CALIFORNIA
HEALTH BENEFITS REVIEW PROGRAM

Analysis

California Senate Bill 912: Biomarker Testing

Summary to the 2021–2022
California State Legislature
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Prepared by
California Health Benefits Review Program
www.chbrp.org

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SUMMARY

The California Senate Committee on Health requested that the California Health Benefits Review Program (CHBRP) conduct an evidence-based assessment of California Senate Bill (SB) 912, Biomarker Testing. SB 912 would require coverage for biomarker testing for the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring of a disease or condition if the test is supported by medical and scientific evidence.

Background on Biomarker Testing.

A *biomarker* is a characteristic that can be measured to specify normal or abnormal health processes or to indicate a condition or disease. These measurements can also be used to determine the effects a treatment is having on a patient. *Biomarker tests* are a way to measure and quantify biomarkers. Nonphysiologic tests are often done in a laboratory using samples of blood, tissue, or other clinical samples to quantify and evaluate the biomarker. In recent years, biomarker testing has been used in the expansion of precision medicine, an approach in which treatment and prevention are based on patients' genetic, environmental, and lifestyle factors rather than a single approach to a disease or condition for all patients. Biomarkers can be tested a variety of ways, including through common blood biomarker tests, individually (single-analyte tests), within a multiplex panel test, or as part of whole genome or exome sequencing.

Biomarker testing can be performed for cancer including prostate, ovarian, colorectal, breast, and lung cancers; Alzheimer's disease; rheumatoid arthritis; type 2 diabetes; and other conditions. Additionally, many biomarkers may be associated with several diseases and conditions. Performing biomarker testing for cancer, for example, enables a provider to accurately match the therapy to an individual patient by focusing on treatments most likely to be effective, and decreases treatment harms by avoiding treatments that are unlikely to result in improvement (e.g., chemotherapy), or may result in an adverse reaction. Biomarker tests can be used across the continuum of care for many diseases and conditions for the purposes of screening asymptomatic individuals, determining the presence of disease (diagnosis), estimating the risk or time to clinical outcomes (prognosis), identifying the likelihood of a patient to benefit from certain therapies (predictive) and to experience therapy-related risks (pharmacogenomics), or for treatment monitoring purposes.

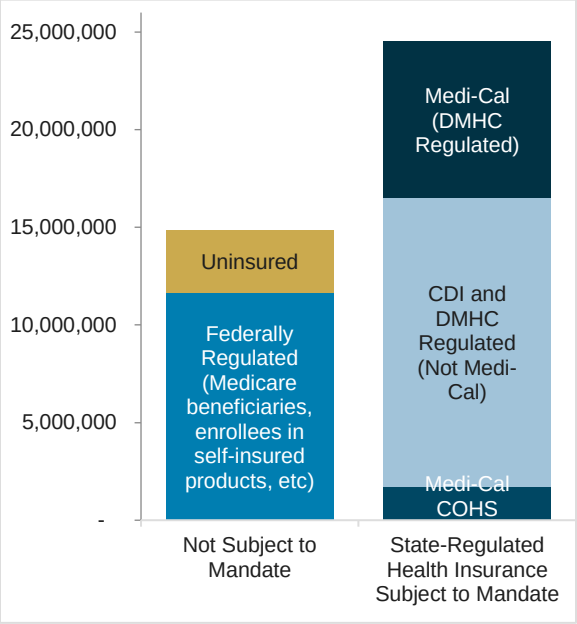
Several studies have found biomarker-driven treatment improves treatment outcomes, including survival rate, and may also be cost-effective, leading to elimination of costs for other less-targeted therapies or offsets in the form of reduced emergency department and in-patient hospital admission. However, the clinical effectiveness of biomarker tests and related treatments varies based on the disease or condition and patient characteristics. Clinical guidelines are one source of information about the effectiveness of biomarker testing and related treatments.

Policy Context.

If enacted, SB 912 would apply to the health insurance of approximately 24.5 million enrollees (62.3% of all Californians) in 2023. This represents enrollees in plans regulated by the Department of Managed Health Care (DMHC) and policies regulated by the California Department of Insurance (CDI), as well as Medi-Cal beneficiaries enrolled in County Organized Health Systems (COHS) or whose benefits are administered by the Department of Health Care Services (DHCS).

Essential Health Benefits (EHBs): Under existing law, plans and policies are required to cover medically necessary diagnostic lab services and ongoing disease management services. Additionally, biomarker testing is broadly covered by California's EHB benchmark plan. Because SB 912 would not require coverage for a new state benefit mandate, it therefore appears not to exceed the definition of EHBs in California.

Figure A. Health Insurance and SB 912



Source: California Health Benefits Review Program, 2022.

Benefit Coverage.

CHBRP queried health plans and policies in California to determine baseline benefit coverage and the impacts of SB 912. **Broadly speaking, all enrollees with health insurance subject to SB 912 have coverage for biomarker testing that is supported by medical and scientific evidence and is determined medically necessary.** There may be some biomarker tests that are newly covered based on the implementation of SB 912, but CHBRP is unable to determine to which biomarker tests this applies.

Utilization and Expenditure Impacts.

Because SB 912 would not result in changes in benefit coverage, there would be no changes in utilization of biomarker tests or changes in health care expenditures as a result of SB 912.

Public Health Implications.

Because enrollees with health insurance subject to SB 912 currently have coverage for biomarker testing generally, there is no measurable public health impact.

