CALIFORNIA
HEALTH BENEFITS REVIEW PROGRAM

Analysis of Senate Bill 913: Biological Medications for Rheumatic Diseases

A Report to the 2005-2006 California Legislature
April 16, 2005

CHBRP 05-09

Established in 2002 to implement the provisions of Assembly Bill 1996 (*California Health and Safety Code*, Section 127660, et seq.), the California Health Benefits Review Program (CHBRP) responds to requests from the State Legislature to provide independent analysis of the medical, financial, and public health impacts of proposed health insurance benefit mandates. The statute defines a health insurance benefit mandate as a requirement that a health insurer and/or managed care health plan (1) permit covered individuals to receive health care treatment or services from a particular type of health care provider; (2) offer or provide coverage for the screening, diagnosis, or treatment of a particular disease or condition; or (3) offer or provide coverage of a particular type of health care treatment or service, or of medical equipment, medical supplies, or drugs used in connection with a health care treatment or service.

A small analytic staff in the University of California's Office of the President supports a task force of faculty from several campuses of the University of California, as well as Loma Linda University, the University of Southern California, and Stanford University, to complete each analysis within a 60-day period, usually before the Legislature begins formal consideration of a mandate bill. A certified, independent actuary helps estimate the financial impacts, and a strict conflict-of-interest policy ensures that the analyses are undertaken without financial or other interests that could bias the results. A National Advisory Council, made up of experts from outside the state of California and designed to provide balanced representation among groups with an interest in health insurance benefit mandates, reviews draft studies to ensure their quality before they are transmitted to the Legislature. Each report summarizes sound scientific evidence relevant to the proposed mandate but does not make recommendations, deferring policy decision making to the Legislature. The State funds this work though a small annual assessment of health plans and insurers in California. All CHBRP reports and information about current requests from the California Legislature are available at CHBRP's Web site, www.chbrp.org.

A Report to the 2005-2006 California State Legislature

Analysis of Senate Bill 913
Biological Medications for Rheumatic Diseases

April 16, 2005

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PREFACE

This report provides an analysis of the medical, financial, and public health impacts of Senate Bill 913, a bill that would prohibit health care service plans and health or disability insurers that contract to provide coverage for medications from identifying a preferred drug within the biological class of drugs for the treatment of Rheumatic Diseases.

In response to a request from the California Senate Banking, Finance, and Insurance Committee on February 15, 2005, the California Health Benefits Review Program (CHBRP) undertook this analysis pursuant to the provisions of Assembly Bill 1996 (2002) as chaptered in Section 127600, et seq. of the California Health and Safety Code.

Yali Bair, PhD, Richard Kravitz, MD, and Janet Keyzer, RN-C, MPA, and Christina Kuenneth, MPH, all of the University of California, Davis prepared the medical effectiveness analysis. Richard White, MD, of the University of California, Davis provided technical assistance with the literature review and clinical expertise for the medical effectiveness analysis. Min-Lin Fang, MLIS, of UCSF conducted the literature search. Helen Halpin, PhD, Sara McMenamin, PhD, and Nicole Bellows, MHSA, all of the University of California, Berkeley, prepared the public health impact analysis. Gerald Kominski, PhD, Miriam Laugesen, PhD, and Nadereh Pourat, PhD, all of the University of California, Los Angeles, prepared the analysis of the cost impact. Robert Cosway, FSA, MAAA, and Chris Girod, FSA, MAAA, of Milliman, provided actuarial analysis. Michael E. Gluck, PhD, and Robert O'Reilly, BS, of CHBRP staff prepared the background section and integrated the individual sections into a single report. Other contributors include Cynthia Robinson, MPP and Sachin Kumar, BA**,** of CHBRP staff, and Cherie Wilkerson, who provided editing services. In addition, a subcommittee of CHBRP's National Advisory Council (see final pages of this report) reviewed the analysis for its accuracy, completeness, clarity, and responsiveness to the Legislature's request.

Jay Ripps, FSA, MAAA of Milliman recused himself from contributing to this and all other CHBRP analyses beginning March 1, 2005. His recusal is valid through his duration as acting chief actuary at Blue Shield of California.

CHBRP gratefully acknowledges all of these contributions but assumes full responsibility for all of the report and its contents. Please direct any questions concerning this report to CHBRP:

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EXECUTIVE SUMMARY

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The California Legislature has asked the California Health Benefits Review Program to conduct an evidence-based assessment of the medical, financial, and public health impacts of Senate Bill 913.

Senate Bill (SB) 913 would prohibit health care service plans and health or disability insurers that contract to provide coverage for medications from identifying a preferred drug within the biologic class of drugs for the treatment of rheumatic diseases. It would apply to health care service plans licensed by Knox-Keene[1] as well as health insurance policies regulated under the California Insurance Code that offer coverage for prescription drugs. Health plans and insurance policies sold without prescription drug benefits are not subject to this mandate.

Rheumatic disease refers to a broad category of illness associated with inflammation and loss of function of the connecting or supporting structures of the body. To date, the U.S. Food and Drug Administration (FDA), has approved biological drugs for three of these conditions: rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS). The medications, comprising a class of drugs known as biological response modifiers (BRMs) are: etanercept (also know by its brand name Enbrel), adalimumab (Humira), anakinra (Kineret), and infliximab (Remicade). Etanercept is approved by the FDA for all three conditions, the others are approved for RA only.

Under current practice, plans and insurers often divide their formularies into three or more tiers requiring different levels of enrollee cost-sharing. They differentiate among similar drugs in a class by placing the least expensive drug in a tier with a lower cost-sharing than applies to other drugs in the class.

For the purpose of this analysis, CHBRP assumes that SB 913 would allow health plans and health insurers to continue to use formularies with tiered cost-sharing as well as prior authorization, step therapy (in which non-preferred drugs can be used only after a preferred drug has been tried unsuccessfully) and other tools to manage pharmacy benefits, the plans would have to apply these requirements equally to each biological drug for rheumatic diseases.[2] For example, if they make use of tiered cost-sharing, all biological drugs used to treat rheumatic disease would have the same cost sharing requirements.

[1] Health maintenance organizations in California are licensed under the Knox-Keene Health Care Services Plan Act, which is part of the California Health and Safety Code.

[2] One exception is the drug infliximab (brand name Remicade), which could be listed on the outpatient drug formulary but is infused under a physician's care (as opposed to self-administered). Like many infused therapies, the physician may procure the drug instead of the patient, and its cost may be included in the cost of the infusion procedure and reimbursed as a medical procedure rather than as an outpatient pharmaceutical.

I. Medical Effectiveness

- Evidence shows that the class of biological drugs known as biological response modifiers (BRMs) are effective in reducing joint pain and swelling, significantly halting bone degeneration and improving quality of life in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS)—the three rheumatic conditions for which the U.S. Food and Drug Administration (FDA) has approved these therapies.

- Although there are no head-to-head trials among the four currently available BRMs, observational studies indicate that they are interchangeable in terms of effectiveness. However, patients who do not respond to one treatment may reasonably be expected to respond to one of the others.

II. Utilization, Cost, and Coverage Impacts

- A total of 20,014,000 individuals, ages 0-64 years, are currently enrolled in health plans or insurance policies that would be affected by this proposed mandate. Of these, 95% or 18,987,000 individuals have prescription drug coverage.

- All health plans and insurers currently cover BRMs for their insured populations with prescription drug benefits. However, formulary requirements and cost sharing for enrollees vary across plans and payers.

- About 101,000 persons or individuals (0.55% of the insured with prescription drug benefits) have RA, PsA, or AS. About 16,000 such individuals currently use BRMs. Based on expert opinion, CHBRP projects no change in the utilization of BRMs by affected individuals due to the mandate.

- CHBRP projects total health expenditures will increase by $11,451,000 (0.019%) due to SB 913. This overall increase is due to a 5% increase in the unit cost of self-injectable BRMs. This cost increase is due to health plans losing discounts or rebates from manufacturers because they would be unable to give one BRM “preferred” status over another.

- CHBRP’s cost analyses are based on the assumption that health plans and insurers would comply with SB 913 by setting the same requirements for the use of all biological therapies. Health plans and insurers would not be prohibited from applying cost sharing or requiring prior authorization for these drugs as long as they were applied equally to each drug. An alternative option that could fulfill the conditions of SB 913 would be to assume that health plans and insurers would be barred from using tiered formularies or step therapy for these drugs. This interpretation of SB 913 would likely have different cost and utilization impacts.

