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Economic Impact Analysis

Proposition 71
California Stem Cell Research and Cures Initiative

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I. Report Overview

A. Introduction

This study provides an economic analysis of the costs and benefits associated with Proposition 71, the Stem Cell Research and Cures Initiative. The study was conducted by Dr. Laurence Baker, Associate Professor of Health Research and Policy and Chief of Health Services Research at the Stanford University School of Medicine, in conjunction with Analysis Group, Inc., a national economic and financial research firm with offices in Los Angeles, San Francisco, Menlo Park and major cities throughout the United States. Bruce Deal, Managing Principal of Analysis Group, co-authored the study.

Proposition 71 authorizes a total of nearly $3 billion in tax-free, general obligation state bonds to support stem cell research at California hospitals, medical schools, universities and other research institutions over 10 years. The Initiative defers principal and interest payments on the bond during the first five years, from 2005 through 2009. Bond payments of about $200 million per year would begin in 2010 and continue until 2039, creating a bond payback period of 30 years. The total payback cost with interest on the bonds is estimated by the authors at about $5.4 billion.[1]

The investments in stem cell research and research facilities made possible by Proposition 71 are expected to generate revenues for the State of California from new income and sales taxes. Proposition 71 could also produce new royalty revenues and tax revenues resulting from expanding economic activity in the biotechnology industry. By leading to new treatments for just a few of the more than 70 diseases and conditions that scientists believe could be treated or cured with stem cells, Proposition 71 has the further potential to provide significant reductions in California's health care spending costs, which now amount to more than $110 billion per year.

B. Key Conclusions of the Economic Analysis of Proposition 71

In even the modest scenarios examined, Proposition 71 provides total state revenues and health care cost savings of between $6.4 billion and $12.6 billion during the payback period, generating a 120% to 236% return on the investment made in the research.

Thus, Proposition 71 is capable of paying for itself during the payback period alone with the possibility of continuing to generate billions of dollars in revenues and savings for the State of California for decades after that.

Specific revenues and savings that are modeled include:

a) ***Direct income and sales tax revenues of at least $240 million*** from the Initiative's spending on research and research facilities.

b) ***Additional income and sales tax revenues of from $2.2 billion to $4.4 billion*** if Proposition 71 could bring about even a 2.5% to 5% increase in private investments and

[1] A report addendum to be released in the future will report both costs and benefits taking into account inflation and the time value of money.

research activity in the California biotechnology industry by making California a world leader in stem cell research.

c) ***Direct health care cost savings to the State government of at least $3.4 billion to $6.9 billion***, based on modest assumptions that the research would reduce state spending by at least 1% to 2% for the care and treatment of patients suffering from six medical conditions that scientists believe could benefit from the development of new stem cell therapies, including stroke, heart attack (acute myocardial infarction), insulin dependent diabetes, Parkinson's disease, spinal cord injury, and Alzheimer's disease.

d) ***Additional billions in health care costs savings for California businesses, citizens and other payers of health care costs.*** California's total health care spending costs now exceed $110 billion per year, including direct state government costs, costs funded by federal programs, insurance companies, employers, and individual citizens. In addition to providing billions in savings to the State government, new stem cell therapies could reduce costs to other health care cost payers by $9.2 to $18.4 billion based on 1% to 2% cost savings for the six conditions considered.

e) ***State royalty revenues of from $537 million to $1.1 billion***, resulting from the provisions in Proposition 71 that give the state an opportunity to share in royalties resulting from research funded by the Initiative.

If Proposition 71 leads to major advances in health care treatments, overall economic benefits to the State could be more than 7 times the cost of the Initiative.

Given the promise of stem cell research, cost reductions of 10% or more in the six conditions considered are possible through significant improvements in therapies. Savings of 10% on health care costs would lead to additional saving to Californians of $92 billion and increase the total economic benefits to the State of Proposition 71 to 750% of cost.

Proposition 71 will create thousands of new jobs in California.

Direct spending from the Initiative will generate thousands of additional jobs in California. Additional growth in the biotechnology industry could generate additional jobs. In total, between 5,000 and 22,000 new jobs on average per year could be created; the total number of job-years (one job for one year = one job-year) ranges from 360,000 to 673,000.

This analysis shows significant potential economic benefits of Proposition 71. However, it should be noted that the primary social benefit from Proposition 71 is its potential to improve the health and save the lives of millions of Californians who now suffer – or will eventually suffer – from diseases and injuries that could be treated or cured with new stem cell therapies whose development could be enabled or accelerated by Proposition 71. This benefit cannot readily be quantified by economic analysis, and has not been included in the study.

II. Executive Summary

A. Overview

On behalf of Californians for Stem Cell Research and Cures, Dr. Laurence Baker, Associate Professor of Health Research and Policy and Chief of Health Services Research at the Stanford University School of Medicine and Bruce Deal, Managing Principal with Analysis Group, Inc., have been retained to analyze the financial impact of Proposition 71 (the Stem Cell Research and Cures Initiative, or the "Initiative") on the people of California and the State budget.

Proposition 71 would authorize the issuance of $3 billion in State general obligation bonds to fund stem cell research in California over 10 years.[2] The measure would establish the California Institute for Regenerative Medicine ("Institute") to use the proceeds from the sale of the bonds to issue grants and loans for stem cell research and research facilities, as well as to provide oversight of stem cell research activities funded by this measure.

While Proposition 71 has significant economic costs and benefits, its central goal is not specifically economic in nature, but rather is to contribute to improvements in health. The concept of public funding of health-related research is well-established in the United States, with billions of dollars each year spent funding basic and later-stage research designed to improve human health. The benefits of this research have been significant and have improved the length and quality of life for millions of Americans. Were Proposition 71 to accelerate the discovery of beneficial new therapies, it could produce important benefits for Californians and others throughout the United States, and even the world, in the form of improved length or quality of life for individuals with affected health conditions as well as their family members, friends, and community members. We do not attempt to quantify the potentially large, but often intangible, benefits of this type that could result from successful research under Proposition 71.

This report does not directly address the political context of Proposition 71 or the fundamental need for the funding, though these issues may be important. The Legislative Analyst's Office reports that in 2002 the Federal government dedicated more than $180 million in funding for adult stem cell research. At the same time, the Federal government also places restrictions on funding for research and limits the availability of embryonic stem cells, prompting arguments that this type of initiative is essential.

We also do not directly investigate the scientific aspects of stem cell research. As economists, we have relied on information obtained from published literature and from conversations with medical and scientific experts as to the potential for development of new stem cell-based therapies. This information is clear on two points. First, there appears to be great potential in stem cell research for the development of new and powerful medical therapies. Some studies from respected research institutions have shown positive proof of concept in important therapy areas, and some respected researchers report the possibility of new therapies emerging within the next several years. Second, the success of these therapies is in most cases yet to be demonstrated, thus further research (and funding) is required before the potential of stem cells will be fully understood or developed.

[2] The interest expense incurred during the initial years would be included in the 30 years general obligation bonds issued during the later years of the program.

Despite uncertainties about whether or when the promise of stem cell research will be realized, our conversations with a variety of experts have led us to the conclusion that the potential for successful therapies is strong enough to warrant analysis of the type we undertake here. With that in mind, we also believe it prudent to keep in mind the difficulties and challenges associated with the research. Even in our models that are correspondingly modest in their expectations for research successes, Proposition 71 appears capable of producing large economic benefits.

Our report examines the costs to the State of the principal and interest on the bonds, as well potential benefits from various sources. The net cost to the State will be the costs less benefits.

B. Economic Costs of Proposition 71

The funding costs of Proposition 71 can be readily quantified.[3] For purposes of our analysis, we have identified three relevant time periods.

1. Years 1 – 5

During the first five years of the Institute, funds would be committed to new dedicated research facilities ($300 million), research grants ($1.25 billion), and program administration (up to 3 percent of the initial bond proceeds to fund overhead, and up to an additional 3 percent for grant administration). During this period, the cost of the bonds to the State budget is insignificant as the principal on the loans is deferred and the interest is paid through bond proceeds rather than by the State General Fund.

2. Years 6 – 14

During years 6 – 14 of the program, the remaining funds (for a combined total of $3 billion) would be spent on research programs. (All facilities spending takes place in years 1 – 5). During this second period, the cost to the State budget is both the interest on the funds spent and the beginning of the 30-year principal repayment.

3. Years 15 – 35

The entire $3 billion is projected to be spent in years 1 – 14. During years 15 – 35 of the program, there would be no additional funds spent from the amount authorized by the Initiative. In this final period, the cost to the State budget is both interest and principal, as the borrowings in years 1 – 14 would be repaid in full by the end of year 35.

We estimate total principal costs of approximately $3.0 billion and interest costs of $2.4 billion over the 35 year life of the program, for a total cost of $5.4 billion.

C. Economic Benefits of Proposition 71

We have identified four areas where Proposition 71 could generate economic benefits for the people of California and the State budget. These are briefly summarized below; each area receives

[3] For simplicity, we generally report all figures in the Executive Summary without adjusting for the time value of money over future periods ("discounting"). A report addendum will be released in the future detailing the costs and benefits after adjusting for inflation and the time value of money.

more complete treatment in the full report. Under the scenarios we model, Proposition 71 could generate economic benefits to the State of California that exceed the costs of the funding, potentially by a significant amount.

1. *Tax Revenues Generated by Proposition 71 Spending*

The first area where Proposition 71 would generate economic benefits is from the income and sales tax revenues generated by the $3 billion in Initiative spending. Our estimates are based in part on analysis done using IMPLAN, an economic modeling program used by various agencies of the State of California.[4] We estimate that during the first five years of the program, the additional tax revenues generated by the spending from Proposition 71 would be just under $73 million, resulting in an overall ratio of $1.30 in tax revenue to $1 in interest expense. In other words, Proposition 71 would not create a net negative impact on the State budget during this period.

Over the 14-year initial funding period of the Initiative, we estimate new tax revenue to the State of $240 million, or 4.5 percent of the overall program cost. The new spending on facilities, research, and administration would be enough to create approximately 2,900 new jobs on average during years 1 – 5, increasing to 3,700 new jobs on average by years 6 – 14, for a total of 47,000 job-years over years 1 – 14.

We assume no further tax revenues after year 14, when disbursements under the Initiative would end. Similarly, we assume no job creation from this source beyond year 14.

2. *Tax Revenues Generated by Additional Biotechnology Economic Activity in California*

The second area where Proposition 71 could generate economic benefits is from the income and sales tax generated by additional private biotechnology economic activity in California. Biotechnology is already a major industry in California, a state that has approximately 12 percent of the U.S. population,[5] and nearly 40 percent of the U.S. life sciences companies.[6]

Proposition 71 could generate economic benefits by attracting additional activity in the life sciences industry. Proposition 71 could encourage companies that exist today, or would have been created anyway, to locate in California. Perhaps more importantly, Proposition 71 could create biotechnology activity that would not have otherwise existed. Many industry experts believe that stem cell research is among the most promising new areas of biotechnology research, attracting a great deal of private interest and investment. By providing a stable, significant funding base, Proposition 71 could facilitate further investment by private companies in stem cell research and

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[4] IMPLAN clients include the California State Departments of Finance, Transportation, and Water Resources, according to: "Client Listing," Minnesota IMPLAN Group Inc., available at http://www.implan.com/references.html.

[5] "Table 1: Annual Estimates of the Population for the United States and States, and for Puerto Rico: April 1, 2000 to July 1, 2003," Population Division, U.S Census Bureau, last revised May 11, 2004, available at http://www.census.gov/popest/states/tables/NST-EST2003-01.pdf.

[6] "California Life Sciences Action Plan: Taking Action for Tomorrow," Bay Area Bioscience Center, BIOCOM, California Healthcare Institute, Southern California Biomedical Council, Bay Area Council, Larta Institute, Sacramento Regional Technology Alliance, and San Diego Area Regional Technology Alliance, p. 1. This source contains a statewide synthesis of four regional Action Plans.

therapy development to a degree that may not have occurred otherwise.

Additional private biotechnology activity would generate economic benefits for the State of California through 1) new jobs that lead to income taxes paid by workers, and 2) sales tax paid by workers in new jobs and by companies undertaking new research.

Over the Institute's 35 year horizon, we estimate that were Proposition 71 to increase the size of the California life science industry by 2.5 percent relative to our estimated industry baseline size, the tax revenue associated with the additional activity would be about $2.2 billion, or approximately 41 percent of the total program cost. This amount of new activity would amount to between $1 and $2 in additional private activity for every $1 of public funding during the years in which the public funding is occurring (years 1 – 14). This amount of additional activity would be enough to create approximately 2,400 new jobs on average during years 1 – 5, increasing to a total of 7,500 jobs on average throughout years 6 – 14, and then a total of 11,100 jobs on average by years 15 – 35. Over years 1 – 14 this is equivalent to a total of 313,000 job-years.

Our estimates assume a baseline size of the biotechnology industry that grows over time. Some have argued that without support for further stem cell research, the biotechnology industry would grow more slowly than the baseline we have projected. If this is the case, then implementation of Proposition 71 could generate larger job creation and tax revenues. Overall, we estimate that the life sciences industry in California could account for nearly 400,000 California jobs by the year 2025. Were Proposition 71 to contribute to maintaining strong industry growth instead of decline, it may contribute a significant share of these jobs to the California economy. However, because of the uncertainty surrounding these predictions, we have not attributed any of these "baseline" jobs or tax revenues to Proposition 71 in our calculations.

3. Reductions in Health Costs Resulting from New Therapies

The primary goal of Proposition 71 is to facilitate new medical advances. In addition to the obvious health and quality of life benefits that would be associated with new therapies, there are also potential economic benefits in the form of lower health care costs if conditions that now require expensive treatments could be more efficiently managed. Though new research does not always lead to reduced costs, many of the conditions that are thought to have the greatest potential for stem cell-based therapies are also currently quite expensive to treat. In the simplest scenario, if stem cell research were to lead to new cures for these conditions, the net savings for each patient could be very large. Even if the therapies are not full cures, therapies that delay the onset or reduce the severity of conditions could also generate significant health care cost savings.

Health care cost savings would benefit both the people of California and the State budget. Currently the State budget is directly responsible for approximately 13 percent of total health care spending, comprising the State share of Medicaid (called MediCal in California), State employees and dependents, and various other State programs.[7] If overall health costs are reduced for those suffering from various conditions, health care spending by the State government will also be reduced.

[7] "2000 – 2001 State Health Care Expenditure Report," Milbank Memorial Fund, National Association of State Budget Officers, and the Reforming States Group, available at http://www.milbank.org/reports/2000shcer/index.html, accessed September 2, 2004.

We have focused on 6 of the 70 conditions identified by medical and scientific experts as having the potential to benefit from stem cell research.[8] These include stroke, heart attack (acute myocardial infarction), insulin-dependent diabetes, Parkinson's disease, spinal cord injury, and Alzheimer's disease. We have modeled direct health care costs in the under 65 population, lost work time costs in the 19-64 year old population, and nursing-home costs for all ages associated with these conditions. In our models, a small cost reduction of 1 percent per year in our modeled costs for these six conditions, beginning between years 5 and 15 of the Initiative, depending upon the condition, produces cost savings to all Californians of $11 billion over the 35 years analyzed. Much of these savings would reduce health spending now paid for by Californians through health insurance or through their out-of-pocket spending. Some of these savings would also benefit the State budget by reducing State spending. Savings to the California State budget alone from reductions in health care spending would be approximately $3.4 billion over the life of the Initiative, or approximately 64 percent of the program cost.

A 1 percent reduction in costs is modest and is consistent with only limited success in developing therapies. This could occur even if stem cell research were to produce only small gains, such as mitigating symptoms of disease or delaying onset of more serious symptoms for a short time. Were stem cell research to achieve greater successes, gains could be much larger. For example, if a stem cell therapy were to reduce the costs associated with insulin-dependent diabetes in California by half, beginning in year 6, this alone would produce savings of $122 billion to California as a whole, and $24 billion to the State budget over the 35 year life of the Initiative.[9] When we model reductions in health care costs of even 2 percent rather than 1 percent, we estimate savings to all Californians of $23 billion, and savings to the State of $6.9 billion. Modeling a more aggressive scenario in which 10 percent savings are realized for these 6 conditions would yield reductions in spending of $114 billion for all Californians and reductions of $34 billion for the State.

We note that these cost savings could underestimate the full benefits to all Californians, because they focus on only 6 conditions and so do not include the benefits of reduced costs for many other diseases and conditions that could potentially benefit from stem cell therapies. In addition, these estimates do not include various other costs, such as care provided by non-paid family members and caregivers.

Our analysis fits within the context of work examining the returns to investment in health research and development. While exact precedents for the type of research envisioned by the Initiative are difficult to identify, there are more general examples of health research producing large gains for society. In many cases, the gains for society at the broadest level have resulted when research produces new therapies for conditions that had previously had no therapeutic treatment. These can lead to substantial improvements in health and quality of life, though often in return for additional health spending. In other cases, particularly serious conditions that create significant costs but lack effective therapies, successful research can be cost-reducing.

For example, studies by the National Institutes of Health ("NIH") have analyzed the benefits of

[8] Proposition 71, Initiative, Section 2. Findings and Declarations, http://rs192.securehostserver.com/~curesfor/initiative.php.

[9] For the purposes of this report, insulin dependent diabetes includes type 1 diabetes and late onset diabetes in adults (LADA).

medical research spending, reporting a number of cases where relatively small investments in medical technology and research have resulted in substantial yearly cost savings, sometimes in the range of 25 – 40 percent return on investment.[10] For example, the National Heart, Lung, and Blood Institute compared medical vs. surgical treatment for people with deferrable coronary artery bypass surgery. The research effort cost $37 million and estimated savings are $402 million to $804 million per year over the period 1974 – 1984 from improved therapy. Another example cited from the National Institute for Allergy and Infectious Diseases concerns the formulation of the Hepatitis B vaccine. Here, the research effort cost $32 million and estimated savings are between $74 million and $148 million per year over the period 1964 – 1981 on average.

While new research is not always cost-saving, and these examples do not ensure this same high level of economic return from all research, they do point to the opportunity for research on high-cost conditions, like those often thought to be amenable to stem cell research, to generate positive economic returns.

4. Royalties from Discoveries Funded by Proposition 71

The fourth area where Proposition 71 could provide economic benefits is from royalties associated with commercial applications of patented discoveries funded in total, or in part, through Initiative funds. While it cannot be known at this point what discoveries will be made and what patents will be secured, Proposition 71 includes explicit provisions for the State to share in the gains from any patents or other intellectual property developed with Initiative funding.

We do not expect that the research funds will be concentrated in such as way as to fund the entire development of a therapy from discovery through commercialization. Instead, the research funds are more likely to be used in a wide variety of promising areas. To provide a framework for discussion, we estimate that the total amount of research funding in the program is equivalent to the estimated cost the private sector currently would incur to develop 3 – 4 new therapies. If new therapies were to produce revenues akin to other major biotechnology therapies, generating approximately $3 billion in current revenues per therapy, and applying a 2 percent royalty rate, we estimate that royalty revenues of $537 million could be possible over the life of the program. Taking inflation into account, on an annual basis, this would be no more than 10 percent of the current amount of annual royalty revenues being realized by Stanford, the University of California system, and the City of Hope Medical Center.

We have also analyzed a scenario in which the state achieves a 4 percent royalty rate (approximately the mean rate observed in university contracts). If this were to happen, revenues would be $1.1 billion.

D. Conclusion

The tables below summarize potential economic costs and benefits of Proposition 71 in three scenarios: limited therapeutic success, increased therapeutic success, and expanded therapeutic success. These analyses are presented without adjusting for inflation and the time value of money. Estimates including these adjustments for inflation and the time value of money will be presented

[10] Mack, Connie, "The Benefits of Medical Research and the Role of the NIH," Joint Economic Committee, May 17, 2000, p. 24. Dollar amounts in 1992 dollars.

in an addendum to be released in the near future. Since costs and benefits are both spread out over time, making these adjustments is less significant for this analysis than for projects where costs occur much sooner than future benefits.

1. *Case 1: Limited Therapeutic Success*

The first case we consider is consistent with only limited success in developing therapies, resulting in a 1 percent reduction in the health care spending we model. New biotechnology activity is assumed to augment the baseline life sciences industry size by 2.5 percent each year. Royalty revenue is calculated using a 2 percent royalty rate. This analysis leads to estimates that the economic benefits of Proposition 71 to the State budget would exceed the costs, with an overall ratio of benefits to costs of 120 percent. These results are summarized in the table below.

In addition to the benefits to the State budget, there are additional benefits to families and businesses in California from reduced health care costs. With a 1 percent savings, these benefits total $9.2 billion over the 35 year life of the program. In addition, a total of 360,000 job-years would be created for California residents, with an average of 5,200 – 11,200 jobs per year over the life of the program.

Table 2.1
Total Program Costs and Benefits – Case 1: Limited Therapeutic Success
($ Millions)

	Phase 1 Years 1-5	Phase 2 Years 6-14	Phase 3 Years 15-35	Total
Economic Costs to State Budget	$56	$1,289	$4,010	$5,355
Economic Benefits to State Budget				
1) Tax revenues from Proposition 71 direct spending	73	167	-	240
2) Tax revenues from 2.5% increase in life sciences activity	54	355	1,796	2,206
3) Cost savings from 1% reduction in State spending on 6 conditions	-	382	3,062	3,444
4) Royalty revenues using 2% royalty rate	-	10	527	537
Total	**127**	**914**	**5,385**	**6,426**
Percent of Total Costs	***227%***	***71%***	***134%***	***120%***
Additional Benefits to Californians Not Included in State Budget*				
Health care cost savings from 1% cost reductions	**-**	**1,136**	**8,043**	**9,180**
Percent of Total Costs	*0%*	*88%*	*201%*	*171%*
Estimated Jobs Created (One job for one year = one job year)				
Job years from Proposition 71 direct spending	14,272	33,209		47,480
Job years from Increase in life sciences activity	11,967	67,732	233,148	312,847
Total	26,239	100,940	233,148	360,328

** These are savings from the reduction in direct spending and lost work time on the 6 conditions that are not included in the State budget but benefit Californians overall.*

2. *Case 2: Increased Therapeutic Success*

In the second scenario, we have analyzed each of the areas with different assumptions. For the Proposition 71 spending tax revenues, the estimates are unchanged. For biotechnology growth, we have assumed that Proposition 71 augments the baseline industry size by 5 percent each year rather than 2.5 percent. For health cost reduction, we have used a 2 percent savings rather than 1 percent. This is consistent with more successful therapies than in Case 1. We understand that this is the minimum success target identified by the Proposition 71 Committee. Two percent reductions in spending could be achieved without large therapeutic breakthroughs, and are also well below the cost savings returns identified in reviews of successful NIH research funding efforts. For royalty revenues, we have used 4 percent rather than 2 percent royalty rates. These results are summarized in the table below, and show an overall ratio of benefits to costs of 236 percent.

With a 2 percent savings, the additional benefits to families and businesses in California from reduced health care costs totals $18.4 billion over the 35 year life of the program. In addition, a total of 673,000 job-years would be created for California residents, with an average of 7,600 – 22,200 jobs per year over the life of the program.

Table 2.2
Total Program Costs and Benefits – Case 2: Increased Therapeutic Success
($ Millions)

	Phase 1 Years 1-5	Phase 2 Years 6-14	Phase 3 Years 15-35	Total
Economic Costs to State Budget	$56	$1,289	$4,010	$5,355
Economic Benefits to State Budget				
1) Tax revenues from Proposition 71 direct spending	73	167	-	240
2) Tax revenues from 5.0% increase in life sciences activity	108	711	3,592	4,411
3) Cost savings from 2% reduction in State spending on 6 conditions	-	764	6,123	6,887
4) Royalty revenues using 4% royalty rate	-	19	1,054	1,073
Total	**181**	**1,662**	**10,769**	**12,612**
Percent of Total Costs	***324%***	***129%***	***269%***	***236%***
Additional Benefits to Californians Not Included in State Budget*				
Health care cost savings from 2% cost reductions	**-**	**2,273**	**16,087**	**18,359**
Percent of Total Costs	*0%*	*176%*	*401%*	*343%*
Estimated Jobs Created (One job for one year = one job year)				
Job years from Proposition 71 direct spending	14,272	33,209		47,480
Job years from Increase in life sciences activity	23,934	135,464	466,296	625,695
Total	38,206	168,672	466,296	673,175

** These are savings from the reduction in direct spending and lost work time on the 6 conditions that are not included in the State budget but benefit Californians overall.*

3. Case 3: Expanded Therapeutic Success

Finally, we also considered estimates of the benefits under a third scenario in which larger therapeutic breakthroughs are realized. In this scenario, the assumptions for life sciences activity and royalty revenue remain the same as in the second case at 5 percent and 4 percent, respectively. The health cost savings are adjusted upward for the 6 conditions to 10 percent rather than 2 percent. The results, summarized in the table below, are a ratio of benefits to costs of 750 percent.

With a 10 percent savings, the additional benefits to families and businesses in California from reduced health care costs total $92 billion over the 35 year life of the program. In addition, a total of 673,000 job-years would be created for California residents, with an average of 7,600 – 22,200 jobs per year over the life of the program.

Table 2.3
Total Program Costs and Benefits – Case 3: Expanded Therapeutic Success
($ Millions)

	Phase 1 Years 1-5	Phase 2 Years 6-14	Phase 3 Years 15-35	Total
Economic Costs to State Budget	$56	$1,289	$4,010	$5,355
Economic Benefits to State Budget				
1) Tax revenues from Proposition 71 direct spending	73	167	-	240
2) Tax revenues from 5.0% increase in life sciences activity	108	711	3,592	4,411
3) Cost savings from 10% reduction in State spending on 6 conditions	-	3,821	30,616	34,437
4) Royalty revenues using 4% royalty rate	-	19	1,054	1,073
Total	**181**	**4,718**	**35,262**	**40,161**
Percent of Total Costs	***324%***	***366%***	***879%***	***750%***
Additional Benefits to Californians Not Included in State Budget*				
Health care cost savings from 10% cost reductions	**-**	**11,364**	**80,434**	**91,797**
Percent of Total Costs	*0%*	*882%*	*2006%*	*1714%*
Estimated Jobs Created (One job for one year = one job year)				
Job years from Proposition 71 direct spending	14,272	33,209		47,480
Job years from Increase in life sciences activity	23,934	135,464	466,296	625,695
Total	38,206	168,672	466,296	673,175

** These are savings from the reduction in direct spending and lost work time on the 6 conditions that are not included in the State budget but benefit Californians overall.*

This Executive Summary summarizes the results of our larger study. The complete study will be released in the near future and will describe in more detail the methodology and data used for the analysis. Under the scenarios considered, the economic benefits to the State of California are greater than the economic costs of the program. Importantly, the non-economic opportunities for improved health and quality of life for Californians and others have not been quantified in this study.