However, despite reported benefit coverage of biomarker testing, utilization of biomarker testing differs between commercial and CalPERS enrollees and for Medi-Cal beneficiaries. Literature indicates that the disparities in testing by race or ethnicity, age, and socio-economic status could widen inequities in utilization of biomarker testing if not specifically addressed. Additionally, studies have suggested that clinician barriers — including familiarity with guidelines and knowledge of best practices for use of biomarker testing, expertise in genomic testing, or access to a multidisciplinary specialty team — impact whether patients receive testing.

Long-Term Implications.

CHBRP assumes it is likely that plans and policies will continue to incorporate new clinical guidelines as they become available in future years. While not directly related to SB 912, there are implications for health plans and policies, including Medi-Cal, as new biomarker tests become available and new therapies indicated by biomarker testing become available. Some medications with biomarker-indications cost more than $100,000 annually. Although utilization of these high-cost medications is relatively low, should utilization increase, related health care expenditures would increase as well. As noted previously, evidence supports clinical utility and cost-effectiveness of several biomarker tests and related treatments, which could contribute to offsets in health care expenditures or improved quality of life for enrollees.

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Senate Bill (SB) 912 would require coverage for biomarker testing for the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring of a disease or condition if the test is supported by medical and scientific evidence. Broadly speaking, CHBRP found that all enrollees have coverage for biomarker testing as supported by medical and scientific evidence.

This section provides an overview of biomarker testing and how it is used for treatment decisions in clinical practice.

Biomarker Testing

A *biomarker* is a characteristic that can be measured to specify normal or abnormal health processes or to indicate a condition or disease. These measurements can also be used to determine the effects a treatment is having on a patient. Examples of biomarkers are varied, and include measures such as blood pressure and heart rate, basic metabolic studies such as HbA1c, x-ray findings, and complex histologic values examining genes, proteins, or other molecules that may be a sign of a disease (FDA-NIH, 2016). Biomarkers can be categorized as molecular, histologic, radiographic, or physiologic (e.g., blood glucose is a molecular characteristic, while blood pressure is physiologic) (FDA-NIH, 2016; IOM, 2010).

Biomarker tests are a way to measure and quantify biomarkers. Nonphysiologic tests are often done in a laboratory using samples of blood, tissue, or other clinical samples to quantify and evaluate the biomarker. In recent years, biomarker testing has been used in the expansion of precision medicine, an approach in which treatment and prevention are based on patients' genetic, environmental, and lifestyle factors rather than a single approach to a disease or condition for all patients (FDA, 2018b). Biomarkers can be tested a variety of ways, including individually (single-analyte tests), within a multiplex panel test, or as part of whole genome or exome sequencing. Table 1 provides an overview of the types of biomarker tests commonly used.

Table 1. Overview of Common Biomarker Tests

Test	Description
Common Blood Biomarker Tests (a)	The complete blood count (CBC) is one of the most common blood tests. It is often done as part of a routine checkup. This test measures many different parts of a patient's blood including red blood cells, white blood cells, and platelets. Each test has normal ranges based on age and gender. Labs may also perform blood chemistry tests/basic metabolic panel, blood enzyme tests, lipoprotein panel, blood clotting tests, and bone marrow tests.
Single-Analyte Test (b)	An analyte is a substance being identified or measured in a laboratory test. In biomarker testing, complete testing of one gene that might account for the phenotype (observable characteristic) is referred to as a single-analyte test. Single-analyte testing may be used when the clinical features and other testing results for a patient are typical for a particular disorder and the association between the disorder and a specific gene is established (e.g., sickle cell disease).
Multiplex Panel Testing (also called multigene panels) (c)	Multigene panels allow simultaneous testing of at least two genes, and could include more than 150 genes (e.g., all genes associated with breast cancer). The methods used in multigene panels may include sequence analysis, deletion/ duplication analysis, and/or other non–sequencing-based tests. There are two types of multigene panels: • Off the shelf: Designed by a laboratory to include genes commonly associated with a broad phenotype (e.g., cardiomyopathy, a condition that makes it difficult for the heart to pump blood to the rest of the body; or ataxia,

	a condition characterized by loss of muscle control, or intellectual disability such as Down syndrome) or a recognizable syndrome with genetic heterogeneity (e.g., Noonan syndrome, a genetic condition that impacts normal development of various parts of the body). • Custom designed: Includes genes selected by a clinician for analysis by clinical sequencing. Results for each gene on the custom multigene panel are reported to the ordering clinician, whereas the results from the remaining genes sequenced (but not requested by the clinician) are not analyzed or included in the final laboratory report.
Whole Genome Sequencing (b)	A laboratory process that is used to determine nearly all of the approximately 3 billion nucleotides of an individual's complete DNA sequence, including noncoding sequence. Used to test for genetic causes of disease when suspicion of a specific mutation is not identified.
Whole Exome Sequencing (b)	A laboratory process that is used to determine the nucleotide sequence primarily of the exonic (or protein-coding) regions of an individual's genome and related sequences, representing approximately 1% of the complete DNA sequence. Used to find a genetic cause of signs and symptoms identified.
Next-Generation Sequencing (NGS) (b) (d)	A high-throughput method used to determine a portion of the nucleotide sequence of an individual's genome. This technique utilizes DNA sequencing technologies that are capable of processing multiple DNA sequences in parallel. This testing is most commonly used in clinical research. NGS can be used to detect individual or algorithm-based abnormalities and can be used to look at the interaction of multiple genes/biomarkers.

