing income. After deducting an inventor share of thirty-five percent, the CIRM threshold is a total royalty income of about $770,000. In fiscal year 2004, the University of California at San Francisco, a major hospital and healthcare research institution in the University of California system, generated net royalty income of $18.2 million from 298 active licensing agreements, an average of $61,084 per agreement.[20] Assuming that a license produces revenues for ten years, the average license revenue would not exceed the CIRM threshold after deducting the inventor's share. The CIRM royalty threshold would have a much smaller impact on the state's share of revenues from the most successful inventions, which account for a very large share of licensing income. While the University of California system had almost one thousand active licenses in fiscal year 2004, the twenty-five licenses with the largest royalty income accounted for almost eighty percent of all royalties.[21] All of these licenses earned cumulative royalties in excess of $770,000.[22] Reducing my estimate of royalty income paid to the

20. U.C. TECHNOLOGY TRANSFER ANNUAL REPORT 2004, *supra* note 13, at 17.

21. *Id.* at 8, 10.

22. University of California Technology Transfer Program Annual Reports for Fiscal Years 2000-2004 confirm that total royalties exceeded the $770,000 threshold for all of the top twenty-five royalty-earning technologies in FY 2004.

state of California by twenty percent to account for technology royalties that do not exceed the CIRM threshold lowers my estimate of the ratio of royalty income to R&D spending to about 0.60 percent in present value terms, which is consistent with the low return I estimate using the Baker-Deal methodology adjusted for the time value of money. Royalty income from CIRM-funded projects will not return a significant fraction of expenditures to the state, and certainly will not generate a significant financial return on the state's investment.

C. Extreme Outcomes and Extreme Expectations

It is not out of the realm of possibility for research expenditures to produce very high royalty returns. In 1998, Florida State University earned royalties from technology licenses that totaled $46.6 million. The entire Florida State University research budget in that year was $112 million, so royalty income at Florida State was 41.6 percent of research expenditures.[23] These extraordinary results are due to research at Florida State University that was instrumental for synthesis of the drug Taxol, a treatment for ovarian, breast, lung, and testicular cancer. Approved by the FDA for initial marketing at the end of 1992,[24] by 2001 Taxol had become the best-selling cancer drug in history.[25] Florida State University earned $67 million in royalty revenues in 2000, roughly 4.2 percent of product sales, nearly all of which was royalties from its technology to synthesize Taxol.[26]

Royalty income from stem cell technologies would more than pay for the cost of R&D if CIRM could reliably turn out patents such as the Florida State University patent for the synthesis of Taxol.[27] Of course, the Taxol patent is an outlier among outliers, a celebrity patent in the world of university technology transfer. Furthermore, taking the time value of money into account, it would require more than fifteen patents as lucrative as Taxol for CIRM to earn a market rate of return on its R&D expenditures solely from licensing income.[28] This is implausible given that the

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23. Rebecca Zacks, *The TR University Research Scorecard 2000*, TECH. REV., Jan 11, 2002, at 4.

24. U.S. GENERAL ACCOUNTING OFFICE, GAO-03-829, TECHNOLOGY TRANSFER: NIH-PRIVATE SECTOR PARTNERSHIP IN THE DEVELOPMENT OF TAXOL 11 (2003).

25. *Id.* at 1.

26. *Id.* at 13 (reporting that ninety-eight percent of the licensing income earned by Florida State University in 2000 was from the license for its Taxol synthesis patent).

27. The National Institutes of Health provided Florida State University with a $2 million grant to subsidize its Taxol synthesis research.

28. Suppose that a blockbuster patent, such as Florida State's Taxol patent, generates $60 million in royalties per year for ten years. Assuming that revenues begin eight

annual research budget of CIRM, about $350 million per year for ten years, is only about ten percent of 2003 expenditures on academic R&D in the health sciences in California.[29]

Forecasting is risky. Research funded by CIRM could lead to technologies that have as much or more commercial success as the Cohen-Boyer technology or other blockbuster patents such as Florida State's patent on Taxol. However, if we have to forecast, it is safer to rely on historical average returns for a large sample of R&D investments, rather than extrapolating from Taxol or gene-splicing technologies to all CIRM-funded R&D.

D. Low Royalty Income Is Not All Bad

There is an upside to my estimate that the state is not likely to earn a substantial return on its investment in stem cell R&D solely from royalty income generated by licenses for its discoveries. Significant royalty income could put CIRM at risk of losing tax-exempt status for its bond funding.[30] The loss of tax-exempt status would have an immediate adverse impact on the cost of financing R&D by CIRM. In the fall of 2005, then-California State Treasurer Philip Angelides estimated a difference of seventy-five basis points in interest costs between long term taxable and tax-exempt general obligation California state bonds; the spread would be higher in a higher-interest rate environment.[31] The 0.75% difference exceeds my estimate of the royalty income that CIRM is likely to earn from its stem cell research. If the receipt of royalty income places CIRM at risk of losing tax-exempt status, the state would be better off abandoning any claim to royalty income.[32] This also would have the additional, albeit

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years after R&D expenditures and applying a ten percent discount rate gives a total present value of about $200 million. Fifteen times this number is still less than the CIRM R&D budget.

29. Expenditures on academic R&D in California were $5.36 billion in 2003, of which fifty-eight percent was in the health sciences. National Science Foundation, Science and Engineering State Profiles: 2003-04, http://www.nsf.gov/statistics/nsf06314/ (last visited June 19, 2006); *see also* Noll, *The Painful Implementation of California's Stem Cell Research Program*, *supra* note 11; Noll, *The Politics and Economics of Implementing State-Sponsored Embryonic Stem-Cell Research*, *supra* note 11, at 34.

30. Whether royalty income would negate tax-exempt status is not clear. *See, e.g.*, Letter from Then-California State Treasurer Philip Angelides to CIRM President Zack Hall (Oct. 26, 2005), *available at* http://www.etopiamedia.net/empnn/pdfs/angelides-hall1.pdf (noting that "the use of state bond financing to fund stem cell research is a new frontier in federal tax law").

31. *Id.*

32. The Proposition 71 charter that created CIRM specifies that the Independent Citizens' Oversight Committee (ICOC) shall establish standards that allow the State of

small, advantage of promoting the development and dissemination of stem cell therapies by eliminating a small royalty tax on users of CIRM-developed technologies.[33]

III. WHY IS LICENSING INCOME SO LOW?

Historically, non-financial corporations in the U.S. have earned rates of return on their capital investments in excess of ten percent per annum.[34] This means that an investment of $100 in physical capital earns, on average, in excess of $10 every year for the foreseeable future. Some estimates of average rates of return on investments in R&D are much larger.[35] Yet, royalties on sponsored R&D have averaged only two to eight percent of the cost of these investments and much less when adjusted to account for the long delays between R&D expenditures and the receipt of royalty income. What explains the fact that, historically, universities and research laboratories have captured only a small fraction of revenues related to their R&D? There are many explanations, several of which I explore below.

A. Highly Uncertain Value of R&D

While some research, such as that leading to Taxol or to the discovery of recombinant DNA techniques, has been extremely valuable, these are distant outliers. Most R&D discoveries generate no royalty income. The distribution of royalty income from R&D programs is highly skewed. Only four of the thirty-two university hospitals and research institutes surveyed by the Association of University Technology Managers earned total revenues from technology licensing that exceeded $40 million in 2004.