Table 1. Summary of Coverage, Utilization, and Cost Effects of SB 913

Total Insured Population = 20,368,000	Before Mandate	After Mandate	Increase/ Decrease	Change After Mandate
Coverage				
Number of insured individuals in California subject to the mandate	20,014,000	20,014,000	None	0.000%
Percentage of insured individuals in California subject to the mandate	95%	95%	None	0.000%
Number of insured individuals in California with prescription drug benefits and subject to the mandate	18,987,000	18,987,000	None predicted	0.000%
Number of insured individuals in California without coverage for the benefit	1,027,000	1,027,000	None predicted	0.000%
Number of insured individuals in California with rheumatic diseases	101,400	101,400	None predicted	0.000%
Number of insured individuals in California with rheumatic diseases who use biological drugs	16,000	16,000	None predicted	0.000%
Utilization				
Percentage of total. members 0-64 years diagnosed with RA, AS, or PsA	0.55%	0.55%	None predicted	0.000%
Percentage of total members 0-64 years with one or more biological. drug prescriptions who are diagnosed with RA, AS, or PsA per year	0.09%	0.09%	None predicted	0.000%
Percentage of members using biologicdrugs with an entanercept prescription	71.6%	71.6%	None predicted	0.000%
Percentage of members using biological drugs with an adalimumab prescription	0.0%	0.0%	None predicted	0.000%
Percentage of members using biologic drugs with an anakinra prescription	4.1%	4.1%	None predicted	0.000%
Percentage of members using biological drugs with an infliximab prescription	24.2%	24.2%	None predicted	0.000%
Prescription Cost to Insurer				
Average annual prescription paid for by insurer	16,234	17,046	812	5%
Annual Expenditures				
Premium expenditures by private employers for group insurance	$35,360,055,000	$ 35,366,136,000	$ 6,081,000	0.017%
Premium expenditures by individuals with group insurance, CalPERS, or Healthy Families	$10,261,105,000	$ 10,262,925,000	$ 1,820,000	0.018%
Premium expenditures for individually purchased insurance	$3,818,726,000	$ 3,819,837,000	$ 1,111,000	0.029%
CalPERS employer expenditures	$2,212,881,000	$ 2,213,269,000	$ 388,000	0.018%
Medi-Cal state expenditures	$2,941,170,000	$ 2,942,152,000	$ 982,000	0.033%
Healthy Families state expenditures	$347,858,000	$ 347,900,000	$ 42,000	0.012%
Out-of-pocket expenditures and other expenditures for noncovered services	$4,074,893,000	$ 4,075,920,000	$ 1,027,000	0.025%
Total annual expenditures	$59,016,688,000	$ 59,028,139,000	$ 11,451,000	0.019%

Source: California Health Benefits Review Program, 2005.

The population includes individuals and dependents in California who have private insurance (group and individual) or are enrolled in public plans subject to the Health and Safety Code, including CalPERS, Medi-Cal, or Healthy Families. All population figures include enrollees aged 0-64 years.

Employees and their dependents that receive their coverage from self-insured firms are excluded because these plans are not subject to the mandate.

Key: CalPERS = California Public Employees' Retirement System.

III. Public Health Impacts

- There have been no California-specific prevalence studies for any of the three rheumatic diseases examined in this analysis. There are national estimates reported in the literature, with an approximately 1% prevalence of the adult US population for RA. The estimated prevalence for AS is 0.07% for men and 0.19% for women, based on a study of a predominately White population. PsA prevalence is estimated to be between 0.08% and 0.12% of the adult population. The national claims database of privately insured individuals under the age of 65 years suggests that 0.49% of the insured population have been diagnosed and are receiving treatment for RA and 0.06% for either AS or PsA. The lower prevalence rates in the claims data are most likely due to the positive relationship between RA and age.

- Because CHBRP projects that SB 913 would not lead to any additional utilization of the four biological drugs used to treat RA, AS, or PsA, the mandate would also have no impact on the health of the community.

- The prevalence of RA is two to three times higher among women than men. For AS, the gender differences are reversed where men are approximately three times more likely to be diagnosed compared with women. No gender differences were reported for the prevalence of PsA. With regard to racial/ethnic differences, Native Americans have the highest prevalence of RA world-wide; RA is at least twice as common among Native Americans compared with Whites. Because there is no projected increase in utilization in the four drugs used to treat RA, AS, or PsA, this mandate will not impact the gender and racial disparities in treatment of rheumatic diseases.

- Patients with RA, AS, and PsA have higher standardized mortality rates compared with patients without these diseases. No studies were found to examine the effect of BRMs on mortality for patients with RA, AS, or PsA. Because there is no projected increase in utilization of the four drugs used to treat RA, AS, or PsA, we conclude that this mandate will have no impact on the reduction of premature death.

- Measures of the indirect cost of rheumatic disease include the loss of ability to work, reduced productivity after returning to work, the value of services of unpaid care providers, as well as quality of life measures, psychological impacts, and other “intangible” costs. Because CHBRP projects no change in utilization of the four BRMs used to treat RA, AS, or PsA, the bill would have no impact on any of these measures of economic loss associated with rheumatic disease.

INTRODUCTION

Senate Bill (SB) 913 would prohibit health care service plans and health or disability insurers that contract to provide coverage for medications from preferring one drug over any other within a biological class of drugs for the treatment of rheumatic disease. As discussed below, "preference" refers to a health plan or insurer's ability to encourage the use of one drug over other similar therapies through financial incentives and other pharmacy management techniques.

SB 913 would apply to health care services plans licensed by Knox-Keene[3] and health insurance policies regulated under the California Insurance code, excluding Medi-Cal/Medicare dual eligibles enrolled in Medi-Cal Managed Care or patients enrolled in County Organized Health Systems. Effective January 1, 2006, Medicare Part D will offer drug coverage for all Medicare enrollees and Medicare supplement plans will no longer be allowed to offer prescription drug coverage. This analysis reflects the fact that SB 913 will only affect those not eligible for drug coverage through Medicare Part D.

Rheutmatic Disease and Biological Treatments

Rheumatic disease is a broad category of illness characterized by inflammation and loss of function of connecting or supporting structures in the body. There are more than 100 rheumatic diseases; however, there are only three conditions where biologics are indicated. These conditions are rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS). These conditions are different from osteoarthritis, the most common form of arthritis, which affects about 10% of the U.S. population. RA affects only about 1% of the U.S. population.

To date**,** the U.S. Food and Drug Administration (FDA) has approved four biological medications for the treatment of RA, PsA, or AS. Comprising a class of drugs known as biological response modifiers (BRMs), the generic names for these drugs are etanercept (also know by its brand name Enbrel), adalimumab (Humira), anakinra (Kineret), and infliximab (Remicade).[4] All of these drugs are typically self-injected by the patient except infliximab, which is infused under the supervision of physicians, usually in their offices or a dedicated infusion facility. Physicians (rather than patients) usually procure infused drugs like infliximab, and reimbursement for their costs are typically part of health plans' payments to physicians for the infusion procedure under the medical benefit, not the outpatient pharmaceutical benefit. Patient cost-sharing obligations are those specified for medical procedures, not those that apply to the pharmaceutical benefit. Therefore, for the purposes of this analysis, any changes in infliximab's status as a pharmaceutical benefit as a result of SB 913 are assumed not to have any effect.

Formularies and Preferred Drugs

Formularies are the most common of several tools health plans use to help administer their drug

[3] Health maintenance organizations in California are licensed under the Knox-Keene Health Care Services Plan Act, which is part of the California Health and Safety Code.
[4] In the rest of this report, CHBRP refers to these drugs by their generic names.

benefits (Hoadley, 2005). In the private sector, nearly 90 percent of health plans use a formulary of some sort. Formularies include a listing of drug classes and categories to which all drugs can be assigned. Under current practice, most plans and insurers divide their formularies into three or more tiers requiring different levels of enrollee cost-sharing. They differentiate among similar drugs in a class by placing the least expensive drug in a tier with a lower cost-sharing than applies to other drugs in the class.

For the purposes of the cost and public health analysis that follow, CHBRP assumes that SB 913 would allow health plans and health insurers to continue to use tiered cost-sharing. However, enrollees would pay the same amount out-of-pocket no matter which drug in the class was prescribed. Plans could also continue to use tools such as prior authorization and step therapy (in which non-preferred drugs can be used only after a preferred drug has been tried unsuccessfully) as long as applied these requirements equally to each biological drug used to treat rheumatic diseases.[5]

An alternative option that could fulfill the conditions of SB 913 would be to assume that health plans would be barred from using tiered formularies or step therapy for these drugs. This interpretation of SB 913 would likely have different cost and utilization impacts.

I. MEDICAL EFFECTIVENESS

Rheumatic Disease

Rheumatic diseases are characterized by inflammation of the connective tissue, including joints, tendons, and ligaments. Chronic, or long-term, inflammation leads to loss of function and mobility; pain; destruction of bone and cartilage; deformity; and decreased quality of life. Some rheumatic diseases can also involve internal organs. There are over 100 rheumatic diseases, with arthritis and autoimmune disorders being the most common types of conditions in this class. For the purposes of this analysis, we focus on the three rheumatic diseases for which biological therapies are FDA approved: RA, PsA, and AS.

RA is the second most common type of chronic arthritic disease, following osteoarthritis. RA can lead to progressive, deforming arthritis, with its associated disabling effects and reduced quality of life. RA affects approximately 1% of the population, is more common among women than men, and tends to be more common with increasing age. The disease is often progressive and is characterized by chronic inflammation of the joints, pain, swelling, and stiffness, and can result in joint destruction and deformity. Other rheumatic conditions that can act in a similar fashion are PsA and AS. PsA appears to affect both genders equally and can occur at any age, but is most

[5] There are proposed regulations currently being promulgated in California through the Department of Managed Health Care (DMHC) titled, "Outpatient Prescription Drug Co-payments, Coinsurance, Deductibles, Limitations and Exclusions, Control #2002-0019, Adopting Section 1300.42.7 in Title 28, California Code of Regulations." These regulations, for Knox-Keene plans, would create standards for drug benefit plans, require information to be provided to enrollees, calculate allowable cost-sharing, and set conditions for excluding drugs or limiting their supply. See www.dmhc.ca.gov.

commonly diagnosed between the ages of 20 and 50 years. This disease causes swelling and pain in the joints outside the spine, frequently accompanied by the typical rash of psoriasis (scaly spots on the scalp, elbows, knees, fingernails, and base of the spine). AS is a chronic disease that most commonly affects men between the ages of 17 and 35 years. This condition primarily affects the spine, leading to stiffness, pain, inflammation, and in some cases, fusion of sections of the spinal column. Other joints and tissues can be affected as well, particularly the hips.