Source: California Health Benefits Review Program, 2022.
Notes: (a) NIH, 2022.
(b) ONS, 2022.
(c) Hays and Wapner, 2021.
(d) Committee on Policy Issues in the Clinical Development and Use of Biomarkers for Molecularly Targeted Therapies, 2016
Key: DNA = deoxyribonucleic acid.

Common laboratory biomarker tests from blood are usually available to physicians within 24 hours. Typically, single-analyte tests take between 7 and 10 days to be completed. Tissue NGS can take 3 to 4 weeks total: one week is usually required for the specimen to be prepared and sent out by the pathology lab to a commercial vendor and the remaining time is used to run and interpret the assay (test).

Biomarker Testing Recommendations

Clinical Practice Guidelines

Clinical practice guidelines (or "clinical guidelines") are recommendations on how to diagnose and treat a medical condition. There are countless clinical guidelines that would meet the definition included in SB 912 (see the *Policy Context* section). Additionally, there is no comprehensive clearinghouse for all clinical guidelines. A substantial number of clinical guidelines related to biomarker testing are for cancer treatment and are mostly published by the National Comprehensive Cancer Network (NCCN). Additional clinical societies and professional associations also publish clinical guidelines for biomarker testing for cancer diagnosis and treatment, which may or may not align with the NCCN guidelines. During its analysis of SB 535 Biomarker Testing, CHBRP identified that some commonly recommended biomarker tests for cancer are for BRCA1 and BRCA2 for breast cancer and prostate cancer; ALK, EGFR, MET, RET, and ROS1 for non–small-cell lung cancer (NSCLC); and HER2 for breast cancer, gastric cancer, gastroesophageal adenocarcinoma, and NSCLC (CHBRP, 2021). Many biomarkers may be associated with several diseases and conditions, such as HER2.

Conversely, some clinical guidelines may recommend against biomarker testing because of lack of or inconsistent clinical evidence.

Some health plans and policies use established clinical guidelines when reviewing determinations for medical necessity. Other plans and policies may develop guidelines internally or use a combination of established guidelines and internal guidelines. One commonly used set of guidelines is the Milliman Care Guidelines.[1] These evidence-based care guidelines are developed using peer-reviewed literature and cover the entire continuum of care.

Other prominent clinical guidelines include those published by the Clinical Pharmacogenetics Implementation Consortium (CPIC), which are designed to help clinicians understand how available genetic test results should be used to optimize drug therapy.[2] These guidelines may be relied on, in addition to the official pharmacogenomic indications included on medication labels approved by the U.S. Food & Drug Administration (FDA).

Medicare national and local coverage determinations

Medicare national coverage determinations (NCDs) are decisions made at the federal level whether to cover a particular item or service for all Medicare beneficiaries. Local coverage determinations (LCDs) are decisions made by a Medicare administrative contractor whether to cover a particular item or service in a contractor's jurisdiction.[3]

For example, as of March 2022, there are three NCDs and three LCDs that pertain to *biomarker testing* related to cancer diagnosis and/or treatment.[4]

Some commercial plans and policies may refer to NCDs or LCDs when making benefit coverage policies.

Reasons to Perform Biomarker Testing

CHBRP found the greatest quantity of peer-reviewed studies on the use of biomarker testing for cancer including prostate, ovarian, colorectal, breast, and lung cancers; Alzheimer's; rheumatoid arthritis; and type 2 diabetes. Performing biomarker testing for cancer, for example, enables a provider to accurately match the therapy to an individual patient by focusing on treatments most likely to be effective, and decreases treatment harms by avoiding treatments that are unlikely to result in improvement (e.g., chemotherapy), or may result in an adverse reaction (NASEM, 2016).

Biomarker tests can be used across the continuum of care for many diseases and conditions for the purposes of screening asymptomatic individuals, determining the presence of disease (diagnosis), estimating the risk or time to clinical outcomes (prognosis), identifying the likelihood of a patient to benefit from certain therapies (predictive), to identify therapy-related risks (pharmacogenomics), or for treatment monitoring purposes (Graig et al., 2016). An actionable biomarker is a biomarker that is associated with a directed treatment to prevent or reverse symptoms or disease (Camilleri and Chedid, 2020). The science surrounding biomarker testing and related treatments is evolving; even though biomarker testing may help identify mutations, there may not be treatments to target the mutation. Additionally, many biomarker tests can be used for multiple purposes. This section outlines each of the clinical pathways that may be taken as a result of biomarker testing using different types of cancer as illustrative examples.

[1] MCG. Available at https://www.mcg.com/care-guidelines/care-guidelines/.
[2] https://cpicpgx.org/
[3] CMS, Medicare Coverage Determination Process. https://www.cms.gov/Medicare/Coverage/DeterminationProcess
[4] Searched "biomarker test" on March 16, 2022. https://www.cms.gov/medicare-coverage-database/search.aspx

Screening

A susceptibility/risk biomarker is one that is associated with an increased, or in some cases decreased, chance of developing a disease or medical condition in an individual who, from a clinical standpoint, does not yet have that disease or medical condition (FDA-NIH, 2016). Examples include testing BRCA1/2 mutations for breast cancer predisposition, or using urinary concentration of tobacco-specific nitrosamines to identify those at greater likelihood of cancer development (Yalcin and de la Monte, 2016).