III. Table Of Contents

IV. Introduction

On behalf of Californians for Stem Cell Research and Cures, Dr. Laurence Baker, Associate Professor, Department of Health Research and Policy, Stanford University School of Medicine and Bruce Deal, Managing Principal with Analysis Group, Inc., have been retained to analyze the financial impact of Proposition 71 on the people of California and the budget of the State of California (the "State"). This analysis focuses on comparing the costs of the program, in the form of principal and interest payments, to the potential financial benefits of the program, which could be derived from a number of different areas.

In conducting this research, we have made use of numerous sources of information, which are referenced as they appear and also noted in Appendix A. In addition, we have benefited from conversations with a number of individuals with expertise in stem cell research, research administration, bond markets, and other areas important to analysis. These are noted in Appendix B. We thank the many individuals who generously provided time and information that aided this analysis. The opinions and conclusions are those of the authors.

A. Proposition 71

Proposition 71 would provide funds from the California state government to support stem cell research. These funds would substantially increase funding available for stem cell research, particularly given current Federal government restrictions on funding for stem cell research.

Proposition 71, if approved, will create the California Institute for Regenerative Medicine ("Institute"). With participation from leading doctors, scientists, patients' rights advocates, medical ethicists and research universities, the Institute would direct and oversee a program of funding for stem cell research with the intention of providing California's scientific community with resources for research that may one day lead to new medical treatments for important health conditions. The Institute would make funding commitments of approximately $295 million per year over 10 years beginning in approximately early 2005. Grants and loans for research and facilities would be made to academic and non-profit research institutions, teaching hospitals, and commercial entities that have demonstrated success in therapy deployment. Priority for research funding would be given to research that both meets the Institute's criteria and is unlikely to otherwise receive adequate federal funding. The Institute's administrative costs would be capped at 3 percent, and Institute grant making activity costs would also be capped at 3 percent of annual funding to ensure the funds are focused on research and results. The Institute would be funded by $3 billion in general obligation bonds, distributed in annual increments for up to ten years, and paid back in full within 35 years of the start of the Institute.

B. Economic Impact Analysis Overview

We analyze the economic impact of the Proposition in two main parts. First, we discuss the estimated costs that the State would incur as a result of issuing bonds to fund the research effort. Second, we discuss the potential for economic benefits to be realized by the people of California in general as well as the potential for generating increases in revenues or decreases in costs that would directly benefit the State budget. There are four areas in which we identify potential benefits:

- Tax revenues generated by the facilities and research spending of the Institute
- Tax revenues associated with increases in private sector biotechnology activity that could result from passage of the Initiative
- Reductions in health care costs associated with new stem cell therapies
- Royalties on intellectual property funded by the Institute

Some of the economic benefits we identify would occur because of the creation of new jobs. In addition to investigating the potential benefits of Proposition 71 in financial terms, we also provide analysis of the potential for new job creation from Initiative spending and increases in biotechnology activity.

We focus on the 35 year time span within which the bonds authorized by the Initiative would be issued, spent on research and facilities, and paid off. We account for costs and benefits that would accrue during this period. Studying this time period should provide for full consideration of the costs associated with the bond issue and its complete repayment. Studying this time period will also allow us to capture many of the benefits, though some potential benefits could continue after this period. We may thus somewhat understate total potential benefits.

This report presents all results in nominal, undiscounted dollars. That is, we make no adjustment here for the time value of money, and value dollars in the future equally with current dollars. Much of the current discussion of Proposition 71 takes place in these terms. However, appropriately accounting for the time value of money (discounting) can be important in some circumstances. Additional information on the results of this analysis accounting for the time value of money will be released separately. In this setting, discounting will not substantially alter the conclusions since both the costs and benefits are spread reasonably consistently over time.

C. Scope and Limitations

While Proposition 71 has significant economic costs and benefits, its central goal is not specifically economic in nature, but rather is to contribute to improvements in health. The concept of public funding of health-related research is well-established in the United States, with billions of dollars each year spent funding basic and later-stage research designed to improve human health. The benefits of this research have been significant and have improved the length and quality of life for millions of Americans. Were Proposition 71 to accelerate the discovery of beneficial new therapies, it could produce important benefits for Californians and others throughout the United States, and even the world, in the form of improved length or quality of life for individuals with affected health conditions as well as their family members, friends, and community members. Our report focuses on economic aspects of the Initiative. We do not consider the happiness, satisfaction, peace of mind, and related benefits to patients, their families, and society more broadly that improved health, longer lives, and higher quality of life could bring. These are often intangible, difficult to quantify, and difficult to predict. They can, nonetheless, be very important and consideration of these kinds of benefits is clearly essential for a full evaluation of Proposition 71. They could, in fact, be larger than any direct and tangible economic gains that result from the Initiative.

We also do not directly investigate the scientific aspects of stem cell research. As economists, we have relied on information obtained from published literature and from conversations with medical and scientific experts as to the potential for development of new stem cell-based therapies. This information is clear on two points. First, there appears to be great potential in stem cell research for the development of new and powerful medical therapies. Some studies from respected research institutions have shown positive proof of concept in important therapy areas, and some respected researchers report the possibility of new therapies emerging within the next several years. Second, while there is promise, the success of these therapies is in most cases yet to be fully demonstrated; further funding and research, possibly including human trials, will be required before the potential of stem cells is completely understood or developed.

Despite uncertainties about whether or when the promise of stem cell research will be realized, our conversations with a variety of experts have led us to the conclusion that the potential for successful therapies is strong enough to warrant analysis of the type we undertake here. At the same time, we also believe it prudent to keep in mind the difficulties and challenges associated with the research. As a result, we modeled scenarios that we believe reflect a balance in expectations about the research. We note that even in models that are modest in their expectations for research successes, Proposition 71 appears capable of producing significant economic benefits.

V. Economic Costs To The California State Budget

A. Introduction

This section of the report describes the spending expected to take place under Proposition 71 and the costs to the budget of the State associated with repayment of the borrowed principal and related interest. Borrowing would take place as needed to match disbursements under the Initiative. We thus begin by discussing expectations about disbursement patterns, followed by analysis of the expected costs associated with bond repayment.

Our analysis is based on the funding structure and timing schedule specified by the Proposition 71 organizers. Proposition 71 funds would be spent in three areas. The first area is the construction or renovation of research facilities appropriate for the research focus of the Institute. These funds would be disbursed during the first five years of the program. The second area is the funding of research. Commitments for multi-year research grants would be made in each of the first 10 years. Some of these commitments would be for multi-year grants, so that funds would be disbursed over the course of the first 14 years of the program. The third area is administration costs, including the Initiative overhead as well as staff and overhead necessary to evaluate, fund, administer, and monitor the grants. These costs would be incurred over the first 14 years of the program, during the time in which there would be active grant making activities.[11]

The total amount borrowed under the Initiative would be approximately $3 billion. Financing is currently planned to take place in three phases, which we model as follows. We recognize that the actual length and maturity schedule of the Initiative bonds may vary somewhat based on the Institute's need to respond to changing financial and economic conditions. During phase one, which takes place during funding years 1 – 5, the funding would consist of variable rate general obligation (G.O.) bonds maturing in year 5, with deferred principal and interest payments. The principal and accrued interest on these notes would be paid in full by the issuance of new bonds at the start of phase two. That is, no repayment of principal or interest would take place in phase one. Phase two starts in year 6 and continues through year 14. During this phase, the principal and accrued interest from years 1 – 5 and the subsequent disbursements during these years would be paid for through State G.O. bonds all maturing in year 35. Phase three starts in year 15 and continues to year 35. During this phase, there are no additional disbursements, and the principal and interest accrued during the first two phases are amortized such that all debt and accrued interest is paid off at the end of year 35. The repayment of the bonds issued in years 6 – 14 would be based on a level payment principal and interest schedule varying from 22 years (for the bonds issued in year 14) to 30 years (for the bonds issued in year 6).

B. Disbursement Assumptions During Phase One: Years 1 – 5

During the first five years, funds would be spent on facilities, research grants, and program administration. The following table summarizes the schedule for the funds committed during phase one and the corresponding funds disbursed. The difference between the commitment and disbursement estimates arises from the fact that many grants would be in the form of a multi-year

[11] Administration funding of up to a total of 6 percent of disbursed funds, consisting of up to 3 percent of the initial bond proceeds to fund the Institute's overhead costs, and up to an additional 3 percent for grant administration. Administration costs are considered a third use of funds.

award, and thus a commitment of $5 million might mean a disbursement of $1 million per year for five years. Following the table is a discussion of each of these spending areas.

Table 5.1
Phase One (Years 1 – 5) Institute Commitment[12] and Disbursement Schedule
($ Millions)

	Year 1	Year 2	Year 3	Year 4	Year 5	Total Years 1 - 5
Project Commitments by Year						
Facilities (including Administration)	$20	$100	$100	$80	$0	$300
Research (including Administration)	150	250	250	300	300	1,250
Total Committed Funds	**170**	**350**	**350**	**380**	**300**	**1,550**
Project Disbursements by Year						
Facilities	$13	$69	$94	$81	$25	$282
Research	20	84	122	190	217	634
Administration	2	10	14	17	15	58
Total Disbursed Funds	**35**	**162**	**230**	**289**	**258**	**974**

1. *Institute Facilities Spending*

During the first five years, the Institute is proposed to commit a total of $300 million in funds for facilities construction and renovation. It is anticipated that the committed funds would be disbursed evenly during an 18-month period following the commitment. We have not conducted a complete evaluation of research facilities needs in California. However, based on discussions with research experts, it is our understanding that there is a significant perceived need for additional research facilities, particularly when considering the multi-billion dollar research program anticipated by the Institute. We thus assume it would be feasible for the Institute to disburse these funds as projected.

This assumption is consistent with recent National Science Foundation ("NSF") studies showing that over 74 percent of biological science institutions report having an inadequate amount of research space. These institutions report that the percentage of facilities space that was considered "suitable for the most scientifically competitive research" was only 23 percent and additional space needed in order to conduct research under current commitments was 29 percent.[13] The same report found that over 908 total institutions reported having to defer over $5.6 billion in needed construction and renovation due to insufficient funding of facilities. This evidence points to a continued need for additional spending on construction and improvement of modern research facilities.

This assumption is also consistent with the implications of current restrictions on the uses of Federal research funds for research involving stem cells. Federal funds may not be used in any

[12] See footnote 11.
[13] "Scientific and Engineering Research Facilities: 2001, National Science Foundation," Division of Science Resources Statistics, January 2002; "A Report to the Advisory Committee of the Director," National Institutes of Health, NIH Working Group on Construction of Research Facilities, July 6, 2001; and "Top 100 R&D-Performing Academic Institutions Continue Increased Facilities Construction," National Science Foundation, June 22, 2000.

way to fund work with stem cells outside of narrow funding guidelines. This prohibition extends to indirect support and general aspects of facilities funding. From conversations with research experts, we understand that, to many observers, these restrictions seem to require institutions that wish to conduct significant stem cell research to house it in space that is clearly separate from space housing other federally-funded projects. Since most research institutions in California receive significant support from the NIH and related federal sources, this requirement would contribute to demand for new construction or other infrastructure-related expenditures to house stem cell work.

2. *Institute Research Spending*

During the first five years, the Institute is proposed to commit $1.25 billion in funds for research grants of various types. These grants would be for various durations, ranging from 3 – 5 years. As a result, the anticipated disbursement of funds during the first 5 years would be less than the commitment, totaling $634 million over the phase one period.

We have not conducted a complete evaluation of the research funding needs in California in the areas covered by the Institute. However, it is our understanding that there is a perceived need for extensive additional research funding in the areas covered by the Institute. Our conversations with research and industry experts about the demand for research funding in this area suggest substantial interest in obtaining Institute funds. We thus assume it would be feasible for the Institute to disburse these funds as projected.

3. *Institute Administration Spending*

Administration spending includes Institute overhead as well as staff and overhead associated with evaluating, funding, administering, and monitoring the grants. Administration funding consists of up to 3 percent of the bond proceeds to fund the Institute's overhead costs, and up to an additional 3 percent for grant administration. We have not conducted an evaluation of the amount of administrative funding that will be needed, or of whether this amount is sufficient to cover the costs of the administering the program. We assume that all 6 percent allowed for administration would in fact be spent on administration and that the distribution of administration spending over time would closely reflect the distribution of research spending over time.

C. Disbursement Assumptions During Phase Two: Years 6 – 14

During phase 2, there would be no additional funds allocated for facilities funding. During this period all of the remaining research funds would be disbursed. The Institute is expected to make new commitments of $300 million per year in each of years 6 – 9, and a commitment of $200 million in year 10. As in the first five years, these would be for 3 – 5 year grants, so that actual disbursements would take place over years 6 – 14. The following table summarizes the planned disbursement during this period.

Table 5.2
Phase Two (Years 6 – 14) Institute Disbursement Schedule
($ Millions)

	Year 6	Year 7	Year 8	Year 9	Year 10	Year 11	Year 12	Year 13	Year 14	Total Years 6 - 14
Project Disbursements by Year	$233	$257	$259	$318	$350	$338	$199	$56	$2	$2,012
Cumulative Disbursements	1,207	1,464	1,722	2,040	2,390	2,728	2,927	2,984	2,986	

D. Costs to the State Budget from Interest and Principal

Proposition 71's spending impact on the State budget comes from the interest and principal repayment associated with the disbursed funds. These costs are discussed in this section.

1. Interest Rate Assumptions during Years 1 – 5

During the first five years, the expense associated with the Institute's program would be the accrued interest on the disbursed funds, since there would be no principal repayment during this period. This section discusses the development of the interest rate assumptions used for modeling.

Our interest rate assumptions for the first five years are based on the issuance of a series of variable rate bond anticipation notes, backed by the general obligation of the State of California, following the pattern of disbursements. The notes would mature in year 5, with deferred interest and principal payments over the term. These notes are assumed to be paid (principal and accrued interest) in full by the issuance of new California G.O. bonds at the end of the five years.

The following factors can influence the pricing of the bond. We analyzed and incorporated each of these factors in determining an expected average annualized yield rate over the term for the Initiative bonds:

- California Discount (or Premium) – The State of California generally has a tax structure that results in relatively high State taxes. Therefore, California taxpayers have an incentive to purchase bonds that are tax exempt to lower the taxable income base. Because of this, demand for tax-exempt investment instruments is high, which has historically resulted in a discount (or benefit) to the base yield price of a bond issued by the State of California. Other factors, such as the State's credit rating and the State's overall economic outlook also factor into the discount (or premium) added to municipal issuances.
- Insurance/Credit Enhancement – Variable rate, general obligation instruments are bound to certain covenants that dictate the credit ratings of the issue be in the top two highest categories. Since the State of California currently has a credit rating of A/A3/A- on G.O. Bonds,[14] a relatively low rating compared to other states, any general obligation

[14] Ratings from Standard & Poor's, Moody's Investor's Service, and Fitch Ratings, respectively. Angelides, Phil, "California's Current Credit Ratings," available at http://www.treasurer.ca.gov/ratings/current.htm, accessed September 8, 2004.

instrument issued would be backed by either a credit enhancement or insurance. The cost of either of these criteria results in an increase to the base yield rate. Should the economic conditions and/or the State's credit rating improve, the need for either insurance or a credit enhancement facility would lessen, resulting in a reduction in the effective yield rate over time.

- Cost of Issuance – While a much smaller component, the cost of issuance, including any underwriter's discount, results in an increase to the base yield rate.
- Remarketing – There are generally three types of floating rate instruments used in the market for municipal bonds, the most common of which is a remarketed floating rate instrument. Essentially the remarketer is tasked with determining, on a weekly basis, the lowest, sellable, liquid rate for the company's note or bond. As this is an ongoing service over the life of the bond, there is an increment to the base yield rate for this service charge.
- Liquidity – Often the largest component of additional yield costs, the liquidity component is a service fee imposed in exchange for a chosen bank to hold enough liquid capital to purchase the instrument from a potential seller, should no immediate buyer be available at any given time.

Due to the nature of the municipal bond industry, it is not possible to precisely predict actual initial bond costs or the base yield rate at issue. However, based on interviews with municipal bond industry experts, we estimate that the effective costs for a note such as that likely to be used by the Institute would be approximately 30 basis points,[15] ongoing on an annualized basis, above the base variable interest or yield rate in the market.

We estimate the base variable interest rate by examining a number of sources of information about current and expected bond market conditions. Predicting interest rate movements even in the near term is difficult at best and it is not possible to know what short-term interest rates will be well into the future. While interest rates cannot be accurately predicted into the future, various historical and predictive scenario analyses suggest a reasonable range of expected future interest rates.

The proxy we have assumed for our ongoing variable interest rate is the Bond Market Association Variable Rate Municipal Swap (BMA) index.[16] The BMA was calculated at approximately 1.25 percent for the week of August 18, 2004,[17] which is near its ten-year low of 0.7 reached on July 9, 2003. The historical weekly BMA has traded at an average of 1.02 percent for the past year, 2.22 percent for the past five years, and 2.87 percent for the past ten years. Over the past ten years, the BMA high was 5.84 percent. The chart below highlights the movements of the BMA and the BMA plus an assumed 30 basis point premium over the past five years.

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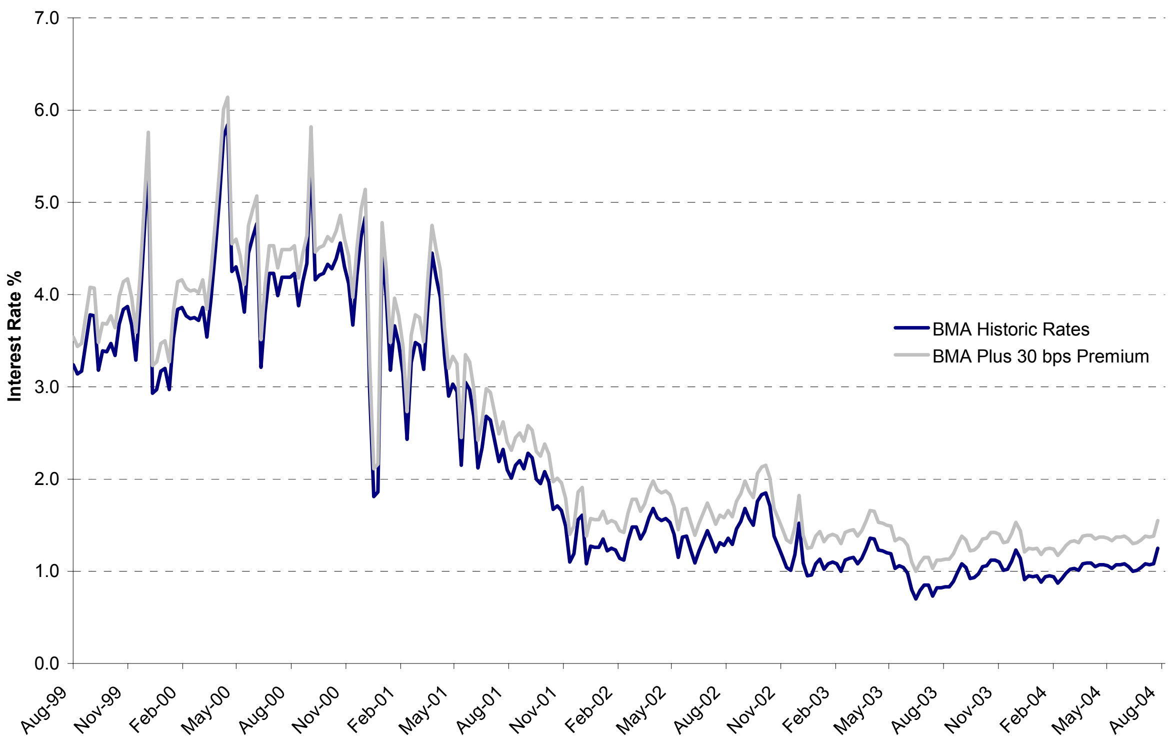
[15] A basis point is one one-hundredth of a percentage point. For example, if the base market yield is 2 percent, a bond issue priced at the market yield rate plus 30 basis points would carry a yield rate of 2.3 percent.

[16] The BMA is an index comprised of variable interest rates from the Variable Rate Demand Note Network database that pulls daily rate change data from over 80 remarketing agents. This database is maintained by Municipal Market Data, a Thomson Financial Services Company. A detailed explanation of the Index and its calculation can be found at http://www.bondmarkets.com/research/qanda.shtml.

[17] Bloomberg data for MUNIPSA Index, accessed August 18, 2004.

Chart 5.1
BMA Index 1999 – 2004



To incorporate industry sentiment regarding future interest rates, we analyzed the yield curve as well as federal funds rate predictions. The yield curve essentially plots a set of interest rates of bonds of different maturities and describes the relationship among short-term, medium-term, and long-term rates at a given point in time. If interest rates are expected to remain constant over time, the yield curve will show some increase, from lower interest rates on shorter-term bonds to higher interest rates on longer-term bonds, because investors require higher returns for making longer term investments. Larger (or smaller) increases in the yield curve will result when the market prices in expectations of rising (or falling) interest rates. The current yield curve has a five-year horizon of about 3.0 percent through a 30-year horizon of about 5.0 percent.[18] In historical terms, this is a modest increase in the yield curve, indicating some expected upward rate movement but not dramatic changes in interest rates, particularly in the near term.

Second, we analyzed short-term market expectations of base interest rate movements given in two independent forecasts of the short-term federal funds rate. These rate projections over the next year from two independent, third-party sources indicate relative stability in the short-term federal funds rate. Specifically, we looked at recently published Merrill Lynch ("ML") and UBS Securities ("UBS") predictions for various interest rates, including the federal funds rate. While

[18] "Dynamic Yield Curve," available at http://www.stockcharts.com/charts/YieldCurve.html, accessed August 24, 2004.

UBS's predictions are slightly higher, both sources appear to indicate that the federal funds rate is expected to remain between 1.75 percent and 4.0 percent over the next 5 quarters. Moreover, Merrill Lynch predicts a decrease in the two-year note rate of 15 basis points and a decrease in the ten-year note rate of 60 basis points over that same time period, as shown in the table below.[19]

Table 5.3
Wall Street Interest Rate Predictions through Q4 2005

	End of Period Rate Prediction					
Interest Rate Type	Q3 2004	Q4 2004	Q1 2005	Q2 2005	Q3 2005	Q4 2005
Fed Funds (ML)	1.75	2.00	2.50	2.50	2.50	2.50
Fed Funds (UBS)	1.75	2.00	2.50	3.00	3.50	4.00
2-Year Note (ML)	3.00	3.25	3.45	3.00	2.90	2.85
2-Year Note (UBS)	2.80	3.20	3.70	4.20	4.70	5.15
10-Year Note (ML)	4.75	5.00	4.90	4.65	4.30	4.15
10-Year Note (UBS)	4.60	5.00	5.00	5.30	5.30	5.50

These two analyses lead to our modeling assumption that, over the next five years, interest rates are expected to have some upward movement from current levels, but are not expected to change dramatically.

If a bond were priced at the current BMA rate, plus the anticipated 30 basis point increase, the yield would be approximately 1.55 percent. Considering the forecasted changes in rates, we have used an effective debt service cost rate of 3.0 percent in each of the first 5 years for our analysis. This may be somewhat conservative in light of current bond market conditions. It would be further conservative if the California economy were to improve, which would tend to make the difference between the BMA rate and the rate on California bonds of this type decrease. The exact result of improvements in the economic situation are uncertain, but include increased demand for California tax-exempt notes that would be expected to improve the State's ability to obtain advantageous pricing for its bonds, which would effectively lower the current additional cost of 30 basis points we have assumed for the variable notes.

It is further worth noting that the proposed variable rate debt instrument would be based on a weekly or monthly floating rate. The uncertainty surrounding economic predictions and projected modest economic growth over the next several years is expected to create some amount of liquidity in the overall floating rate market, which may result in an increased demand for floating rate instruments, relative to other fixed rate or other maturity, thereby increasing the overall value of the floating rate note. The existence of these circumstances also weights our analysis toward being conservative.

[19] "August 2004 U.S. Interest Rate Forecast Update," UBS Securities, August 2004; and "U.S. Interest Rate Forecast," Merrill Lynch, August 5, 2004.

2. *Interest Rate Assumptions during Years 6 – 35*

From discussions with experts in municipal finance, we understand that variable rate debt can be made to essentially be fixed rate through the use of a "synthetic" fixed rate based on swap instruments. Under the right conditions, this may be less expensive than issuing fixed rate debt. Based on our assumption that interest rates will rise somewhat over time, for purposes of our analysis, we have assumed the fixed rate debt issued between years 6 and 14, and paid off by the end of the 35 year horizon would carry an effective rate of 4.50 percent. We note that the Legislative Analyst's office has used a higher interest rate assumption in its analysis, assuming a 5.25 percent average interest rate on the bonds.[20]

As a comparison point, a large portfolio of these synthetic swaps issued by the California Housing Finance Agency over the past several years carries an approximate effective portfolio rate of 4.25 percent. These bonds also do not have all of the tax advantages of Institute bonds, and thus may have a higher interest rate than Institute debt. For example, the Institute's variable rate notes are not subject to the alternative minimum tax. This tax benefit is expected to generate a higher demand for Institute bonds than for instruments without similar tax advantages, and could potentially result in the difference of a 25 – 30 basis points savings.