Summary of Treatment Options

In many patients, satisfactory control of these diseases cannot be achieved using currently available drugs. All forms of treatment are aimed at: (1) controlling joint damage, (2) reducing pain, (3) preserving joint mobility and function, and (4) improving quality of life. Until recently, non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, and cortisone-like drugs, such as prednisone, combined with disease-modifying agents for rheumatic diseases (DMARDs) were considered the treatment of choice. NSAIDs are effective in reducing pain and swelling, but do not affect the progressive course of the disease. DMARDs, such as low-dose oral methotrexate, are now used early in the course of RA as a "first line" of treatment. These DMARDs reduce inflammation and can reduce or prevent the joint erosion that often occurs within the first few months of disease onset. However, many patients do not have a satisfactory response to DMARD treatment, or the response to these drugs declines over time.

BRMs, such as anakinra (Kineret), etanercept (Enbrel), infliximab (Remicade), and adalimumab (Humira) are now available. They are not "drugs" in the classic sense; instead they are large, biological proteins, similar to antibodies that are made in the body. Whereas DMARDs often affect many tissues in a non-specific fashion, the new BRMs target a very specific trigger or signal involved in inflammation. In contrast to older DMARDs, these agents have a rapid onset of action (2-3 weeks), with fewer short-term side effects, and they can reduce inflammation and disease activity in combination with methotrexate or when administered alone. There are both clinical and structural differences among these four drugs. Infliximab must be infused intravenously in an outpatient clinic or infusion center, whereas the other three are self-injectable and can be administered by the patient.

Outcome Measures

Important outcomes for rheumatic disease include measures of how the treatment affects clinical symptoms and signs (such as joint pain and swelling), radiographic appearance of the joints, and functional status and well-being (health-related quality of life). The following is a description of the outcome measures evaluated in the studies included in this analysis:

The American College of Rheumatology (ACR) Response Rate is a composite clinical scoring system that has been repeatedly validated (Arnett et al., 1988)

ACR-20 (also ACR-50 and ACR-70) refers to the percent improvement in response to therapy. The ACR-20 response rate is based on:

- ☐ A decrease of at least 20% in the number of tender joints;
- ☐ A decrease of at least 20% in the number of swollen joints; and
- ☐ A 20% improvement in three of the following: patient's assessment of

disease status, health assessment questionnaire estimate of disability, physician's assessment of disease status, and two laboratory test markers.

Radiographic progression of structural joint damage is typically assessed using X-ray or magnetic resonance imagine (MRI) evaluation of erosion and joint space narrowing using a validated scoring system (Sharp Score) (range 0-440, with higher scores indicating greater damage).

Health-related quality of life may be measured using standardized and validated survey instruments such as the Health Assessment Questionnaire (HAQ) (Wolfe et al., 2004) and the Short Form-36 (SF-36) Health-related Quality of Life Score (Ware et al., 1999).

Summary of Effectiveness Literature

The most recent clinical trial literature to evaluate the effectiveness of the four currently approved BRMs was reviewed. The search was conducted through PubMed and the Cochrane Library for relevant research published over the last twenty years. Numerous studies evaluated the effectiveness of each of the four therapies, at varying doses, on clinical, radiographic and quality of life outcomes. Our analysis focused on recent systematic reviews and meta-analyses, and any randomized clinical trials published after the publication of the reviews. A description of methods used to conduct the medical effectiveness review, and the process used to "grade" the evidence can be found in Appendix A: Literature Review Methods.

Rheumatoid Arthritis

The majority of the BRM effectiveness studies focused on RA. These studies compared each of the BRMs to either a placebo treatment or to a standard DMARD treatment such as methotrexate. These studies were overwhelmingly positive, showing significant improvement in symptoms and quality of life and sustained cessation of bone erosion, as measured by improvements in radiographic evaluation of joint damage. In some studies, treatments with a BRM and methotrexate were compared with methotrexate alone or with the BRM alone. These studies also showed significant improvement in all outcome markers, although the treatment effect was not as large as that associated with switching from methotrexate to a biological agent. In one study (Genovese et al, 2004), etanercept treatment was compared to treatment with etanercept and another BRM, anakinra. This study did not show a significant improvement in outcomes with the addition of a second biological agent. The consensus in the medical effectiveness literature is that BRMs are more effective than other therapies in the management of RA. However, this increased effectiveness may be associated with increased risk of certain serious, albeit rare, side effects including reactivation of latent tuberculosis, exacerbation of demyelinating illnesses (e.g., multiple sclerosis), and lymphoma (see below).

Psoriatic Arthritis and Ankylosing Spondylitis

The medical effectiveness literature for the BRM agents is relatively new and growing due to the increased availability of the biologic agents and the increasing number of conditions with approved indications for treatment with these therapies. We found only four published clinical

trials focusing on the treatment of PsA that met our inclusion criteria. These studies compared treatment with etanercept with a placebo, and all showed positive results with respect to symptoms, joint inflammation, and function. With respect to the quality of life measures, the results from these trials showed etanercept and methotrexate had similar effects. Likewise, the studies evaluating the use of both etanercept and infliximab relative to placebo for AS showed consistently positive outcomes with respect to symptoms, joint inflammation, and function.

Summary of Treatment Effects

As a whole, the clinical trial evidence for the effectiveness of BRMs in the treatment of the rheumatic conditions in this analysis is favorable with respect to clinical, radiographic and quality of life outcomes. Table 2 provides a summary of the clinical trial evidence with respect to these outcomes. A determination of "favorable" indicates that the study findings are uniformly favorable and most or all are statistically as well as clinically significant. A determination of "ambiguous" indicates that some studies are favorable and some studies show no effect.

Table 2. Summary of Clinical Trail Findings by Therapy and Disease

	Infliximab	**Etanercept**	**Anakinra**	**Adalimumab**
Rheumatoid Arthritis				
FDA approved?	Yes	Yes	Yes	Yes
Clinical outcomes	Favorable	Favorable	Favorable	Favorable
Radiographic outcomes	Favorable	Favorable	Favorable	Favorable
QOL outcomes	Ambiguous	Ambiguous	Insufficient data	Insufficient data
Psoriatic Arthritis				
FDA approved?	No	Yes	No	No
Clinical outcomes	No studies	Favorable	No studies	No studies
Radiographic outcomes	No studies	Favorable	No studies	No studies
HRQOL outcomes	No studies	No studies	No studies	No studies
Ankylosing Spondylitis				
FDA approved?	No	Yes	No	No
Clinical outcomes	Favorable	Favorable	No studies	No studies
Radiographic outcomes	Favorable	Favorable	No studies	No studies
HRQOL outcomes	Favorable	Favorable	No studies	No studies

Table 3 summarizes the range of response effects from the numerous clinical trials and systematic reviews included in this analysis. Relative to placebo, etanercept, infliximab, and adalimubab show significant improvement in the proportion of patients achieving at least 20% improvement in symptoms and function (approximately 2-3 times as many patients with treatment achieve this threshold, relative to placebo). Greater increases in the proportion of patients achieving 50% and 70% improvement were seen when comparing these therapies with placebo. Anakinra did not show a significant effect on ACR-20 over placebo in the one trial included in this analysis (Cvetovic et al, 2002), but did show a significant effect on the

proportion of patients achieving 50% and 70 % improvement in function. Studies comparing etanercept to the standard methotrexate therapy showed a significant improvement in the proportion of patients achieving 20%, 50% and 70% improvement. Several studies compared treatment with both a biological and methotrexate to methotrexate alone. In these studies, etanercept, infliximab and adalimubab, when administered with methotrexate, all showed significant improvement in symptoms relative to treatment with methotrexate alone. Anakinra with methotrexate did not result in significant improvements to the ACR-20, but did result in improvements in the ACR-50 and -70, relative to methotrexate alone.

Biological therapies have a profound protective effect on bone erosion. All of the clinical trials involving radiographic measures of bone erosion show a 6-fold to 50-fold decrease in the amount of joint damage. In some cases, long-term studies of 1-2 years showed a complete and sustained cessation of bone degeneration. One study evaluated the effects of etanercept with methotrexate to the use of etanercept alone (Klareskog et al, 2004). In this case, there was no difference in the degree of bone erosion, implying that the addition of methotrexate to the treatment did not improve the effect of etanercept on the joints.

The evidence regarding the effects of biologic agents on quality of life measures was less consistent than the evidence for the clinical effects. Studies that evaluated quality of life as an outcome showed that patients undergoing treatment with biological therapies had improved health-related quality of life, but these studies were not consistently statistically significant. In one systematic review of studies comparing etanercept with methotrexate therapy to methotrexate alone, the control group reported slightly better quality of life scores than the treatment group (Blumenauer et al., 2003).