Diagnosis

A diagnostic biomarker is used to detect or confirm presence of a disease or condition of interest or to identify individuals with a subtype of the disease (FDA-NIH, 2016). Gene expression profiling may be used as a diagnostic biomarker to differentiate patients with diffuse large B-cell lymphoma into subgroups with different tumor cell of origin signatures (Scott et al., 2014).

Prognostic

A prognostic biomarker can be used to select patients with greater likelihood of having a disease-related endpoint event or a substantial worsening in condition (FDA-NIH, 2016). In cancer, prognostic tests identify the patient's overall cancer outcome or likelihood of developing cancer. A Gleason score (a grade assigned to how abnormal prostate cancer cells appear under a microscope) may be used as a prognostic biomarker when evaluating patients with prostate cancer to assess the likelihood of cancer progression (Epstein et al., 2016; Gordetsky and Epstein, 2016).

Predictive

Predictive tests inform the effect of a therapeutic intervention in a patient and can be used to tailor treatment. In cancer, predictive biomarkers may change over time within a single tumor or may be different if cancer is a reoccurrence. Whether biomarkers change may also indicate whether treatments are nonresponsive. For example, patients with certain genetic changes in the EGFR gene can get treatments that target those changes, called EGFR inhibitors. In this case, biomarker testing can find out whether someone's cancer has an EGFR gene change that can be treated with an EGFR inhibitor (NCI, 2021).

Pharmacogenomics

Pharmacogenomics looks at how genes affect a person's response to medications. Many of these interactions are determined through biomarker testing. The FDA compiles a list of all FDA-approved medications with pharmacogenomic information found in the drug labeling (FDA, 2022b). The type of information can loosely be divided into two categories: companion diagnostics and significant biomarker information in the drug label.

A **companion diagnostic** is a test that provides information about a corresponding therapeutic medication or biological product that is essential for its safe and effective use (FDA, 2022a). It is used to determine whether the medication or biological product is the appropriate treatment for a patient. Companion diagnostic tests are also used to determine how well a treatment is working or if serious side effects might occur (FDA, 2018a; NCI, 2022).

Medications with **significant biomarker information found in the drug label** include specific actions to be taken based on the biomarker test results. In the case of these medications, pharmacogenomics plays an important role in identifying responders and non-responders to medications, avoiding adverse events, and optimizing drug dose. However, biomarker testing may not be recommended for all patients who receive these medications. See the *Benefit Coverage, Utilization, and Cost Impacts* section for an example.

More than 400 medications are included on the FDA's list as of March 2022.

Treatment monitoring

A treatment monitoring biomarker is one that is tested at multiple timepoints to assess the rate or magnitude of change to the biomarker in response to therapy (FDA-NIH, 2016). The example mentioned earlier in this section for urinary concentration of tobacco-specific nitrosamines may also be used for assessing exposure to tobacco and tobacco smoke, in addition to its use as a screening biomarker (Yalcin and de la Monte, 2016). Biomarker monitoring during the course of an intervention can be used to determine how a drug is metabolized by a patient by monitoring drug concentration, to detect therapeutic effect or disease progression while on or following treatment, or to detect toxicity.

Clinical Utility of Biomarker Testing

As mentioned above, biomarker testing is often used to inform which treatments may be most effective. This use of biomarker testing to guide individualized treatment is currently widely used in the realm of precision oncology (i.e., to inform cancer treatment) (Selleck et al., 2017). A 2015 meta-analysis (570 studies; 32,149 patients) examined the impact of using biomarker testing to select the appropriate targeted treatment across a variety of different types of cancers. Across cancer diagnoses, personalized biomarker-driven treatment selection, compared to nonpersonalized treatment selection, was found to significantly improve response rate to treatment (31% vs. 10.5%, respectively), progression-free survival (5.9 vs. 2.7 months, respectively), and overall survival (13.7 vs. 8.9 months, respectively) (Schwaederle et al., 2015). Similarly, a 2016 meta-analysis (346 studies; 13, 203 patients) analyzed the effect of a biomarker-based selection strategy for cancer treatment in Phase 1 clinical trials, and also found a significant improvement in response rate (30.6% vs. 4.9%) and progression-free survival (5.7 vs. 2.9 months) (Schwaederle et al., 2016).

Recent studies have demonstrated the clinical utility of biomarker testing within specific types of cancers, most notably in patients with non–small cell lung cancer (NSCLC). In a retrospective cohort study of patients with advanced stage NSCLC, Duarte et al. (2021) examined the amount of time from diagnosis to receipt of the genetic profile from the biomarker tests, time to treatment, and changes to treatment based on the test results. The median time from diagnosis to receipt of a genetic profile was 40.5 days (range: 29.5–68.5 days) and the median time to the start of treatment was also 40 days. A clinically relevant result was identified in 44.9% (n=35) of patients. However, in 51% of those patients (18 out of 35), first-line treatment with chemotherapy was initiated before the biomarker test results were available. In nine of these cases, their results indicated a different type of treatment was more appropriate based on the genetic profile (tyronise kinase inhibitor [TKI]). For these nine cases, the chemotherapy was replaced by TKI treatment as soon as the results became available.