California to benefit from the patents, royalties, and licenses that result from the activities of CIRM. *Proposition 71*, *supra* note 1, § 5, ch. 3, art. 1. *See also* IPPNPO, *supra* note 12 (describing its current policies with respect to patents, royalties, and licenses). My recommendation could run afoul of this requirement, although the quantitative impact would be small in present value terms.

33. A running royalty increases the marginal cost of using the licensed technology or selling a product made with the licensed technology.

34. *See, e.g.*, Eugene F. Fama & Kenneth R. French, *The Corporate Cost of Capital and the Return on Corporate Investment*, 54 J. FIN. 1939 (1999). The authors also estimate a real rate of return on the book cost of investment equal to about 7.5% over the period 1950–1996 and a nominal rate of return, which includes inflation, of about 13%. *Id*. at 1955.

35. *See, e.g.*, Zvi Griliches, *R&D and Productivity: Econometric Results and Measurement Issues*, *in* HANDBOOK OF ECONOMICS OF INNOVATION AND TECHNOLOGICAL CHANGE 53-89 (Paul Stoneman ed., 1995); Edwin Mansfield, John Rapoport, Anthony Romeo, Samuel Wagner & George Beardsley, *Social and Private Rates of Return from Industrial Innovations*, 91 Q.J. ECON. 221 (1977).

Three-quarters of the hospitals and research institutes in the AUTM survey earned total revenues less than $6 million from technology licensing in 2004. The median total income from technology licenses in 2004 was in the range of $2 to 3 million; that is, half of the university hospitals and research institutes in the survey earned less than $2 to 3 million in total royalty income from technology licenses in 2004.[36] The fact is that most basic research would earn little or no licensing income even if the research institution could bargain for a larger share its value.

Table 2 shows the top five sources of licensing revenues earned by the University of California (U.C.) system for the years 1996, 2000, and 2004. The table also shows the total licensing revenue for the U.C. system in each year and the fraction of total licensing revenue earned by the license with the largest revenues. A single technology, the Hepatitis-B vaccine, accounted for more than forty percent of U.C. licensing revenues in 1996 and for more than a third of all U.C. licensing revenues over these years.

36. AUTM U.S. LICENSING SUVEY: FISCAL YEAR 2004, *supra* note 15, at 25.

Table 2
Licensing Revenues Earned by the University of California System ($000's)[37]

FY 1996	Hepatitis-B Vaccine (1979,1981)	$25,412
	Process for splicing genes (1974)	$12,662
	Human Growth Hormone (1977)	$5,292
	Nicotine Patch (1984)	$1,576
	Radiographic Media (1979)	$1,214
	Total Licensing Revenues	$63,204
	Largest as Percent of Total	40.2%
FY 2000	Hepatitis-B vaccine (1979,1981)	$26,462
	Treatment-Intracranial Aneurysms (1989)	$5,671
	Human Growth Hormone (1977)	$2,890
	Process for splicing genes (1974)	$2,785
	Camarosa strawberry (1992)	$2,266
	Total Licensing Revenues	$67,765
	Largest as Percent of Total	39.0%
FY 2004	Hepatitis-B vaccine (1979,1981)	$18,910
	Treatment-Intracranial Aneurysms (1989)	$7,896
	Energy Transfer Primers (1994)	$3,513
	Interstitial Cystitis Therapy (1980)	$3,469
	Camarosa strawberry (1992)	$3,222
	Total Licensing Revenues	$79,265
	Largest as Percent of Total	23.9%

Other university licensing programs also illustrate the importance of single blockbuster discoveries. Revenues from licenses for the Cohen-Boyer patent for gene splicing accounted for roughly half of the technology licensing revenues earned by Stanford University over the life of the patent.[38] More than half of the licensing revenues earned by Harvard University in fiscal year 2004 came from licenses for the Cardiolite, a tool for diagnosing coronary artery disease. Harvard had 554 active licenses in fis-

37. OFFICE OF THE PRESIDENT, UNIVERSITY OF CALIFORNIA TECHNOLOGY TRANSFER PROGRAM, ANNUAL REPORTS, FISCAL YEARS 1996, 2000 & 2004 (1996, 2000, 2004).

38. The Cohen-Boyer patent, which expired in 1997, earned licensing revenues of about $255 million on worldwide product sales of over $35 billion. *See* Feldman et al., *supra* note 6, at 23.

cal year 2004, only two of which generated income of more than $1 million, while fifty-eight percent produced income of less than $10,000.[39] The University of California at San Francisco, a major hospital and research institution, reported that about ninety-eight percent of disclosed inventions earn less than $100,000 per year in licensing income and about eighty percent earn less than $10,000 per year.[40]

The highly skewed distribution of licensing royalty income for university hospitals and research institutes suggests that licensees have to bear the risk that most of the technologies they license will be dry holes. The very few gushers have to compensate for expenditures by licensees that generate little or no return.[41] For this reason, licensees are unlikely to be willing to share a large fraction of the revenues from licensed technologies with the licensor. Doing so would sap the licensee of the economic returns generated by the occasional technology that has very substantial value.[42]

B. Distant Payoffs

New drug development requires a sequence of discovery, preclinical development and testing in assays and animals, clinical testing on humans, and regulatory approval. Each of these steps incurs delays and risk of failure. Clinical testing typically begins with small-scale tests on volunteers, then moves to larger-scale tests on targeted populations, and finally to larger-scale tests that are designed to establish efficacy and identify undesirable side-effects.[43] It is only after a drug manufacturer completes these clinical tests that it may submit a new drug application (NDA) or a bio-

39. HARVARD UNIVERSITY OFFICE FOR TECHNOLOGY AND TRADEMARK LICENSING, ANNUAL REPORT FISCAL YEAR 2004 5 (2004), *available at* http://www.techtransfer.harvard.edu/files/OTD_AR2004.pdf.

40. UNIVERSITY OF CALIFORNIA, SAN FRANCISCO OFFICE OF TECHNOLOGY MANAGEMENT, THE OTM GUIDE TO INTELLECTUAL PROPERTY MANAGEMENT 5 (2003), *available at* http://www.otm.ucsf.edu/docs/otmIPMgmt.asp#Patenting.

41. These expenditures include additional R&D costs and the costs of clinical trials, as well as product development and marketing. *See* Henry G. Grabowski & John Vernon, *Returns to R&D on New Drug Introductions in the 1980s*, 13 J. HEALTH ECON. 383, 399 (1994). In their study of the returns to pharmaceutical R&D, Grabowski and Vernon observe that if the top-selling drug were excluded from the cohort introduced between 1980 and 1984, the remaining drugs would fail to break even on average.

42. Cochrane observes that when the distribution of returns is highly skewed, variance contributes to the expected value of returns as well as to risk. Variance is a problem for a licensee because it implies that a small set of licenses has a high probability of earning little or no return. *See* John H. Cochrane, *The Risk and Reward of Venture Capital*, 75 J. FIN. ECON. 3, 5 (2005).