Table 3. Summary of Range of Treatment Effects, All Trials

Treatment	Control Group	ACR-20 Tx% Control %	ACR-50 Tx % Control %	ACR-70 Tx % Control %	Radiographic Sharp Score Rx Control	Quality of Life Tx Control
Etanercept	Placebo	33%-75% 11%-14%	39%-50% 3%-7%	4%-15% 0%-1%	No Data	**HAQ Mean Δ** −0.5 −0.6 Control **HAQ Score** −6-33 Rx −6-6 Control
Etanercept	MTX	61%-72% 65%	32%-49% 43%	16%-25% 22%	No Data	**HAQ** 36-53 Rx 50 Control
Etanercept + MTX	MTX	71% 27%	39% 3%	15% 0%	0.54 2.80	**HAQ** 47 Rx 27 Control
Etanercept + MTX	Etanercept	No Data	NoData	No Data	0.54 0.52	No Data
Infliximab	Placebo	44%-79% 8%-20%	26%-58% 5%-8%	8%-18% 0%-2%	0.5 4	**HAQ** −30-0.52 Rx −0.18 Control **SF 36** 7.1-13.3 Rx 5.1 Control
Infliximab + MTX	MTX	40%-59% 16%-20%	27%-38% 5%-8%	8%-19% 0%-2%	.50 4-25	No Data
Adalimumab	Placebo	49%-56% 10%	No Data	No Data	No Data	No Data
Adalimumab + MTX	MTX	48%-66% 15%	32%-43% 8%	19%-27% 5%	No Data	No Data
Anakinra	Placebo	26%-43% 27%-43%	2%-17% 7%-13%	0%-4% 1%-7%	No Data	No Data
Anakinra + MTX	MTX	19%-42% 19%-23%	11%-24% 4%-8%	5%-10% 0%-2%	No Data	No Data

Key:
ACR-20/50/70 = American College of Rheumatology Percent Improvement Score (percentage of patients reaching 20%/50%/70% improvement)
Δ = Change
HAQ = Health Assessment Questionnaire (Higher number indicates poorer health status and quality of life)
MTX = methotrexate
Rx = prescription
Sharp Score (Higher number indicates more bone damage)
SF-36 = Medical Outcomes Study 36-item short form (Higher number indicates better health-related quality of life)

Safety Considerations

All drugs have side effects and contain an element of risk. Consideration of the effectiveness of any therapy must include a discussion about the potential risks involved with the treatment, relative to its potential benefits. Table 4 summarizes the common side effects and uncommon adverse events reported for the four biologic treatments and the DMARD methotrexate. The effectiveness literature is consistent about the potential risks involved with the BRMs. The most common complication for all the treatments is a local reaction at the injection site, including minor irritation and, occasionally, infection. This is true for the self-administered injectables and the infused therapy. The infused therapy (infliximab) also carries a risk of infusion reaction, which can result in death. Among the more serious complications for all the therapies are an increased risk of infection, particularly pneumonias and tuberculosis, some of which have resulted in death. In addition, these therapies may carry a risk of malignancies, including lymphomas and other cancers. The standard alternative therapy to the biological agents is methotrexate, which also carries some risks, including liver damage, bone marrow suppression (low white blood cell counts), and inflammation in the lungs or other tissues. Methotrexate in low doses has not been shown to increase the risk of cancer.

Table 4. Side Effects and Complications of Therapy

Treatment	Common Side Effects	Uncommon Complications
Adalimubab	☐ Injection site infection or irritation	☐ Infections (tuberculosis) ☐ Malignancies ☐ Systemic lupus erythematosus syndrome ☐ Adverse effects on patients with heart disease ☐ Demyelination/neurological complications ☐ Hematologic complications
Anakinra	☐ Injection site infection or irritation	☐ Infections (upper respiratory, sinusitis, pneumonia, cellulitis) ☐ Low white blood cell count
Etanercept	☐ Injection site infection or irritation	☐ Infections (upper respiratory infection, sinusitis, pyelonephritis (kidney), bronchitis, pneumonia, cellulitis, sepsis) ☐ Death from serious infection ☐ Malignancies ☐ Systemic lupus erythematosus ☐ Adverse effects on patients with heart disease ☐ Multiple sclerosis-like changes/neurological complications ☐ Hematologic complications
Infliximab	☐ Dyspnea (shortness of breath) ☐ Urticaria (skin irritation) ☐ Headache ☐ Upper respiratory infections ☐ Nausea	☐ Infections (histoplasmosis, coccidiolycosis, or reactivation of tuberculosis) ☐ Infusion reaction ☐ Malignancies ☐ Systemic lupus erythematosus ☐ Adverse effects on patients with heart disease ☐ Multiple sclerosis-like changes/neurological complications ☐ Hematologic complications
Methotrexate		☐ Bone marrow suppression ☐ Liver dysfunction

Sources: Braun, Brandt, et al (2003, 2005), Bresnihan (2001), Calabrese et al. (2002), Clark et al. (2004), Fleischman et al. (2002), Gomez-Reino et al. (2003), Ledingham (2005), Luong et al. (2000), Moreland et al. (2001), Mpofu et al. (2005), Scheinfeld et al. (2004).

Is One Biologic Response Modifier Better Than Another?

There are no head-to-head studies comparing individual BRMs to one another. However, several studies have observed the response of patients who have changed from one biological treatment to another due to lack of effectiveness of the initial therapy (Table 5). These studies clearly indicate that there is no clinical or statistical difference in response to therapy when switching from one BRM to another. In other words, lack of response to one of the four biological therapies does not predict lack of response to the others. This is true of both the infused therapy and the self-injectable forms. One study provided an indirect comparison among three of the four BRMs using a statistical method of data pooling to estimate relative treatment effects for each drug from individual clinical trials (Hochberg et al., 2003). This study found no significant clinical or statistical difference in outcomes between the three agents.

Although there is no evidence of effectiveness differences among the four therapies, there are structural, clinical, and cost differences among the treatments. Because the biological therapies are proteins, responses to each agent may be significantly different from patient to patient. Specifically, as shown in the literature, some patients may respond better to one treatment or another. Additionally, allergic or antibody response to each agent may differ significantly in terms of incidence, severity, and effect on the anti-inflammatory properties of the therapy. The different treatment modalities of these agents have implications on treatment cost (for providers and patients), patient convenience, and patient preference. Infliximab must be infused intravenously in an outpatient clinic or infusion center, whereas the other three are self-injectable and can be administered by the patient. Costs for the infused therapy are higher than those of the self-injectable therapy, and this might be a significant consideration for some patients. Additionally, there are some patients who may experience difficulty with self-administration of these therapies due to the disabling effects of the disease on grasp and hand function. Conversely, some patients may prefer the convenience of the self-administered modality over the time investment involved in the infusion process.

Table 5. Studies Evaluating the Effectiveness of Changing from One Biologic Response Modifier to Another

Study	Treatments	Findings	Notes
Hansen et al., 2004 Retrospective study	Etanercept (no response)→ infliximab vs infliximab with no prior treatment	• Patients with prior unsuccessful treatment with etanercept responded to infliximab	Infliximab dose was higher
Haraoui et al., 2004 Prospective study	Infliximab (no response)→ etanercept No comparison group	• Patients with prior unsuccessful treatment with infliximab responded to etanercept	
Hochberg, et al., 2003	Etanercept vs adalimubab Infliximab vs adalimubab Etanercept vs infliximab	• No difference • No difference • No difference	Indirect comparisons using statistical modeling

Table 5. Studies Evaluating the Effectiveness of Changing from One Biologic Response Modifier to Another

Study	Treatments	Findings	Notes
van Vollenhoven et al., 2003 Registry Data	Etanercept (no response) → infliximab Infliximab (no response) → etanercept	• Patients with prior unsuccessful treatment with etanercept responded to infliximab • Patients with prior unsuccessful treatment with infliximab responded to etanercept	
Ang et al., 2003	Etanercept (no response)→infliximab Infliximab (no response)→ etanercept	• Patients with prior unsuccessful treatment with etanercept responded to infliximab • Patients with prior unsuccessful treatment with infliximab responded to etanercept	

Limitations of Analysis

There are no clinical trials directly comparing the four biological agents to one another. Each therapy has been shown effective in treating rheumatic disease, relative to either a placebo or a non-biological agent such as methotrexate. Thus, there is no clear scientific evidence to guide decisions such as preferential prescribing or benefit design.

Conclusions

The evidence demonstrates that BRMs are more effective than standard treatments for the treatment of RA, PsA, and AS. There is indirect evidence that the four biologic agents are interchangeable with respect to clinical response. Patients who do not respond to one of these four agents might reasonably expect better results with treatment from one of the other agents, regardless of method of administration. In addition to evidence of effectiveness, safety considerations, and cost, practical access to the therapies and patient preferences should be considered when setting treatment policy.

II. UTILIZATION, COST, AND COVERAGE IMPACTS

The California Health Benefits Review Program (CHBRP) assesses the utilization, cost, and coverage impacts of a proposed health benefit(s) mandate based on criteria specified under Assembly Bill 1996 (2002) (AB 1996), *California Health and Safety Code (Section 127660, et seq*.) This section is organized by, and addresses, each criterion specified in the statute.

For the purposes of this analysis, CHBRP assumes by prohibiting the designation of a preferred drug, all health service plans must set similar requirements for the use of biological therapies. The bill does not specify whether requirements such as prior authorization, cost sharing, or medical necessity cannot be used by health plans. CHBRP assumes that health plans and insurers

would be prohibited from differentiating among these biologic drugs by using tiered formularies (in which patients face lower out-of-pocket expenditures for preferred drugs) and step therapy (in which non-preferred drugs can be used only after the preferred drug has been tried and shown to be ineffective, have side effects, or otherwise be contraindicated). All BRMs are assumed to be available on insurers' outpatient drug formulary with equal patient cost-sharing obligations.[6]

An alternative option that could fulfill the conditions of SB 913 would be to assume that health plans and insurers would be barred from using tiered formularies or step therapy for these drugs. This interpretation of SB 913 would likely have different cost and utilization impacts.

In the following analysis, the population of Californians who are covered by Knox-Keene and Department of Insurance health service plans, as well as health maintenance organization (HMO) enrollees covered by California Public Employees' Retirement System (CalPERS), Medi-Cal, and Healthy Families programs are included. Effective January 1, 2006, Medicare Part D will offer drug coverage for all Medicare enrollees and Medicare supplement plans will no longer be allowed to offer prescription drug coverage. This analysis reflects the fact that SB 913 will only affect those not eligible for drug coverage through Medicare Part D.