In a recent analysis of biomarker testing rates, targeted therapy use, and mortality outcomes using data from a large U.S. health care delivery system including a total of 17,555 patients, John et al. (2020) found that a large majority of patients with NSCLC (83.9%) received at least one biomarker test. Rates of testing were higher in later years of the study period (62.2% between 2014 and 2018 vs. 21.7% between 2011 and 2013). Similar trends were found in the studies by Haslem et al. (2017) and Sadaps et al. (2018). Overall, 30% of patients in John et al.'s (2020) study had a positive test result for at least one biomarker and more than half of patients who had biomarker testing received a biomarker-driven therapy (52.8%). Biomarker testing and targeted therapy as the first line of treatment were associated with greater survival compared to those who did not receive biomarker testing (median survival of 18 months vs. 6 months).

Healthcare Costs and Cost-Effectiveness of Biomarker Testing[5]

Some literature has found that biomarker testing for many conditions can be cost-effective.[6] Some literature reviews found biomarker testing is cost-effective for specific populations, while others found cost-effectiveness for more widespread testing. As noted above, some biomarker testing can be used for multiple reasons, including screening purposes.

As mentioned previously, cancer is by far the most common medical condition studied in biomarker research. Studies have evaluated the cost-effectiveness of biomarker testing within specific types of cancers, including breast cancer, melanoma, colorectal cancer, among others. A systematic review examining cost-effectiveness of testing for BRCA1 or BRCA2 found testing women with a family history to be cost-effective and that this varied by test source and payer; cost per quality-adjusted life year (QALY) ranged from $5,100 to $55,000 in 2014 U.S. dollars (D'Andrea, 2016). Another systematic review reported that using a 21-gene assay to guide breast cancer treatment resulted in costs per QALY of $8,900 and $10,800 in two studies (Berm, 2016). However, testing the general population for BRCA1 or BRCA2 genetic mutations is not cost-effective (D'Andrea, 2016). A systematic review reported testing melanoma patients with a 34- or 48-gene panel reduced costs and increased QALYs compared to testing only for BRAF (Tan, 2018). For colorectal cancer, a U.S. study found testing for KRAS alone saves $7,500 per patient and adding testing for BRAF saves an additional $1,000 (Berm, 2016). Lastly, recent systematic reviews have found biomarker testing saves costs in treatment of NSCLC (Mucherino, 2021). In addition to cancer, the cost-effectiveness of biomarker testing has also been evaluated for several other conditions, including but not limited to rheumatoid arthritis, neuropsychiatric conditions, and cardiovascular and pulmonary conditions, and these studies have shown variations in levels of cost-savings (Bergman, 2020; Berm, 2016; Frazier, 2021; Lee, 2017; Mattke, 2020; Oderda, 2018; van der Maas, 2017).

Recent cost-effectiveness and healthcare cost evaluation literature related to biomarker testing has focused on cost-savings related to medication management. One recent study compared 5,288 Medicare Advantage enrollees in a voluntary testing/medication management program to 22,357 members not enrolled in that program (Jarvis, 2022). In the first 32 months, the testing program led to a mean decrease of about $7,000 per person in direct medical charges. Another study (Brixner, 2016) compared a prospective cohort of 205 patients 65 years or older undergoing biomarker testing to a propensity score–matched historical cohort of 820 untested patients in a claims database. The testing group had significantly fewer hospitalizations, emergency department visits, and outpatient visits, leading to a mean savings of $218 per person over four months. Finally, a small trial randomized 110 older patients discharged to home health after hospitalization to either pharmacogenetic profiling through biomarker tests or a control group (Elliott, 2017). The biomarker tests were reviewed by a pharmacist for drug and/or gene interactions while the control group received pharmacist-guided medication management using a standard drug information resource. The mean number of emergency department visits and re-hospitalizations at 60 days was significantly lower among the biomarker group.

[5] A recent systematic review (Seo, 2021) reported inconsistent approaches used to estimate the value of biomarker tests. Some analyses covered only accuracy measures (sensitivity/specificity) and costs related to biomarker testing, while some included only patients testing positive rather than all patients tested.
[6] CHBRP did not perform a comprehensive systematic review of cost-effectiveness literature. There are also many studies that have found no evidence of cost-effectiveness for biomarker testing.

POLICY CONTEXT

The California Senate Committee on Health has requested that CHBRP[7] conduct an evidence-based assessment of the medical, financial, and public health impacts of SB 912, which would require coverage of biomarker testing.

Bill-Specific Analysis of SB 912, Biomarker Testing

Relevant Populations

If enacted, SB 912 would apply to the health insurance of approximately 24.5 million enrollees (62.3% of all Californians) in 2023. This represents Californians who will have health insurance regulated by the state that may be subject to any state health benefit mandate law, which includes health insurance regulated by the California Department of Managed Health Care (DMHC) or the California Department of Insurance (CDI), as well as Medi-Cal beneficiaries with full-scope coverage administered by the Department of Health Care Services (DHCS) and those enrolled in County Organized Health Systems (COHS).

Bill Language

SB 912 would require coverage of biomarker testing for the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring of an enrollee's disease or condition, only if the test is supported by medical and scientific evidence. Types of evidence include but are not limited to:

- A label indication for a test that has been approved or cleared by the FDA or is an indicated test for an FDA-approved medication;
- A national coverage determination made by the federal Centers for Medicare and Medicaid Services (CMS) or a local coverage determination made by a Medicare administrative contractor; and
- Nationally recognized clinical practice guidelines and consensus statements.

Insurers and DHCS must ensure biomarker testing is provided in a manner that limits disruptions in care, including the need for multiple biopsies or biospecimen samples.