43. Joseph A. DiMasi, Ronald W. Hansen & Henry G. Grabowski, *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151, 156 (2003).

logical license application (BLA) to the U.S. Food and Drug Administration.[44]

Mansfield traced the lag between the publication of academic research results and the first commercial introduction of new products and processes based on those results. He surveyed a sample of innovations in several industries during the time periods 1975-1985 and 1986-1994. For "Drugs and Medical Products," Mansfield reports lags that range from 6.2 to 10.3 years, depending on the time period of the survey and on whether the academic research was necessary or only a very substantial aid for the development of the new drug or medical product.[45]

DiMasi, Hansen, and Grabowski estimated a mean time between the start of clinical testing and submission to the FDA of a NDA or new BLA equal to 72.1 months.[46] At the time of their study, the mean time required for FDA approval was 18.2 months, resulting in a total lag from the start of clinical testing to marketing approval of a new drug equal to about 7.5 years.[47] This is within the range of estimates by Mansfield, but understates the lag from basic R&D to marketing approval for a new drug because considerable R&D is necessary before clinical testing.[48]

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44. "A biologic product is any virus, serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product applicable to the prevention, treatment, or cure of diseases or injuries. Biologic products are a subset of 'drug products' distinguished by their manufacturing processes, biological process vs. chemical process. In general, the term 'drugs' includes biologic products." Federal Drug Administration, Glossary of Terms, http://www.fda.gov/cder/drugsatfda/glossary.htm#B (last visited May 7, 2006).

45. Edwin Mansfield, *Academic Research and Industrial Innovation: An Update of Empirical Findings*, 26 RES. POL'Y 773, 775-76 (1998).

46. DiMasi, *supra* note 43, at 164.

47. In recent years the FDA has reduced the average lag for new drug approvals. The approval time for a new molecular entity (NME) fell from about two years in the early 1990s to about one year in 1999, but then increased to over fifteen months in 2000. A NME is medication containing an active substance that has never before been approved for marketing in any form in the United States. FDA, FDA's Drug Review and Approval Times, http://www.fda.gov/cder/reports/reviewtimes/default.htm (last visited May 7, 2006). Approval times for NMEs could be somewhat longer than approval times for NDAs, which may be based on familiar chemical compounds. New drugs made with stem cell technologies are likely to be NMEs and hence have longer approval times than for NDAs. However, the approval time could be as low as six months if classified as a priority new drug application.

48. *See also* James D. Adams, *Fundamental Stocks of Knowledge and Productivity Growth*, 98 J. POL. ECON. 673 (1990) (reporting a twenty-year lag between publication of research results and its peak effect on industrial productivity).

With private discount rates in the range of 10-15% per year, delay between R&D expenditures and commercial products causes a very large reduction in the financial value of that R&D.[49] Consider the following optimistic scenario for an illustration of the effects of discounting. Suppose a CIRM program costs $100 million and, after a ten year delay for product development, testing, and regulatory approval, leads to a drug that earns $200 million per year for ten years, for a total of $2 billion. The nominal payoff from CIRM R&D is impressive. The R&D program earns $20 in revenue from each dollar of R&D. But accounting for the time value of money with a 15% discount rate makes the R&D investment much less attractive. First, the present value of the revenues from the drug falls by almost half from $2 billion to about $1.15 billion. Second, the ten-year delay between R&D and the commercial product further reduces the ultimate payoff from $1.15 billion to about $285 million. The R&D program still turns a tidy profit, but now the payoff falls from $20 in nominal revenue for each dollar of R&D expenditure to less than $3 in present value revenue for each dollar of R&D expenditure.

The time value of money takes a devastating toll on the payoff from basic research and development. The risk that any products that might emerge from basic R&D may fail to win regulatory approval or encounter market obstacles further reduces the benefits from R&D.

The lags between R&D on stem cell technologies and revenues from products that use these technologies are likely to be on the high side of these estimates. Any new therapeutic products based on research in regenerative medicine will require extensive testing and will face regulatory hurdles and likely legal challenges that will impose long delays to commercial product introduction. Research and development tools developed at CIRM may earn royalty streams with a shorter delay. However, the value of these tools will be limited by the long delays between the use of the tools and the generation of revenues from approved products that are designed, developed, or produced using these tools.

C. Need for Large Additional Investments

Most technologies licensed by universities are at an early stage of development and there is no reason to believe that technologies developed by CIRM will be any different.[50] The commercialization of a new thera-

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49. The private discount rate should reflect the private return on investment, which Fama and French estimate to be about thirteen percent in nominal terms. *See* Fama & French, *supra* note 34.

50. In a survey of technology transfer offices of sixty-two major universities, Thursby et al. found that a majority of the technologies licensed by these offices were at

peutic treatment typically requires expenditures of many millions of dollars in development, testing, and approvals, and millions more to market the new treatment. A prospective drug manufacturer first must submit an investigational new drug application (IND), which demonstrates results of pre-clinical testing in laboratory animals. Based on the IND, the FDA decides whether it is reasonably safe to move forward with testing the drug on humans.

Clinical trials on humans proceed in three stages. Phase 1 studies are small-scale treatments usually conducted on healthy volunteers. If results from Phase 1 studies are acceptable, Phase 2 trials begin with subjects ranging from a few dozen to about 300. Phase 2 trials are designed to assess clinical efficacy of the therapy, as well as to continue Phase 1 assessments in a larger group of volunteers and patients. Phase 3 studies begin if Phase 2 shows evidence of effectiveness without unacceptable side effects. These studies gather more information about safety and effectiveness, studying different populations and different dosages and using the drug in combination with other drugs. The number of subjects usually ranges from several hundred to about 3000 people.[51] It is only after these clinical tests are completed that a drug manufacturer submits a NDA or BLA to the FDA. On average, drug development costs increase dramatically in each clinical phase prior to FDA approval.[52] DiMasi et al. estimate that the average cost of developing a drug to the point of marketing approval was $802 million for a sample of sixty-eight drugs first tested in humans between 1983 and 1994.[53]

Given the nascent state of most technologies developed in universities and other basic research institutes, the large investments necessary to transfer these technologies into useful products, and the high risks of failure, it is not surprising that licensees are unwilling to commit to large upfront payments or to share a high percentage of the value of successful products with their licensors.

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an early stage of development and about half were only a proof of concept when they were licensed. Jerry G. Thursby, Richard Jensen & Marie C. Thursby, *Objectives, Characteristics and Outcomes of University Licensing: A Survey of Major U.S. Universities*, 26 J. TECH. TRANSFER 59, 59, 62 (2001).

51. Michelle Meadows, *The FDA's Drug Review Process: Ensuring Drugs are Safe and Effective*, FDA CONSUMER, July-Aug. 2002, *available at* http://www.fda.gov/fdac/features/2002/402_drug.html.

52. DiMasi, *supra* note 43, at 171.

53. *Id.* at 151.

D. Bargaining Power

Another possible reason for small royalty shares is that technology transfer managers have little bargaining power or simply are not effective bargainers. Bargaining power is a function of a party's threat point: the value the party can earn by walking away from an agreement. For technology managers this threat point may be quite low in many circumstances. Thursby et al. note that while multiple potential licensees often examine a technology, it is much less frequent for multiple companies to become involved in license negotiations.[54] A technology manager's threat is to license the technology to another company, but that threat is absent if there is only one serious potential licensee. The licensee's threat is to license a substitute technology from another source or develop the technology in-house, both of which may be viable alternatives. For many technologies the licensee will have the upper hand in the licensing negotiations.