Present Baseline Coverage, Utilization, and Costs

Current coverage of the mandated benefit (3(i))

Coverage data were collected in March 2005 by CHBRP from six of the seven major California health insurance and managed care organizations. There was one major health plan from which CHBRP was unable to gather coverage information. The six organizations provide coverage for biological treatments for rheumatic disease; however, the data collected also showed that plans currently identify at least one preferred drug within the biological class of drugs for the treatment of rheumatic diseases. Additional inquiries of informed sources by CHBRP provided formulary information of major pharmacy benefit management (PBM) administrators, who developed and maintained drug formularies for most health plans in California. These PBMs reported that all formularies they managed included biological treatments for rheumatic disease and identified at least one preferred drug within the biological class of drugs.

This mandate applies only to plans that already provide a prescription drug benefit. All individuals covered by the public payers included in CHBRP analysis have prescription drug coverage. Some private health plans in California offer optional plans that do not cover prescription drugs. These optional plans are not subject to this mandate. CHBRP estimates that 95% of all insured populations in California have coverage for prescription drug benefits, and so would receive coverage for these mandated benefits if this bill is signed into law.

Currently, there are four FDA-approved biological therapies on the market: etanercept (Enbrel©), infliximab (Remicade©), adalimumub (Humira©), and anakinra (Kineret©). Etanercept,

[6]As suggested earlier, infliximab's status on the pharmaceutical benefit formulary is assumed to be irrelevant to SB 913 because it is reimbursed under the medical benefit as an infusion procedure.

adalimubab, and anakinra are self-injectable by the patient and are covered by drug benefits. Self-injectable therapies are purchased by the patients directly from pharmacies in person or by mail.

Infliximab is infused either in the physician's office or in an outpatient setting and is thus considered a medical benefit and not a drug benefit by most plans surveyed. Only drug benefits will be reimbursed by health plans under the proposed mandate. Also, infused therapies are ordered by physicians or outpatient facilities on behalf of the patients and maintained for infusion. The physician or the outpatient facility may purchase the drug through channels other than the health plan and therefore are not subject to formulary criteria. Consequently, infliximab is not expected to be subjected to this mandate by insurers and its utilization and costs are not expected to change.

A significant or dominant pattern in "preferred status" or formulary requirements is not apparent in the coverage data collected. At least one biological therapy is listed on preferred status, however, the preferred drug varies considerably among insurers. The copays and coinsurance amounts that apply to these drugs also vary considerably. All insurers surveyed used requirements such as prior authorization and step therapy for at least some of these drugs.

Current utilization levels and costs of the mandated benefit (Section 3(h))

The data used in this and the following sections are from the most recent Milliman claims database nationally (2003), which includes about 7.4 million individuals from the commercially insured population in the United States.

The prevalence of RA among the general adult population nationally is estimated at 1% or 2.1 million individuals for RA, 0.1% to 0.2% for AS, and between 0.06% and 0.1% percent for PsA. However, the majority of these populations are 65 or older. The California prevalence of these rheumatic diseases for the population subject to this mandate (0-64 years of age) is not established. Thus, estimates of prevalence used in this analysis are from Milliman claims data.

The overall prevalence of the three rheumatic diseases studied in the population under 65 years of age covered by private and public insurers is estimated at about 101,000 individuals (0.55%) out of the total insured population subject to this mandate (20,014,000) (Table 8). An equal rate of rheumatic disease is assumed for both private and public payers, due to lack of prevalence data for public payers. It is possible that the Medi-Cal program may have a larger number of individuals with rheumatic disease due to the high rates of disability caused by these diseases.

About 16,000 or 0.09% of the total insured population are estimated to receive biological therapies and have RA, PsA, or AS, three conditions for which biological therapies are indicated by the FDA.

Among the population receiving biological therapies that have these three rheumatic diseases, most receive etanercept (71.59%). Infliximab is the second most widely received drug at 26.27%. Anakinra is used by 4.54%, and adalimubab by 0.03%. The distribution by type of drug

is based on 2003 data -- it is likely these percentages have changed since then.

The estimated annual cost of each biologic drug per insured person ranges from the low of $14,370 for adalimubab to the high of $21,445 for Anakinra (Table 7). The average annual prescription cost for all four biologic therapies per insured person is $16,234. The costs were developed by assuming a 16% discount on the average wholesale price (AWP) of the drug, assuming a full year of treatment. The cost also includes $131 for physician administration of these drugs to patients. A small increment of this cost is due to the few patients using self-injectables who have the drug injected in a physician's office. The vast majority of the cost of administration of the drug to patients is for the infused drug, inflixmimab.

The extent to which costs resulting from lack of coverage are shifted to other payers, including both public and private entities. (Section 3(f))

Among individuals with prescription drug benefits, all payers cover biological therapies, albeit with various cost sharing limits and requirements. Consequently, there would be no cost shifting among payers, public or private, due to this mandate.

Public demand for coverage (Section 3(j))

CalPERS, which provides health insurance and other benefits to state and some local government employees, is the largest purchaser of private health insurance in California. CalPERS's decisions regarding the inclusion or exclusion of particular services among the health insurance benefits it provides is one measure of the public demand for those services. For CalPERS's self-insured PPO plan, prior authorization is required for etanercept (Enbrel) and its use is coordinated through a specialty pharmacy service. The 2005 Evidence of Coverage (EOC) makes no mention of other BRMs, although this document does include the plan's formulary. For CalPERS HMO plan offered by Blue Shield, BRMs are covered on a tiered formulary that includes a lower patient copayment for a preferred BRM. The use of restrictions and financial incentives to steer patients toward a particular drug suggests that CalPERS benefit design does not reflect any public demand for the abolition of preferred status as proposed by SB 913. However, this is only one potential measure of public demand. A full examination of other measures, such as the potential consideration of copayments and restrictions on these drugs in labor negotiations or the design of other California health insurance benefits, is beyond the scope of CHBRP's 60-day timeframe for analyzing this bill.

Impacts of Mandated Coverage

How will changes in coverage related to the mandate affect the benefit of the newly covered service and the per-unit cost? (Section 3(a))

Supply of services, effectiveness, and unit costs

There is no evidence that there are current supply constraints on availability of biological therapies in the health care market in California or nationally. The supply of these biological therapies is not expected to change as the result of this mandate. Increased advertising efforts by manufacturers to consumers and physicians as a direct consequence of this mandate is expected to be small with little perceptible change in increased utilization or unit costs of these drugs.

Medical effectiveness of biological therapies is not expected to be affected by this mandate, because no single biological therapy has proven to have a therapeutic advantage over the others in the class, and no change in pattern of utilization of these drugs is predicted in this analysis.

SB 913 is expected to change the unit costs of the affected drugs. Applying similar criteria to all biological therapies would lead to loss of "preferred status." This loss will likely affect the ability of health plans to negotiate reduced rates for the 'preferred drug' and result in loss of discounts or rebates from manufacturers of biological therapies. The impact of savings from manufacturer rebates is estimated to range from 2% to 21% of total savings depending on the drug. (GAO, 2003) This loss is expected to result in an across the board increase of an estimated 5% in the unit costs for self-injectables in this class of biological therapies, based on data collected from major PBM companies in the state (Freudenheim, 2005). This lower level of increase in unit costs is due to other savings options available to health plans.

The increase in unit costs of these drugs is expected to translate into higher premiums for employers and employees as well as higher cost sharing by patients.

How will utilization change as a result of the mandate? (Section 3(b))

Overall utilization

The overall utilization of biological drugs for persons with rheumatic disease and coverage for prescription benefits is not expected to change as a consequence of this bill. Any increases in utilization due to additional advertising of manufacturers of these biological therapies to increase their market share is likely to be counteracted by formulary criteria such as prior authorization and increased copays imposed by health plans. The scientific evidence cited in the medical effectiveness analysis suggests that BRMs are interchangeable in terms of effectiveness. Thus the law might lead to some degree of switching among the three self-injectable drugs when none is preferred by the health plan. Such switching should have minimal or no effect on overall utilization of these drugs. However, it is a factor in the negotiating position of plans relative to competing products, leading to a change in unit cost of these drugs.

Complementary, alternative, and substitution effects

SB 913 is not expected to impact use of complementary, alternative, or substitute services for the rheumatic diseases examined. In the majority of cases, biological therapies are the third and final class of drugs available for the treatment of rheumatic diseases. Individuals using these drugs are generally those who did not sufficiently benefit or tolerate alternative treatments.

To what extent does the mandate affect administrative and other expenses? (Section 3(c))

CHBRP estimates this mandate would increase the administrative expenses for health plans, but not disproportionately to the increase in health care costs. Health care plans and insurers include a component for administration and profit in their premiums. The estimated impact of this mandate on premiums includes the assumption that plans and insurers will apply their existing administration and profit loads to the marginal increase in health care costs produced by the mandate. Therefore, although there may be administrative costs associated with the mandate, administrative costs as a proportion of the premium would not change.

Impact of the mandate on total health care costs (Section 3(d))

SB 913 is expected to increase total health care expenditures from $59,016,688,000 to $59,028,139,000 for the 20,014,000 individuals affected by this mandate; an increase of $11,451,000, which equals 0.019% of total expenditures for this insured population (Table 1).

Costs or savings for each category of insurer resulting from the benefit mandate (Section 3(e))

Total expenditures, by payer

SB 913 will lead to changes in total annual expenditures, for each major category of payer, by the following amounts and percentages:

- Private employer premiums: $6,081,000 (0.017%);
- CalPERS employee premiums: $ 1,820,000 (0.018%);
- Individually purchased insurance premiums: $1,111,000 (0.029%);
- CalPERS premiums: $388,000 (0.018%);
- Medi-Cal: $982,000 (0.033%);
- Healthy Families: $42,000 (0.012%); and
- Out-of-pocket expenditures (copays and deductibles): $1,027,000 (0.025%).