3. *Summary of Interest and Principal Repayment Assumptions*

The following tables summarize the interest and principal costs we expect to be associated with Proposition 71. We understand that the Institute and the State would work to ensure that the borrowing and repayment are done in the most economically efficient manner. This may result in a somewhat different pattern than the currently planned pattern that we employ in our analysis.

[20] "Proposition 71: Stem Cell Research Funding. Bonds. Initiative Constitutional Amendment and Statute," Legislative Analyst's Office, July 2004, available at http://www.lao.ca.gov/ballot/2004/71_11_2004.htm, accessed August 16, 2004.

Table 5.4
Summary of Interest and Principal Repayments
($ Millions)

	Years 1-5	Years 6-14	Years 15 - 35	Total Years 1 -35
Total Interest	56	862	1,450	2,368
Total Principal	0	427	2,560	2,986
Total	56	1,289	4,010	5,355

Table 5.5
Year by Year Interest and Principal Repayments
($ Millions)

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8
Yearly Interest	1	3	9	17	25	54	65	75
Yearly Principal	0	0	0	0	0	20	25	31
Total	1	3	9	17	25	74	90	107

	Year 9	Year 10	Year 11	Year 12	Year 13	Year 14	Year 15	Year 16
Yearly Interest	88	102	115	122	121	118	115	112
Yearly Principal	39	48	58	65	69	73	76	79
Total	126	150	173	187	191	191	191	191

	Year 17	Year 18	Year 19	Year 20	Year 21	Year 22	Year 23	Year 24
Yearly Interest	108	104	101	97	92	88	83	78
Yearly Principal	83	86	90	94	99	103	108	113
Total	191	191	191	191	191	191	191	191

	Year 25	Year 26	Year 27	Year 28	Year 29	Year 30	Year 31	Year 32
Yearly Interest	73	68	62	57	51	44	38	31
Yearly Principal	118	123	128	134	140	147	153	160
Total	191	191	191	191	191	191	191	191

	Year 33	Year 34	Year 35
Yearly Interest	24	16	8
Yearly Principal	167	175	183
Total	191	191	191

VI. Economic Benefits From Tax Revenues Generated By Proposition 71 Spending

The first area of economic benefit we analyze is the additional tax revenue generated by the spending associated with Proposition 71. These revenues include income and sales tax revenues generated by new employment and purchases that result from Institute spending, such as the hiring of new researchers, purchases of new equipment, or new construction contracts. We make these calculations by first computing the amount of new economic activity that could result from Institute spending, including the application of economic multipliers generated from a widely-used economic model. We then break down new spending into different components, such as salaries and equipment purchases, and compute expected tax revenues for each type of new spending.

A. Financial Leverage/Matching Funds and Substitution

From the perspective of measuring economic activity, the net new research and facility spending associated with the Institute program may be somewhat different from the amounts disbursed by the Institute to fund research and facilities. This is a result of the interaction of three factors: 1) leverage from matching funds, 2) offsets to account for fact that some of the Institute spending could substitute for other spending rather than being truly incremental, and 3) leverage from research funding diversification. Each of these will be discussed below. The Institute would also disburse funds for its own administrative overhead and grant making activities. We assume that this spending would not be influenced by these three factors.

1. Additional Leverage from Matching Funds

It is common for research organizations to attempt to combine various sources of funding for major research initiatives. For example, a major cancer research effort might attempt to combine funds from sources such as the NIH, other federal government research organizations, state university research funds, private cancer research organizations, and other private philanthropic research organizations. By combining funding, a larger and more substantial research programs could be developed than would otherwise have been possible.

It is a stated goal of the Institute to encourage facilities and research grantees to seek out matching funds from donors or other outside sources like industry. Language in the Initiative appears to require grant recipients to provide a minimum of 20 percent matching funds.[21] While federal research funds may be unavailable as matching funds due to various restrictions, there are other individual donors, patient advocacy and disease research organizations (e.g., American Diabetes Association, The Christopher Reeve Paralysis Foundation, and the Michael J. Fox Parkinson's Foundation), private sector firms, and other funding organizations potentially interested in being research partners in these endeavors. Many organizations such as the Juvenile Diabetes Research Foundation require that private companies must match funds as a condition for funding. Conversations with medical and scientific leaders of California research institutions and industry experts in this area confirm that the presence of Institute funding could generate interest among donors, industry, or other funding organizations and that it is likely that some matching funds would be obtained by funded institutions.

[21] Proposition 71, Initiative, 125281.12 (b)(1)(i), http://rs192.securehostserver.com/~curesfor/initiative.php.

To the extent matching funds would flow in to California as a result of Institute funding that would otherwise not have been spent in California, this represents leverage that would increase the economic benefits to the State with no increase in interest or principal repayment on Institute bonds.

It is impossible to know with certainty what amount of financial leverage could be obtained by funded institutions. Our analysis models a modest matching leverage rate of 20 percent for both research dollars and construction dollars (i.e. each dollar of Institute funds would be matched by $0.20). We developed this estimate taking into consideration the following factors.

- The Initiative appears to require grant recipients to provide at least 20 percent matching funds. The Institute's program would also provide incentives for institutions receiving the funds to obtain matching funds. We expect that these incentives would promote the use of matching funds. Specifically, recipients of Institute funds would be able to obtain a higher funding priority and higher research indirect rate if they obtain matching funds. Previous programs, like the California Institute for Telecommunications and Information Technology (Cal IT2), which have required or otherwise provided incentives to obtain industry partnerships or other matching funds, appear to have a successful track record.
- The Industry-University Cooperative Research Program (IUCRP) awards hundreds of UC Discovery Grants each year in science, engineering, and microelectronics. UC Discovery Grants form a three-way partnership between UC, Industry Sponsors, and the State of California. A recent report from IUCRP states that every $1 in State funded research spending is matched with $1.57 in industry dollars and $0.68 in UC system dollars.[22] In addition, institutions were able to generate additional funds from other various sources. In all, this program achieves a matching rate of much more than 20 percent.
- Private sector funds appear available as a source of matching funds for universities and other research institutions to augment Institute-funded research. There are currently numerous private sector entities involved in research efforts focusing on health issues targeted by the Institute. These entities conduct a substantial amount of research. A recent report by the National Science Foundation estimated that the U.S. spent 2.79 percent of total Gross Domestic Product (GDP) on research and development spending in 2002.[23] When the GDP / R&D ratio is split between federal and non-federal sources, the study shows that historically the majority of growth can be attributed to non-federal R&D spending, which is primarily from private company sources. In a related report, the National Science Foundation estimated that private sector industry funds were the largest source of funds at 70 percent, with these same industry sources contributing over 7 percent of their funding to university and colleges and over 14 percent to non-profit institutions.[24] The table below identifies sources of research and development funding for the year 2000.[25]

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[22] "Industry-University Cooperative Research Program: 1996-2002," University of California President's Board on Science and Innovation, available at http://www.ucdiscoverygrant.org.
[23] "Slowing R&D Growth Expected in 2002," National Science Foundation, December 2002.
[24] "Sixth Year of Unprecedented R&D Growth Expected in 2000," National Science Foundation, November 2000.
[25] *Ibid.*

Table 6.1
Sources of U.S. Research & Development Funds, 2000

	Sources of Funds				
Total Research by Sector	Industry	Federal Government	Universities and Colleges	Other Non Profit Institutions	Total Research by Sector
Industry	88.2%	11.8%	0.0%	0.0%	100%
Federal Government	0.0%	100.0%	0.0%	0.0%	100%
University	7.4%	57.9%	27.5%	7.3%	100%
Other Non Profit Institutions	13.1%	43.0%	0.0%	43.9%	100%
Weighted Total Research by Source	70.1%	24.4%	3.2%	2.3%	100%

Note: Excludes FFDRC (Federally Funded Research & Development Centers) administered by non-federal entities.

- Conversations with industry experts suggest interest in partnering with academic institutions. Many private sector firms appear to have participated in 1:1 shared financing of past or ongoing research projects in which they were or are interested.
- Conversations with medical and scientific experts produced mixed results on the ability to obtain, and interest in obtaining, matching funds from donors. Some reported that obtaining matching funds of 20 percent or more would be possible. Others suggested less.

2. *Incremental Economic Activity vs. Substitution*

Research and construction funds flowing from the Institute and leveraged by matching funds would constitute new research and construction funding flowing to California research institutions. A key issue in evaluating the economic impact of this spending is the extent to which it produces new, incremental activity, as opposed to substituting for activity that would have occurred anyway.

For example, if research funding from the Institute allowed an institution to create a new faculty position, and that position were filled with a researcher who otherwise would not have worked in California, the Institute would generate new, incremental activity. On the other hand, if a researcher currently working at a California institution were to face a choice between seeking funds from the Institute or seeking funds from some other source, and applied to and obtained funds from the Institute, the Institute funding may not produce incremental activity. If Institute grant funding were not there, the researcher might simply get a different grant, and there would be no net economic impact on the State. It seems reasonable to expect that not all of the research funding provided by the Institute would be incremental. At the same time, we believe it likely that the Institute would generate a significant amount of incremental activity, particularly given the limitations in the availability of research funds from other sources for this kind of work. Predicting exactly how much activity is incremental rather than a substitute for other activity is difficult. There are not existing data and studies of which we are aware that quantify these effects in related circumstances. We have thus aimed to develop reasonable estimates of the amount of incremental activity based on the information about the program and from conversations with experts.

Because it would take time to add and fill new positions at research institutions, we expect that the share of research funding that is incremental would tend to rise over time. Our base models incorporate the assumption that 30 percent of the research activity in the first year would be incremental, and that this would rise to 70 percent by year five and remain at 70 percent thereafter. We considered the following factors when developing these estimates.

- The size and duration of the program appears to us to provide enough funding for a long-enough period to attract new researchers and research programs to California. In addition, while California does have researchers capable of working in the areas covered by the Institute, carrying out research on the scale viewed as plausible by research experts (and envisioned by the Institute's program) would seem to require substantial additional effort and the creation of additional positions.
- Conversations with leaders at some California research institutions indicated interest in creating new positions in response to the Institute's program, though these conversations also point out that it would take time to add and fill new positions. When asked how many new positions it is reasonable to think could be created, estimates vary but in some cases are reasonably large.
- Conversations with medical and scientific research leaders indicated interest in expanding operations in California were the Institute to come into existence.
- Opportunities for Institute funds to be incremental depend on availability of other funds. Given the leveling off of the NIH budget and California state budget cuts that could affect higher education funding, there may be increased demand for Institute funds that would more easily allow them to contribute to incremental activity.

For the facility spending, we believe it likely that virtually all of that activity would be incremental. Thus, we assume no substitution effect for facility spending. This view is confirmed by conversations with industry experts.

3. *Additional Leverage from Research Funding Diversification*

To the extent that Institute funds augmented by matching funds lead to the creation of incremental research positions, it is likely that these positions would then produce an additional source of leverage. Researchers, often encouraged by research administrators, frequently seek to diversify their sources of research funding. Much like in the financial world, diversification reduces the volatility associated with any single funding source. At major research institutions, it is common for investigators to have support on multiple grants from multiple funding sources. While the Institute is intended to be a relatively long-term, substantial funding source, it is plausible that many researchers funded by the Institute would seek to diversify their funding sources and would ultimately receive other research grants. By doing so, they would increase the overall amount of economic activity in California, with no increase in interest and principal payments on Institute bonds.

For example, a researcher attracted to California by the Institute may ultimately find him or herself receiving funding from the Institute to support half of his or her research effort, and receiving funds from other funders to support the other portion. This would produce leverage, effectively doubling the economic activity generated by Institute funds. That is, if the Institute provided funding for 50 percent of a research program, this would provide 100 percent leverage since for every dollar provided by the Institute, there would be an additional dollar in leverage. Note that this is different from donor matching funds. This research funding diversification does not occur because of multiple donors funding a common project. It occurs because a researcher would have multiple projects underway at the same time.

For modeling, we assume that the amount of research diversification leverage is smaller in earlier years, as incremental researchers develop their programs, and grows larger as research programs are developed and additional funding support can be put into place. Specifically, we assume that research diversification leverage will rise from 5 percent in year 1 (i.e. Institute funds support about 95 percent of the research program) to 40 percent in year 4, (i.e. Institute funds support about 60 percent of the research program). We assume that it would remain at 40 percent thereafter. Based on conversations with medical and scientific research experts, we believe these figures to be conservative.

We base the assumptions for research funding diversification on the following pieces of information:

- Conversations with research experts suggest that most investigators have multiple sources of funding. Particularly as research programs develop, it would be common for researchers to have no more than 30 – 50 percent of their funds from any given source. Newer investigators tend to have fewer grants, and so it is plausible that the fraction of research supported by the Institute would be higher in earlier years. For Institute-funded research, the percentages of funding from the Institute might be somewhat higher than average since the extent to which federal funds would be available to support research using exactly the same stem cell related methodologies most centrally contemplated by the Institute appears limited by various restrictions. Nonetheless, based on conversations with research experts, we anticipate that researchers studying diseases and conditions covered by the Institute would be able to obtain funding to study risk factors or therapy approvals for those diseases in ways that are acceptable to federal and other funders.
- The San Diego Supercomputer is a major research center that was originally funded by one major federal project. That project provided significant and stable funding for the Supercomputer, which in turn enabled them to attract other research funding. The research program at the Supercomputer continues to grow, but at the current time, the research funding profile has over 40 percent from new projects.
- Some Institute funds would flow to private firms and it is unclear that these funds would be leveraged through the same mechanisms.

We assume there is no research funding diversification leverage on facility spending.

4. *Net Impact*

Combining these effects together provides the net impact of increased leverage less any substitution effect. To produce the net number, we first account for matching fund leverage, then account for the share expected to be incremental, and then account for the research diversification leverage that would apply to the incremental spending. For a dollar of new research funding in year 1, augmented by 20 percent matching fund leverage, we would have $1.20. If (as we assume in year 1), 30 percent of this would go to incremental activities, we have $0.36. If (as we assume in year 1), this is leveraged 5 percent by research diversification, we end up with $0.38 of incremental research spending, or a net effect of -62 percent.

Table 6.2 reports the leverage and substitution effects for research funding that we incorporate into the analysis for the first 5 years. For research spending the net impact becomes larger over time as the substitution effect diminishes and the research diversification leverage increases, with a net effect of +18 percent by year 5. We hold the values fixed at their year 5 levels for years 6 – 14. For facility spending, the effect is constant over time based on a matching fund leverage of +20 percent and no impact from substitution on research diversification.

Table 6.2
Net Impact of Leverage and Substitution on Research Funding

	Year 1	Year 2	Year 3	Year 4	Year 5
1) Matching fund leverage	120%	120%	120%	120%	120%
2) Incremental Portion of Spending	30%	40%	50%	60%	70%
3) Leverage from Research Diversification	105%	110%	120%	130%	140%
Net Incremental Impact (1 x 2 x 3)	38%	53%	72%	94%	118%

5. Additional Leverage from Research Indirect Cost Funding

Institute grants provide for institutions to receive 25 percent research indirect spending on research grants. This rate is substantially below the rate currently identified by many institutions as needed to cover their actual research indirect costs. Thus, institutions receiving Institute grants would seem to have to allocate additional funds to cover the indirect costs of the research. Since federal restrictions limit the ability of institutions to share indirect costs with other federal grants, funds to cover additional indirect costs would likely be another source of leverage for the Institute funds when considering effects on economic activity. For example, if a $1 million research project includes 25 percent indirect spending from the Institute, or $250,000, but the true research indirect costs associated with the work are $500,000, the institution obtaining the grant would have to provide the additional $250,000 from another source. In this way, a $1 million grant would contribute net economic activity of $1.25 million (not counting any additional effects through matching fund leverage or research diversification leverage).

We have not accounted for this in our analysis because it is possible that some of these funds could come from matching fund leverage and should not be double-counted. It is also possible that not all of these funds would be incremental spending – if institutions allocate internal resources to cover some of these costs, for example, the additional spending may not produce incremental economic activity. We note, though, that it is also possible that these kinds of funds could come from incremental sources and that to the extent that this occurs, our leverage estimates would be conservative. At the very least, they provide further support for the existence of leverage associated with Institute funding.

B. Economic Activity Multiplier

As does any economic activity, the activity generated by the expenditures of the Institute would create multiplier effects for the California economy. Expenditures by the Institute for research and construction lead to subsequent rounds of activity in the economy as institutions receiving the grants undertake new projects, and in turn affected businesses and institutions hire new employees and purchase goods and services. For example, a new researcher hired from out of state by an in-state research institution would buy food, buy or rent housing, and purchase goods and services in California. That spending would itself generate additional wages, spending, and taxes as it ripples through the economy.

This additional economic activity is an indirect or "multiplier" effect of the original Institute funding. In order to calculate the multiplier effect of Institute expenditures, we have used the IMPLAN economic modeling software to estimate the total new economic activity generated within the State of California as a result of proposed Institute funding. IMPLAN utilizes the most recent regional economic data from the State of California to quantify the linkages between the sectors of the State economy and leakages out of the State economy. The software is widely used by academic, municipal, and private institutions to measure the economic effect of fiscal expenditures and public programs.[26]

In order to target the spending more precisely, we estimated multipliers from two different types of spending. The first multiplier was estimated for construction activities and the second multiplier was estimated for research activities. The multiplier for spending on construction for new facilities is 1.80 and for research spending the multiplier is 1.93. For example, for every dollar spent on new research facilities, an additional 80 cents of economic activity is created in California as this spending ripples through the California economy. In both cases, these multipliers are focused on the impact on the California economy and do not include any economic activity generated in other states as a result of spending in California.

C. Estimating Total New Economic Activity

To estimate the total amount of new economic activity in California from Institute spending, we apply the factors adjusting for leverage and substitution to the research spending and facilities spending. We then apply the economic multipliers to the resulting figure. For Institute administrative spending, we apply only the research economic multiplier, assuming no leverage or substitution in that area.

To compute tax revenues that could result from the total new economic activity, we must allocate the new activity into its constituent parts. The next three sections describe allocation of facilities, research, and Institute administrative spending to different component activities.[27]

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[26] IMPLAN clients include the California State Departments of Finance, Transportation, and Water Resources, according to: "Client Listing," Minnesota IMPLAN Group Inc., available at http://www.implan.com/references.html.

[27] An implicit assumption in this analysis is that economic activity generated through the multiplier effects follows the same breakdown into constituent parts as does the spending that generated it. For example, spending generated as a result of applying the multipliers to research spending is assumed to break down into categories in the same way the research spending itself breaks down.

D. Facilities Spending Breakdown

Research institutions that spend Institute-provided funds on new facilities would generate new spending in several areas, which would each have different tax generating characteristics. For our analysis, we estimated the breakdown of facility construction costs by using national data for construction firms' expense breakdowns as collected by the U.S. Census Bureau.[28] The categories used for our analysis and the corresponding percentage spending breakdowns include the following:

- Salaries (35.2 percent) – Wages paid to construction workers and professionals. These wages generate both income tax revenue and sales tax revenue when the wages are spent on taxable items.
- Benefits (8.4 percent) – Benefits expense associated with the salaries. These are assumed not to generate any tax revenue for the State.
- Equipment and supplies (49.2 percent) – Building materials used in construction, building hardware and equipment, rental equipment and equipment purchases by construction companies. This spending generates sales tax revenue for the State.
- Overhead (7.2 percent) – All other costs associated with construction company spending. These would include a variety of costs for office overhead, supplies, travel, and other costs. They are assumed to generate a combination of income and sales tax for the State. We have not attempted to break down these expenses into individual items.

Conversations with medical and scientific experts at California research institutions about the spending breakdowns in recent construction are generally consistent with the values we incorporate.

E. Research Spending Breakdown

We break down the research spending into various spending categories for purposes of our tax revenue analysis. The categories used for our analysis and the corresponding percentage spending breakdowns include the following:

- Salaries (48 percent) – Wages paid to research staff and faculty. These wages generate both income tax revenue and sales tax revenue when the wages are spent on taxable items.
- Benefits (12 percent) – Benefits expense associated with the research staff and faculty. We have used a benefit rate of 25 percent of salary expense. These are assumed not to generate any tax revenue for the State.
- Equipment and supplies (15 percent) – Includes research supplies, lab animals and other related expenses, as well as specialized equipment not included in the facility spending. This spending generates sales tax revenue for the State.

[28] "Construction," 1997 Economic Census, U.S. Census Bureau, January 27, 2000.

- Research indirect (25 percent) – General costs of running the university or research organization, including facility staff, utilities, and all other expenses typically associated with indirect expenses in research grants. The Institute is currently planning to use a 25 percent indirect cost ratio on its grants. We have not attempted to break down the research indirect expenses into individual items. Because of the size of the Institute research grants, it is assumed that these grants would generate incremental expenses of the type typically covered by research indirect funds at the institutions receiving the grants.

We arrived at this breakdown after consulting numerous sources including faculty members knowledgeable about current spending breakdowns on existing grants similar to those likely to be funded by the Institute; aggregated data from California research institutions; National Science Foundation studies; and IRS 990 (tax exempt organization) returns for research organizations. Since research activities can vary considerably from one project to the next, there is variation in the reported breakdown of funds utilization from different sources. We have attempted to adopt distribution estimates reflecting a composite of these sources. To be conservative, we have tended to use a share of expenditures going to personnel on the lower end of the plausible range, since we expect the greatest revenues to be generated for the State from income taxes and sales tax revenue flowing from personnel expenditures.

F. Institute Administration Spending Breakdown

Based generally on the experience of funding organizations, we use a spending breakdown of 60 percent salaries, 15 percent benefits,[29] and 25 percent overhead.

G. State Tax Revenue Impact

1. Tax Revenue Generated by Salary Spending

The construction workers, researchers, and other staff whose wages are funded by the Institute's facility, research, and administrative spending would generate tax revenues to the State of California. Our analysis focuses on two categories of taxes: personal income taxes paid by workers, and sales and use taxes generated when these workers purchase goods and services subject to tax. The Institute on Taxation and Economic Policy compiles California tax data annually and reports effective tax rates as a percentage of income for California residents by income tier, as shown below.[30]

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[29] Benefit spending is estimated to be 25 percent of salary spending. We assume that benefit spending does not generate tax revenue.

[30] The sales tax rate is based on the assumption that the California State General Fund receives a 5 percent sales tax rate. Actual sales tax rates of 8 percent or more as seen by consumers includes the 5 percent state rate plus 3 or more percent to fund other activities. Source: "Detailed Description of the Sales and Use Tax Rate," California State Board of Equalization, available at http://www.boe.ca.gov/news/sp111500att.htm, accessed September 12, 2003.

Table 6.3
Average Income Tax Rate Paid by California Residents by Income Tier

Income Range	$18,000 – $30,000	$30,000 – $47,000	$47,000 – $80,000	$80,000 – $168,000	More than $168,000
State General Fund Rate	0.8%	1.7%	2.7%	4.0%	5.6%

Table 6.4
Average Sales Tax Rate Paid by California Residents by Income Tier

Income Range	$18,000 – $30,000	$30,000 – $47,000	$47,000 – $80,000	$80,000 – $168,000	More than $168,000
Total Sales Tax Rate	7.3%	5.6%	4.4%	3.2%	2.1%
State General Fund Rate	5.0%	3.9%	3.0%	2.2%	1.4%

To determine the effective tax rate to use for modeling purposes, we used two approaches. First, we identified a sample breakdown of salary spending by income tier for construction spending and research spending. We then used these shares as weights to compute a weighted average tax rate. Second, we identified the average wage estimate of construction workers and researchers, and identified the tax rate associated with the tier into which the average fell. Because wages in California tend to be higher than the national averages and because the construction spending and research efforts funded by the Institute are likely to be more sophisticated than the average, these salary estimates are likely to be somewhat low. We do not make separate estimates of tax rates for administrative spending, but rather apply the tax rates for research salaries to the administrative salaries. The breakdowns and the estimates used for modeling purposes are shown in the following tables:

Table 6.5
Average Income Tax Rate Paid by California Residents by Income Tier

Income Range	$18,000 – $30,000	$30,000 – $47,000	$47,000 – $80,000	$80,000 – $168,000	More than $168,000	Average
State General Fund Rate	0.8%	1.7%	2.7%	4.0%	5.6%	
Construction Salary						
Sample Range	13%	41%	20%	26%	0%	2.4%
Average Salary[31]			$47,900			2.7%
Rate Used for Analysis						2.4%
Research Salary						
Sample Range[32]	10%	60%	10%	20%	0%	2.2%
Average Salary			$52,000			2.7%
Rate Used for Analysis						2.3%

Table 6.6
Average Sales Tax Rate Paid by California Residents by Income Tier

Income Range	$18,000 – $30,000	$30,000 – $47,000	$47,000 – $80,000	$80,000 – $168,000	More than $168,000	Average
State General Fund Rate	5.0%	3.9%	3.0%	2.2%	1.4%	
Construction Salary						
Sample Range	13%	41%	20%	26%	0%	3.3%
Average Salary[33]			$47,900			3.0%
Rate Used for Analysis						3.0%
Research Salary						
Sample Range[34]	10%	60%	10%	20%	0%	3.6%
Average Salary			$52,000			3.0%
Rate Used for Analysis						3.3%

2. *Tax Revenue Generated by Spending on Supplies and Equipment*

Purchases of supplies and equipment would generate sales tax revenue for California. Given the size and complexity of California's economy, it seems reasonable to assume that virtually all of the materials and equipment for construction would be obtained locally. For example, even timber originating in Oregon would be purchased through a California distributor. Though some research equipment would probably come from specialized out-of-state suppliers, it is reasonable to assume

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[31] "Construction," 1997 Economic Census, U.S. Census Bureau, January 27, 2000.
[32] Data estimated from several sources including the NSF, UC system reporting, and conversations with research and industry experts.
[33] "Construction," 1997 Economic Census, U.S. Census Bureau, January 27, 2000.
[34] Data estimated from several sources including the NSF, UC system reporting, and conversations with research and industry experts.

that the significant majority of research supplies and equipment would also be able to be purchased through California companies, particularly given the preference for California spending that is expected to be written into Institute grants. Discussions with various administrators in the research community confirm that California sourcing of supplies and equipment should be common, with the possible exception of certain specialized laboratory equipment.