IV. LICENSING STRATEGIES TO INCREASE RETURNS

Historically, U.S. universities, hospitals, and research institutions have earned only a small return on their R&D expenditures from licensing the outputs of their research. The previous Part discussed some of the reasons why licensing income has been only a small fraction of R&D expenditures for most universities, hospitals, and research institutions. In this Part, I consider various approaches to technology licenses, namely fixed fees, running royalties, and equity sharing. Each approach has certain benefits as a means for the licensor to obtain value from the licensed technology. I show that a licensing strategy that emphasizes fixed fees is attractive in theory, but is unlikely to perform better than a running royalty in actual licensing situations. Equity sharing is attractive in some respects, in part because isolated examples have produced stunning returns. I argue, though, that equity sharing is not likely to dominate running royalties as a way to capture value for most CIRM technologies.

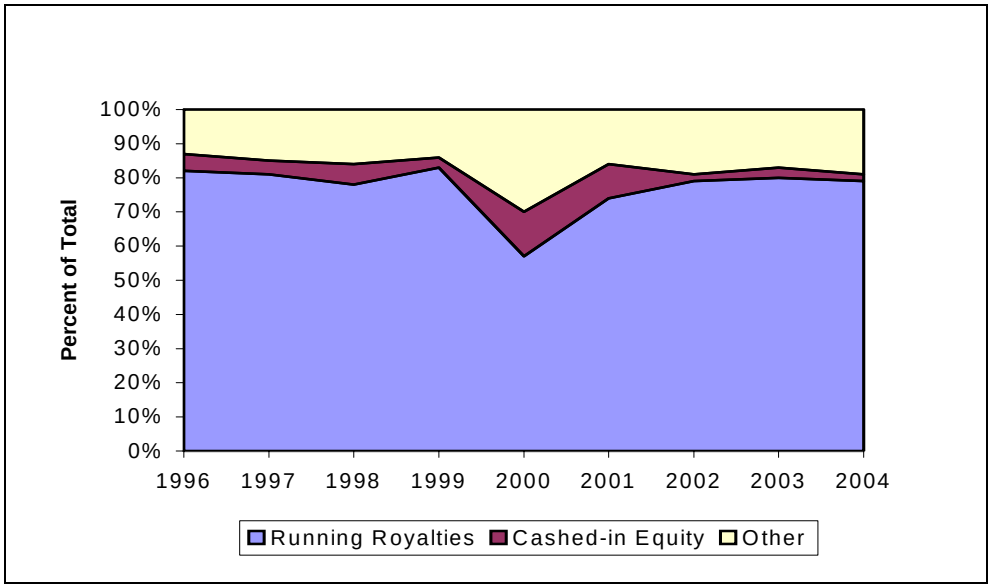
Licenses come in different forms. A license can specify a fixed fee, a running royalty, a share of equity in the assets of the licensee, or require payments that are conditional on meeting certain thresholds such as use of the licensed technology in commercial production of goods or services. In a paid-up or pure fixed-fee license, the licensee makes a one-time payment for the right to use or sell the licensed technology. Running royalties are

54. Thursby, Jensen & Thursby, *supra* note 50, at 63. (observing that it is unusual for a technology to attract multiple bidders, due to uncertainty and the need for additional investment).

payments that vary with sales of products made using the licensed technology, usually calculated as a percentage of gross sales or a per unit fee. These license terms are not mutually exclusive. Licenses can combine fixed fees and running royalties, and in addition may include some equity ownership.

Figure 1 shows the distribution of revenues earned by all university technology licenses over the period FY 1996 through FY 2004. Running royalties account for by far the largest share of university licensing revenues, averaging seventy-seven percent of license income over this period. The other two categories in Figure 1 are cashed-in equity, which is the amount collected from sales of equity holdings in technology licenses, and "other," which includes fixed fees as well as other sources of license income such as litigation settlements.[55]

Figure 1
Licensing Revenue Shares by Type of License



Source: AUTM Licensing Survey, FY 1996-2004 (all respondents)

55. These figures are not directly comparable if the lags between R&D expenditures and the receipt of income differ for royalties and equity payouts. It is not obvious, though, that lags differ significantly. Furthermore, adjusting for lags is unlikely to change the conclusion that running royalties are the dominant source of licensing income.

Running royalties are close to eighty percent of the total in every year from FY 1996-2004 except for FY 2000. This fraction holds at a more disaggregated level for hospitals and research institutes as well as for total university licensing reported by AUTM. FY 2000 was unusual because the University of California recorded a $200 million settlement of an infringement suit involving its human growth hormone patent, which is included in the "other" category for that year.[56] Leaving out FY 2000, the "other" category, which includes fixed fees, accounted for only about sixteen percent of university licensing revenues over the period 1996-2004.

This result may appear odd, at least to economists. Under some conditions, an exclusive license with a fixed fee and no running royalty is a good way for a licensor to recover the value of licensed intellectual property. With no running royalty, or a running royalty equal to the marginal cost of transferring the technology, a single licensee can earn a monopoly profit as the sole supplier of the licensed technology, which the licensor can extract with a fixed fee. A running royalty that exceeds the marginal cost of transferring the technology imposes an artificial cost on the licensee and reduces the total available profit for the licensor.[57] Thus, in theory and with a number of implicit assumptions, a license with a fully paid-up royalty and with little or no running royalty would extract the maximum profit from a licensed technology.

This argument has not had much traction for managers of university technology transfer offices. Fixed fees represent a small share of licensing revenues, with the lion's share coming from running royalties. Furthermore, less than half of university licenses are exclusive and the share of licenses that are exclusive has fallen over the past several years (Figure 2).

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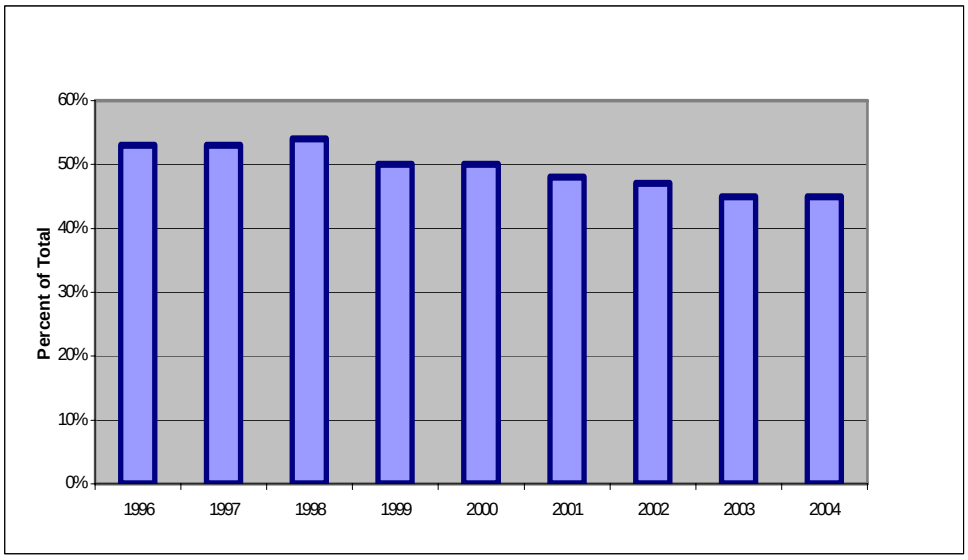
56. OFFICE OF THE PRESIDENT, UNIVERSITY OF CALIFORNIA TECHNOLOGY TRANSFER PROGRAM, ANNUAL REPORT, FISCAL YEAR 2001 20 (2001).