Employer premiums and individuals who privately purchase insurance policies will recognize the largest premium increases due to this mandate. Among public payers, the Medi-Cal program will realize the largest increase in premiums. These costs represent the short-term (one-year) increases and do not account for potential long-term impact of this mandate on cost of biologic therapies.

Impact on access and health service availability (Section 3(g))

SB 913 is not expected to impact overall access to biological therapies. The total predicted annual increase of $11,451,000, for the 20,014,000 covered persons, amounts to an overall increase of $0.05 per person per month in individual costs (employee share of premium and copayments) across the board.

III. PUBLIC HEALTH IMPACTS

Present Baseline Information

A literature review was conducted to assess the baseline data on prevalence of RA, AS, and PsA. There have been no California-specific prevalence studies for any of the three diseases. Additionally, there were no prevalence estimates found specific to the under 65 population, however, other national and international estimates are available. For RA, the consensus in the literature is that the prevalence of RA in the United States is approximately 1%, thereby affecting about 2.1 million people nation-wide (Abdel-Nasser et al, 1997; Lawrence et al, 1998, Silman and Hochberg, 2001). RA is more common in women, older adults, and Native American populations (Silman and Hochberg 2001).

No nation-wide estimates of the prevalence of AS or PsA have been made in the US (Lawrence et al., 1998; Silman and Hochberg, 2001). The prevalence estimates for these diseases are based primarily on European estimates and a study conducted in Rochester, Minnesota, with prevalence estimates for AS at 0.07% for males and 0.19% for females and estimates of PsA ranging between 0.08% and 0.12% (Silman and Hochber, 2001). Some researchers have argued that these figures substantially underestimate the prevalence of PsA and in the absence of broadly accepted diagnostic criteria, the exact prevalence remains unknown (Gladman, 2005).

Although the measures reported in the literature estimate the prevalence within the overall population, Milliman's claims data from large private insurers nationwide were used to estimate the number of individuals within the privately insured population receiving treatment for these three rheumatic diseases in California. The claims database included 7.4 million people under age 65 years and suggests 0.49% of the insured population have been diagnosed and are receiving treatment for RA and 0.06% for either AS or PsA. Due to the positive relationship of RA and age, it is not surprising that the estimates from the claims data (containing only information on the under-65 population) are lower than those reported in the literature. Based on the claims data, among the insured population that would be affected by SB 913 in California (approximately 20 million), the number of people expected to need treatment for these three rheumatic diseases is about 100,000.

Impact of the Proposed Mandate on Public Health

Impact on Community Health (Section 1A)

There are a number of ways in which the treatment for rheumatic diseases can be evaluated such as a reduction in pain, swelling, and physical disability, as well as delays or prevention of irreversible joint damage (Scott 2004). Section I reviews the major health outcomes that have been examined in the literature with respect to the use of BRMs in the treatment of rheumatic diseases:

- ACR Response Rate: A composite measure of percentage improvement in response to therapy, including the number of tender joints, the number of swollen joints, patient and physician assessment of disease status, questionnaire estimate of disability, and laboratory test markers. The ACR-20 measures a 20% improvement in this measure.
- Radiographic Sharp Score: A measure of the progression of structural joint damage based on the evaluation of X-rays or MRIs.
- Health-related Quality of Life: A survey-based measure of a patient's perceptions of how an illness affects day-to-day life and functionality.

There is no projected increase in utilization of the four drugs used to treat RA, AS, or PsA. Therefore we conclude that this mandate will have no impact on the health of the community.

Impact on Community Health where Gender and Racial Disparities Exist (Section 1B)

A literature review was conducted to assess whether gender or racial disparities existed with regards to the three rheumatic diseases discussed in this report: RA, AS, and PsA. Both gender and racial disparities were identified with most of the literature focusing on RA and much less on AS and PsA.

Gender Disparities

In examining gender differences, the prevalence of RA is two to three times higher in women than in men (Abdel-Nasser et al., 1997; Lawrence et al., 1998; Rasch et al., 2003; Sangha, 2000; Voulgari et al., 2004). Brennan and Silman (1995) attribute the increased risk of RA in women to hormonal levels and state that the gender gap narrows as age increases, particularly after women reach menopause. For AS, the gender differences are reversed where men are approximately three times more likely to be diagnosed compared to women (Sangha, 2000). No gender differences were reported for the prevalence of PsA (Gladman et al., 2005).

In addition to prevalence differences, researchers have examined gender disparities in health outcomes. Anderson (1996) conducted a literature review of mortality among those with RA and found that there was not a clear association between gender and mortality rates. Gender does appear to be a factor in other treatment and health outcomes for patients with rheumatic diseases, with women having longer lengths of stay after knee and hip surgery (Escalante and Beardmore, 1997), and higher levels of depressive symptoms (Dowdy et al., 1996). Men were found to have

more severe symptoms with AS (Jiminezbalderas and Mintz, 1993).

The Milliman national claims data also show gender differences in the use of BRMs for the treatment of rheumatic diseases. Table 6 shows the female to male ratio for the use of biologicals for RA and AS/PsA. Confirming the findings in the literature, the claims data show a higher utilization of biologics for females for the treatment of RA and more males using biologics for the other two diseases.

Table 6. Female to Male Ratio of Rheumatic Disease Diagnoses

Age	RA	AS/PsA
0-17	2.35	0.81
18-34	2.93	0.57
35-44	2.64	0.57
45-54	2.53	0.67
55-64	2.28	0.77

Source: Milliman 2003, National Claims Database.

Racial Disparities

The most prominent finding in this area is the high prevalence of RA and other rheumatic diseases among Native American groups in the United States (Abdel-Nasser et al., 1997; Peschken and Esdaile, 1999; Molokia and McKeigue, 2000). Abdel-Nasser et al (1997) report that Native Americans have the highest prevalence of RA world-wide, and RA is at least twice as common in Native Americans compared with North American Whites. There are also substantial differences in prevalence of RA and other rheumatic diseases among Native Americans groups, with very high rates of RA found in Pima Indians, Chippewa Indians, and Inupiat Indians (Silman and Hochberg, 2001).

Little research was found on racial disparities in the treatment or outcomes of rheumatic diseases. Escalante and Beardmore (1997) report that RA patients of non-White race had longer lengths of stay following knee and hip surgery and De Roos and Callahan (1999) found that the odds of work disability was higher for RA patients of non-White race. Additionally, researchers have found that Blacks are underrepresented in clinical trails and genetic studies of RA (Bridges et al., 2003; Dunbar-Jacobs et al., 2004).

Because there is no projected increase in utilization in the four drugs used to treat RA, AS, or PsA, this mandate will not impact the gender and racial disparities in treatment of rheumatic diseases.

Reduction of Premature Death and the Economic Loss Associated with Disease (Section 1C)

Premature Death

Patients with RA have higher standardized mortality rates and an estimated 5 to 10 years of reduced life expectancy (Anderson, 1996; Kvien, 2004). Among those with RA, those with more severe symptoms have elevated rates of mortality (Wolfe et al., 1994;Yelin et al., 2002). Patients with AS and PsA also have increased mortality, particularly for mortality associated with cardiovascular disease (Wong at al, 1997; Peters et al. 2004). No studies were found to examine the effect of BRMs on the mortality for patients with RA, AS, or PsA. In addition, there is no projected increase in utilization of the four drugs used to treat RA, AS, or PsA based on this mandate. Therefore we conclude that this mandate will have no impact on the reduction of premature death.

Indirect Productivity Costs

Most of the literature on the indirect costs associated with rheumatic disease focuses on RA as opposed to the less common AS and PsA. According to the Arthritis Foundation, RA costs the U.S. economy approximately $86.2 billion per year. Indirect cost estimates of RA can include the loss of ability to work, reduced productivity after returning to work, the value of services of unpaid care providers, as well as quality of life measures, psychological impacts, and other "intangible" costs that are more difficult to estimate and are not included in traditional cost of illness estimates (DHHS, 2000; Emery, 2004; Kvien, 2004). Based on various studies of indirect costs associated with RA, Kvien (2004) reports a range of $1,082 to $33,000 per patient per year, with a substantial proportion attributed to lost productivity.

Indirect cost components such as work disability have been found to be associated with the level of disability in RA patients (Newhall-Perry et al, 2000). While some research has found that pharmacological treatment for RA results in better long-term disability outcomes (Fries et al. 1995), no literature was identified to show that the use of BRMs was associated with work disability. Additionally, a literature review conducted by de Croon et al. (2004) found that biomedical variables associated with RA did not consistently predict work disability but rather a variety of individual factors influence whether or not a patient with RA will experience work disability.

There is no projected increase in utilization of the four drugs used to treat RA, AS, or PsA. Therefore we conclude that this mandate will have no impact on the reduction of economic loss associated with disease.

TABLES

Table 7. Costs of Biological Therapies

	Before Mandate	After Mandate	Increase/ Decrease	% Change After Mandate
Average annual costs of biologic therapies	$16,234	$16,818	$584	4%
Entanercept	$15,099	$15,852	$754	5%
Adalimumab	$14,370	$15,089	$719	5%
Anakinra	$21,445	$22,517	$1,072	5%
Infliximab	$18,698	$18,698	$0	0%

Source: California Health Benefits Review Program, 2005.