Information about how to request an exemption if coverage for biomarker testing is restricted should be available on insurers' or, for Medi-Cal beneficiaries, DHCS' websites. This information should be clear and readily accessible, and the process for requesting the exemption should be convenient.

Amendments to the Welfare and Institutions Code state that utilization controls would be permissible under SB 912, although there is no provision in the Health and Safety Code or Insurance Code (other than existing law) that would prohibit utilization controls from applying to biomarker testing. SB 912 would add to the Welfare and Institutions Code prohibitions on prior authorization for enrollees with stage 3 or stage 4 metastatic or advanced cancer.

SB 912 includes the following definitions:

- **Biomarker:** A characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacological responses to a specific therapeutic intervention. A biomarker includes but is not limited to gene mutation and protein expression.[8]

[7] CHBRP's authorizing statute is available at www.chbrp.org/about_chbrp/faqs/index.php.
[8] This definition is similar to one provided by the FDA, available at https://www.fda.gov/drugs/biomarker-qualification-program/about-biomarkers-and-qualification#what-is.

- **Biomarker testing:** The analysis of an individual's tissue, blood, or other biospecimen for the presence of a biomarker. Biomarker testing includes but is not limited to single-analyte tests, multiplex panel tests, and whole genome sequencing.
- **Consensus statements:** Statements developed by an independent, multidisciplinary panel of experts who utilize a transparent methodology and reporting structure, and are subject to a conflict of interest policy. These statements are aimed at specific clinical circumstances and are based on the best available evidence to optimize the outcomes of clinical care.
- **Nationally recognized clinical practice guidelines:** Evidence-based clinical practice guidelines developed by independent organizations or medical professional societies utilizing a transparent methodology and reporting structure, and are subject to conflict of interest policy. Clinical practice guidelines establish standards of care informed by a systematic review of evidence and an assessment of the benefits and costs of alternative care options, and those guidelines include recommendations intended to optimize clinical care.

The full text of SB 912 can be found in Appendix A.

Interaction With Existing State and Federal Requirements

Health benefit mandates may interact and align with the following state and federal mandates or provisions.

California Policy Landscape

California law and regulations

Under existing law, plans and most policies are required to cover medically necessary diagnostic lab services and ongoing disease management services.[9]

Existing law requires coverage of all generally medically accepted cancer screening tests.[10] This code also prohibits use of prior authorization for biomarker testing for enrollees with advanced or metastatic stage three or four cancer, including for cancer progression or recurrence for these enrollees. As mentioned above, SB 912 would direct the Welfare and Institutions Code to incorporate prior authorization prohibitions mentioned in the existing law. Biomarker test is defined as "a diagnostic test, such as single or multigene, of the cancer patient's biospecimen, such as tissue, blood, or other bodily fluids, for DNA or RNA alterations, including phenotypic characteristics of malignancy, to identify an individual with a subtype of cancer, in order to guide patient treatment."

The Welfare and Institutions Code requires coverage of rapid whole genome sequencing for a parent or parents and their baby for any Medi-Cal beneficiary one year of age or younger and is receiving inpatient hospital services in an intensive care unit.[11]

Current law regulates the internal appeal process for DMHC-regulated plans and CDI-regulated policies.[12] Insurers with DMHC-regulated plans with websites are required to provide an online form for filing a grievance.[13]

[9] HSC 1345 and 1367.005; IC 10112.281.
[10] Health and Safety Code 1367.665; Insurance Code 10123.20.
[11] WIC 14132(ae)(1).
[12] 45 CFR §147.136
[13] HSC 1368.015

Existing law requires health plans and policies that include maternity coverage to *offer* coverage for "prenatal diagnosis of genetic disorders of the fetus by means of diagnostic procedures in cases of high-risk pregnancy."[14]

SB 1191, introduced in 2022, would require Medi-Cal coverage of pharmacogenomic testing. CHBRP's analysis of this bill will be available in late April 2022.

Similar requirements in other states

Illinois passed similar legislation to SB 912 in 2021.[15] Louisiana passed a bill in 2021 that requires coverage of genetic or molecular testing, including biomarker testing, for cancer.[16]

Similar legislation has been introduced in Arizona, New York, Rhode Island, and Washington in 2022.

Federal Policy Landscape

Federal legislation

The 117th Congress has introduced two bills related to biomarker testing. The first, House Resolution (HR) 5989 or The Precision Medicine Answers for Kids Today Act, would require the Secretary of Health and Human Services to conduct a demonstration program of genetic and genomic testing for certain children, to provide for a study by the National Academy of Medicine on the use of such testing to improve health care, and for other purposes.[17] The second, HR 6875 or The Right Drug Dose Now Act, would update the National Action Plan for Adverse Drug Event Prevention to provide educational information on adverse drug events and pharmacogenomic testing, to improve electronic health records for pharmacogenomic information, and for other purposes.[18]

Federal regulation of biomarker tests

The FDA has cleared and approved over 40 biomarker tests (FDA, 2022). The FDA reviews these tests for safety and effectiveness by assessing their analytical and clinical validity (Cancer Action Network, 2020).

Additionally, hospitals and other laboratories can produce their own category of diagnostic test, known as laboratory-developed tests (Cancer Action Network, 2020). While not reviewed by the FDA, the laboratories are required to meet certain criteria under the Clinical Laboratory Improvement Amendment (CLIA), including an inspection that reviews analytical validity of laboratory-developed tests.