57. *See, e.g.*, Patrick Rey & Jean Tirole, *A Primer on Foreclosure*, *in* 3 HANDBOOK OF INDUSTRIAL ORGANIZATION 21, 40 (Mark Armstrong & Robert Porter eds., forthcoming), *available at* http://venus.unive.it/roson/papers/primer20030716.pdf (last visited June 21, 2006).

Figure 2
Share of University Technology Licenses that are Exclusive[58]



Are university technology managers missing an opportunity to earn more from licenses, or is the simple economics story too simple? What lessons can we learn from university technology managers that might apply to licensing by the California Institute for Regenerative Medicine? The argument that an exclusive license with a fixed fee and with little or no running royalty is a good way for a licensor to recover the value of licensed intellectual property is indeed too simple. It omits many considerations in real-world licensing that affect the potential for licensing income, including uncertainty, moral hazard, diseconomies of scale, and different profit opportunities for licensees.

A. Uncertainty

A fixed fee burdens the licensee with the risk associated with the new technology. As demonstrated above, most technology licenses generate little or no income, not because the royalty rate is low, but because most technologies do not realize significant commercial value. Reflecting this risk, the demand for licenses from potential licensees is often quite low. In a survey of university licenses granted from 1991-1995, only twenty-two

58. AUTM, AUTM LICENSING SURVEYS: FISCAL YEARS 1996-2004 (1996-2004).

percent had more than one bidder.[59] The uncomfortable fact is that most exclusive university licenses are exclusive because only one potential licensee was willing to pay for the right to use the technology, not because the university technology transfer manager limited the license to a single licensee.

University technology managers typically are not flush with bids for exclusive licenses. The University of California at San Francisco Office of Technology Management notes that not all patented life science technology is licensable, affording value to a commercial developer, for several reasons. The technology often requires more research and development to attract commercial interest. As well, the market for the technology is frequently undeveloped and inadequate. The patent claims may be too narrow or difficult to enforce. The technology may not sufficiently differ from other technologies. Furthermore, there may be no economical method to manufacture products deriving from the technology.[60]

An exclusive license also creates uncertainty for the licensor. The licensor faces the risk that the chosen licensee is not the best entity to develop the commercial potential of the licensed technology. The licensor could protect against licensee underperformance by including minimum payments, contingent payments, and termination provisions, although these terms are typically difficult to negotiate. Furthermore, even a licensee that performs well may choose not to develop the commercial potential of the licensed technology in every application.[61]

B. Moral Hazard

Moral hazard exists when the structure of a license fails to offer incentives for efficient investment in the licensed technology. A common theme expressed both by university technology transfer managers and by those people who have studied technology transfer is that new technologies licensed by universities and research institutes typically require a great deal more research and development to become commercially useful.[62] Often

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59. Richard Jensen & Marie Thursby, *Proofs and Prototypes for Sale: The Licensing of University Inventions*, 91 AM. ECON. REV. 240, 245 (2001).

60. UNIVERSITY OF CALIFORNIA SAN FRANCISCO OFFICE OF TECHNOLOGY MANAGEMENT, *supra* note 40, at 4.

61. Gregory Graff. et al. offer the example of an exclusive license to Monsanto for genetic engineering of plants, which Monsanto chose not to exploit for some minor crops. *See* Gregory Graff., Amir Heiman & David Zilberman, *University Research and Offices of Technology Transfer*, 45 CAL. MGMT. REV. 88, 114 n.22 (2002).

62. *See, e.g.*, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO OFFICE OF TECHNOLOGY MANAGEMENT, *supra* note 40, at 4; Gregory Graff. et al., *supra* note 61, at 92-93; Jensen & Thursby, *supra* note 59.

the inventor of the technology has the intellectual ability, and sometimes the entrepreneurial capacity, to contribute to this additional research and development. A paid-up license, though, offers no pecuniary incentive for the inventor to invest in the technology after the license has been negotiated, because the inventor's compensation does not depend on its commercial performance. With a running royalty the inventor's compensation depends on the commercial performance of the technology. This compensation model motivates the inventor to participate in a technology's development after negotiating the license.[63] Alternatively, an equity share also offers the inventor an incentive to increase the value of the equity by participating in the development of the licensed intellectual property.[64]

C. A Single Licensee Can't Do It All

An exclusive fixed fee license presumes that the exclusive licensee can satisfy all of the demand for products made with the licensed technology in a cost-efficient manner. But the exclusive licensee cannot efficiently supply all of the demand for products if it incurs diminishing returns to scale or faces other constraints that limit its ability to exploit the full potential of the licensed technology, including limits on its ability to explore creative applications for the new technology. The technology licensor could permit the licensee to sublicense others, and extract some of the value of the sublicenses with the fixed fee. However, this requires that the licensee identify the appropriate sub-licensees and that the licensor, the original licensee, and the sub-licensees negotiate terms for sharing profits. This is a complex undertaking with the potential to sacrifice potential economic surplus. Furthermore, there is little assurance that the licensor would be able to capture a high share of the remaining surplus, particularly with limited competition among potential licensees for the rights to an exclusive license.

An alternative is to license the technology non-exclusively to all takers with a running royalty and low or no upfront fees. This strategy limits the profit that the licensor can extract from each licensee, but royalties from a large number of licensees can more than compensate for a high fixed fee from an exclusive licensee. The licensing history of the Cohen-Boyer patent for recombinant DNA is a case in point. Patented in 1980, the Cohen-Boyer technology for inserting genes in cells was the foundation for the

63. *See* Jensen & Thursby, *supra* note 59, at 248 (arguing that development requires a positive royalty rate when the contract terms specify a royalty and/or fixed fee).

64. There may be a dilution effect that reduces inventor incentives if the value of equity depends on activities that are unrelated to the licensed technology. *See id.* at 251 n.26.

biotechnology revolution. The patent was licensed non-exclusively, in part out of concern that one company could not explore all of the possible applications of the technology and in part because potential licensees feared that they would be excluded if the patent were licensed to a single company.[65] A total of 468 companies ultimately licensed the Cohen-Boyer technology and paid a total of $254 million during the patent's term, ninety percent of which was from running royalties.[66] Adoption of the Cohen-Boyer technology would probably not have been as pervasive with an exclusive license, and an exclusive license would also probably not have generated as much revenue for its licensors.

D. Not All Licensees Are Alike

Suppose that efficient exploitation of a technology requires more than one licensee. If the licensor knew exactly what each potential licensee could earn from using the licensed technology, it is possible that the licensor could design a unique contract for each licensee that would extract a large share of each licensee's profit and limit competition among licensees. However, the informational requirements of such a contract would be enormous, particularly for new technologies whose potential profitable applications are largely unknown. An alternative approach is to design a one-size-fits-all contract that most potential licensees would accept. A well-designed standard contract can increase the ability of the licensor to profit from the technology.