Table 8. Baseline (Pre-Mandate) Per Member Per Month Premium and Expenditures, California, Calendar Year 2005, by Insurance Plan Type

	Large Group				Small Group				Individual		Public				
	HMO	PPO	POS	FFS	HMO	PPO	POS	FFS	HMO	PPO	CalPERS HMO	Medi-Cal HMO Over 65	Medi-Cal HMO Other	Healthy Families HMO	Total Annual
Population Currently Covered	7,400,000	3,220,000	457,000	19,000	1,498,000	875,000	454,000	4,000	887,000	1,065,000	795,000	0	2,846,000	494,000	20,014,000
Average Portion of Premium Paid by Employer	$0.0382	$0.0352	$0.0384	$0.0295	$0.0329	$0.0332	$0.0317	$0.0317	$0.0000	$0.0000	$0.0407	$0.0495	$0.0288	$0.0070	$7,493,000
Average Portion of Premium Paid by Employee	$0.0102	$0.0072	$0.0085	$0.0078	$0.0170	$0.0104	$0.0166	$0.0065	$0.0554	$0.0408	$0.0077	$0.0000	$0.0000	$0.0008	$2,930,000
Total Premium	$0.0484	$0.0424	$0.0469	$0.0373	$0.0499	$0.0435	$0.0483	$0.0381	$0.0554	$0.0408	$0.0484	$0.0495	$0.0288	$0.0078	$10,422,000
Covered Benefits Paid by Member (Deductibles, copays, etc)	$0.0024	$0.0084	$0.0042	$0.0126	$0.0036	$0.0096	$0.0054	$0.0138	$0.0048	$0.0150	$0.0024	$0.0000	$0.0000	$0.0003	$1,027,000
Benefits Not Covered (2)	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$-
Total Expenditures	$0.0508	$0.0508	$0.0511	$0.0499	$0.0535	$0.0531	$0.0537	$0.0520	$0.0602	$0.0558	$0.0508	$0.0495	$0.0288	$0.0080	$11,450,000

Source: California Health Benefits Review Program, 2005.

Note The population includes individuals and dependents in California who have private insurance (group and individual) or are enrolled in public plans subject to the Health and Safety Code, including CalPERS, Medi-Cal, or Healthy Families.

All population figures include enrollees aged 0-64 years.

Employees and their dependents that receive their coverage from self-insured firms are excluded because these plans are not subject to mandates.

Key: FFS = fee for service; HMO = health maintenance organization; POS = point of service; PPO = preferred provider organization. CalPERS = California Public Employees' Retirement System.

Table 9. Post-Mandate Impacts on Per Member Per Month and Total Expenditures, California, Calendar Year 2005, by Insurance Plan Type

	Large Group				Small Group				Individual		Public				
	HMO	PPO	POS	FFS	HMO	PPO	POS	FFS	HMO	PPO	CalPERS HMO	Medi-Cal. HMO Over 65	Medi-Cal. HMO Other	Healthy Families HMO	Total. Annual
Population Currently Covered	7,400,000	3,220,000	457,000	19,000	1,498,000	875,000	454,000	4,000	887,000	1,065,000	795,000	0	2,846,000	494,000	20,368,000
Average Portion of Premium Paid by Employer	$0.0626	$0.0606	$0.0638	$0.0530	$0.0545	$0.0577	$0.0532	$0.0577	$0.0000	$0.0000	$0.0668	$0.0800	$0.0464	$0.0114	$12,434,000
Average Portion of Premium Paid by Employee	$0.0168	$0.0123	$0.0141	$0.0139	$0.0282	$0.0180	$0.0279	$0.0118	$0.0925	$0.0754	$0.0127	$0.0000	$0.0000	$0.0012	$4,975,000
Total Premium	$0.0795	$0.0729	$0.0779	$0.0670	$0.0827	$0.0758	$0.0810	$0.0695	$0.0925	$0.0754	$0.0795	$0.0800	$0.0464	$0.0127	$ 17,410,000
Covered Benefits Paid by Member (Deductibles, copays, etc)	$0.0028	$0.0099	$0.0049	$0.0148	$0.0042	$0.0113	$0.0063	$0.0162	$0.0056	$0.0176	$0.0028	$0.0000	$0.0000	$0.0003	$ 1,204,000
Benefits Not Covered	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$0.0000	$ -
Total Expenditures	$0.0823	$0.0828	$0.0828	$0.0817	$0.0869	$0.0870	$0.0874	$0.0856	$0.0981	$0.0930	$0.0823	$0.0800	$0.0464	$0.0130	$13,280,000
Percentage Impact of Mandate															
Insured Premiums	0.033%	0.021%	0.027%	0.022%	0.034%	0.025%	0.029%	0.032%	0.043%	0.063%	0.029%	0.034%	0.054%	0.019%	0.032%
Total Expenditures	0.033%	0.021%	0.027%	0.022%	0.034%	0.025%	0.029%	0.032%	0.043%	0.063%	0.029%	0.034%	0.054%	0.019%	0.032%

Source: California Health Benefits Review, 2005.

Note: The population includes individuals and dependents in California who have private insurance (group and individual), or are enrolled in public plans subject to the Health and Safety Code, including CalPERS, Medi-Cal, or Healthy Families.

All population figures include enrollees aged 0-64, except the Medi-Cal population.

Employees and their dependents that receive their coverage from self-insured firms are excluded because these plans are not subject to mandates

Key: FFS = fee for service; HMO = health maintenance organization; POS = point of service; PPO = preferred provider organization. CalPERS = California Public Employees' Retirement System.

APPENDICES

Appendix A
Literature Review Methods

SB 913 is an act to add Section 1374.17 to the Health and Safety Code to read: "*on or after January 1, 2006, no health care service plan shall, with respect to the biologic class of drugs for the treatment of rheumatic disease, limit access to biologic therapies by designating a preferred drug*". SB 913 would also add Section 10127.19 to the Insurance Code to read "*on or after January 1, 2006, no health or disability insurer contracting to provide coverage for drugs shall, with respect to the biologic class of drugs for the treatment of rheumatic disease, limit access to biologic therapies by designating a preferred drug"*.

Appendix A describes the literature search for studies on the medical effectiveness of etanercept, infliximab, adalimubab, and anakinra for the treatment of RA, PsA, and AS.
This appendix also discusses the outcomes used in analysis of the mandate.
To "grade" the evidence for all outcome measures, the CHBRP effectiveness team uses a system with the following categories:

1. Favorable (statistically significant effect): Findings are uniformly favorable, and many or all are statistically significant.
2. Pattern toward favorable (but not statistically significant): Findings are generally favorable, but there may be none that are statistically significant.
3. Ambiguous/mixed evidence: Some findings are significantly favorable, and some findings with sufficient statistical power show no effect.
4. Pattern toward no effect/weak evidence: Studies generally find no effect, but this may be due to a lack of statistical power.
5. No effect: There is statistical evidence of no clinical effect in the literature with sufficient statistical power to make this assessment.
6. Unfavorable: No findings show a statistically significant benefit, and some show significant harms.
7. Insufficient evidence to make a "call": There are very few relevant findings, so that it is difficult to discern a pattern.

Studies were identified from PubMed (January 1985-January2005) and Cochrane databases. Only English language studies were included in the analysis. The initial search terms were "Arthritis, Rheumatoid", and "Immunologic and Biological Factors". The *Medical Subject Headings* (MeSH) terms used by the librarian in the PubMed search were:

Arthritis, Rheumatoid/ drug therapy
Arthritis, Juvenile Rheumatoid/drug therapy
Spondylitis, Ankylosing/ drug therapy
Arthritis, Psoriatic/drug therapy
Psoriasis/drug therapy
Methotrexate/economics
Methotrexate/therapeutic use

Biological Response Modifiers/ therapeutic use
Antibodies, Monoclonal/therapeutic use
Immunoglobulin G/therapeutic use
Antirheumatic Agents/ therapeutic use
Antirheumatic Agents/adverse effects
Antirheumatic Agents/administration
Methotrexate/therapeutic use
Receptors, Tumor Necrosis Factor/administration & dosage
Receptors, Tumor Necrosis Factor/therapeutic use
Drug Therapy, Combination
Tumor Necrosis Factor-alpha/ antagonists & inhibitors
Comparative Study
Infection/immunology
Lymphoma/chemically induced
Quality of Life
Quality-Adjusted Life Years
Activities of Daily Living
Severity of Illness Index
Safety
Drug Resistance/physiology
Therapeutic Equivalency
Disability Evaluation
C-Reactive Protein/analysis
Cost-Benefit Analysis
Health Care Costs
Cost of Illness
Health Care Costs/statistics & numerical data
Evidence-Based Medicine
Treatment Outcome
Outcome Assessment (Health Care)
Clinical trials
Controlled Clinical Trails
Randomized Controlled Trials
Multicenter Studies

Publication types:
Meta-analysis
Practice Guideline
Randomized Controlled Trial
Clinical Trial

Substance Names:
Infliximab, TNFR-Fc fusion protein, adalimumab,
interleukin 1 receptor antagonist protein

Additional key words were used to identify recent articles that had not yet been assigned MeSH tems:
Infliximab, TNFR-Fc fusion protein, adalimumab, interleukin 1 receptor antagonist protein, kineret, humira, enbrel, remicade, methotrexate , health assessment questionnaire, physical function, total radiographic score*, american college of rheumatology 20% improvement criteria, acr20, modified disease activity score, european league against rheumatism response, duration of morning stiffness, short form 36 healthy survey, tender and swollen joint counts, global assessment*, visual analog scale for pain, disability, c reactive protein level, sharp scoring method, american college of rheumatology core set of variable*, systemic lupus erythematosus disease activity index, systemic lupus activity measure score, sharp scoring method, systematic review, disease activity score, cost effectiveness, efficacy, rheumatoid arthritis, juvenile rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, drug therapy, biological response modifiers, therapeutic use, quality of life, daily activit*, treatment outcome*, safety, self injectable, infused, cost benefit analysis, cost*
* truncation

At least two reviewers screened the title and abstract of each citation returned by the literature search to determine eligibility for inclusion. Full-text articles were obtained and reviewers reapplied the initial eligibility criteria.