Affordable Care Act

A number of Affordable Care Act (ACA) provisions have the potential to or do interact with state benefit mandates. Below is an analysis of how SB 912 may interact with requirements of the ACA as presently

[14] Health and Safety Code 1367.7; Insurance Code 10123.9.
[15] Illinois House Bill 1779, 102nd General Assembly. Available at https://www.ilga.gov/legislation/publicacts/fulltext.asp?Name=102-0203.
[16] Louisiana Senate Bill 84, 2021. Available at http://www.legis.la.gov/legis/BillInfo.aspx?s=21rs&b=SB84&sbi=y.
[17] HR 5989, Precision Medicine Answers for Kids Today Act, 117th Congress (2021-2022). Available at: https://www.congress.gov/bill/117th-congress/house-bill/5989/text
[18] HR 6875, Right Drug Dose Now Act, 117th Congress (2021-2022). Available at: https://www.congress.gov/bill/117th-congress/house-bill/6875/text

exist in federal law, including the requirement for certain health insurance to cover essential health benefits (EHBs).[19,20]

Essential Health Benefits

Under existing law, plans and policies are required to cover medically necessary diagnostic lab services and ongoing disease management services. Additionally, biomarker testing is broadly covered by California's EHB-benchmark plan. Because SB 912 would not require coverage for a new state benefit mandate, it therefore appears not to exceed the definition of EHBs in California.

Analytic Approach and Key Assumptions

CHBRP makes the following assumptions and approach decisions for the analysis of SB 912:

- Based on the bill language, CHBRP interprets SB 912 to require coverage of biomarker tests performed for "the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring." Biomarker tests used for screening purposes (tests performed on asymptomatic enrollees or those who have not had previous diagnoses) would not be included under these provisions. However, some biomarker tests are used both for screening and diagnostic/treatment purposes (tests for the BRCA genes, for example). While DMHC interprets[21] the bill language as CHBRP does, CDI states[22] that the bill could apply to screening biomarker tests as well.
- Utilization management policies, such as prior authorization, would be allowed under SB 912, except where prohibited by current law (see above).
- The definitions of biomarker and biomarker testing encompass a vast array of biomarkers and tests, ranging from more traditional biomarkers tests (e.g., white blood cell count) to biomarkers testing for genetic variation (sometimes identified using whole genome and exome sequencing). Due to the number of biomarker tests, CHBRP is unable to conduct a medical effectiveness review of biomarker testing within its 60-day timeline.
- SB 912 would not require coverage of multiplex panel tests if the panel is not included in clinical guidelines. Insurers would be able to limit reimbursement to a portion of the panel or direct providers to file separate claims for the individual analyte tests.
- SB 912 would not impact coverage of tests, treatments, or services that may be indicated based on the results of the biomarker tests.
- CHBRP assumes plans and policies would be required to incorporate future guidelines into their coverage policies, but SB 912 does not specify within what timeframe that must happen, or which guideline should be followed if there is disagreement or conflicting information provided.

CHBRP previously analyzed related bill language, SB 535, in 2021 (CHBRP, 2021). Where applicable, this analysis incorporates information from the previous analysis.

Beginning in 2022, DHCS began implementing the California Advancing and Innovating Medi-Cal (CalAIM) initiative.[23] To the extent possible as of this analysis, CHBRP has incorporated known CalAIM changes into its methods and approach.

[19] The ACA requires nongrandfathered small-group and individual market health insurance – including, but not limited to, QHPs sold in Covered California – to cover 10 specified categories of EHBs. Policy and issue briefs on EHBs and other ACA impacts are available on the CHBRP website: www.chbrp.org/other_publications/index.php.
[20] Although many provisions of the ACA have been codified in California law, the ACA was established by the federal government, and therefore, CHBRP generally discusses the ACA as a federal law.
[21] Personal communication with representatives from DMHC, March 23, 2022.
[22] Personal communication with representatives from CDI, March 9, 2022.
[23] More information about CalAIM is available at https://www.dhcs.ca.gov/CalAIM/Pages/calaim.aspx

BENEFIT COVERAGE, UTILIZATION, AND COST IMPACTS

As discussed in the *Policy Context* section, SB 912 would require health plans and health policies regulated by DMHC or CDI, as well as Medi-Cal benefits administered by DHCS, to cover biomarker testing for the purposes of diagnosis, treatment, appropriate management, and ongoing monitoring that is supported by medical and scientific evidence.

Analytic Approach and Key Assumptions

There are countless biomarker tests that could fall under the purview of SB 912. CHBRP's contracted actuarial firm, Milliman, pulled claims data from Milliman's 2019 Consolidated Health Cost Guidelines Sources Database (CHSD) for 546 biomarker testing and whole genome or exome procedure codes[24], identifying those most likely to fall under the purview of SB 912 — those most likely to be used for the purposes of diagnosis, treatment, appropriate management, and ongoing monitoring. However, some biomarker tests can be used for both screening and the purposes mentioned by SB 912.

As noted, claims data used for this analysis are from 2019. Biomarker testing is a rapidly evolving field and the claims captured by CHBRP's analysis does not include more recently added biomarker tests or utilization. Utilization may also be higher or different than what CHBRP displays below, which is using 2019 claims data to project utilization in 2023.

For further details on the underlying data sources and methods used in this analysis, please see Appendix C.