The optimal standard license would not be a single fixed fee, because a single fixed fee would not extract all of the available profit from each licensee. If the licensor wants to set a single fixed fee and license all firms that can efficiently produce goods or services using the licensed technology, the fixed fee would have to be the smallest fee that any licensee would be willing to pay. This would fail to extract all of the profits available from licensees that could earn more using the licensed technology. A standard license that extracts more of the available profit combines a fixed fee with a running royalty. The fixed fee can be set low enough to make the license attractive to licensees with modest profit expectations, while the running royalty can collect revenues from licensees that have large business opportunities.[67] Indeed, a mix of fixed fees and running royalties

65. Feldman, *supra* note 6, at 5-6.

66. *Id.* at 20, 23.

67. *E.g.*, Walter Y. Oi, *A Disney Land Dilemma: Two-Part Tariffs for a Mickey Mouse Monopoly*, 85 Q.J. ECON. 77 (1971); Richard Schmalense, *Monopolistic Two-Part Pricing Arrangements*, 12 BELL J. ECON. 445 (1981).

is a common feature of most technology licenses, although running royalties account for most of the revenues.[68]

E. Equity Participation

Licenses that include an equity stake in the licensee account for only a few percent of all licenses negotiated by universities, hospitals, and research institutes surveyed by AUTM over the past several years (Figure 1). This is surprising given that many potential licensees are short on cash. The option value of cashing in an equity stake is a tempting alternative to the expectation of meager royalties. Equity sharing can be an attractive way to realize the value of new technology when it is appropriate to grant an exclusive license to a firm whose business model is focused on the new technology, as in a new startup venture. A startup with a focus on the new technology avoids a dilution of effort and interest that could happen if the licensee is a large diversified company.[69]

Although equity sharing can be an attractive alternative to royalty-based licenses, the benefits should derive from better risk sharing and alignment of incentives for the licensor and the licensee. There is no reason why the expected value of an equity share should exceed the expected present value of a royalty stream unless the equity contract itself promotes investments that increase the value of the licensed technology. If the licensor and the licensee agree that a license would generate $1 million in royalties, the licensee should not be willing to give up more than $1 million in expected equity value, and the licensor should not be willing to accept less than that amount. Whether the payment to the licensor is based on revenues produced by the licensed technology or the equity value of the licensee is irrelevant in this example.[70]

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68. Jensen & Thursby, *supra* note 59, at 245.

69. Equity sharing, which often goes hand-in-hand with exclusive licensing, could conflict with the CIRM goal to negotiate non-exclusive licenses to CIRM-funded intellectual property whenever possible. *See* IPPNPO, *supra* note 12, at 17.

70. Equity participation can be a last resort to obtain value from a cash-starved licensee. Bray and Lee report that "When [a university executive] asked one licensing manager why he had taken equity so many times he shrugged and said it was all he could get." Michael J. Bray & James N. Lee, *University Revenues from Technology Transfer: Licensing Fees vs. Equity Positions*, 15 J. BUS. VENTURING 385, 388 (2000); *see also* AUTM, AUTM U.S. LICENSING SURVEY: FISCAL YEAR 2004, *supra* note 15, at 30 (demonstrating that equity is often the only currency that startup companies have to offer licensor institutions as upfront consideration).

There are examples of spectacular equity rewards, such as Stanford University's $336 million sale of its equity share in Google,[71] which may not have been equaled with a royalty-based license.[72] On the other hand, there are also examples of licenses that have produced spectacular royalties, such as the $254 million in royalty income from the Cohen-Boyer technology. It is not obvious that a negotiated share of equity in a Cohen-Boyer licensee would have generated an equally large return.

Equity participation is an appealing technology transfer alternative when it increases the *total value* of the licensed technology by better aligning the incentives of the licensor and the licensee. If an inventor has an equity share in the licensee, the inventor may have greater motivation to work with the licensee to develop the commercial potential of the technology. A license with running royalties also offers an incentive for the inventor to work with the licensee to produce greater revenues. Equity participation can be more effective by offering rewards for work outside the boundaries of the licensed product or process. Licensed technologies can benefit from continued inputs of knowledge and creativity from the original inventors as well as feedback from the licensees to the inventors. An equity stake can provide a platform for these critical communications that is superior to the incentives that flow from a product or license.[73]

Equity sharing can create value relative to a royalty license in other ways. Equity offers some diversification benefit by assigning the licensor a share of the value of an entity rather than a share of revenues from a product or process. Equity may simplify negotiations in the event of contingencies that were not anticipated in a royalty license. For example, a licensee could have a technology opportunity that competes with the licensed technology. The allocation of effort between the licensed technology and the alternative would be a concern to a licensor with a royalty

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71. *Google Stock Turns into Windfall for Stanford University*, S.F. CHRON., Dec. 1, 2005.

72. It is conceivable that Stanford would have earned even more if it had negotiated a royalty license with Google. Google earned $3.2 billion in revenues in 2004 and $6.1 billion in 2005. Google Investor Relations, http://investor.google.com/fin_data.html (last visited July 9, 2006). Had Stanford negotiated a license with a royalty equal to two percent of Google's sales, it would have earned $64 million in 2004 and $122 million in 2005. Stanford's equity payout corresponds to only a few years worth of royalties at these levels.

73. Interviews with university technology managers suggest that equity participation changes the university from being a potential adversary of the licensee to a concerned partner. Bray & Lee, *supra* note 70, at 389; *see also* Maryann Feldman, Irwin Feller, Janet Bercovitz & Richard Burton, *Equity and the Technology Transfer Strategies of American Research Universities*, 48 MGMT. SCI. 105, 106 (2002).

contract, though less of a concern to a licensor with an equity share in the company because equity could increase with development of either technology.[74] Equity sharing can mitigate other potentially costly conflicts that might arise, such as over rights to new technologies that are developed using the licensed technology. An equity license can also realize value from the licensed technology before the technology generates significant revenue flows through the sale of equity in an initial public offering or acquisition.[75]

The pecuniary incentive for post-license cooperation comes from the prospect of increased royalties, which means that the contract has to be back-loaded to emphasize running royalties rather than up-front fees. But a running royalty increases a licensee's marginal production cost, which can interfere with the dissemination of the technology and reduce its ultimate value. This risk is particularly severe when production requires many licenses, each with a running royalty, and the total stack of royalties adds to the licensee's marginal cost.[76] An equity participation license does not add to the licensee's marginal cost and can avoid the distortion imposed by a running royalty.

Despite some attractive features, there are negatives to equity participation. Many technologies are not likely candidates for an equity license. If a technology offers only an incremental value to an on-going concern, a royalty license is a better way to measure its incremental contribution. Equity participation is attractive to a startup if the licensed technology has clear commercial potential and the licensee can build a firm around it.[77] Larger licensee companies offer greater diversification benefits for sponsors of new technologies, but also dilute the incentives for the licensor to develop the technology because the efforts make only a small contribution to the total value of a large company.