For the purposes of this analysis, we have assumed that 100 percent of construction supplies and equipment and 75 percent of research supplies are subject to California sales tax. The State General Fund receives 5 percent of the value of purchases of items subject to sales tax.

3. Tax Revenue Associated with Overhead Spending

For construction overhead, research indirect spending, and administration overhead, there are various expenses that we have not attempted to break down into detailed categories. Some of these expenses include salaries and wages of personnel, equipment and supplies subject to sales tax, and non-taxable items or items that are not incremental to Institute spending. Rather than attempt to generate precise estimates, we have used an overall estimated tax revenue rate of 2 percent for these categories of spending. These rates are well below the combined income and sales tax rates for salary spending and are below the 5 percent sales rate on equipment and supplies purchased in California.

4. Additional Tax Revenue to Entities Other Than the State General Fund

The new economic activity generated within the State of California that results from the Institute's expenditures would also benefit local municipalities within the State. We make no estimate of these spillovers in this report, but we note that increased receipts from sales and property taxes to cities and counties would result in additional tax revenues to city and county municipalities. This in turn may reduce transfers from the State government or produce new economic activity (e.g. new school construction) that could produce benefits for the State.

H. Combined Net State Tax Revenue Impact, Phase One (Years 1 – 5)

In the first five years of the Institute, using the assumptions outlined above, we estimate that the total tax revenue that would go to the State as a result of Institute funding would be just under $73 million. Table 6.7 shows the input assumptions used to generate this estimate. The bottom portion of the table reports the resulting tax revenue estimates, year by year and in total.

One instructive comparison is between the tax revenue generated by Institute spending and the amount of spending required to service the bonds issued during year 1 – 5 of the Initiative. Using the estimates derived in the previous section, we estimate that during this time period the tax revenue produced by Institute spending would exceed the interest costs of the bonds. The estimated ratio of tax revenue to debt service cost is 1.3 over the initial five-year period.

Table 6.7
Tax Revenue Estimates for Proposition 71 Spending: Years 1 – 5

	Year 1	Year 2	Year 3	Year 4	Year 5	Total Years 1-5
Net Impact of Leverage less Substitution						
Facilities	20.0%	20.0%	20.0%	20.0%	20.0%	
Research	-62.2%	-47.2%	-28.0%	-6.4%	17.6%	
Multiplier Impacts						
Facilities	1.80	1.80	1.80	1.80	1.80	
Research	1.93	1.93	1.93	1.93	1.93	
Facilities Tax Revenue						
Salary						
Average Income Tax Rate	2.4%	2.4%	2.4%	2.4%	2.4%	
Average Sales Tax Rate	3.0%	3.0%	3.0%	3.0%	3.0%	
Construction & Equipment, Average Sales Tax Rate	5.0%	5.0%	5.0%	5.0%	5.0%	
Overhead, Average Tax Rate	2.0%	2.0%	2.0%	2.0%	2.0%	
Research Tax Revenue						
Salary						
Average Income Tax Rate	2.3%	2.3%	2.3%	2.3%	2.3%	
Average Sales Tax Rate	3.3%	3.3%	3.3%	3.3%	3.3%	
Other/Animal Testing, Net Average Sales Tax Rate	3.8%	3.8%	3.8%	3.8%	3.8%	
Equipment, Net Average Sales Tax Rate	3.8%	3.8%	3.8%	3.8%	3.8%	
Research Indirect Costs, Average Tax Rate	2.0%	2.0%	2.0%	2.0%	2.0%	
Administration Tax Revenue						
Salary						
Average Income Tax Rate	2.3%	2.3%	2.3%	2.3%	2.3%	
Average Sales Tax Rate	3.3%	3.3%	3.3%	3.3%	3.3%	
Administration Costs, Average Tax Rate	2.0%	2.0%	2.0%	2.0%	2.0%	
Facilities, Research & Administration Combined Net Impact on State Budget						
Total Tax Revenue ($ Millions)	1.9	10.6	16.5	21.9	21.8	72.7

I. Combined Net State Tax Revenue Impact, Phase Two (Years 6 – 14)

Institute spending during years 6 – 14 would also produce increased tax revenue. At the end of year 14, there is no more Institute research funding, and thus no additional tax revenue presumed to be associated with the program thereafter.[35] We make our revenue estimates for years 6 – 14 using the modeling assumptions described above, holding all values constant at their year 5 levels. In total, we estimate that $167 million would be generated in tax revenues associated with the Proposition 71 funding in years 6 – 14.

The total tax benefits of $73 million during phase one and $167 million during phase two represent

[35] We would note, though, that some of the economic activity generated by the institute could reasonably be assumed to continue past this point. For example, researchers who establish programs in California might well decide to remain in California after Institute funds are exhausted, funding their research activities through other means. Although these kinds of efforts could produce measurable revenues for the state, we do not estimate them here.

a combined total of $240 million. This is equivalent to approximately 4.5 percent of the total economic costs of $5.3 billion.

J. New Job Creation

We have also estimated the number of jobs that could be created by direct spending from the Initiative. To do this, we used the estimated incremental salary spending from the Initiative, including salary spending generated by the economic multipliers, and divided this by the corresponding average wage rate, adjusted for inflation. This yields a total of 14,272 job-years, where one job for one year is equal to one job-year. This is equivalent to 2,854 jobs per year for each of years 1 – 5. During years 6 – 14, these job-years are equal to 33,209 job-years, equivalent to 3,690 jobs for each of years 6 – 14. Construction funding occurs in years 1 – 5 only, so we assume no new construction jobs beyond that point. Similarly, no estimated job creation from this source is included beyond year 14 when research grant disbursement ends, although jobs from other sources including biotechnology spending could continue beyond this point.

VII. Economic Benefits From Increased Private Biotechnology Activity In California

The second area of potential economic benefit is the tax revenue generated from additional private biotechnology investment spurred by Proposition 71. A recent endorsement from the San Francisco Chamber of Commerce summarizes the economic opportunities for the biotechnology industry in the San Francisco Bay area:

> "The entire Northern California region is poised to benefit substantially from this measure, given our proximity to world-renowned medical and research institutions…With more than 90,000 people employed in biomedical careers in Northern California, earning billions in wages and salaries and producing exports totaling more than $2.3 billion in 2003, passage of this measure would generate even more economic strength for the region." – *Lee Blitch, President and CEO of the San Francisco Chamber of Commerce.*[36]

New private investment would generate tax revenues for the California budget. Note that the additional investment contemplated in this section differs from the potential for research leverage from private firms in the previous section. Here, we focus on the potential for private firms to start up, locate, or expand activity in California. Research leverage as contemplated in the previous section would come in the form of existing firms making contributions to augment Institute funds to university and other researchers.

A. Opportunity for Additional Private Activity

Additional economic growth could occur in two ways. First, by contributing to the stability of the policy environment in California, as well as by creating a stable funding base for stem cell research, Proposition 71 could encourage biotechnology and life sciences companies that exist today to locate operations in California as opposed to elsewhere. Similarly, new companies that form, including companies that would have formed even in the absence of the new funding, may be more likely to choose to locate in California. The resulting expanded economic activity in the state would produce benefits for California. To the extent this activity is moved to California from other states, it would be a loss for other areas that would otherwise have benefited from the activity.

Perhaps more importantly, Proposition 71 also appears to have the potential to foster new biotechnology activity that would not have existed otherwise. Stem cell research is felt by many scientific and medical experts we have interviewed to be one of the most, if not the most, promising new area of biotechnology research. Although there appears to be a great deal of private interest in stem cell research, uncertainties in the policy environment appear to be important deterrents to substantial investments in the area. By helping solidify the policy environment in California and by providing a stable, significant funding base, Proposition 71 could improve the climate for investing in new biotechnology activities related to stem cells, which could include new businesses forming or existing businesses expanding. Investors may be more willing to support

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[36] "San Francisco Chamber of Commerce Endorses Proposition 71: Chamber President & CEO Cites Potential for Cures, Economic Growth," YES on 71: Californians for Stem Cell Research and Cures, August 24, 2004.

stem cell-related research if Proposition 71 is passed, and be supportive at levels that would not have been reached in the absence of further stability.

It is difficult to forecast precisely the extent of new business in California that might result from passage of Proposition 71. We have developed our modeling scenarios by evaluating the current life sciences industry in California and evaluating private investment levels compared to the funding levels provided under Proposition 71.

B. Life Sciences Industry in California

California is already a leader in the global life sciences industry, with its research and development activities and commercialization capabilities. Of the over 6,250 life sciences firms around the world, 40 percent are located in California.[37] The Brookings Institute evaluates and ranks metropolitan areas where biotechnology activity in terms of biomedical research capacity and activity[38] and biotechnology commercialization[39] is concentrated. California has three of the top nine metropolitan areas, or clusters, including San Francisco, Los Angeles, and San Diego.

Of the nine biotechnology clusters nationwide, the San Francisco Bay Area ranks first in venture capital investment, second in both biotechnology patents and number of biotechnology companies, and fourth and fifth in number of life scientists and NIH funding, respectively.[40] San Francisco has been a leading California research center since the 1970s and played a central role in the industry's founding. The San Francisco Bay Area has three of the nation's top ranked medical research institutions: Stanford, University of California San Francisco, and University of California Berkeley. The San Francisco Bay Area also accounts for a majority of the State's venture capital biotechnology investment, reaching $819 million in 2003.[41]

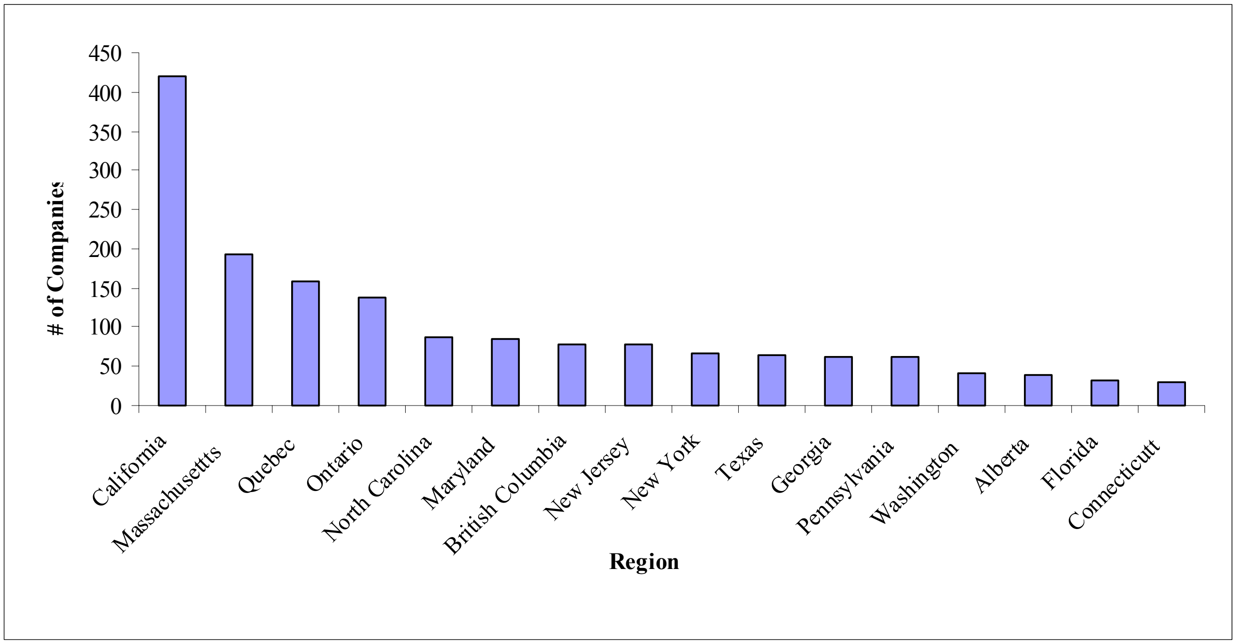
The San Diego and Los Angeles clusters are also major life science centers and contribute substantially to California's biotechnology industry.[42] San Diego ranks fourth in the country for NIH spending and venture capital investment and fifth in the country for biotechnology patents and number of biotechnology companies – including over thirty biotechnology firms with over 100 employees each.[43] Los Angeles ranks fifth overall in number of life scientists employed and is home to Amgen, the largest biotechnology firm in the United States, with annual revenues of $9.5

[37] "California Life Sciences Action Plan: Taking Action for Tomorrow," Bay Area Bioscience Center, BIOCOM, California Healthcare Institute, Southern California Biomedical Council, Bay Area Council, Larta Institute, Sacramento Regional Technology Alliance, and San Diego Area Regional Technology Alliance.
[38] Specifically, NIH research funding and biotechnology-related patents.
[39] Specifically, venture capital investments, value of biotechnology research alliances, new biotechnology firms established, and biotechnology firms with more than 100 employees.
[40] "Alchemy 2004: Annual Review and Analysis of Real Estate Trends in the Life Science Industry", Colliers International, Volume 1, Summer 2004. Note: Alchemy 2004 relies heavily on The Brookings Institute report for its analysis of life sciences clusters.
[41] "Alchemy 2004: Annual Review and Analysis of Real Estate Trends in the Life Science Industry", Colliers International, Volume 1, Summer 2004, pp. 56.
[42] All subsequent rankings in this paragraph are sourced to: "Alchemy 2004: Annual Review and Analysis of Real Estate Trends in the Life Science Industry," Colliers International, Volume 1, Summer 2004.
[43] "Signs of Life: The Growth of Biotechnology Centers in the U.S.," The Brookings Institution, Center for Urban and Metropolitan Policy, 2002.

billion, employment of 12,900, and a market capitalization of $72.1 billion.[44]

Ernst and Young recently reported on the number of biotechnology firms in North America. As the chart below illustrates, California has more than twice as many biotechnology companies as any other state or province in North America.[45]

Chart 7.1
North American Biotech Companies by State and Province 2004



As a starting point for our analysis, we estimated the current size of life sciences activity in California and examined its historical growth. In 2003, the California Life Sciences Action Plan put the contribution of the life sciences sector to the California Gross State Product at $12 billion.[46] This should reflect the value of life sciences goods produced in California. This report also indicated that the life sciences sector grew at a rate of 8 percent per year between 1991 and 2000.

Evaluating the potential impact of Proposition 71 on the biotechnology industry requires an estimate of the baseline size of the industry that would have been observed in the absence of the Initiative. It is difficult to forecast the size of an industry far out into the future with any degree of

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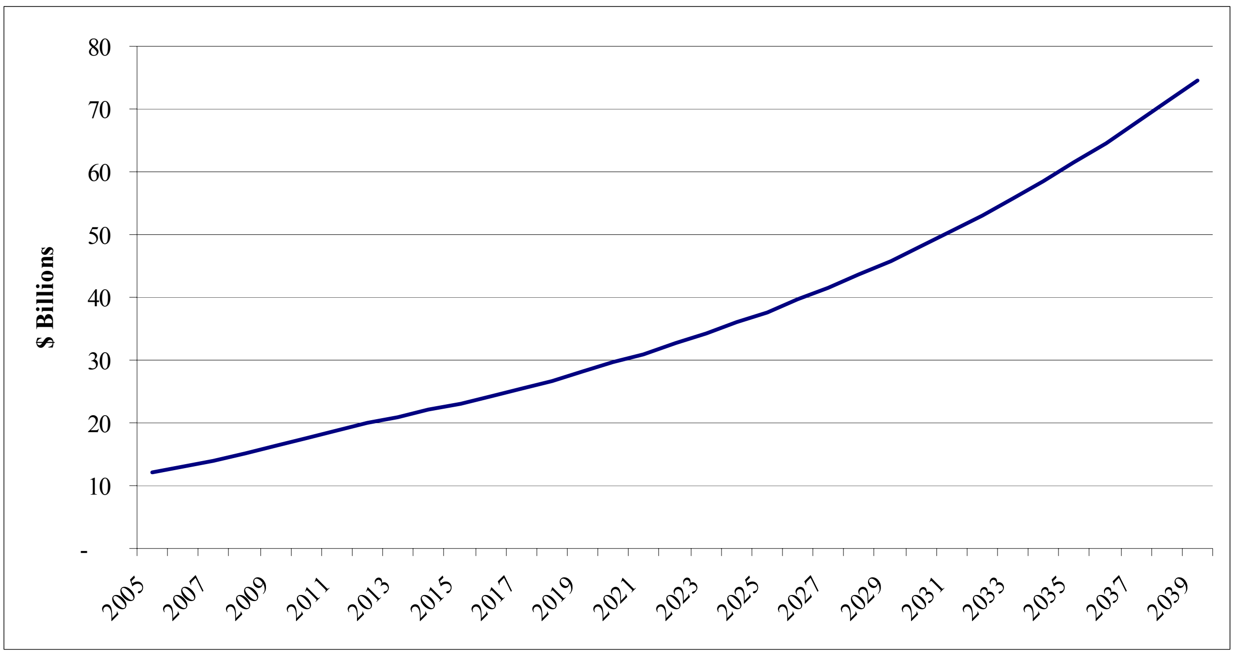
[44] Yahoo! Finance, Key Statistics for Amgen, Inc. (AMGN), available at http://finance.yahoo.com, accessed on July 29, 2004. Amgen data collected includes revenue over trailing twelve months, revenue growth over last fiscal year, and intraday market capitalization.

[45] "Biotechnology Industry Facts," Biotechnology Industry Organization, available at http://www.bio.org/speeches/pubs/er/statistics.asp, accessed September 6, 2004. This document cites "America's Biotechnology Report: Resurgence," Ernst & Young Report, 2004.

[46] "California Life Sciences Action Plan: Taking Action for Tomorrow," Executive Summary, pp. 9, Bay Area Bioscience Center, BIOCOM, California Healthcare Institute, Southern California Biomedical Council, Bay Area Council, Larta Institute, Sacramento Regional Technology Alliance, and San Diego Area Regional Technology Alliance.

certainty. The business opportunities and economic climate that will prevail over this long time span are quite unclear. To provide some framework for discussion, we constructed a baseline long-term growth scenario for the life sciences industry in California for the next 35 years. We use $12 billion as our initial size, and then project a growth rate of 8 percent per year for years 1 – 5, scaling down to 5 percent per year by year 10 and remaining at 5 percent, somewhat faster than projected economic growth overall, thereafter. The biotechnology industry is a particularly fast-growing segment within the life sciences area and has exceeded these growth rates over the past several years. Since 1992, U.S. revenues from biotech therapies have increased from $8 billion to $39.2 billion in 2003.[47] The chart below illustrates the growth of the life sciences industry in California under the scenario we modeled. This scenario does include continued growth in the sector for the next 35 years. Since industries cannot grow indefinitely at a rate faster than overall economic growth, presumably growth would slow as an equilibrium size is reached beyond the 35 year time horizon we consider.

Chart 7.2
Expected Growth of the Life Sciences Industry in California
($ Billions)



C. Additional Growth in Biotechnology Business from Proposition 71

The exact private industry response to Proposition 71 depends on a wide variety of factors that are difficult to forecast. Nonetheless, after listening to industry experts, it is plausible that Proposition 71 would contribute to a business climate for stem cell-based biotechnology activities in California

[47] "Biotechnology Industry Facts," Biotechnology Industry Organization, available at http://www.bio.org/speeches/pubs/er/statistics.asp, accessed September 6, 2004. This document cites "America's Biotechnology Report: Resurgence," Ernst & Young Report, 2004.

that would result in additional economic activity.[48]

Were Proposition 71 to generate additional investment, it would be on top of the baseline industry size. One way of conceptualizing additional biotechnology industry growth is to relate that additional growth to the size of the Proposition 71 investment. While some in the industry posit a very large private sector response, considering a proportional response may be a reasonable starting point. We note that additional private investment of between $1 and $2 for each dollar of public investment during the years of public funding would produce a life sciences industry 2.5 percent larger than it otherwise would have been under our growth scenario outlined above. That is, if the industry were estimated to produce $15 billion in gross product in a given year, assuming it would be 2.5 percent larger would result in an increment of $375 million. As presented earlier, in the U.S. overall, approximately 70 percent of U.S. research and development is provided by the private sector and 25 percent by the federal government, for an overall ratio of $2.80 in private investment to $1 in public funding.

Starting with the possibility of the Initiative increasing the size of the industry by 2.5 percent relative to baseline in each year, we develop a modeling scenario in which we assumed an increase in the size of the California life sciences industry of 0 percent in year 1, 0.5 percent in year 2, 1.0 percent in year 3, 1.5 percent in year 4, 2.0 percent in year 5, and 2.5 percent in subsequent years. Our estimates of the additional economic activity associated with a larger industry size are shown in the table below. Over the 35 years analyzed, this totals to $37.4 billion in additional activity, or an average of just over $1 billion per year.

Some industry representatives suggested a stronger response could be possible. As a result, in addition to the scenario outlined above, we also developed a scenario in which we assumed a stronger private industry response, modeling an increase of 0 percent in year 1, 1.0 percent in year 2, 2.0 percent in year 3, 3.0 percent in year 4, 4.0 percent in year 5, and 5.0 percent thereafter. Under this scenario, new economic activity would be twice that shown in Table 7.1.

Note that the larger industry size we model results from increases relative to the baseline industry size (as shown in Figure 7.2). They are not based on increases in the assumed growth rate of the industry. Assumed industry growth rates stay constant at 8 percent and 5 percent per year in this modeling.

Some have argued that effects on the growth rate are possible. Specifically, without support for further stem cell research, the biotechnology industry would grow more slowly than the baseline we have projected. If this is the case, then implementation of Proposition 71 could generate larger economic effects by helping to sustain a higher growth rate. However, because of the uncertainty surrounding these predictions, we have not modeled any growth rate effects.

[48] See Appendix B: Interviews.

Table 7.1
Economic Activity Associated with a 2.5 Percent Increase in the California Life Sciences Industry
($ Millions)

	Years 1 – 5	Years 6 – 14	Years 15 – 35	Total Years 1 – 35
Aggregate size of life sciences sector	$70,399	$269,394	$1,274,654	$1,614,447
Average per Year	14,080	29,933	60,698	46,127
Estimated percent increase	0 – 2.0 %	2.5%	2.5%	0 – 2.5%
Value of increase	758	5,733	30,864	37,355
Average per Year	152	637	1,470	1,067

D. Methodology for Estimating Tax Revenue Impact

Additional biotechnology activity in California would generate economic benefits for the State through new jobs, income taxes paid by workers, and sales tax paid by the workers and companies. To estimate the tax revenue implications of expanding the biotechnology industry, we assumed that the industry "gross product" estimates that we derive above would approximate spending by the industry on personnel and other inputs.[49] We then used the same basic methodology as in Section V, where we estimated the tax revenues associated with direct Proposition 71 spending. We adjust our estimates of new economic activity using the research economic multiplier as discussed earlier. This is the same economic model as used by many California State government departments.[50] We then incorporate the same research spending breakdown by spending category. Using these spending breakdowns, we calculated the salary income tax revenue, salary sales tax revenue, other sales tax revenue, equipment sales tax revenue, and other tax revenue.

This increased activity is expected to continue past the Proposition 71 funding ending date in year 14, since the private industry activity is assumed to depend on the climate created by Proposition 71 more than on the funding itself. We thus constructed these estimates to span the entire 35 year life of the Institute.[51]

E. Estimated Revenues

Our estimates under the 2.5 percent increase scenario are summarized in the table below. Total tax revenue is estimated to be $2.2 billion over the 35 year life of the Initiative. This additional tax revenue would represent approximately 41 percent of the total economic costs of the Initiative.

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[49] Note that it is possible that estimates of gross product will underestimate industry spending since in this context if there is additional spending made possible by new investments in the industry from sources other than sales.
[50] IMPLAN clients include the California State Departments of Finance, Transportation, and Water Resources, according to: "Client Listing," Minnesota IMPLAN Group Inc., available at http://www.implan.com/references.html.
[51] This will still understate the total benefit if industry expansions were to persist past year 35.

Table 7.2
Additional Tax Revenue From Increased Biotechnology Investment in CA – Case 1: 2.5% Industry Augment
($ Millions)

	Phase 1 Years 1-5	Phase 2 Years 6-14	Phase 3 Years 15-35	Total
Economic Costs	$56	$1,289	$4,010	$5,355
Economic Benefits				
Income tax revenue	16	104	524	643
Sales tax revenue	31	204	1,029	1,264
Other tax revenue	7	48	243	298
Total	54	355	1,796	2,206
Percent of Total Costs	97%	28%	45%	41%

Table 7.3 illustrates the results of the analysis that incorporates the assumption of a 5.0 percent larger life sciences sector. The additional tax revenue under this scenario would total to 82 percent of the economic costs.

Table 7.3
Additional Tax Revenue From Increased Biotechnology Investment in CA – Case 2: 5.0% Industry Augment
($ Millions)

	Phase 1 Years 1-5	Phase 2 Years 6-14	Phase 3 Years 15-35	Total
Economic Costs	$56	$1,289	$4,010	$5,355
Economic Benefits				
Income tax revenue	32	207	1,048	1,287
Sales tax revenue	62	408	2,059	2,529
Other tax revenue	15	96	485	596
Total	108	711	3,592	4,411
Percent of Total Costs	194%	55%	90%	82%

F. New Job Creation

As with the direct Proposition 71 funding, the increased economic activity would be associated with additional jobs for Californians. We used the same approach as outlined in the previous section to estimate that under the base (2.5 percent) case, 312,847 additional job-years would be created over the period. For the 5.0 percent scenario, this increases to 625,695. The table below summarizes the results of our estimated impact on jobs in California from increased biotechnology investment.

Table 7.4
Additional Jobs Associated with Increased Biotechnology Investment in CA

	Phase 1 Years 1-5	Phase 2 Years 6-14	Phase 3 Years 15-35	Total
Job-Years				
2.5% industry augment	11,967	67,732	233,148	312,847
5.0% industry augment	23,934	135,464	466,296	625,695
Average Jobs per Year				
2.5% industry augment	2,393	7,526	11,102	
5.0% industry augment	4,787	15,052	22,205	

VIII. Reductions In Health Costs Resulting From New Therapies

A. Overview

The third source of potential benefit from Proposition 71 is the reduction in medical expenditures that could result from successful research that makes possible, or even just accelerates the development of new therapies. New medical technologies do not always lead to reductions in costs, but new therapies that improve health for patients with conditions that are currently expensive to treat could have a large impact.