A large number of publications were identified through the literature search. The analysis focused on the most recent systematic reviews of the literature for each of the four biologic agents under consideration, in addition to any clinical trials meeting the inclusion criteria, but published after the systematic reviews. Clinical trials published before the systematic reviews and those included in the reviews were excluded from the analysis. In addition, publications relating to diseases other than RA, PsA, and AS were excluded.

At least one systematic review was identified for each of the four therapies, with respect to RA. In addition, we identified a smaller number of clinical trials evaluating the effectiveness of one or more biologic agents with respect to PsA and AS. One systematic review of adalimubab was excluded from the analysis due to difficulty obtaining full text article (Bang et al., 2004, BioDrugs).

Appendix B
Summary of Clinical Trials

Rheumatoid Arthritis

Trial	Therapy	Findings
Blumenauer, et al., 2002 Cochrane Collaboration Review	Infliximab vs placebo Infliximab + Methotrexate vs Methotrexate	Favorable Favorable
Blumenauer et al., 2003 Cochrane Collaboration Review	Etanercept vs placebo Etanercept vs Methotrexate	Favorable Pattern toward favorable
Quinn et al., 2005	Infliximab vs Methotrexate	Favorable
Breedveld et al., 2004	Infliximab + Methotrexate vs Methotrexate	Favorable
Maini et al., 2004	Infliximab + Methotrexate vs Placebo + Methotrexate	Favorable
Klareskog et al., 2004	Etanercept + Methotrexate vs Etanercept Etanercept + Methotrexate vs Methotrexate	Favorable Favorable
Lyseng-Willimason, Foster, et al., 2004 Systematic review	Infliximab + Methotrexate vs Methotrexate + placebo	Favorable Favorable
Lyseng-Willimason, Plosker, et al., 2004 Systematic review	Etanercept + Methotrexate vs Methotrexate + placebo	Favorable Favorable
Durez et al., 2004	Infliximab vs Methylprednisolone	Favorable
van de Putte et al., 2004	Adalimubab vs placebo	Favorable
St, Clair et al., 2004	Infliximab + Methotrexate vs Methotrexate	Favorable
Cohen et al., 2004	Anakinra + Methotrexate vs Methotrexate	Favorable
Keystone et al., 2004	Etanercept vs placebo	Favorable
Genovese et al., 2004	Etanercept + Anakinra vs Etanercept	Pattern toward favorable
Rau et al., 2004	Adalimubab (sc)+ Methotrexate vs Methotrexate + placebo Adalimubab (iv) + Methotrexate vs Methotrexate + placebo	Favorable Favorable
Torrance et al., 2004	Adalimubab + Methotrexate vs Methotrexate	Favorable

Trial	Therapy	Findings
Clark et al., 2004 Health Technology Assessment Systematic Review	Anakinra vs placebo Anakinra + Methotrexate vs placebo	Favorable Favorable
Cohen et al., 2003	Anakinra + Methotrexate vs Methotrexate + placebo	Favorable
Keystone et al., 2003	Adalimubab + Methotrexate vs Methotrexate	Favorable
Nahar, 2003 Systematic Review	Infliximab + Methotrexate vs Placebo + Methotrexate	Favorable Favorable
van de Putte et al., 2003	Adalimubab vs placebo	Favorable
Blumenauer et al., 2003 Systematic Review	Etanercept vs placebo Infliximab vs placebo	Favorable Favorable
Weisman et al., 2003	Adalimubab + Methotrexate vs Methotrexate	Favorable
Hochberg et al., 2003	Etanercept + Methotrexate vs placebo Adalimubab + Methotrexate vs placebo Infliximab + Methotrexate vs placebo	Favorable Favorable Favorable
Den Broeder et al., 2002	Adalimubab vs placebo	Favorable
Cohen et al., 2002	Anakinra + Methotrexate vs Methotrexate + placebo	Favorable
Cvetkovic et al., 2002	Anakinra vs placebo	Favorable
Bresnihan et al., 2002	Anakinra vs placebo Anakinra + Methotrexate vs Methotrexate + placebo	Favorable Favorable
Rau, 2002 Systematic Review	Adalimubab vs placebo Adalimubab vs Methotrexate	Favorable Favorable
Jobanputra et al., 2002 Health Technology Assessment Systematic Review	Etanercept vs placebo Etanercept vs Methotrexate Infliximab vs placebo	Favorable Pattern toward favorable Favorable
Calabrese, 2002	Anakinra vs placebo Anakinra + Methotrexate vs placebo	Favorable Favorable

sc= subcutaneous injection iv=intravenous infusion

Ankylosing Spondylitis

Trial	Therapy	Findings
Mease et al., 2000	Etanercept vs placebo	Favorable
Mease et al., 2002	Etanercept vs placebo	Favorable
Mease et al., 2004	Etanercept vs placebo	Favorable
Mease et al., 2004	Etanercpet vs placebo	Favorable

Psoriatic Arthritis

Trial	Therapy	Findings
Braun et al., 2002	Infliximab vs placebo	Favorable
Gorman et al., 2002	Etanercept vs placebo	Favorable
Brandt et al., 2003	Etanercept vs placebo	Favorable
Davis et al., 2003	Etanercept vs placebo	Favorable
Calin et al., 2004	Etanercept vs placebo	Favorable
Van der Heijde et al., 2005	Infliximab vs placebo	Favorable

Appendix C
Cost Impact Analysis: General Caveats and Assumptions

This appendix describes general caveats and assumptions used in conducting the cost impact analysis. For additional information on the cost model and underlying methodology, please refer to the CHBRP Web site, http://www.chbrp.org/analysis_methodology/cost_impact_analysis.php

The cost analysis in this report was prepared by Milliman and University of California, Los Angeles, with the assistance of CHBRP staff. Per the provisions of AB 1996 (California Health and Safety Code, Section 127660, et seq.), the analysis includes input and data from an independent actuarial firm, Milliman. In preparing cost estimates, Milliman and UCLA relied on a variety of external data sources. The *Milliman Health Cost Guidelines* (HCG) were used to augment the specific data gathered for this mandate. The HCGs are updated annually and are widely used in the health insurance industry to estimate the impact of plan changes on health care costs. Although this data was reviewed for reasonableness, it was used without independent audit.

The expected costs in this report are not predictions of future costs. Instead, they are estimates of the costs that would result if a certain set of assumptions were exactly realized. Actual costs will differ from these estimates for a wide variety of reasons, including:

- Prevalence of mandated benefits before and after the mandate different from our assumptions.
- Utilization of mandated services before and after the mandate different from our assumptions.
- Random fluctuations in the utilization and cost of health care services.

Additional assumptions that underlie the cost estimates presented here are:

- Cost impacts are only shown for people with insurance.
- The projections do not include people covered under self-insurance employer plans because those employee benefit plans are not subject to state-mandated minimum benefit requirements.
- Employers and employees will share proportionately (on a percentage basis) in premium rate increases resulting from the mandate. In other words, the distribution of premium paid by the subscriber (or employee) and the employer will be unaffected by the mandate.

There are other variables that may affect costs, but which Milliman did not consider in the cost projections presented in this report. Such variables include, but are not limited to:

- Population shifts by type of health insurance coverage. If a mandate increases health insurance costs, then some employer groups or individuals may elect to drop their coverage. Employers may also switch to self-funding to avoid having to comply with the mandate.
- Changes in benefit plans. To help offset the premium increase resulting from a mandate, members or insured may elect to increase their overall plan deductibles or copayments. Such changes would have a direct impact on the distribution of costs between the health plan and the insured person, and may also result in utilization reductions (i.e., high levels

of patient cost sharing result in lower utilization of health care services). Milliman did not include the effects of such potential benefit changes in its analysis.

- Adverse Selection. Theoretically, individuals or employer groups who had previously foregone insurance may now elect to enroll in an insurance plan postmandate because they perceive that it is to their economic benefit to do so.
- Health plans may react to the mandate by tightening their medical management of the mandated benefit. This would tend to dampen our cost estimates. The dampening would be more pronounced on the plan types that previously had the least restrictive medical management (i.e., FFS and PPO plans).
- Variation in existing utilization and costs, and in the impact of the mandate, by geographic area and delivery system models: Even within the plan types we modeled (HMO, PPO, POS, and FFS), there are variations in utilization and costs within California. One source of difference is geographic. Utilization differs within California due to differences in the health status of the local commercial population, provider practice patterns, and the level of managed care available in each community. The average cost per service would also vary due to different underlying cost levels experienced by providers throughout California and the market dynamic in negotiations between health plans and providers. Both the baseline costs prior to the mandate and the estimated cost impact of the mandate could vary within the state due to geographic and delivery system differences. For purposes of this analysis, however, we have estimated the impact on a statewide level.

Appendix D
Information Submitted by Outside Parties for Consideration for CHBRP Analysis

In accordance with its policy to analyze evidence submitted by outside parties during the first two weeks of each 60-day review of a proposed benefit mandate, CHBRP received the following submissions:

No information was submitted to date.

CHBRP analyzes all evidence received during the public submission period according to its relevance to the proposed legislation and the program's usual methodological criteria. For more information about CHBRP's methods, to learn how to submit evidence relevant to an on-going mandate review, or to request email notifications of new requests CHBRP receives from the California Legislature, please visit: www.chbrp.org.

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The **National Advisory Council** provides expert reviews of draft analyses and offers general guidance on the program to CHBRP staff and the Faculty Task Force. CHBRP is grateful for the valuable assistance and thoughtful critiques provided by the members of the National Advisory Council. However, the Council does not necessarily approve or disapprove of or endorse this report. CHBRP assumes full responsibility for the report and the accuracy of its contents.

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