In many respects equity sharing is the ultimate exclusive license. The choice of equity as the path to commercialize a technology discourages broad dissemination of the technology to other licensees, which are poten-

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74. Feldman et al. note the example of an equity share for an artificial heart technology where the licensee was working on a competing technology. Equity minimized the conflicts that could have been serious with a royalty contract. Feldman et al., *supra* note 73, at 112.

75. Bray & Lee, *supra* note 70, at 389.

76. *See, e.g.*, Carl Shapiro, *Navigating the Patent Thicket: Cross Licenses, Patent Pools, and Standard-Setting*, *in* 1 INNOVATION POLICY AND THE ECONOMY (Adam Jaffe, Joshua Lerner & Scott Stern eds., 2001); Richard Gilbert, *Antitrust for Patent Pools: A Century of Policy Evolution*, 2004 STAN. TECH. L. REV. 3, ¶¶ 25-26 (2004), *available at* http://stlr.stanford.edu/STLR/Articles/04_STLR_3/article_pdf.pdf.

77. Bray & Lee, *supra* note 70, at 388.

tial sources of competition that can reduce the value of the equity stake. The licensor with an equity stake in a single company may be reluctant to explore other partners to commercialize the licensed technologies, and the licensee may be equally reluctant to consider sub-licensing the technology to others. Equity participation can make it difficult to terminate an underperforming licensee because it would require admission that the equity stake is worthless.

An equity license, with its focus on a single licensee, may contradict the objective of broad dissemination of technologies developed by CIRM. In addition, an equity license may interfere with the potential health benefits from stem cell technologies, which should be the primary objective of CIRM. Exclusivity is not necessarily bad, because it can encourage investment to commercialize the technology. All the same, CIRM has to ensure that the benefits of exclusivity do not come at the expense of broader dissemination.[78]

Equity licenses pose other challenges for CIRM. Equity magnifies the risk inherent in technology transfer, with the prospect of very large rewards offset by the much larger probability of no return. With equity sharing, the licensor acts much as a venture capitalist. Successful venture capitalists are highly skilled at identifying the potential winners. If CIRM intends to make equity sharing a major component of its licensing program, it should develop venture capital expertise in-house or acquire it from others. In the latter case, a significant fraction of the reward for picking attractive equity sharing opportunities will go to those with the expertise to choose them.[79] Furthermore, equity participation can expose the licensor to liability for product defects, or more generally sully the licensor's reputation as a research institution serving the public good if products sold by the equity partner harm patients or the environment.[80] Equity can become a trap for the licensor if the need for additional investments to commercialize the technology lures the licensor into making expenditures that generate little or no financial returns.

Actual financial returns to equity licensing by universities, hospitals, and research institutes have been mixed compared to royalty licenses. Bray and Lee report that the average value of equity sold in sixteen uni-

78. *See* IPPNPO, *supra* note 12, at 17, 23, 36 (describing concerns about exclusive licenses).

79. Choosing the right licensee is also an issue for an exclusive royalty-based license. A difference is that equity participation may presume more active involvement by the licensor and hence the need to match the capabilities of the licensor, the licensee, and the licensed technology.

80. *See* Feldman et al., *supra* note 73, at 107.

versity spin-off companies in 1996 was $1,384,242, while the average annual income of a royalty license was only $63,832 in the same year. These numbers, though, are not directly comparable. The equity number includes only successful equity licenses. If half the equity deals fail, this reduces the average realized value to $692,121. Excluding a few of the highest equity sales drops the average value of equity sold to only $279,443.[81] Equity is the capitalized value of the contract, while royalties represent income in one year. If a license generates $60,000 in royalty income for ten years and the discount rate is ten percent, the capitalized value of the royalty income is over $400,000. Furthermore, the comparison is potentially misleading because many licenses that generate royalty income would not have been suitable candidates for an equity share.[82]

Equity is not becoming a preferred method to realize technology value for universities, hospitals, and research institutes. Although the number of licenses reported by AUTM that include an equity share has more than doubled since 1996,[83] the share of licenses with equity and startups with equity has not increased dramatically from 1996 to 2004 (Figure 3). Furthermore, with the exception of fiscal years 2000 and 2001, which offered unusually favorable conditions to realize equity values, the share of licensing income from cashed-in equity has been in the low single digits and has been falling since 1996 (Figure 4). However, it is likely that FY 2005 will be a notable exception to this trend with Stanford's sale of Google stock.[84]

Equity sharing is a potentially rewarding path to commercialize CIRM technologies and it should play a role in its overall technology transfer program. However, other than Stanford's sale of Google stock, there is not much evidence that, compared to licenses with running royalties, increased equity sharing would significantly change historical patterns of

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81. Other studies have shown that estimated equity returns from new ventures are very sensitive to adjustments for failures. In one study, eliminating failed projects reduced the average rate of return for venture capital from about 700% to 59%. The high average that remains after adjusting for failures reflects the small probability of earning an extremely large return, combined with the much larger probability of a more modest return. *See* John H. Cochrane, *The Risk and Reward of Venture Capital*, 75 J. FIN. ECON. 3, 5, 30 (2005); *see also* Peng Chen, Gary Baierl & Paul D. Kaplan, *Venture Capital and Its Role in Strategic Asset Allocation*, 28 J. PORTFOLIO MGMT. 83 (2002).

82. University policies typically limit their maximum equity share to about ten percent. *See* Jensen & Thursby, *supra* note 59, at 250.

83. AUTM, AUTM U.S. LICENSING SURVEY: FISCAL YEAR 2004, *supra* note 15, at 29.

84. The share of licensing income from cashed-in equity should increase dramatically in FY 2005 after recording Stanford's $336 million share of Google stock. This figure dwarfs total cashed-in equity sales of $29 million in FY 2004. *Id.* at 26.

licensing income from research by universities, hospitals, and research institutes.