Given the overall magnitude of health expenditures, the potential savings from even small reductions could be quite large. California has the highest total healthcare spending of any state in the country. The total personal health care spending in California topped $112 billion in 1998,[52] accounting for approximately 9.8 percent of California's total gross state product.[53] In 2001, health care spending by the State government reached over $32 billion, $16.6 billion of which came directly from the State General Fund and other State funds, with the remainder coming from Federal government funds.[54] State government spending on health care is also increasing at a rapid pace, growing at a compound annual growth rate of 8.4 percent from 1980 to 1998.[55] More recently, an annual employer health benefits survey found that 2004 premiums for job-based health insurance increased an average of 11.2 percent nationally last year, following a 13.9 percent increase the prior year.[56]

This section develops information about the potential for stem cell research to lead to reductions in spending. We examine health care cost reductions that affect the people of California as a whole and more specifically those that would impact the State budget. The State budget bears a substantial portion of California's health care costs, including such costs as the State share of the Medicaid program (part of which is also funded by the federal government), and costs for State employees. California residents bear additional costs through health insurance premiums and out-of-pocket costs of medical care. We assume that costs of employer-provided health insurance affect Californians since they either increase the prices of goods and services or reduce the wages of employees.

We focus our attention on six conditions that seem likely candidates for successful stem cell therapies. These include insulin-dependent diabetes, Parkinson's disease, spinal cord injury, heart attack (acute myocardial infarction), stroke, and Alzheimer's disease. These represent only a

[52] "California Personal Health Care Expenditures (PHCE), All Payers, 1980 – 1998," Centers for Medicare and Medicaid Services, available at http://cms.hhs.gov/statistics/nhe/state-estimates-provider/ca.asp, accessed October 20, 2003.
[53] "Trends in State Health Care Expenditures and Funding: 1980-1998," Health Care Financing Review, Summer 2001, Volume 22, Number 4.
[54] Martin, A., Whittle, L., and Levit, K., "Trends in State Health Care Expenditures and Funding: 1980-1998" Health Care Financing Review, Volume 22, Number 4, Summer 2001; and "2000-2001 State Health Care Expenditure Report," Milbank Memorial Fund, National Association of State Budget Officers, and the Reforming States Group, available at http://www.milbank.org/reports/2000shcer/index.html, accessed September 2, 2004.
[55] "California Personal Health Expenditures (PHCE), All Payers, 1980 – 1998," Centers for Medicare and Medicaid Services, available at http://cms.hhs.gov/statistics/nhe/state-estimates-provider/ca.asp, as accessed on October 20, 2003.
[56] Colliver, Victoria, "Health care costs bruising economy," SFGate.com, September 10, 2004.

portion of the conditions that could potentially be influenced by stem cell research.

For these conditions, we develop estimates of three types of costs for which we could obtain data sufficient to support analysis and that represent important costs borne by the people of California and the State budget. We estimate costs over the 35 year life of the Institute. First, we estimate direct health care spending in the population under age 65. We do this by estimating the number of Californians with each condition, as well as the average incremental costs associated with the condition. We estimate total direct medical costs in this population in California, as well as the direct medical costs that are paid for by the State government (through Medicaid for example).

Second, we estimate costs associated with lost work time for these conditions in the employed population age 19-64. This is done based on estimates of the prevalence of each condition in California in the relevant population along with estimates of the average incremental lost work cost per person with the condition. We estimate these costs in total as well as the portion that is paid for by the State government.

Finally, we estimate nursing home costs. We estimate these for all ages. For this analysis, we rely on published data that are strongest for estimating costs paid by Medicaid for Alzheimer's disease patients. We also extrapolate from these data to estimate costs to Medicaid for the other conditions, as well as overall costs to the people of California.

Based on these estimates of costs, we model three scenarios capturing potential impacts of new stem-cell-based therapies. Case 1 considers the impacts of one percent reductions in spending for each condition, beginning 5 to 15 years after the start of the Institute depending on condition, to allow time for new research to develop into therapies. We believe this represents a modest expectation for the potential benefits of stem cell research, consistent with a scenario in which new research funded by the Initiative achieves limited improvements in therapy for these conditions. A second scenario considers the impact of increased therapeutic success. Considering improvements in therapies beyond that assumed for Case 1, but not at the expanded success level of Case 3, we examine the potential effects of two percent reductions in spending for each condition, beginning 5 to 15 years after the start of the Initiative. Finally, we examine the potential effects Institute funding could have if it led to even more effective therapies, modeling a 10 percent reduction in costs for the 6 conditions, beginning between years 5 and 15.

Even our first scenario generates estimates of substantial savings, enough to offset the majority of the cost of the Initiative to the State budget. The analysis of more effective therapies illustrates the potential for stem cell research to lead to much greater savings in the treatment of these conditions.

Subsequent sections detail the steps we undertook in our analyses, including the selection of six health conditions for our analysis; estimation of that number of Californians with each condition by year; development of direct medical and lost work cost estimates; development of nursing home spending estimates; development of scenarios for stem-cell based cost reductions; and finally modeling of potential savings under the scenarios.

B. Limitations

We do not attempt to distinguish between different types of stem cell research. When considered in even moderate detail, what is broadly termed "stem cell research" is quickly seen to consist of a number of related but varying activities, using different types of stem cells and sometimes different scientific techniques. Different approaches may hold differing levels of promise for any given condition and Proposition 71, while focusing on research restricted from federal funding, may well fund research in a variety of stem cell areas.[57] We have observed evidence that multiple forms of stem cell work have potential to be useful in regenerative medicine. Many experts, including the NIH, provide evidence that suggest that all forms of stem cell research hold promise for future medical therapies.[58]

When we estimate direct medical costs, we do not consider direct medical costs for persons age 65 and over. The direct medical expenses for this group are mainly covered by the federal Medicare program. Californians do bear costs associated with Medicare in the form of Medicare premiums and taxes. Elderly Californians also bear costs for Medicare supplemental insurance and for out-of-pocket expenditures. To the extent that the Initiative improved therapies for health conditions that affect the elderly, it would likely reduce the sometimes substantial costs for medical care that face this population. These costs have been rising in recent years and reducing them could have important benefits. Lower out-of-pocket costs or Medicare supplemental insurance premiums could directly benefit elderly residents of California. Reducing nationwide Medicare spending below the level at which it would otherwise have been could also be valuable. This could ultimately benefit Californians by reducing their Medicare tax burden, prolonging the life of the program without further tax increases, or in other ways. However, although benefits from reduced Medicare costs may be substantial, their impact is likely to be spread across the entire country and to depend on actions by the Federal government, so that benefits accruing to Californians are difficult to estimate. Thus, while we recognize the importance of health care costs for the over 65 population, we do not analyze these costs here. We believe that this would lead our estimates to be conservative

C. Identifying Six Conditions for Analysis

We began by developing a prioritized list of medical conditions likely to be impacted by stem cell research based on a review of literature from disease and medical advocacy groups, a review of available scientific literature, and interviews with leading medical researchers. As an example of the literature that we reviewed, one paper from the *National Academy Press* lists conditions that could potentially benefit from stem cell-based therapies. This list, ranked in order of U.S. prevalence, includes cardiovascular disease, autoimmune diseases, diabetes, osteoporosis, cancers,

[57] The Initiative; Section 3: Purpose and Intent, states that it will "maximize the use of research funds by giving priority to stem cell research that has the greatest potential for therapies and cures, specifically focused on pluripotent stem cell and progenitor cell research among other vital research opportunities that cannot, or are unlikely to receive timely or sufficient federal funding, unencumbered by limitations that would impede the research." Available at http://www.curesforcalifornia.com/initiative.php

[58] Kirschstein, Ruth and Skirboll, Lana, "Stem Cells: Scientific Progress and Future Research Directions," NIH, June 2001.

Alzheimer's disease, Parkinson's disease, burns (severe), spinal cord injuries, and birth defects.[59]

This compilation identified over 70 different conditions that could be impacted. From this list, we limited our analysis to six conditions. Limiting to six allowed us to focus on conditions that are commonly identified as those for which stem cell research shows important promise. Limiting the analysis in this manner will also provide a conservative assessment of the potential cost savings. The conditions we analyzed are:

- Type 1 diabetes and LADA (Latent Autoimmune Diabetes in Adults),
- Parkinson's disease,
- Spinal cord injury,
- Heart attack (also referred to as acute myocardial infarction or AMI),
- Stroke, and
- Alzheimer's disease.

The remainder of this section briefly summarizes some background information about these conditions, and the potential for stem cell therapy development. This summary will undoubtedly be incomplete in some ways – these conditions and the stem cell research that might affect them are complex, and relevant new information seems to be published nearly every day – but nonetheless provides a useful background.

1. Diabetes

Diabetes mellitus ("diabetes") is a chronic, debilitating disease and the seventh leading cause of death in the United States today.[60] The American Diabetes Association estimates that nearly 18.2 million people or 6.3 percent of the U.S. population has diabetes, 13 million of which are officially diagnosed. Sources such as the American Diabetes Association and the Centers for Disease Control and Prevention estimate that between 41 and 69 million adults in the United States have prediabetes, a condition in which people have some of the symptoms of diabetes but not enough to be classified as diabetic, and one in four of them will develop type 2 diabetes.[61] Studies that report the costs of diabetes vary. For example, one study estimated that the country incurred over $92 billion in direct costs and over $40 billion in indirect costs from diabetes in 2002.[62] The NIH estimates that the national direct and indirect costs of diabetes are $56 billion and $69 billion, respectively.[63] Recent California estimates of total direct and indirect costs of diabetes in 2003 are

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[59] "Stem Cells and the Futures of Regenerative Medicine," The National Academy of Sciences, 2002, available at http://books.nap.edu/books/030976307/html.

[60] Kirschstein, Ruth and Skirboll, Lana, "Stem Cells: Scientific Progress and Future Research Directions," NIH, June 2001, p. 67.

[61] "Heart Disease and Stroke Statistics - 2004 Update," American Heart Association, 2003. Cites secondary sources: Personal communication with Earl Ford, (MD, CDC/NCHS, 2003); "National Diabetes Education Program," available at http://ndep.nih.gov; "National Diabetes Fact Sheet," American Diabetes Association, 2003, available at http://www.diabetes.org/diabetes-statistics/national-diabetes-fact-sheet.jsp, accessed August 13, 2004.

[62] These data are based on a study conducted by the Lewin Group, Inc., for the American Diabetes Association and are 2002 estimates of both the direct costs (cost of medical care and services) and indirect costs (costs of short-term and permanent disability and of premature death) attributable to diabetes, available at http://diabetes.niddk.nih.gov.

[63] "Disease-Specific Estimates of Direct and Indirect Costs of Illness and NIH Support, Fiscal Year 2000 Update," Department of Health and Human Services, NIH, February 2000. Costs adjusted to 2003 dollars based on CPI for medial care and medical care services.

over $17.9 billion a year.[64]

Medically, diabetes is a group of diseases characterized by abnormally high levels of the sugar glucose in the bloodstream. The high glucose levels result from problems with insulin, a hormone normally produced in the pancreas that is necessary for the body to be able take glucose into cells where it is used for growth and energy. Most diabetes falls into one of two categories, referred to as type 1 and type 2. Type 1 diabetes normally is diagnosed in childhood or adolescence, and in the past has been referred to as juvenile-onset diabetes. In a type 1 diabetic, the body's autoimmune system sees its own cells as foreign and attacks the beta cells in the pancreas which normally produce insulin. Without insulin, glucose accumulates in the blood. Individuals with type 1 diabetes must monitor their blood glucose levels and receive insulin injections, typically three to four times each day, in order to process the glucose created from eating food. Type 2 diabetes, also called adult-onset diabetes, is associated with older age, inactive lifestyle, obesity, family history of diabetes, and ethnicity. Type 2 diabetes occurs when the body produces insulin but cannot use it effectively, resulting in a build up of glucose in the blood. Type 2 diabetics can often control their blood glucose concentrations through a combination of diet, exercise, and oral medication, though over time the disease can progress to the point where type 2 diabetics also become dependent on insulin therapy. Recently, type 2 diabetes has been diagnosed more and more frequently in overweight and sedentary children.

A third type of diabetes is less recognized and often undiagnosed. Referred to as late onset diabetes in adults, latent autoimmune diabetes in adults, or LADA, is an autoimmune disorder like type 1 diabetes, but appears in adults later in life, typically after age 25. LADA diabetes differs from type 1 diabetes only in the age of onset and disease progression. In LADA the insulin producing beta cell destruction occurs over years or decades as opposed to month or days in adolescence. LADA diabetes is often hard to diagnose properly because adults with LADA may not require insulin therapy immediately, are often not overweight, and may initially respond to type 2 diabetes medications, diet, or exercise. Over time, however, LADA patients need insulin injections to normalize their blood glucose.

Diabetes is a progressively debilitating disease, is the major cause of non-traumatic amputations, blindness, and end-stage kidney disease, and can be deadly. Diabetes is a significant risk factor for coronary heart disease, stroke, and nerve damage. One study found diabetics aged 45 to 64 years were at a 60 percent greater risk of hospitalization due to general medical conditions, when compared to their non-diabetic counterparts.[65]

Stem cell research appears to hold considerable promise as a source of therapies for type 1 diabetes and LADA. Specifically, many researchers now believe that stem cells could be implanted and develop into new beta and related cells, restoring the body's ability to produce insulin. Short of full replacement, stem cell research also offers other promising opportunities for insulin dependent diabetes therapy. For example, implantation of stem cells could reduce inflammation that may improve opportunities for other types of islet transplants and improve prognosis for type 1 diabetes patients.

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[64] "An Early Warning Sign: Diabetes Deaths in California Legislative Districts," California Center for Public Health Advocacy, February 2004, p. 7.

[65] Huse, D.M., et al., "The Economic Costs of Non-Insulin-Dependent Diabetes Mellitus," Journal of the American Medical Association, Volume 262, Number 19, November 17, 1989, pp. 2708-2713.

Recently, promising results in this area of stem cell research have come from scientists who have reported an ability to foster the development of embryonic stem cells into insulin-producing cells in the lab. Other work has shown success for treatment of diabetes with human experimental cell-replacement therapy. For example, over 300 procedures involving transplantation of insulin-producing islets from the pancreases of cadavers have been performed and have dramatically reduced insulin dependence in diabetic patients.[66] Press reports about islet transplants report, for example, on adults who had lived with daily insulin injections from type 1 diabetes for over 40 years who have been injection free for years and have stopped the progression of diabetes-related problems.[67] Though this work clearly demonstrates potential, concerns about required autoimmune suppressant therapies and the supply of new islet cells from cadavers are obstacles for wider availability of transplants.[68] Scientists have stressed the need for continued work on stem cells to further prospects for therapy in this area, which will take time and effort.[69]

2. *Parkinson's Disease*

Parkinson's disease is a progressive movement disorder that usually appears in people over 50 years old. Symptoms include an uncontrollable hand tremor, increasing body rigidity, difficulty walking, and trouble initiating voluntary movement. These symptoms stem from degeneration of neuron pathways, located deep inside the brain, that connect certain cerebral structures and release dopamine. One of dopamine's major roles is to regulate the nerves that control body movement. As these cells die, there is less dopamine produced, leading to the movement difficulties characteristic of Parkinson's. The exact cause of this degeneration is unknown. The NIH estimates that direct and indirect costs to the U.S. of Parkinson's disease are $3.2 billion and $6.3 billion, respectively.[70]

Research into the central nervous system's regeneration mechanisms, including the discovery of stem cells in the adult brain that can give rise to new neurons and neural support cells, shows promise for new therapies for Parkinson's disease and other neurodegenerative diseases. In fact, the National Institutes of Health, among others, identifies nervous system disorders as an area in which there is evidence that cell-replacement therapy can restore lost function.[71]

A central hope for stem cell research is that it would enable therapies in which cells could be implanted into the brain to replace the lost dopamine-releasing neurons. Several approaches are currently being explored in human and animal models and many have shown positive proof-of-

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[66] "Centers Report Islet Transplant Results in Patients with Type I Diabetes," National Institute of Diabetes and Digestive and Kidney Diseases, available at http://www.niddk.nih.gov/welcome/releases/09-07-04.htm, accessed September 8, 2004.
[67] Waldholz, Michael and Regalado, Antonio, "Biggest Struggles in Stem cell Fight May be in the Lab," The Wall Street Journal, August 12, 2004.
[68] "Centers Report Islet Transplant Results in Patients with Type I Diabetes," National Institute of Diabetes and Digestive and Kidney Diseases, available at http://www.niddk.nih.gov/welcome/releases/09-07-04.htm, accessed September 8, 2004.
[69] *Ibid.*
[70] "Disease-Specific Estimates of Direct and Indirect Costs of Illness and NIH Support, Fiscal Year 2000 Update," Department of Health and Human Services, NIH, February 2000. Costs adjusted to 2003 dollars based on CPI for medial care and medical care services.
[71] Kirschstein, Ruth and Skirboll, Lana, "Stem Cells: Scientific Progress and Future Research Directions," NIH, June 2001.

concept in key areas.[72] For example, one 2002 study reported exposing embryonic stem cells to growth factors so that they developed into differentiated neurons of the type that is lost in Parkinson's disease and injecting the new cells into the brain, alleviating Parkinson's-like symptoms in mouse models.[73]

In addition to therapies that would allow for regeneration, stem cell work could contribute to Parkinson's disease treatment in other ways. Additional research is looking for ways to use stem cells to spark the repair mechanisms already in a patient's brain to repair the damage. While less developed than approaches involving cell implantation, these approaches may be beneficial even if regeneration therapy is ultimately unsuccessful.[74]

Moreover, researchers could use these findings from stem cell research to explore ways to improve the effectiveness of traditional drug treatments that help a patient's own repair mechanisms. For example, creation of dopamine producing cells on a large scale could provide researchers better chances to study the processes that lead to degeneration of cells, better identify what agents are killing these cells in Parkinson's disease patients today, and evaluate what traditional drugs offer the best protection.[75]

3. *Spinal Cord Injury*

Spinal cord injury (SCI) primarily affects young adult males, with over 50 percent of injuries occurring between 16 and 30 years of age.[76] Causes of SCI are many, but the top three causes since 1990 are motor vehicle crashes, falls, and acts of violence (primarily gunshot wounds). Patients with spinal cord injuries are often left partly or wholly paralyzed because nerve and supporting cells in the spinal cord have been damaged and cannot regenerate. Depending on the severity, patients can be permanently disabled or institutionalized, and may require life support.

While spinal cord injury has a lower prevalence than some of the other conditions we analyze, it is one of the most costly. Estimates from the National Spinal Cord Injury Statistical Center (NSCISC) estimate that following injury, first year direct health care and living expenses range from approximately $185,000 to $627,000, and each subsequent year can average $13,000 to $112,000, depending on severity of injury.[77] These figures do not include substantial indirect costs from lost wages and benefits, which can be large since many spinal cord injuries occur early in life. For a patient injured at age 20, the average remaining life expectancy varies between 23 and 53 years, depending on severity.[78] While the NIH does not give specific direct and indirect cost estimates for SCI alone, it does estimate costs for injury, which is comprised mainly of SCI and

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[72] "Transplanted Adult Stem Cell Reduce Symptoms in San Clemente Man with Parkinson's Disease," California HealthCare Foundation, April 9, 2002, available at http://www.californiahealthline.org/index.cfm?Action=dspItem&itemID=91560.
[73] Kim, Jong Hoon et al., "Dopamine Neurons Derived from Embryonic Stem Cells Function in an Animal Model of Parkinson's Disease," Nature, Volume 418, July 4, 2002, pp. 50-56.
[74] Bjorklund, A. and Lindvall, O., "Self-Repair in the Brain," Nature, Volume 405, pp. 892-895.
[75] Wade, N., "Progress is Reported on Parkinson's Disease," New York Times, June 21, 2002.
[76] For a person who survived at least 1 year post injury. "Spinal Cord: Facts and Figures at a Glance," National Spinal Cord Injury Statistical Center (NSCISC), December 2003, available at http://www.spinalcord.uab.edu/show.asp?durki=21446, accessed August 4, 2004.
[77] Average yearly expense in 2000 dollars; *ibid*.
[78] Average yearly expense in 2000 dollars; *ibid*.

trauma. These costs are estimated to be $121 billion in direct costs and $336 billion in indirect costs, annually.[79]

As with Parkinson's disease, therapies that allow for the regeneration of damaged nervous system tissue could lead to great advances in treatment of SCI. Existing stem cell research has shown that regeneration of cells is possible, and has launched new research around SCI. Some of this work appears promising. For example, recent results show positive proof-of-concept in spinal-cord-injured rats.[80] This research demonstrated that neural cells, derived from stem cells, injected into the spinal cord injury site of rats, produce significant improvement in the animal's ability to move and bear weight. Some ongoing studies hold promise even in the relatively near term. Geron, for example, states that after completion of its ongoing studies, they expect to begin Phase I clinical trials as early as late 2005 or early 2006.[81]

4. *Heart Attack (Acute Myocardial Infarction or "AMI")*

Over 61 million Americans, or about one quarter of the population, have some form of cardiovascular disease. Cardiovascular disease, including heart attack, is the leading cause of death in the U.S. and the primary disease category for hospital patient discharges.[82] Heart attack occurs when blood flow to at least some part of the heart is interrupted by blockages in coronary arteries, cutting off the supply of oxygen and nutrients and resulting in the death of heart muscle and related cells. This can leave the heart muscle unable to effectively pump blood. Over 1.1 million people each year experience a heart attack.[83] About one third of heart attack cases result in the death of the patient during the acute phase. In another third of cases, patients survive but fail to make a complete recovery, ending up with permanent impairments related to reduced heart capability.[84] The NIH does not give estimates for AMI specifically, but it does give overall costs of Heart Disease, which includes AMI. These national direct and indirect annual cost estimates are $121 billion and $97 billion, respectively.[85]

Research on stem cells has provided early evidence of possible muscle regeneration therapies that could replace damaged heart muscle cells. In addition, stem cell therapy also holds potential for developing new blood vessels that could supply the heart The potential capability of stem cells to

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[79] "Disease-Specific Estimates of Direct and Indirect Costs of Illness and NIH Support, Fiscal Year 2000 Update," Department of Health and Human Services, NIH, February 2000. Costs adjusted to 2003 dollars based on CPI for medial care and medical care services.

[80] "Geron Announces Presentation of Preclinical Studies on Human Embryonic Stem Cell-Based Treatment of Acute Spinal Cord Injury," BioExchange, available at http://www.bioexchange.com/news/news_page.cfm?id=18901, accessed August 19, 2004.

[81] "Geron – Human Embryonic Stem Cell Program", Geron Corp, available at http://www.geron.com/showpage.asp?code=prodst, accessed July 30, 2004.

[82] French, W.J., "Trends in Acute Myocardial Infarction Management: Use of the National Registry of Myocardial Infarction in Quality Improvement," American Journal of Cardiology, Volume 85, pp. 6-12. As cited in: "Overview of the Acute Myocardial Infarction (AMI) Core Measure Set," available at http://www.jcaho.org/pms/core+measures/ami-overview.htm, accessed August 13, 2004.

[83] "Info for Health Professionals," MassPRO, Healthcare Quality Improvement Organization, available at http://www.masspro.org/healthpro/hcquip/hospqi/hf_ami.htm, accessed August 13, 2004.

[84] *Ibid.*

[85] "Disease-Specific Estimates of Direct and Indirect Costs of Illness and NIH Support, Fiscal Year 2000 Update," Department of Health and Human Services, NIH, February 2000. Costs adjusted to 2003 dollars based on CPI for medial care and medical care services.

develop into specialized cells such as these would provide regenerative medicine the ability to meet the heart's high demand for blood flow, by developing a new network of arteries to bring nutrients and oxygen to the cells of a damaged heart.

Recent studies have used stem cells injected both directly into the heart ventricle and into the bone marrow to demonstrate how these cells can regenerate into multiple forms of new, healthy heart tissue. Most recently, using embryonic stem cells in animal studies, Mayo Clinic researchers transformed stem cells into fully functional cardiac cells and transplanted them into damaged regions of the heart where the cells integrated into the damaged tissue and showed rapid and robust improvements, which were stable over an extended period post-therapy. The researchers in this study state, "the stable benefit of embryonic stem cell therapy on myocardial structure and function in this experimental model supports the potential for stem cell-based reparative treatment of myocardial infarction."[86]

5. Stroke

A stroke occurs when either the blood supply to the brain is interrupted (known as ischemic stroke) or when a blood vessel in the brain bursts (hemorrhagic stoke). In both cases brain cells are destroyed when the supply of oxygen and nutrients to the brain is cut off. Stroke often also affects other body systems and can cause severe disabilities such as paralysis, cognitive deficits, speech problems, and pain. Each year about 700,000 people experience a new or recurrent stroke; in 2001 alone, strokes resulted in death for over 160,000 Americans. According to the American Stroke Association, approximately 4.8 million stroke survivors are alive today. Stroke is a leading cause of premature, permanent disability among working adults – stroke has left over 1.1 million Americans disabled today.[87] The NIH estimates that direct costs for stroke are $35 billion and indirect costs for stroke are $19 billion annually.[88]

Therapies that could provide for the repair of brain tissue damaged by stroke could contribute to new therapies for stroke patients. Stem cell researchers appear to have made inroads into reversing the brain damage in patients that have suffered a stroke. For example, researchers have used nerve stem cells, implanted directly into the region of the brain with stoke damage, to restore functionality. Recently, a study published in July 2004 from researchers at Stanford found that fetal stem cells injected into the brains of rats could migrate to the right location and turn into the appropriate types of neurons that, if able to replace the function of the lost cells, could eventually help people recover from a stroke.[89]

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[86]Mayer, R., "Embryonic Stem Cell Therapy Shows Steady Benefits In Rebuilding Infarcted Heart," American Physiological Society, August 18, 2004. Original study cited: Terzic, A. et al., "Stable Benefit of Embryonic Stem Cell Therapy in Myocardial Infarction," American Journal of Physiology-Heart and Circulatory Physiology, August 2004, available at http://www.the-aps.org/press/journal/04/23.htm, accessed August 26, 2004.