Figure 3
Share of Licenses with Equity

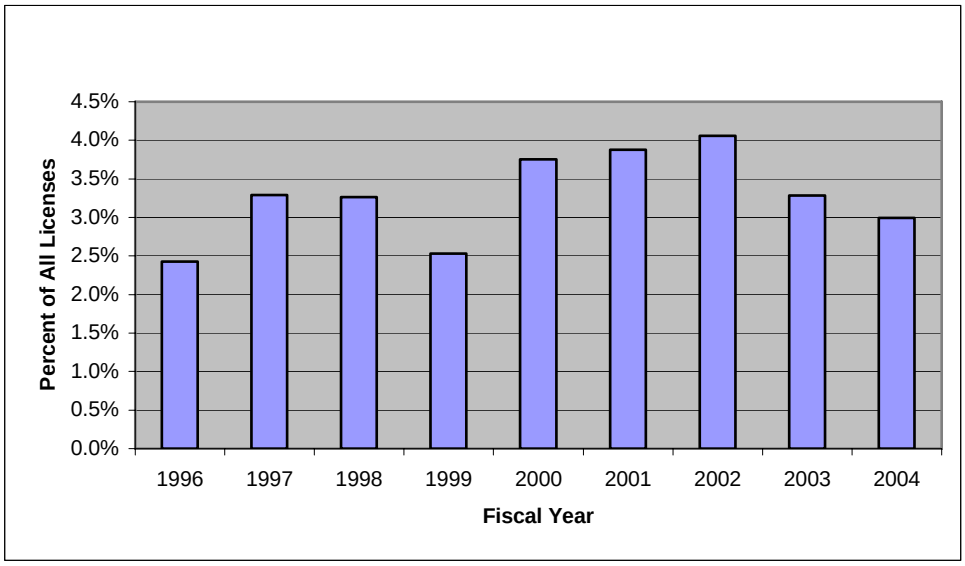
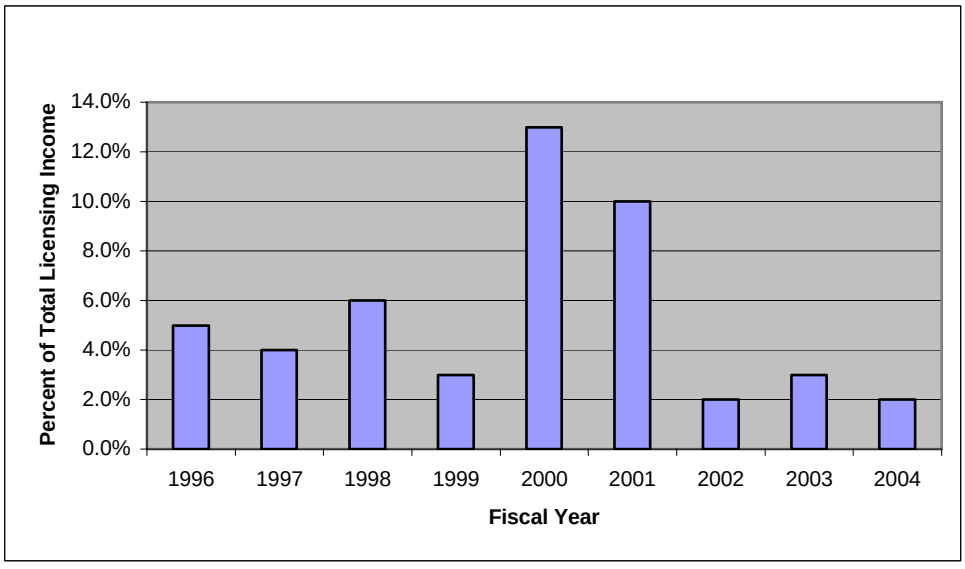


Figure 4
Share of Licensing Revenue from Cashed in Equity



V. CONCLUSIONS

The approach that CIRM will pursue to collect revenues from the licensing of intellectual property created with CIRM R&D support is yet another source of controversy in the brief history of this institute.[85] A main conclusion of this Article is that this particular controversy is a tempest in a teapot. The present value of licensing revenues is unlikely to be a source of income that will substantially offset the cost of R&D by CIRM, taking into account the likely long lag between R&D funding and the realization of commercial therapies made possible with CIRM support. This conclusion applies only to licensing income and does not diminish the prospect that research funded by CIRM will lead to important health benefits.[86]

I take two different paths to reach my conclusion about likely royalty income from CIRM-supported R&D. One approach follows the analysis performed in the Baker-Deal study, which forecasts the likely number of major therapies that CIRM support will produce and the revenues from these therapies. The Baker-Deal study estimates that the state will earn royalties from research funded by CIRM that will total either $537 million or $1.1 billion, depending on the royalty rate. The study, however, does not account for the time cost of revenues that occur far in the future. Applying a discount rate corresponding to the interest rate on ten-year treasury bonds reduces the present value of revenues from CIRM-funded R&D predicted in the Baker-Deal study by sixty-five percent. Under the current CIRM policy for revenue sharing, the state will receive only about one-sixth of these revenues (twenty-five percent of licensing revenues remaining after deducting thirty-five percent for the inventor's share). This leaves the state with about $31 million in the base case of the Baker-Deal study and $62 million in their high estimate, very small fractions of the more than $3 billion in R&D funding for CIRM.

A second approach I use to estimate likely future royalty income from CIRM-supported R&D relies on actual royalty income collected by U.S. universities, hospitals, and non-profit research institutes surveyed by the Association of University Technology Managers. CIRM will not perform research itself, but will contract with entities, most of which will be uni-

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85. *See, e.g.*, Michelle Chen, *Stem-Cell Research Blasted From New Angle*, THE NEW STANDARD, May 8, 2006, *available at* http://www.genetics-and-society.org/news disp.asp?id=1000.

86. Another possible benefit, which I do not address in this Article, is increased economic activity in the state of California from the activities of CIRM. While these benefits may be important, they are unlikely to be large given that R&D funding by CIRM is a small fraction of total academic R&D expenditures in California. *See* sources cited *supra* note 29.

versities, hospitals, and non-profit research institutes engaged in biomedical research. For this reason the licensing revenue performance of the organizations surveyed by AUTM, particularly hospitals and non-profit research institutes, is a good model to estimate the likely revenues from licenses for technology generated with R&D support from CIRM.

Over the past several years, the hospitals and research institutes surveyed by AUTM earned licensing revenues equal to about 6.6 percent of their current R&D expenditures net of operating expenses. After correcting for the lag between R&D expenditures and receipt of royalty income and applying a time cost to future income, I estimate a return on R&D for these entities in current dollars equal to about 4.5 percent of R&D expenditures. Adjusting this number to account for CIRM's revenue sharing policies reduces the state's return in current dollars to about 0.60 percent of R&D expenditures.

Although I estimate that the state of California will earn little in technology licensing royalties from CIRM-funded research, I do not regard this conclusion as particularly bad news for the state. My analysis does not undermine the value of the potentially enormous health benefits from therapies made possible by advances in human embryonic stem cell science. This is the true measure of value from the state's support of CIRM. Furthermore, the low expected royalty income to the state reduces the risk that royalty income will jeopardize tax-exempt status for the bonds that pay for CIRM. Tax-exempt status reduces the cost of CIRM funding by more than the state is likely to earn in royalty income. There is little to gain, and much to lose, from struggles over policies to distribute royalty income for CIRM-funded research. There is a potential conflict between the goal of advancing stem cell science and achieving an attractive financial rate of return on California's investment. Bad policies could undermine CIRM's research program by distorting incentives for inventors to work on CIRM-funded projects. The controversy over the allocation of royalties from CIRM-funded research is a distraction from the main benefits from CIRM R&D support, which are the therapies that research funded by CIRM will help to create.

I have also considered ways by which CIRM may increase its licensing income. Central among these alternatives is a greater reliance on equity sharing. Taking equity in licensees of CIRM-supported technologies has a number of attractive features, but is unlikely to produce a major increase in expected licensing revenues compared to licenses that specify running royalties and up-front fees. Stanford University's $336 million sale of Google stock is indeed impressive, but a running royalty could have produced as much income from Google's large and growing revenue

base. Equity sharing has the potential for large rewards, but the risks are great. CIRM or its grantees would have to gain expertise as venture capitalist, or purchase this expertise, if CIRM is to rely heavily on equity sharing to realize monetary benefits from technology transfer.

While CIRM investments in human embryonic stem cell research will generate some financial return for the state of California, the primary benefit from these investments will be progress toward improved therapies for the treatment of major chronic and acute diseases. The justification for the state's investment in CIRM is the promise of better health, not the promise of financial reward.