[87] "Impact of Stroke," American Stroke Association, available at http:www.strokeassociation.org, accessed July 13, 2004. Note: stroke disability based on self reporting in 1999 of difficulty with functional limitation, activities of daily living, etc. resulting from stroke.

[88] "Disease-Specific Estimates of Direct and Indirect Costs of Illness and NIH Support, Fiscal Year 2000 Update," Department of Health and Human Services, NIH, February 2000. Costs adjusted to 2003 dollars based on CPI for medial care and medical care services.

[89] "Stem Cells Fill Gap Left by Stroke, Say Stanford Researchers," Stanford University Press Release, July 26, 2004. Cites study in online issue of "Proceedings of the National Academies of Science" by Dr. Gary Steinberg.

6. *Alzheimer's Disease*

Alzheimer's disease gradually destroys the brain cells that control memory and thought processes, first degrading these functions, then progressing to other regions of the brain that affect the patient's ability to perform even the most rudimentary functions. Ultimately, Alzheimer's disease results in death. Alzheimer's disease affects one in 10 persons over the age of 65, and this figure doubles every five years of age thereafter.[90] Alzheimer's disease generates large health care costs, including direct costs of medical care and long term care, as well as indirect costs for patients and families. These costs are particularly concerning since the incidence of Alzheimer's disease is expected to rise over time as life expectancy increases.

There are several sources for national and California specific estimates of the cost of Alzheimer's disease. Nationally, the NIH estimates that annual direct costs for Alzheimer's disease are $19 billion, while indirect costs exceed $108 billion.[91] Another study, by University of California San Francisco researchers from the Institute for Health and Aging, estimates costs for caring for California community residents with Alzheimer's disease were $22.4 billion in 2000 and are expected to increase to $42.8 billion by 2020 and $68.1 billion by 2040. Similarly, costs of caring for Alzheimer's disease patients in California institutions were $2.5 billion in 2000 and are expected to increase to $4.6 billion by 2020 and $7.4 billion by 2040.[92]

Currently, little help is available for the treatment of Alzheimer's disease beyond establishing supportive, safe environments, and assistance with daily activities and behavioral problems. While some drug therapies that could slow the disease progression are being tested, therapies to delay the disease onset or to prevent it entirely are not available. New therapies that could slow the degeneration, or even provide new information about the disease, could make an important contribution. The past decade has demonstrated impressive advances in basic research on the etiology of Alzheimer's disease, leading many to believe that advances in stem cell therapies are likely to lead to more effective treatments in the future.

In general, scientists are optimistic that transplantation of neural stem cells could demonstrate measurable evidence of efficacy in models of neurodegenerative disease, including Alzheimer's disease.[93] As neurodegenerative diseases such as Alzheimer's are complex, more research focused on better understanding the causes and impact of the disease is needed before a working therapy can be achieved.

D. Estimating the Number of Californians with Each Condition

Our estimates of direct medical costs and lost work time costs rely upon estimates of the number of

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[90] "2001 – 2002 Progress Report on Alzheimer's Disease," National Institute on Aging, available at http://www.alzheimers.org/pr01-02/index.htm, accessed September 7, 2004.
[91] "Disease-Specific Estimates of Direct and Indirect Costs of Illness and NIH Support, Fiscal Year 2000 Update," Department of Health and Human Services, NIH, February 2000. Costs adjusted to 2003 dollars based on CPI for medial care and medical care services.
[92] "Costs of Caring for California's Alzheimer Patients Will Triple by 2040, Say UCSF Researchers," University of California – San Francisco, April 2001, available at http://www.scienceblog.com/community/older/2001/D/200114508.html, accessed September 7, 2003.
[93] Kirschstein, Ruth and Skirboll, Lana, "Stem Cells: Scientific Progress and Future Research Directions," NIH, June 2001, pp. 97-99.

Californians under age 65 that have each of the six conditions in each of the years we analyze. We developed these estimates in 3 steps: 1) we estimated the current prevalence rate of each condition; 2) we estimated prevalence rates in future years; 3) we multiplied the estimated prevalence rates by estimates of the population in California in each year to generate an estimate of the number of people with each condition in each year.

We begin by estimating the current prevalence rate for each condition. The prevalence rate measures the share of the population that has the condition at a given point in time.[94] For example, a prevalence rate for diabetes of 5 percent in 2004 would mean that 5 percent of the population has diabetes in 2004. We derived our estimates of prevalence rates based on published data from a variety of sources, including the National Institutes for Health (NIH). In most cases, we were able to obtain data on prevalence rates applicable to the United States as a whole, but were not able to obtain data specific to California. In these cases, we apply national prevalence rates to the California population. For diabetes, we were able to incorporate some information specific to California. The majority of these sources give estimates of prevalence rates applicable within the past five years. In some cases, we also used sources that were older but appeared to be highly credible. We assumed that rates reported in all of these studies could be applied to the current year.

Forecasting prevalence rates over time is difficult to do precisely. For our modeling, we used published projections of prevalence growth rates, where available, to estimate future prevalence of specific conditions. In cases where we could not obtain published predictions for prevalence rates, we assumed rates would remain constant over time.

To estimate the number of Californians with each condition in each year, we multiplied the prevalence rates in each year by estimates of the population for the relevant year. For example, if the prevalence of Parkinson's disease in the under 65 year old population is estimated to be 0.11 percent in a given year, and there are expected to be 1 million people in the 19-64 year old population group in that year, we would expect 0.11%* 1,000,000 = 1,100 Parkinson's disease patients in that age group that year.

Within the under 65 population, we attempt where possible and relevant to estimate separate prevalences for the population age 18 and under and the population age 19-64. We treat these groups separately to facilitate our analysis of lost work time, which should primarily affect the 19-64 year old population.

The next sections detail our estimates of current and future prevalence rates for the six conditions.

1. *Diabetes*

We aim to estimate the prevalence of type 1 diabetes in the 18 and under and 19-64 populations, and the prevalence of LADA in the 19-64 population.[95] Since estimates of the prevalence of type 1 diabetes and LADA are typically derived from estimates of the prevalence of all diabetes, we begin

[94] Note that the prevalence rate does not capture the number of new diagnoses in a given period, which is known as the incidence rate.
[95] As discussed earlier, LADA is a diagnosis of adult onset insulin dependant diabetes, thus by definition does not occur in children. We thus assume there is no LADA in the population 18 years old and under.

by developing estimates of the prevalence of all diabetes.

We do not account for the portion of the population that is considered prediabetic or is undiagnosed. We understand that much of this population is at risk for type 2 diabetes, and is thus outside the scope of our analysis here. To the extent that some of this population has or will have type 1 diabetes or LADA, we will underestimate the costs due to type 1 diabetes and LADA.

We reviewed eight studies with information about the prevalence of diabetes that included age specific prevalence estimates. Four of these provided information at the national level, three provided California-specific prevalence information, and one provided both. We first consider the national studies, followed by the California-specific information. Studies reporting national estimates put the total number of diabetic patients nationwide at between about 11 million and 13 million. Four studies provide age-specific breakdowns that help us estimate the prevalence of diabetes in the population age 19-64. These studies report information about the prevalence of diabetes in the population over-18 and/or in the population over age 60 or 64. Reported prevalence rates in the over-18 population range from 5.9 percent to 8.7 percent. We use a median of 7.3 percent. Reported prevalence rates in the over-60 or over-64 population range from 14.2 percent to 18.3 percent. We use a prevalence of 14.2 percent for the population over age 64. Using prevalence rates for the over 18 and the over 64 population, we can calculate the implied prevalence in the 19-64 population, which comes to 4.3 percent. Two national studies report on the number of diabetics under age 18, with implied prevalence rates ranging from 0.25 percent to 0.3 percent. We use the median, 0.28 percent.

Three studies provide information that helps us estimate diabetes prevalence in the 19-64 age group specific to California. Prevalence estimates in the over 18 population range from 5.9 percent to 6.6 percent. Prevalence estimates in the over 64 population are 14.3 percent and 14.8 percent. Based on these two prevalences, we calculate an implied prevalence in the 19-64 population of 4.3 percent. There are no California-specific estimates of the number of individuals 18 and under with diabetes, although one study did report that "at least 12,000" Californian adolescents age 12-17 have diabetes.[96] We view this as generally consistent with the national estimate of 0.28 percent above. The California-specific estimates are locally applicable, but rely on smaller samples and may thus be less precise than national figures. In our modeling, we use the average of the California-specific and national estimates for the 19-64 population, a prevalence of 4.8 percent. For the 18 and under population, we use the national estimate of 0.28 percent.

We focus on individuals with type 1 diabetes, which is a subset of the population with diabetes. Among those age 18 and under, type 1 diabetes is the most common type of diabetes reported. Current estimates from the CDC report that between 8 and 43 percent of newly diagnosed diabetes in children is type 2 diabetes.[97] The remainder, between 57 and 92 percent, is type 1 diabetes. If we estimate that 75 percent of diabetes in the 18 and under population is type 1 diabetes, we obtain an estimate of the prevalence of type 1 diabetes in the 18 and under population of 0.75*0.36% = 0.21%.

[96] Dimant, A. et al., "Diabetes in California; Findings from the 2001 California Health Interview Survey," Los Angeles: UCLA Center for Health Policy Research, 2003.
[97] "Fact Sheet: SEARCH for Diabetes in Youth," Centers for Disease Control and Prevention, available at http://www.searchfordiabetes.org.

Among all ages, estimates are that between 5 and 10 percent of all diabetics have type 1 diabetes.[98] We apply the midpoint of 7.5 percent to the population 19-64. Thus, we estimate type 1 diabetes prevalence of 0.075*4.8% = 0.36% in the 19-64 population.

LADA is estimated to account for another 15 to 20 percent of the remaining type 2 diabetes population over age 18.[99] We estimate the prevalence of type 2 diabetes (all diabetes less the portion estimated as type 1), to be 4.4 percent. If LADA accounts for 17.5 percent of this group, we estimate a prevalence of 0.175*4.4% = 0.78 percent among individuals age 19-64.

We expect that this prevalence will change over time. Two studies reported similar projections of overall diabetes and type 1 specific prevalence rates over the period 2000 through 2050.[100] We used these studies to estimate type 1 and LADA specific prevalence growth for the under-65 population. They give compound average growth rates of between 0.7 percent and 1.1 percent per year, depending on the specific years in question. We apply these yearly prevalence growth rates to our current estimated type 1 and LADA prevalence rates as determined above.

2. *Parkinson's Disease*

We examined 8 sources providing information about the prevalence of Parkinson's disease. None had information specific to California, so we developed estimates of national prevalence and apply these to the California population. Estimates of national prevalence ranged between 500,000 and 1,000,000 people, however some of the higher estimates appeared to be factoring in a significant undiagnosed population. Many of the estimates appear to be based on a prevalence range of between 100 – 300 persons per 100,000, with a midpoint of 200 per 100,000, or 0.2 percent. We use this 0.2 percent prevalence rate and apply it to the overall population for our estimate of 564,356 Parkinson's patients.

Data from which to derive age-specific estimates of Parkinson's disease prevalence are sparse. While juvenile Parkinson's disease does exist, we did not find data sufficient to use to estimate a prevalence for Parkinson's disease patients in the 18 and under age group, and thus assume zero prevalence in this population. We used two approaches to derive estimates of the share of the population aged 19-64 with Parkinson's disease, which both lead to roughly the same conclusion. First, we found one source[101] that reported that 5 – 10 percent of Parkinson's patients are under age 40 and another[102] that reported that, of a sample of Parkinson's patients 45 and over, 20 percent were between the ages of 45 and 64. If, based on the first study, 12.5 percent of Parkinson's patients are under age 45, this accounts for 70,544 patients. The second study would then imply that 20 percent of the remaining 493,811 patients are 45-65, or 99,750 patients. Together, this

98 "National Diabetes Fact Sheet," American Diabetes Association, 2003, available at http://www.diabetes.org/diabetes-statistics/national-diabetes-fact-sheet.jsp, accessed August 13, 2004.
99 "Type 1.5 Diabetes: aka Slow Onset Type 1 and LADA," available at http://www.diabetesnet.com/diabetes_types/diabetes_type_15.php, accessed June 2, 2004.
100 Boyle, J. et al., "Projection of Diabetes Burden Through 2050: Impact of Changing Demography and Disease Prevalence in the U.S.," Diabetes Care, Volume 24, Number 11, November 2001; "Disease Glossary – Release 1.2," Lehman Brothers, November 10, 2000.
101 "Parkinson's Disease - Hope Through Research," National Institute of Neurological Disorders and Stroke, NIH, November 2003.
102 Whetten-Goldstein, K., et al., "The Burden of Parkinson's Disease on Society, Family, and the Individual," American Geriatrics Society, 1997.

would give 170,294 Parkinson's patients age 19-64, or a prevalence rate of 0.1 percent.

The second approach builds from a study that reported that the prevalence of Parkinson's disease in the population age 65 and higher is 1.0 percent. Based on current population figures, this amounts to approximately 351,000 people. If the national prevalence for all ages is approximately 564,000, it implies roughly 213,000 people under age 65 have Parkinson's disease. If there are very few Parkinson's disease patients age 18 and under, this would give a prevalence slightly higher than the 0.1 percent suggested by the other study. We apply the lower, 0.1 percent, rate in the analysis.

We did not find any literature with specific estimates of projected increases in Parkinson's disease prevalence, therefore we assume that the baseline prevalence of Parkinson's disease would remain constant at 0.1 percent in the 19-64 year old group over time.

3. *Spinal Cord Injury*

We examined five sources of information about the prevalence of spinal cord injury. None had information specific to California, so we developed estimates of national prevalence and applied them to the California population. Four of the five report that there are between 243,000 and 250,000 people with spinal cord injury in the U.S. One reports 450,000. The median estimate is that there are 250,000 SCI patients in the U.S., which implies a prevalence rate of 0.9 percent.

Available data provides some information with which we can piece together an estimate of the population prevalence of SCI among the 18 and under and the 19-64 populations. One source suggests that approximately 220,000 people under age 65 suffer from SCI. Three sources suggest that roughly 137,500 spinal cord injury patients are between the ages of 16 and 30. Assuming a uniform age distribution, of this number, 3/15, or 27,500, would be age 16, 17, or 18, and the remainder, or 110,000, would be 19-30. This results in approximately 82,500 persons with an undefined age. Assuming 80 percent are age 30-64, and 20 percent are under 16, we estimate approximately 44,000 patients age 18 and under, a population prevalence rate of 0.06 percent, and approximately 176,000 patients 19-64, or a population prevalence rate of 0.10 percent.

We did not find any literature with specific estimates of projected increases in spinal cord injury prevalence. Therefore we assume that the baseline prevalence rates of SCI will remain constant over time.

4. *Heart Attack (Acute Myocardial Infarction or AMI)*

We relied on two primary sources for our estimates of heart attack (AMI) prevalence.[103] We did not find estimates specific to California, so we developed estimates of national prevalence and apply these to the California population. The American Heart Association estimates that 3.5 percent of the U.S. population age 20 and over has had a heart attack. Based on current population figures, this would amount to over 7 million people.

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[103] There are number of additional sources reporting information, but we do not use them here because they did not separate AMI from overall coronary disease, they were not focused on national prevalence estimates, or they relied upon the NHLBI data, which we cite directly, as a metasource.

Data from the National Heart, Lung, and Blood Institute[104] provides recent age-specific AMI prevalence rates. They report prevalence of 0.3 percent in the 25-34 age group, 0.6 percent in the 35-44 age group, and a prevalence of 5.5 percent in the 45-64 age group. Averaging these rates, weighted by their population shares, gives an estimate of prevalence in the 25-64 age group of 2.58 percent. If we factor in an assumed prevalence of 0.05 percent for the 19-24 population, we arrive at an estimate of prevalence for the 19-64 population of 2.22 percent. We assume there are no AMI patients 18 and under.

We expect that the baseline prevalence of heart attack will change over time. We are unaware of projections of future changes in the prevalence of AMI specifically. One source makes projections about the prevalence of chronic heart diseases for the period 2000 through 2050. This source reports a high and a low series for the expected number of people with chronic heart diseases over time. We used the average of the high and low series for our calculations, which results in projected rates of growth in the population with chronic heart disease of between 0.5 percent and 1.6 percent per year, depending on the specific year in question. We used these figures, along with estimates of the population by year, to convert the projections of changes in the number of people with chronic heart disease into projections of the population prevalence of chronic heart diseases, computed the implied growth rate in prevalence for years 2000 – 2050, and applied this growth rate to our heart attack prevalence rates.

5. *Stroke*

We reviewed five sources of information about the prevalence of stroke. None had information specific to California, so we developed estimates of national prevalence and applied these to the California population. The American Heart Association estimates that 2.0 percent of the U.S. population, or 5.6 million people, have suffered a stroke. We are aware of two other estimates of the national prevalence, one of 3.9 million people and one of 4.8 million people.

The American Heart Association provides a strong source of information on which to base estimates of the prevalence among the 19-64 population. They report that the prevalence of stroke in the 20-34 population is 0.23 percent, the prevalence in the 35-44 population is 0.45 percent, and the prevalence in the 45-64 population is 2.50 percent. Averaging these, weighted by census estimates of the population in each group, yields an average prevalence in the 20-64 age group of 1.13 percent. If we factor in an assumed prevalence rate of 0.05 percent in the 19 year old population, we arrive at a prevalence estimate of 1.09 percent for the 19-64 population.

The data used above are consistent with the one other available age-specific estimate we identified, which is that approximately 1.6 million people between the ages of 45 and 64 have had a stroke. This would imply a prevalence in the 45-64 population of 2.5 percent, which is the same prevalence for this population we estimated above.

Some sources would suggest that there are stroke patients age 18 and under.[105] [106] However, since

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[104] "Morbidity & Mortality 2004 Chart Book on Cardiovascular, Lung and Blood Disease," National Heart, Lung and Blood Institute, May 2004.

[105] "Heart Disease and Stroke Statistics - 2004 Update," American Heart Association, 2003. This document cites: Pediatrics, 2002;109[1]:116-123.

we were unable to identify strong enough data with which to estimate prevalence in the 18 and under population, we include no stroke patients age 18 and under.

Although we expect that the baseline prevalence of stroke will change over time, we were unable to identify studies that project the prevalence of stroke. We thus assume prevalence will remain constant over time.

6. *Alzheimer's Disease*

We reviewed 7 studies that provided evidence about the prevalence of diagnosed Alzheimer's disease. None had information specific to California, so we developed estimates of national prevalence and apply these to the California population. Five of these reported on the overall national prevalence, ranging from 2.8 million to 4.5 million individuals with Alzheimer's disease. We work from the median estimate of 4.0 million, which implies a prevalence rate of 1.4 percent. Four separate studies reported information we could use to estimate the number of people over age 64 with Alzheimer's disease.[107] Using the midpoint of available data, we estimate that there are just under 3.1 million people over age 65 with Alzheimer's disease. Assuming no cases of Alzheimer's disease in the 18 and under population, we can thus estimate that there are slightly more than 900,000 people age 19-64 with Alzheimer's disease, implying a prevalence rate of 0.54 percent. As we discuss below, care for Alzheimer's patients over age 64 is a factor in the California State budget, so we perform additional calculations based on the population over 64 with Alzheimer's disease, incorporating the estimate that there are 3.1 million such individuals, or a prevalence rate of 8.8 percent.

We expect that the prevalence of Alzheimer's disease will change over time. One study[108] reported projections of Alzheimer's disease growth over the period 2000 through 2050. The projected growth in prevalence is 1.2 percent per year over this time period. We apply these growth rates to our estimated prevalence figures.

7. *Estimating the Number of People with Each Condition*

Using these prevalence rates, we can compute the number of Californians age 0-18 and age 19-64 with each condition each year by multiplying the prevalence rate by the projected California population in each age group. We use population projections based on the U.S. Census. To obtain current population estimates, we used 2000 – 2001 census data[109] to estimate the share of the population 18 and under, 19-64, and over 65 in California. We then obtained Census Bureau

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[106] "Heart Disease and Stroke Statistics - 2004 Update," American Heart Association, 2003. This document cites "The Greater Cincinnati/Northern Kentucky Stroke Study," J Child Neurol. 1993; 8[3]:250-255; Neurology. 1998; 51[1]:169-176.

[107] Estimates in these studies range from 2.8 to 3.5 million, though some vary on the precision with which the relevant age group is defined. For example, some refer to the prevalence among the "elderly." We assumed that all of the reported prevalences were applicable to the over 65 population.

[108] Sloane, P., et al., "The Public Health Impact of Alzheimer's Disease, 2000 – 2050: Potential Implication of Treatment Advances," Annual Review of Public Health, 2002.

[109] "Fact Sheet – California," U.S. Census Bureau, available at http://factfinder.census.gov.

estimates of total California population for 2003,[110] and applied the shares in each age group to estimate the population in each age group.[111] To estimate population for 2004 and future years, we obtained population projections from the California State government. These are available for 2010, 2020, 2030, and 2040. We interpolated to project population in the intervening years.

The results of our prevalence estimates are shown in the table below.

Table 8.1
Estimated Prevalence of Selected Conditions in California, Selected Years

		Estimated Number of Californians with Condition		
Condition	Age Group	2005	2014	2039
Type 1 Diabetes and LADA	0-18	22,625	21,999	40,000
	19-64	253,291	310,886	430,774
Parkinson's Disease	19-64	21,644	24,359	27,819
Spinal Cord Injury	0-18	7,847	8,252	10,212
	19-64	22,370	25,175	28,751
Heart Attack (AMI)	19-64	484,218	557,919	781,216
Stroke	19-64	238,522	268,433	306,565
Alzheimer's Disease	19-64	120,235	150,447	230,659

E. Incremental Direct Medical Costs, Under 65 Population

1. *Total Direct Medical Costs in California*

We estimated the incremental direct medical costs associated with each condition in the under 65 population in California. Incremental costs are those costs that are beyond the costs expected for an average population without the condition (but with an average mix of other conditions that may be found in the population). As a simple example, for an individual, if "normal" health costs are $1,000 per person per year and the average cost for a person with a given condition is $5,000, then the *incremental* cost of the condition is $4,000 ($5,000 total cost less $1,000 normal cost) per year.

To make our estimates, we used a standard cost of illness methodology[112] to compute the average incremental cost per individual associated with each condition, and then computed estimates of total costs by multiplying the per-person incremental cost estimate by the estimated number of people with each condition. Estimates of incremental direct medical costs per person were calculated using a database that includes health insurance claims of about 2 million lives, including 400,000 employees. This database is discussed in more detail in Appendix C. Everyone included

[110] "Table 1: Annual Estimates of the Population for the United States and States, and for Puerto Rico: April 1, 2000 to July 1, 2003," Population Division, U.S Census Bureau, last revised May 11, 2004, available at http://www.census.gov/popest/states/tables/NST-EST2003-01.pdf.
[111] These 2003 population estimates for California, or analogous estimates for the entire country were also used in the development of the prevalence rates where we needed to weight by population or make other population-dependent calculations.
[112] See Appendix C: Employer Claims Database Description.

in the database has health insurance. The claims information covers inpatient, hospital outpatient (e.g., outpatient surgery), physician, and prescription drug services, as well as other ancillary services (e.g., physical therapy), and reports the amount the health insurer paid for the care. This should capture the majority of health care spending, but will underestimate total spending somewhat because out-of-pocket payments, like co-payments or deductibles paid by patients themselves, and spending not covered by insurance are not included.

To compute average annual spending for individuals with a given condition, we searched the database to identify individuals with any indication of the condition in their medical claims. We then identified all medical claims for those individuals, and computed the average total annual amount the paid by the plan for care for the individuals with the condition.

We also calculated matching measures of annual spending for a matched sample of individuals with no indication of having the condition. For every patient with the disease, we randomly selected another individual who did not have the condition (who may or may not have had other conditions) with an age difference of less than 5 years and the same gender, geographic region of residence, and employee status. This provided a baseline estimate of health spending from which the incremental spending associated with each condition could be computed.

We included both employees and dependents (spouses and children) in the analysis. For heart attack, stroke, Parkinson's disease, and Alzheimer's disease, we included individuals age 18-64. For spinal cord injury and diabetes we included individuals age 0-64. We excluded individuals over age 65 from all of the analyses. Individuals in our sample represent substantial numbers of both employees and dependents. Using diabetes as an example, we have nearly 9,300 patients, out of whom about 1,700 are active employees, and 7,600 are spouses and children of insured employees.

Since our estimates are based on a database derived from employees, our estimates will be most representative of the population of employed individuals and their dependents. We believe this will provide valuable information about health spending for the diseases we analyze. The Kaiser Family Foundation estimates that two thirds of American's under the age of 65 received health insurance coverage through an employer (their own or that of family member) in 2001.[113]

We also use these figures for discussions of costs for other populations. The primary populations of interest other than those with employer-provided insurance are the uninsured and those with state-sponsored coverage (e.g. Medicaid). For the Medicaid population, we expect that these figures will be valuable for discussion. Medicaid recipients with these conditions should receive care generally comparable to that received by the insured population, though in some cases they may receive somewhat less. At the same time, Medicaid recipients with these conditions may have more serious illness, as a group, than the employed with these conditions, tending to drive up their incremental health care costs.

For the uninsured, comparisons raise two issues. First, for any given service, the uninsured as a group probably pay less. The uninsured are typically billed at per-service rates higher than patients with insurance, but not all of them end up paying the bills. Second, the uninsured typically receive

[113] Garrett, B., "Employer-Sponsored Health Insurance Coverage: Sponsorship, Eligibility, and Participation Patterns in 2001," The Henry J. Kaiser Family Foundation, July 2001.

fewer services than the insured. Any variations in spending due to uninsurance would affect both the condition and no-condition groups, but effects could be different in size between the two groups. We are unsure of the extent or direction of the net impact on our estimates. In the end, we view our incremental cost estimates as a reasonable starting point for discussing the cost society incurs for treating an uninsured person with these conditions.

Potential stem cell therapies are expected to influence the long-term health care costs of individuals with our conditions, rather than the initial costs during the acute phase of the condition. For example, patients suffering a heart attack would require immediate medical attention to stabilize their condition. Were stem-cell therapies available, heart attack patients would presumably later become candidates for regenerative therapy, which would then influence their subsequent health care costs. To account for this, we omitted costs associated with the acute phases of conditions in the time period surrounding the initial diagnosis where appropriate. Specifically, based on inspection to select a stable portion of the cost over time curve, we excluded the first 8 weeks of data at the time of a new diagnosis of type 1 diabetes, heart attack, and SCI, the first 4 weeks of data at the time of a new diagnosis of Parkinson's disease and Alzheimer's disease, and the first 14 weeks at the time of a new stroke diagnosis.

The average per-person annual incremental direct health care costs for these diseases and conditions ranged from $4,432 to $10,375 per year. We extrapolate forward over the 35 year time horizon of this analysis, using a projected inflation rate of 4.2 percent, based on the 10-year historical medical and medical services CPI rates.[114] We can then estimate the total incremental costs associated with each of our 6 diseases and conditions, among individuals under age 65 in California, in each of the years we consider. Table 8.2 reports information about this. Over the 35 year time horizon of our analysis, these costs would amount to $1.18 trillion.

Table 8.2 Incremental Direct Costs of 6 Conditions to California, Years 1 – 35 ($ Millions)

Condition	Age Group	Total Direct Medical Cost to California
Type 1 Diabetes and LADA	< 65	$243,714
Parkinson's Disease	19-64	9,636
Spinal Cord Injury	<65	26,706
Heart Attack (AMI)	19-64	582,204
Stroke	19-64	186,215
Alzheimer's Disease	19-64	134,374
Total		**$1,182,849**

2. *Direct Medical Costs Paid by the State Budget*

The portion of the total costs paid for by the State government is of particular interest here, since reducing these costs would directly benefit the State budget, and thus could provide economic offsets to the expense of Proposition 71. We lack the information necessary to derive precise

[114] This is not necessarily the overall growth rate of health expenditures, which could be effected by changes in quantity as well as price.

estimates of the amount of direct medical costs for each of our conditions that falls directly on the State budget. We can, however, use available data to generate estimates that provide guidance for discussion. A recent report breaks healthcare spending down into state, federal, and private payment sources. The following table reports the spending payer types.[115]

Table 8.3
Healthcare Spending By State, Federal, and Private Payment Sources

	Age Group	Percent of Total	Percent of Under 65 Paid by Third-Party Payers
Federal - Medicare	Over 65	17%	Not Included
Federal - Other	Under 65	6%	9%
Federal - Medicaid	Under 65	10%	14%
States - Medicaid	Under 65	7%	10%
States - Other	Under 65	7%	10%
Private Insurance/Spending	Both	39%	57%
Out of Pocket	All	14%	Not Included
Total		100%	100%
States % of Total		14%	20%

Not including Federal Medicare spending or out of pocket spending (which is not included in our incremental cost data), and accounting for the fact that the Federal government shares in Medicaid costs, state governments pay, on average, 20 percent of health care costs. This spending takes place primarily through the Medicaid program and other state insurance programs. Lacking guidance specific to our conditions, we apply this figure to our estimates of direct medical spending in the California under 65 population. We thus estimate that 20 percent of the total direct medical costs of our conditions are borne by the State budget.

F. Lost Work Time Costs, Employed 19-64 Population

1. Total Lost Work Time Costs in California

In addition to direct medical costs, many health conditions also lead to other "indirect" costs. For example, people unable to work lead to lower productivity in the economy. Or, other family members may have to care for individuals with some conditions, leading to further costs. Overall, there are many kinds of indirect costs that could be associated with the conditions we analyze. Here, we provide estimates of some of the costs associated with lost work time among the 19-64 population.

Other studies that have attempted to estimate broader indirect costs vary widely in their estimates. For example, one study conducted for the Parkinson's Disease Foundation estimates indirect costs

[115] "2000-2001 State Health Care Expenditure Report," Milbank Memorial Fund, National Association of State Budget Officers, and the Reforming States Group, available at http://www.milbank.org/reports/2000shcer/index.html, accessed September 2, 2004; and Analysis Group estimates.

of Parkinson's disease that include lost wages as well as the incremental cost to society of supporting patients through social programs. The study estimates that these costs represent more than 60 percent of the total costs associated with the disease.[116] Another source from the National Spinal Cord Injury Statistical Center estimates that total indirect costs associated with SCI, such as losses in wages, fringe benefits and productivity, average $52,915 per year (but vary based on education, injury severity and pre-injury employment history).[117] These kinds of studies lead us to believe that the analysis of lost work time will understate the total indirect costs associated with these conditions, potentially by a significant amount.

To arrive at the figures we present here, we estimated incremental individual-level average lost work time costs associated with disability-related and medically-related absenteeism for active employees age 19-64 in the same database we used to study direct medical costs.[118] These costs were calculated using data on employees' disability claims, employees' absenteeism due to medical diseases, and actual employer payments. For each non-disability day that an employee had a medical claim, we assumed a day of work was lost for hospital stays and half a day of work was lost for all other claims. Costs of absenteeism due to medical conditions were estimated at 100 percent of salary for each employee. (These estimates will not capture reductions in productivity that may accompany our conditions but not result in missed work time.)

The lost work time cost data was available for only a subset (of about 20 percent) of the individuals in our database. Since these individuals may not be representative of all individuals in the database, we adapted the methodology described above. First, we computed estimates of incremental direct costs for the whole sample. Second, we computed estimates of incremental direct costs for the sample for which we also had lost work cost data. Third, we computed estimates of lost work time costs for the employee sample with lost work time cost data. We then computed the ratio of lost work to direct costs observed in the employee population with lost work time cost data, and applied this ratio to the direct costs observed in the entire population to derive an estimate of lost work time costs that should be more representative.

We compute estimates of the total lost work time costs associated with each condition by year by multiplying the per-person estimate of incremental lost work time costs[119] by an estimate of the number of employed individuals with each condition in California. To estimate the number of employed individuals, we began with the projected number of people age 19-64 with each condition. Using third party sources, we estimated the percentage of the California population employed full time. In July of 2003, the estimated number of full time workers in California was 13.4 million.[120] As a percentage of our applicable age 19-64 group, this is slightly more than 51 percent. We use this figure for the percentage of the 19-64 population with each condition who

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[116] "A Desk Study of The Average Per Patient Costs of Parkinson's Disease," John Robbins Associates, commissioned by the Parkinson's Disease Foundation, April 1998.
[117] "Spinal Cord: Facts and Figures at a Glance," National Spinal Cord Injury Statistical Center (NSCISC), December 2003, available at http://www.spinalcord.uab.edu/show.asp?durki=21446, accessed August 4, 2004.
[118] Note that we do not compute indirect costs for anyone under 18, unlike direct medical costs which we do compute for diabetes and spinal cord injury. We thus do not include any costs incurred by individuals under 18 from lost work or school time.
[119] Extrapolated forward over the 35 year time horizon of this analysis using a projected inflation rate of 4.2 percent, based on the 10-year historical medical and medical services CPI rates
[120] "California Labor Market Review," California Employment Development Department Labor Market Information Division, August 2004, available at http://www.calmis.ca.gov.

would be employed in each year. To the extent that part time employees may also incur lost work costs, this number may be understated. On the other hand, to the extent that individuals with our conditions are disproportionately likely to be unemployed, this estimate would be overstated.

Applying the per-person estimates to 51 percent of the 19-64 population with each condition yields the costs shown in Table 8.4. Per-person estimates of indirect costs from lost work time range from $1,244 to $4,582. Over the 35 year time horizon of the analysis, total lost work time costs are $133 billion.

Table 8.4 Incremental Lost Work Time Costs of 6 Conditions to California, Years 1 – 35 ($ Millions)

Condition	Age Group	Total Lost Work Time Cost to California
Type 1 Diabetes and LADA	< 65	$27,012
Parkinson's Disease	19-64	2,718
Spinal Cord Injury	<65	6,856
Heart Attack (AMI)	19-64	81,174
Stroke	19-64	15,203
Alzheimer's Disease	19-64	-
Total		**$132,964**

2. *Lost Work Time Costs Paid by the State Budget*

The State bears some lost work time costs attributable to state employees. We lack data with which to make specific estimates about the share of lost work time costs paid for directly by the State government. We have assumed that the state does not bear any lost work time expense associated with Medicaid expenditures. For the remaining expenditures, we assume that the state only bears lost work time or equivalent expenses proportional to 2/3 of its direct medical costs.

G. Nursing Home Costs

Another important category of spending for many diseases is the cost of long term care, which for some conditions can be very high. Detailed estimates of spending in nursing homes due to our conditions in California are not available. There is, however, some useful information that we can use to derive estimates. For Alzheimer's disease, one study indicates that in 1994, the nationwide costs to Medicaid of Alzheimer's disease patients in nursing homes was $8 billion.[121] We adjusted these costs to 2004 dollars using the medical care and medical services CPI average.[122] This results in an estimated Medicaid national nursing home expense of over $12 billion in 2004. If California's portion of these costs is proportional to its overall share of the U.S. population, or approximately 12 percent, California's own costs Alzheimer's related Medicaid costs would be approximately $1.5 billion. States share the costs of Medicaid with the federal government.

[121] Sloane, P., et al., "The Public Health Impact of Alzheimer's Disease, 2000 – 2050: Potential Implication of Treatment Advances," Annual Review of Public Health, 2002.
[122] This resulted in an increase of 4.2 percent per year.

Adjusting for the portion of California health care expenditures for nursing homes paid by Medicaid from State contributions, or 60 percent,[123] yields $872 million in State costs for nursing home care for Alzheimer's disease in 2004. Using this as a baseline, we project forward adjusting for inflation to estimate spending in each of the 35 analysis years.

For other conditions, information is rarer. The National Nursing Home Survey indicates that approximately 9.2 percent of nursing home residents have Alzheimer's disease as a primary diagnosis.[124] In addition, this study also reports that the share of the nursing home resident population with Parkinson's disease is 2.1 percent, and the share with diabetes is 5.0 percent total (or 1.2 percent with type 1 diabetes and LADA).[125] AMI, stroke, and spinal cord injury are included in this survey within broader diagnosis categories that include additional related conditions. For these categories, we have assumed that 25 percent of residents in each of these broader categories had the specific diagnosis corresponding to the diseases we analyze. This results in an estimate of 2.5 percent of nursing home residents with AMI, 2.7 percent with stroke, and 0.4 percent with SCI. Together, these estimates would suggest that 8.9 percent of residents have Parkinson's disease, type 1 diabetes or LADA, AMI, stroke, or spinal cord injury. That is, the share of nursing home residents with these conditions is about 98 percent of the share of residents with Alzheimer's disease. If the cost structure of Medicaid nursing home care for these conditions is similar to that of Alzheimer's disease, then costs to the State government through Medicaid for these conditions in California could be approximated at 98 percent of the Alzheimer's costs identified above, or $855 million in 2004. We apply this figure, extrapolated forward to account for inflation, into the analysis.

Taking these estimates for all 6 conditions together, the State's share of Medicaid spending is approximately $1.7 billion in 2004. Over the 35 year analysis time frame, costs would total more than $144 billion.

We incorporate these estimates of Medicaid nursing home spending into our analysis. We lack data with which to estimate non-Medicaid nursing home spending in California for our conditions, and thus do not make estimates for the entire population. We note, however, that these costs could be large. For example, one of the most comprehensive surveys of nursing home patients in the United States found that almost 59 percent of residents had Medicaid as their primary payer.[126] If $1.7 billion is spent on nursing homes in 2004 in California by people with Medicaid as their primary payer, and costs outside of Medicaid are similar to those within Medicaid, total California spending for our conditions would be nearly $2.9 billion.

H. Savings Potential from Stem Cell Therapies and Cures

The potential for stem cell research to lead to lower spending for these 6 conditions depends on a

[123] "Table 10: Expenditures of Health Services and Supplies Under Public Programs, by Type of Expenditure and Program: Calendar Year 2002," Centers for Medicare & Medicaid Services, available at http://www.cms.hhs.gov/statistics/nhe/historical/t10.asp, accessed September 9, 2004.
[124] "The National Nursing Home Survey: 1999 Summary," Vital and Health Statistics, Series 13, Number 152, June 2002, p. 31.
[125] Fraction with type 1 and LADA based on previous prevalence analysis.
[126] "The National Nursing Home Survey: 1999 Summary," Vital and Health Statistics, Series 13, Number 152, June 2002, p. 3.

number of factors. In this section, we discuss these factors, and a modeling approach to estimating the health cost implications of new discoveries.

1. Stem Cell Research and Health Care Spending

There are several issues that influence the extent to which stem cell research funded by the Initiative would impact health spending. First, though it seems promising, there is uncertainty about the impact stem cell research can ultimately have on health care. While the potential for new therapies is widely accepted, much research remains to be done to realize this potential. This uncertainty suggests caution in projecting cost savings, but the potential for successful therapies also supports the view that valuable savings could result and should be seriously considered in any economic analysis.

Second, the diseases and conditions affected by stem cell research would influence savings. Our background work has identified approximately 70 diseases and conditions that might be amenable to new therapies from stem cell research. The number of diseases and conditions for which therapies are achieved, and the characteristics of the diseases and conditions, would determine the potential expenditure reductions for each. While some expect stem cell therapy to lead to cures for large numbers of diseases, which could generate very large savings, it is also important to note that new therapies for even a small number of diseases or conditions could make important contributions.

Third, the impact of new therapies on spending is important. Some proponents of stem cell research have discussed the potential for therapies that will completely cure all of the patients with currently costly conditions. These types of therapies are not implausible, and were they to be developed, they could generate very large reductions in health care costs for the affected conditions. But, it is also important to keep in mind that even smaller successes could lead to important reductions in costs. For many conditions, therapies that simply reduce the burden of symptoms could be quite beneficial. Therapies that delayed the onset of a disease, or slowed the progression of symptoms, even for relatively short time periods, could reduce spending. Therapies that cured diseases, but only worked for a subset of the population with the disease or condition, could also reduce spending as well. Stem cell research need not achieve complete cures for diseases or conditions in order to contribute to health expenditure reductions.

Fourth, the impact on mortality rates is important. New therapies that keep people alive longer would affect health care costs simply because people who would otherwise not have been alive to incur costs would be if there were successful therapies for them.

Fifth, the time frame within which research is successful would affect savings. Research would take time to generate new therapies. Therapies that are achieved sooner would make larger contributions than those achieved later, because they would have a longer time horizon over which to achieve savings.

Sixth, the ways new Initiative-funded discoveries interact with other research would affect savings. The impact of the Initiative on savings would be driven by the extent to which the new research funded makes a contribution beyond what would otherwise have been developed in the absence of the Initiative. This would happen if Initiative-funded research accelerated the discovery of important information. For example, Initiative funding may make therapies possible years before they otherwise would have been. This would also happen if Initiative funding led to the discovery of information that would otherwise have gone undiscovered, at least during the time horizon that we analyze.

Seventh, the pricing of therapies would affect savings. Newly developed stem cell therapies would presumably be made available to patients at some cost. Some potential therapies may also require ongoing additional medical treatments. For example, anti-rejection medications may be required for some types of cell transplants. Costs for the stem cell therapies and any ongoing care required would offset some of the savings that new therapies could bring about.

2. *Stem Cell Therapy Scenarios*

We have embedded these factors in a model that allows us to illustrate the impact of various scenarios related to stem cell therapy. We describe here three scenarios that we hope will help better illustrate the reasoning behind the cases modeled below. In the first, limited therapeutic success case, we considered the impact of a new therapy that is discovered in year 5 of the Institute, rather than having been discovered in year 15 in the absence of Institute funding. The new therapy is assumed to result in a reduction of 10 percent in the health care costs affecting a person with a condition, and to reduce the mortality rate slightly (from 1.5 percent per year to 1.4 percent per year.) We assume that the new therapy would be provided at 2 times the baseline annual costs for a person with the condition (e.g. if baseline annual health costs were $5,000, we assume the new therapy would be available for $10,000.). Under these assumptions, total spending over the 35 year period, including spending for the therapy and for health care, would be lower with the Institute by 1.4 percent.

As a second, increased therapeutic success case, we consider the impact of a new therapy that is discovered in year 5 of the Institute, rather than having been discovered in year 15 in the absence of Institute funding. The new therapy is assumed to result in a reduction of 25 percent in the health care costs affecting a person with a condition, and to reduce the mortality rate from 1.5 percent per year to 1.3 percent per year. We assume that the new therapy would be provided at 3 times the annual costs for a person with the condition, and would require annual maintenance costs of 10 percent of the annual health spending for the condition (e.g. if in the absence of a new therapy, a person with the condition would have spent $5000, we assume annual maintenance costs of $500.). Under these assumptions, total spending, including spending for the therapy and for health care, would be lower with the Institute by 1.9 percent over the 35 year time horizon of our analysis.

Finally, we report the results from an expanded therapeutic success case in which, as before, a new therapy is discovered in year 5 of the Institute, rather than having been discovered in year 15 in the absence of Institute funding. The new therapy is assumed to result in a reduction of 60 percent in the health care costs affecting a person with a condition, and to reduce the mortality rate from 1.5 percent per year to 1.2 percent per year. We assume that the new therapy would be provided at 5 times the annual costs for a person with the condition, and would require annual maintenance costs of 0.1 times annual health spending for the condition. Under these assumptions, total spending, including spending for the therapy and for health care, would be lower with the Institute by 12.6 percent over the 35 year time horizon of our analysis.

We take two important lessons from these scenarios. First, even accelerating timing of therapies with moderate impacts (e.g. 10 percent reduction in health spending) by 10 years could lead to spending reductions that, as illustrated below, could be significant. Accelerating the timing of new therapies by more years, or therapies with stronger impacts on the conditions, would have larger effects. Second, however, even therapies with large health care cost reductions do not always reduce total spending proportionately, once the costs of the therapy itself and the costs of maintenance therapies are taken into account.

Another important feature of these models is the impact of mortality rate changes. New treatments that reduce mortality rates would tend to lead to higher health care costs because more people would be alive to incur costs. This is, of course, only part of the picture since reduced mortality rates would have beneficial impacts on society that could outweigh their increased health care costs.

I. Estimating Potential Cost Savings

These spending figures, and the scenarios described above are estimates, but should provide a valuable framework for discussing the potential for cost savings from new therapies. Roughly based on the scenarios described above, we illustrate the cost implications of reductions in direct, lost work, and nursing home costs in three cases. First, we analyze a "limited therapeutic success" scenario in which costs for all 6 conditions are reduced by 1 percent per year starting between years 5 and 15 of the Initiative and continuing through year 35. This same basic methodology is applied to the second and third cases. However, in the second, we analyze an "increased therapeutic case" scenario with a 2 percent reduction. Finally, we analyze an "expanded therapeutic success" scenario with a 10 percent reduction per year.

1. Case 1: "Limited Therapeutic Success" – Savings of 1 Percent

The 1 percent savings modeled in the limited therapeutic success case represents a very modest reduction. Many proponents of stem cell therapies believe much larger reductions are possible. At the same time, examining the impact of a small reduction allows for consideration of a wider range of potential stem cell research successes. Short of a full cure for a disease, reductions in the burden of symptoms, for example, could lead to 1 percent reductions in spending. Similarly, small delays in the onset or progression of disease could produce reductions in spending on this scale, as could therapies that turn out to help only a subset of the patients with a disease. Finally, considering small reductions in spending would also better take into account that, should stem cell therapies be developed, they would themselves have some cost, which would offset some savings.

In our consideration of savings potential, we assume that the development of therapies would take several years. We thus model the impact of reductions in spending beginning after 5 years for spinal cord injury, diabetes, and Parkinson's disease, and reductions for stroke and AMI beginning after 7 years. Since therapies for Alzheimer's disease appear further off, we model the impact of reductions in spending beginning in 15 years. The table below summarizes the resulting cost savings for the people of California and for the budget of the State.

Table 8.5
Impact of Savings of 1 Percent in Healthcare Costs – Case 1: Limited Therapeutic Success
($ Millions)

	Phase 1 Years 1-5	Phase 2 Years 6-14	Phase 3 Years 15-35	Total
Direct Medical Cost and Lost Work Time Costs to Californians	$70,331	$191,242	$1,054,240	$1,315,813
Impact of 1% Savings	0	1,413	10,010	11,423
Direct Medical, Lost Work Time, and Nursing Home Cost to State Budget	23,343	60,317	306,159	389,819
Impact of 1% Savings	0	382	3,062	3,444

Results from this first scenario indicate total savings at 1 percent of over $11 billion to the people of California from direct medical costs and lost work time costs. Savings would be $3.4 billion to the State budget, including the State's share of direct medical costs, lost work time costs, and nursing home costs. These savings to the State budget are equivalent to 64 percent of the cost of Proposition 71.

2. *Case 2: Increased Therapeutic Success – Savings of 2 Percent*

For the second scenario, we use 2 percent reductions where we had previously used a 1 percent reduction. This could result from stronger therapies, discovered sooner.

Table 8.6
Impact of Savings of 2 Percent in Healthcare Costs – Case 2: Increased Therapeutic Success
($ Millions)

	Phase 1 Years 1-5	Phase 2 Years 6-14	Phase 3 Years 15-35	Total
Direct Medical Cost and Lost Work Time Costs to Californians	$70,331	$191,242	$1,054,240	$1,315,813
Impact of 2% Savings	0	2,827	20,020	22,847
Direct Medical, Lost Work Time, and Nursing Home Cost to State Budget	23,343	60,317	306,159	389,819
Impact of 2% Savings	0	764	6,123	6,887

Results from this second scenario indicate total savings of over $22 billion to the people of

California and $7 billion to the State budget. These savings to the State budget are equivalent to 130 percent of the cost of Proposition 71.

3. *Case 3: Expanded Therapeutic Success – Savings of 10 Percent*

Finally, to illustrate the potential from a stronger therapy, we model a 10 percent reduction for all six diseases and conditions, starting between years 5 and 15 of the Institute. Based on the scenarios in the preceding section, this is comparable to the result if the Institute accelerated by 10 years discovery of a new therapy that reduced spending by 60 percent and was available at moderate costs to patients.

Table 8.7
Impact of Savings of 10 Percent in Healthcare Costs – Case 3: Expanded Therapeutic Success
($ Millions)

	Phase 1 Years 1-5	Phase 2 Years 6-14	Phase 3 Years 15-35	Total
Direct Medical Cost and Lost Work Time Costs to Californians	$70,331	$191,242	$1,054,240	$1,315,813
Impact of 10% Savings	0	14,134	100,098	114,233
Direct Medical, Lost Work Time, and Nursing Home Cost to State Budget	23,343	60,317	306,159	389,819
Impact of 10% Savings	0	3,821	30,616	34,437

Results from this scenario indicate total savings of over $114 billion to the people of California and $34 billion to the State budget. These savings to the State budget are equivalent to 645 percent of the cost of Proposition 71.

J. Costs Not Considered

While we believe that this analysis provides useful information about the potential of stem cell therapies to lead to reductions in spending, it is clearly incomplete. In particular, there are a number of potential sources of spending that we did not consider, and that will generally lead us to underestimate the potential size of reductions. These include:

1. *Other Indirect Costs*

We considered indirect costs due to work loss among employees. We did not include considerable other indirect costs that can be associated with these conditions. For example, we do not include costs that affect family members and caregivers of patients with dementia or related conditions. We did not include the costs associated with lost schooling for children with spinal cord injury or type 1 diabetes. We were unable to obtain sufficiently precise estimates of other indirect costs besides lost work time costs for the specific diseases we analyze, but we note that available data do suggest that such costs can be considerable.

For example, a comprehensive study by the NIH estimates both direct and indirect costs for many diseases, and as reported in prior sections many of these estimates were much higher than the estimates we used in our report.[127] The NIH figures include different informal costs for each disease, depending on the data available, but these costs could include mortality costs, lost workdays, reduced productivity, lost earning of unpaid care givers, and other non-health related costs. We note that the indirect cost estimates we use were well below 20 percent of total direct costs, whereas the indirect costs illustrated in the table below are much higher due to the additional cost categories included. The table below summarizes these estimates.

Table 8.8
NIH Direct and Indirect Cost Estimates of Selected Diseases
(Cost Adjusted to 2003 $ Millions)

Illness	Original Cost Year	Direct Costs	Indirect Costs	Total Costs
Injury	1995	$120,701	$336,336	$457,038
Heart Disease	1999	121,407	96,959	218,366
Stroke	1998	34,910	18,504	53,414
Alzheimer's Disease	1997	19,098	108,219	127,317
Diabetes	1997	56,147	68,878	125,025
Parkinsons	1992	3,169	6,338	9,508

In addition to the NIH, other third party studies have attempted to identify informal costs that are limited to only the costs associated with unpaid care for patients by unpaid or family caregivers.[128] One study concludes that patients with Alzheimer's disease have estimated informal annual costs ranging from $5,200 – $14,000 in 2005 dollars depending on severity of the disease and assuming zero comorbid conditions. When applied to our 2005 total prevalence estimates for the California population with Alzheimer's disease, these informal costs alone, on average, would amount to nearly $4.6 billion a year.[129]

2. *Costs Associated With Other Conditions*

We have based our analysis on 6 conditions thought to have potential for stem cell therapies. Our initial review turned up approximately 70 conditions that could be affected by stem cell work. Were there to be reductions in the costs of additional conditions, potential cost savings could be much larger.

It should also be pointed out that stem cell research could develop therapies for conditions that now

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[127] We were unable to use this study to directly augment our analysis because of differences in the definitions of diseases (e.g., all diabetes v. type 1/LADA diabetes, heart disease v. AMI).
[128] Leon, J., Cheng, C., and Neumann, P., "Alzheimer's Disease Care: Costs and Potential Savings," Health Affairs, Volume 17, Number 6, 1998, pp. 206-216; "A Desk Study of The Average Per Patient Costs of Parkinson's Disease," John Robbins Associates, commissioned by the Parkinson's Disease Foundation, April 1998.
[129] The cost estimate for 1996 has been adjusted to 2005 dollars using the 10-year average CPI for Medical Care and Medical Care Services, and applied to 2005 prevalence estimates.

have low spending. In such a circumstance, it is possible that the research could increase health care spending, for example by providing therapies to people who would have received minimal or no treatments otherwise. In such a case, although spending for the condition might increase, length and quality of life could also increase and would create value that could balance against the cost increase. In general, current research frequently supports the value of many of the medical technologies developed in recent decades.

3. Out of Pocket Costs

We did not include out-of-pocket costs, including any co-insurance and deductible payments or other costs not covered by insurance. While the State budget in California does not pay the out-of-pocket costs, it is worth noting that these costs would also be reduced as health costs are reduced, and this would represent an economic benefit to Californians.

4. Costs for the Over Age 65 Population

Other than the Medicaid nursing home costs, we do not include costs for those over age 65. Medicare covers many of these costs. Since the funding for Medicare comes from the federal government, any cost savings associated with persons over 65 would not typically produce direct benefits to the State budget. However, if partial Medicare costs were to be reduced, benefits in the form of lower taxes, a more stable Medicare program, or other forms could accrue to Californians. Elderly Californias bear other costs, such as for Medicare supplemental insurance and out-of-pocket payments. These costs can be substantial, and could also be reduced if there were successful new stem-cell therapies.

5. Nursing home costs not paid by Medicaid

Nursing home costs not paid by Medicaid are significant for many families, and these represent an additional cost to Californians that has not been included in our analysis.

IX. Economic Benefits From Royalties From Discoveries Funded By Proposition 71

The fourth major area of economic benefits associated with Proposition 71 is the potential revenue associated with a share of the intellectual property developed with Proposition 71 funds. Proposition 71 includes explicit provisions for sharing in the gains from any patents or other intellectual property developed with Initiative funding:

> "The ICOC shall establish standards that require that all grants and loan awards be subject to intellectual property agreements that balance the opportunity of the State of California to benefit from the patents, royalties, and licenses that result from basic research, therapy development and clinical trials with the need to assure that essential medical research is not unreasonably hindered by the intellectual property agreements."[130]

New discoveries could have significant economic value. By patenting and licensing these discoveries, the State may well be able to offset some of the costs of Proposition 71. While it cannot be known at this point what discoveries will be made and what patents will be secured, if any, we present an analysis that illustrates the potential for economic benefits were there to be patentable and licensable discoveries.

A. Current Royalty Revenues for Research Organizations

As a foundation, it is useful to understand the current level of intellectual property royalties being received by the University of California (U.C.) system and other research organizations.

1. Academic Institutions

In 2001, 143 U.S. universities that responded to the 2001 Association of University Technology Managers survey received more than $827 million in royalties and fees from discoveries licensed to commercial companies generated from 7,715 licenses. The top 10 research universities generated $511 million, most of which was from life-science related discoveries.[131] Of the top 5, the UC system and Stanford ranked third and fifth respectively as shown in the table below:[132]

[130] Proposition 71, Section 5, Chapter 3, Article 1, 125290, h.
[131] Agres, T., "Licenses Worth a Billion," The Scientist, May 27, 2003.
[132] *Ibid.*

Table 9.1
Top 5 Research Institutions in Terms of Net Royalty Payment 2001
($ Millions)

Research Institution	Net Royalty
Columbia University	$129.9
Massachusetts Institute of Technology	74.0
University of California System	66.7
Florida State University	62.1
Stanford University	38.8

The average licensing fee of the 143 respondents was $5.8 million. These revenues may not reflect the maximum revenues obtainable by the owners of intellectual property. At the same time, the State may adopt a similar set of goals in its licensing activities, were there to be licensable products developed under the Initiative.

California research and academic institutions have been particularly successful in receiving royalty revenue. The UC system, Stanford and City of Hope National Medical Center earned $178.1[133] million in combined 2002 gross royalties from their intellectual property.[134] A factor contributing to the success is the concentrated presence of commercial life science companies and investment capital in California that creates a continuous demand for innovation, which often requires licensing the rights to use intellectual property developed by others.

2. *Other Payments*

In addition to examining the ongoing licensing revenues, it is also useful to examine the value of individual payments for technology licenses. Many of these payments, which are often associated with intellectual property litigation, can be very large, and illustrate the value of truly breakthrough technology.

In a recent (1999) high profile case, Genentech was ordered to pay The City of Hope National Medical Center $300 million in compensatory damages and $200 million in punitive damages for their failure to pay royalties.[135] Under the licensing agreement between Genentech and The City of Hope, Genentech was given the patents for manufactured polypeptides using City of Hope-synthesized DNA in return for 2 percent licensing royalty on net sales of products using the polypeptide. Combined with the $300 million in already paid royalties, the value of the City of Hope-synthesized polypeptide was $600[136] million (not including the punitive damages of $200 million).

[133] $178.1 million is the total received gross royalty payments of Stanford, the City of Hope, and the UC System (without a one-time payment) for their fiscal year 2002. Note that fiscal years differ for the three institutions.
[134] "Stanford University Office of Technology Licensing Annual Statistics Five-Year Report," January 23 2004; 1998-2003 data received from Stanford University Office of Technology Licensing; "Annual Report University of California Technology Transfer Program, Fiscal Year 2002", p. 20, available at http://www.ucop.edu/OH/ann02/ar02.pdf; E-mail correspondence from Eben DuRoss, containing City of Hope royalty revenues, August 26, 2004.
[135] Agres, T., "Legal Issues in the Lab," The Scientist, Volume 16, Issue 15, July 22, 2002.
[136] In the original lawsuit, the City of Hope claimed it was owed $457 million in royalties and interest, but the jury award was $300.1 million.

In a separate lawsuit, Genentech was ordered to pay the UC System $200 million in an unrelated lawsuit over genetically engineered human growth hormones.[137] In both of these cases, a single licensing agreement had a value of many hundreds of millions of dollars. While these are not the average result of research efforts, they do illustrate the potential associated with breakthrough discoveries.

Table 9.2 illustrates the steady flow of licensing revenues to Stanford, UC, and the City of Hope, both including and excluding the Genentech settlement.[138]

Table 9.2
1996 – 2003 Gross Royalty Payments Made to the UC System and Stanford[139]
($ Millions)

Institution	1996	1997	1998	1999	2000	2001	2002	2003
UC System Including 2002 One-Time Payment	$63.2	$67.3	$73.1	$80.9	$66.8	$72.9	$288.0	$67.0
UC System Excluding One-Time Payment	63.2	67.3	73.1	80.9	66.8	72.9	88.0	67.0
Stanford University	28.8	34.0	43.2	27.7	34.6	38.8	50.2	43.2
City of Hope	NA	NA	NA	23.8	26.7	28.4	39.9	55.9
Combined Excluding Payment	92.0	101.3	116.3	132.4	128.1	140.1	178.1	166.1

B. Modeling Possible Royalty Revenues from Research Funded by Proposition 71

The primary motive behind Proposition 71 is "to save lives and reduce health care costs."

137 Agres, T., "Legal Issues in the Lab," The Scientist, Volume 16, Issue 15, July 22, 2002.

138 "Stanford University Office of Technology Licensing Annual Statistics Five-Year Report," February 4, 1999; 1993-1998 data received from Stanford University Office of Technology Licensing; "Stanford University Office of Technology Licensing Annual Statistics Five-Year Report," January 23 2004, 1998-2003 data received from Stanford University Office of Technology Licensing; "Technology Transfer Revenues", University of California Annual Report 1996, available at http://www.ucop.edu/ott/ars/ann96/Hr.html, accessed July 22, 2004; "Technology Transfer Revenues," University of California Annual Report 1997, available at http://www.ucop.edu/ott/ars/ann97/Hr.html, accessed July 22, 2004; "Technology Transfer Revenues," University of California Annual Report 1998, available at http://www.ucop.edu/ott/ars/ann98/page03.html, accessed July 22, 2004; "Annual Report University of California Technology Transfer Program, Fiscal Year 2000," p. 10, available at http://www.ucop.edu/OH/ann00/ar00.pdf; "Annual Report University of California Technology Transfer Program, Fiscal Year 2001," p. 20, available at http://www.ucop.edu/OH/ann01/ar01.pdf; "Annual Report University of California Technology Transfer Program, Fiscal Year 1999," p. 14, available at http://www.ucop.edu/OH/ann99/ar99.pdf; "Annual Report University of California Technology Transfer Program, Fiscal Year 2002," p. 20, available at http://www.ucop.edu/OH/ann02/ar02.pdf; "Annual Report University of California Technology Transfer Program, Fiscal Year 2003," p. 20, available at http://www.ucop.edu/OH/ann03/ar03.pdf.; E-mail correspondence from Eben DuRoss, containing City of Hope royalty revenues, August 26, 2004.

139 Figures given for the fiscal year of each institution. Note that fiscal years differ for the three institutions.

However, the performance of national and California research institutions suggest that the State of California may also earn significant royalties from intellectual property derived from the investment.

It is worth noting that there is a relationship between the cost savings identified earlier and the intellectual property royalties identified here. To the extent royalties from intellectual property increases costs of new therapies, this obviously reduces some of the benefits from lower health care costs. This tension creates a situation where health cost reductions are somewhat limited by royalty payments.

However, from the perspective of the State of California, this tension does not exist for therapies sold outside of California. In other words, the State would benefit from royalties on stem cell related treatments and therapies sold outside of California, even if those payments reduce somewhat the health savings the State realizes from new therapies.

The basic methodology we have employed for purposes of our analysis is as follows:

1. *Step 1: Estimate Average Total Revenue over the Patent Life of a Biotechnology Therapy*

In order to estimate the potential royalty revenues from research funded through Proposition 71, we estimate the sales per year of an average current therapy. In March 2004, SG Cowen issued a report projecting 18 potential biotechnology therapy approvals in 2004 (some of the development products like Genentech's Avastin have since been approved).[140] These 18 potential biotechnology therapies in development are estimated to have aggregate future peak annual sales potential ranging from $7.5 – $12.4 billion. Based on this range, we derive average peak sales of $10 billion or $556 million per therapy.[141]

While patents typically have a 17 year life, the effective patent life of a drug is much shorter, after factoring in the time required for approval and the potential of displacement by new therapies. For purposes of our analysis, we have assumed a 7 year usable patent lifetime average with peak sales occurring in year 4, the midpoint of the 7 year usable patent life. Furthermore, we assume that sales will increase linearly starting from year 1 to year 4 and remain at peak levels until year 7. In order to maintain a conservative approach, we have not taken into account the value of product life extensions of the original drug. Based on these estimates, we have estimated an average $3.0 billion per drug over the effective patent life based on current 2004 levels.

2. *Step 2: Estimate the Average Royalty Revenues per Therapy*

Biotechnology therapies typically use an intellectual property contract structure that allows the owner of the intellectual property to receive a percentage of the sales of the therapy. We have analyzed an extensive database of biotechnology licenses and found of the university or institute licenses, 105 reported a license royalty fee. Removing one large outlier of 47 percent, the royalty

[140] Schmidt, E., et al., "Biotech Pipeline Monitor," SG Cowen Analyst Report, March 2004, p. 8.
[141] *Ibid.*

percentages ranges from 1 to 10 percent with an average and median both around 4 percent.[142] For the purposes of our limited therapeutic success analysis, we have used a royalty percentage of 2 percent of revenues. For the increased therapeutic success case, we have used a royalty percentage of 4 percent.

We then apply the royalty percentage to the estimated therapy sales to estimate royalty payments per therapy per year over a 7 year timeframe. Given the $3 billion lifetime revenue estimate, this results in $60 million total dollars from royalty revenue per therapy in 2004 dollars spread over the usable lifetime of the therapy in proportion to the sales. We adjust these estimates using our long-term estimate of health care inflation of 4.2 percent per year.

3. *Step 3: Scale the Proposition 71 Research Funding to Drug Development Costs*

It is difficult to know exactly how many therapies may ultimately be developed using intellectual property associated with Proposition 71. In order to provide an framework for discussion, we have scaled the overall research funding from Proposition 71 (totaling approximately $2.5 billion) to the average therapy development cost. Frost & Sullivan, in their yearly report on the biotechnology pipeline,[143] estimates that the R&D research expenditures that are necessary to develop a biotechnology drug are approximately $500 million, to which we have applied the annual health care inflation factors.

If in a given year the research funding is $52.5 million and the then-current drug development costs are estimated to be $525 million, we have estimated that the funding from that year would be equivalent to 10 percent of the cost of developing a single therapy in that year. Based on the planned spending, the actual yearly spending ranges up to 41 percent of a cost of a single therapy. Doing this on a year-by-year basis results in a scenario in which Proposition 71 would provide funding equivalent to approximately 3.4 total therapies. Obviously in practice the result may vary. For example, Proposition 71 may play some role in the development of more therapies, but share in a smaller percentage of each one. If development costs are higher, Proposition 71 may participate in fewer. However, this provides an overall scaling factor for our estimates.

4. *Step 4: Estimate the Royalty Revenues on a Year-By-Year Basis*

In our analysis, we have included a 10 year delay between the funding point and any royalty revenues associated with the research funding, which then continue for the 7 year estimated patent life of the therapy. This yields royalty revenue estimates beginning at $145,000 in year 11, peaking at just over $56.2 million in year 23 and declining to $107,000 in year 30. The following graph shows the year-by-year estimates, which together total $536.7 million. This equates to approximately 10 percent of the total cost of the Initiative.

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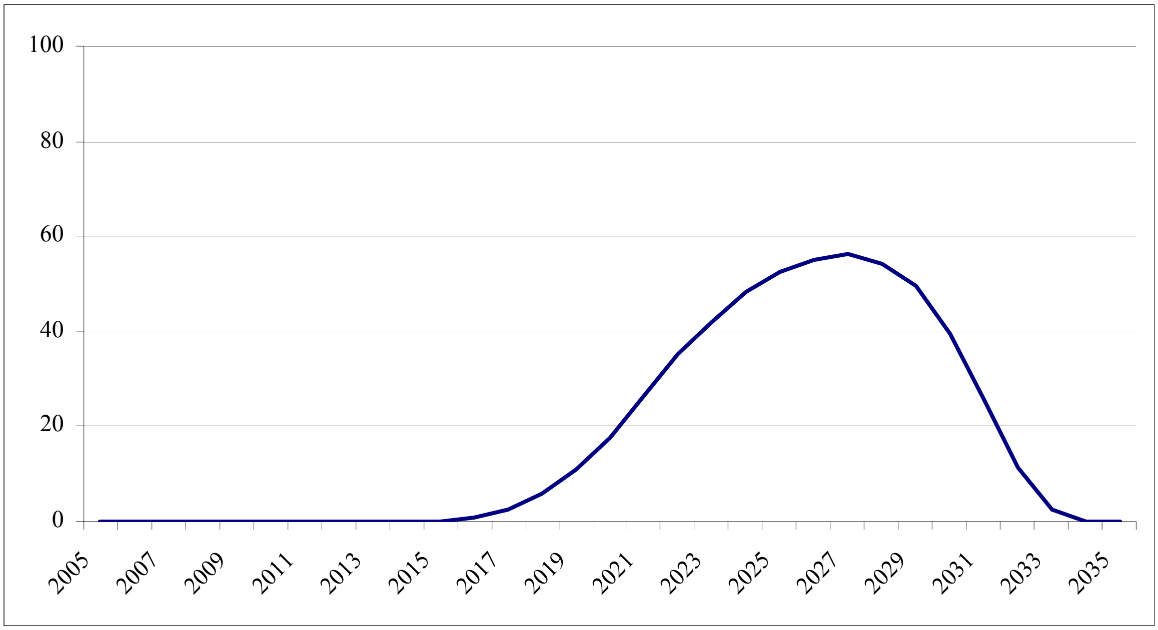
[142] The average is 4.3 percent and the median is 4.0 percent. The outlier is Cytel & The Scripps Research Institute, 1992. Source: "Alliance Summary for Vestar/Stanford," available at http://www.rdna.com, accessed March 27, 2002.

[143] "U.S. Biotechnology Pipeline Analysis," Frost and Sullivan Report, January 21, 2004, pp. 2-7.

Chart 9.1
2005 – 2035 Estimated Royalty Payments from Proposition 71 Base Case
($ Millions)



We note as a point of reference that the $56.2 million peak estimate in year 23 would equate to approximately 12 percent of the equivalent royalty revenue number for the UC system, Stanford, and City of Hope Medical Center combined, using the 2002 estimate and using the same estimate of health care inflation as was used for our estimates.

C. Increased Royalty Rate Case

A two percent royalty rate is near the low end of royalty rates observed in our background research. We have also modeled a royalty rate of 4 percent of revenue, or twice the rate used for the first scenario. Four percent is approximately the mean for royalty rates currently observed for biotechnology. Under the second scenario, total royalty revenues are expected to be $1.1 billion, or 20 percent of total program costs.

X. Conclusion

We find that Proposition 71 has the potential to produce significant economic benefits to Californians, to the State budget, and to the global society as a whole. We have analyzed the economic costs and benefits of Proposition 71 to the State of California, in four primary areas. We believe it prudent to maintain a perspective on the difficulties and challenges associated with stem cell research, and we stress the limitations and uncertainties that hamper the development of precise estimates in this area into the future. Accordingly, many of our assumptions, including the benefits we model are modest in their expectations. Nonetheless, the analyses we conducted support the view that with even modest success, Proposition 71 could generate economic benefits to the State of California that exceed the costs of the funding.

1. *Case 1 Analysis: Limited Therapeutic Success*

The table below summarizes the economic costs and benefits of Proposition 71 in our base analysis. Here, we include the tax revenues from direct spending, tax revenues from new biotechnology activity associated with a 2.5 percent increase in life sciences activity, cost savings from a 1 percent reduction in health care costs for our 6 conditions, and royalty revenues based on a 2 percent royalty rate.

Table 10.1 Total Program Costs and Benefits – Case 1: Limited Therapeutic Success ($ Millions)

	Phase 1 Years 1-5	Phase 2 Years 6-14	Phase 3 Years 15-35	Total
Economic Costs to State Budget	$56	$1,289	$4,010	$5,355
Economic Benefits to State Budget				
1) Tax revenues from Proposition 71 direct spending	73	167	-	240
2) Tax revenues from 2.5% increase in life sciences activity	54	355	1,796	2,206
3) Cost savings from 1% reduction in State spending on 6 conditions	-	382	3,062	3,444
4) Royalty revenues using 2% royalty rate	-	10	527	537
Total	**127**	**914**	**5,385**	**6,426**
Percent of Total Costs	***227%***	***71%***	***134%***	***120%***
Additional Benefits to Californians Not Included in State Budget*				
Health care cost savings from 1% cost reductions	**-**	**1,136**	**8,043**	**9,180**
Percent of Total Costs	*0%*	*88%*	*201%*	*171%*
Estimated Jobs Created (One job for one year = one job year)				
Job years from Proposition 71 direct spending	14,272	33,209		47,480
Job years from Increase in life sciences activity	11,967	67,732	233,148	312,847
Total	26,239	100,940	233,148	360,328

** These are savings from the reduction in direct spending and lost work time on the 6 conditions that are not included in the State budget but benefit Californians overall.*

On an overall basis, our analysis estimates that, in the Case 1 scenarios we examined, the economic benefits of Proposition 71 exceed the costs, with an overall ratio of benefits to costs of 120 percent.

2. Case 2 Analysis: Increased Therapeutic Success

In addition to Case 1 estimates, we also developed estimates of the benefits under an increased therapeutic success scenario as shown below. Here, we use 5.0 percent increases in life sciences activity, rather than 2.5 percent, a 2 percent reduction in health care costs for the 6 conditions, and a 4 percent royalty rate.

Table 10.2
Total Program Costs and Benefits – Case 2: Increased Therapeutic Success
($ Millions)

	Phase 1 Years 1-5	Phase 2 Years 6-14	Phase 3 Years 15-35	Total
Economic Costs to State Budget	$56	$1,289	$4,010	$5,355
Economic Benefits to State Budget				
1) Tax revenues from Proposition 71 direct spending	73	167	-	240
2) Tax revenues from 5.0% increase in life sciences activity	108	711	3,592	4,411
3) Cost savings from 2% reduction in State spending on 6 conditions	-	764	6,123	6,887
4) Royalty revenues using 4% royalty rate	-	19	1,054	1,073
Total	**181**	**1,662**	**10,769**	**12,612**
Percent of Total Costs	***324%***	***129%***	***269%***	***236%***
Additional Benefits to Californians Not Included in State Budget*				
Health care cost savings from 2% cost reductions	**-**	**2,273**	**16,087**	**18,359**
Percent of Total Costs	*0%*	*176%*	*401%*	*343%*
Estimated Jobs Created (One job for one year = one job year)				
Job years from Proposition 71 direct spending	14,272	33,209		47,480
Job years from Increase in life sciences activity	23,934	135,464	466,296	625,695
Total	38,206	168,672	466,296	673,175

** These are savings from the reduction in direct spending and lost work time on the 6 diseases and conditions that are not included in the State budget but benefit Californians overall.*

In the second scenario, the life sciences activity is estimated to be 5 percent; cost savings for the six diseases and conditions are estimated to be 2 percent; and royalty revenues are projected using a 4 percent royalty rate. These scenarios yield a ratio of benefits to costs of 236 percent for the State budget.

3. Case 3 Analysis: Expanded Therapeutic Success

Finally, we developed a scenario that assumes a larger percentage of cost savings, which could result if stem cell research led to expanded therapies. The results of such a scenario are shown below:

Table 10.3
Total Program Costs and Benefits – Case 3: Expanded Therapeutic Success
($ Millions)

	Phase 1 Years 1-5	Phase 2 Years 6-14	Phase 3 Years 15-35	Total
Economic Costs to State Budget	$56	$1,289	$4,010	$5,355
Economic Benefits to State Budget				
1) Tax revenues from Proposition 71 direct spending	73	167	-	240
2) Tax revenues from 5.0% increase in life sciences activity	108	711	3,592	4,411
3) Cost savings from 10% reduction in State spending on 6 conditions	-	3,821	30,616	34,437
4) Royalty revenues using 4% royalty rate	-	19	1,054	1,073
Total	**181**	**4,718**	**35,262**	**40,161**
Percent of Total Costs	***324%***	***366%***	***879%***	***750%***
Additional Benefits to Californians Not Included in State Budget*				
Health care cost savings from 10% cost reductions	**-**	**11,364**	**80,434**	**91,797**
Percent of Total Costs	*0%*	*882%*	*2006%*	*1714%*
Estimated Jobs Created (One job for one year = one job year)				
Job years from Proposition 71 direct spending	14,272	33,209		47,480
Job years from Increase in life sciences activity	23,934	135,464	466,296	625,695
Total	38,206	168,672	466,296	673,175

** These are savings from the reduction in direct spending and lost work time on the 6 diseases and conditions that are not included in the State budget but benefit Californians overall.*

In this scenario, the assumptions for life sciences activity and royalty revenue remain the same as in Case 2 at 5 percent and 4 percent, respectively. The cost savings for the six conditions is adjusted upward to 10 percent rather than 2 percent. The results are a ratio of benefits to costs of 750 percent

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A. Documents Cited in Report

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Appendix B. Interviews

1. Interview with Dan Perry, Alliance for Aging Research Executive Director, May 2004.
2. Interview with Dr. David Baltimore, President, California Institute of Technology, October 2003.
3. Interview with Dr. Karl K. Johe, Chairman and Chief Science Officer, NeuralStem, October 2003.
4. Interview with Dr. Seung Kim, Assistant Professor from the Departments of Developmental Biology and Medicine, Stanford University School of Medicine, May 2004.
5. Interview with Dr. Shane Smith, Scientist at UCLA, August – October 2003.
6. Interview with Dr. Evan Snyder, Professor and Director of the Stem Cells and Regeneration program, The Burnham Institute, May 2004.
7. Interview with Frank Rice, Chief Financial Officer, Vistagen, October 2003.
8. Interview with Dr. Hans Keirstead, Assistant Professor, Reeve-Irvine Research Center Department of Anatomy & Neurobiology, University of California, Irvine, August 2004.
9. Interview with Dr. Jeffrey Bluestone, Head of Diabetes Center at University of California, San Francisco, May 2004.
10. Interview with Larry Soler, Junior Diabetes Research Foundation Senior Legislative Counsel, May 2004.
11. Interview with senior representative from the SALK Institute for Biological Sciences, October 2003.
12. Interview with senior representatives from University of California, San Diego, October 2003.
13. Interviews with Dr. Irv Weissman, Professor Stanford Medical School and Director of the Stanford Institute for Cancer/Stem Cell Biology and Medicine, August – October 2003.
14. Interviews with Dr. Larry Goldstein, Professor of Cellular and Molecular Medicine at the University of California, San Diego, School of Medicine, August – October 2003.
15. Interviews with senior representative from SWAP Financial Group, investment advisors, October 2003.
16. Personal communication from Dr. Thomas Okarma, CEO at presentation at the First International Stem Cell Action Conference, University of California, Berkeley, June 2004.

Appendix C. Employer Claims Database Description

The analyses for the cost of illness section are performed using an Analysis Group (AG) in-house administrative claims database of sixteen employers (nine of which have work loss data) from 1999 – 2002. Together these companies have operations nationwide in a broad array of industries and job classifications. The claims database covers medical claims of about 2 million lives, including 400,000 employees. The data include the medical and prescription drug claims for all enrollees as well as disability claims for enrollees that are also active employees. The inclusion of both the medical and disability claims for these individuals enables us to estimate both the direct and indirect costs of patients with a given disease. Some of the key data elements are listed below.

Medical claims (e.g., hospital inpatient, hospital outpatient, office, laboratory):

- ICD-9 diagnoses
- CPT procedures
- Provider payments

Prescription drug claims:

- NDC drug codes
- Days supply
- Dosage strength
- Payments

Work-loss (for employees)

- Disability claims (dates, employer payments)
- Imputed medically-related work-loss days and wages