Benefit Coverage

CHBRP queried health plans and policies in California to determine baseline benefit coverage and the impacts of SB 912. **Broadly speaking, all enrollees with health insurance subject to SB 912 have coverage for biomarker testing that is supported by medical and scientific evidence and is determined medically necessary.[25]** This includes commercial and CalPERS enrollees, as well as Medi-Cal beneficiaries enrolled in DMHC-regulated plans, County Organized Health Systems (COHS), and beneficiaries in the fee-for-service program.

Whether or not insurers place prior authorization requirements on biomarker testing varied. Some enrollees with health insurance subject to SB 912 had prior authorization requirements, while others did not.

Insurers also varied in their use of clinical guidelines as mentioned by the bill language. All insurers either use guidelines or rely on contracted providers to make medical necessity determinations. Of the insurers that use guidelines, the guidelines are either purchased from an external clinical care guideline company (such as Milliman Care Guidelines) or incorporate publicly available guidelines, such as the list of FDA-

[24] Some biomarker tests may be captured under multiple procedure codes.
[25] To further investigate whether benefit coverage existed at baseline, CHBRP examined the codes for which there is a published Medi-Cal fee-for-service rate. CHBRP compared this list of codes with the list of codes identified by Milliman. Approximately 9% of the biomarker tests on Milliman's list were not included in the Medi-Cal fee-for-service rate list. However, analyzing claims data of biomarker test utilization found that a similar proportion of Medi-Cal beneficiaries in DMHC-regulated Medi-Cal managed care plans (6%) received the "not covered" biomarker tests as compared to commercial and CalPERS enrollees (9%), indicating that there is benefit coverage for these biomarker tests in DMHC-regulated Medi-Cal managed care plans. CHBRP is unable to determine whether benefit coverage for biomarker tests differs between DMHC-regulated Medi-Cal managed care plans and COHS, which have near-identical standard contracts from DHCS.

approved medications with biomarker indications on the label or Medicare national coverage determinations. CHBRP is unable to do a direct comparison of all clinical guidelines that could fall under the purview of SB 912 with guidelines insurers use and the resulting baseline benefit coverage determinations.

At baseline, CHBRP estimates enrollees with health insurance that would be subject to SB 912 already have coverage, generally, for biomarker testing supported by medical and scientific evidence.

There may be some biomarker tests that are newly covered based on the implementation of SB 912, but CHBRP is unable to determine to which biomarker tests this applies. Additionally, Medi-Cal beneficiaries in COHS likely have similar benefit coverage as those of commercial, CalPERS, and DMHC-regulated Medi-Cal managed care enrollees. Again, there may be some variation in coverage of biomarker testing at baseline, but CHBRP is unable to identify which biomarker tests may not be currently covered.

Utilization and Per-Unit Cost of Biomarker Testing

More than 200,000 commercial and CalPERS enrollees and 100,000 Medi-Cal beneficiaries use biomarker testing each year (Table 2). Some enrollees may use multiple forms of biomarker testing (single-analyte tests, multiplex panel tests, or whole exome or genome sequencing). Utilization of biomarker testing per 1,000 commercial and CalPERS enrollees is 14 for single-analyte tests, 3.2 for multiplex panel tests, and 0.4 for whole exome or genome sequencing. Utilization of biomarker testing per 1,000 Medi-Cal beneficiaries is 10.3 for single-analyte tests, 2.3 for multiplex panel tests, and 0.4 for whole exome or genome sequencing. Because biomarker testing is already broadly covered, utilization is not expected to change as a result of the passage of SB 912.

The average annual cost per user of biomarker testing for enrollees with commercial or CalPERS coverage was $677 for single-analyte tests, $948 for multiplex panel tests, and $984 for whole exome or genome testing (Table 2). The average annual cost per user of biomarker testing for Medi-Cal beneficiaries was $426 for a single-analyte test, $460 for a multiplex panel test, and $488 for whole exome or genome testing.

The average annual cost sharing for commercial and CalPERS enrollees using biomarker testing ranges between $64 and $90.

Enrollees who receive single-analyte tests may receive multiple single-analyte biomarker tests on the same day. Some providers will submit claims to insurers for multiple single-analyte tests when a multiplex panel test was run because an insurer may not provide reimbursement for a panel that includes non-medically indicated tests, because no billing code exists for the panel test that was run, or there is not a panel available that includes the desired biomarker tests.[26] Other enrollees will receive multiple single-analyte tests over time because the testing required is iterative or to check specific biomarkers over time.

Additionally, some enrollees may receive multiple types of tests, not only within a category, but across categories. For example, an enrollee could receive a multiplex panel test as well as additional single-analyte tests. As mentioned above, reasons include both billing capabilities or requirements, as well as medically indicated testing over time.

[26] This has been confirmed through CHBRP's survey of insurers in California, as well as multiple subject matter experts.

Table 2. Projected Utilization and Cost of Biomarker Tests, 2023

	Single-Analyte Tests	Multiplex Panel Tests	Whole Exome or Genome Testing
Commercial and CalPERS Enrollees			
Users per 1,000 enrollees utilizing biomarker testing	14.0	3.2	0.4
Average annual cost per user of biomarker testing	$677	$948	$984
Average annual per enrollee cost sharing for biomarker testing	$90	$81	$64
Medi-Cal Beneficiaries			
Users per 1,000 beneficiaries utilizing biomarker testing	10.3	2.3	0.4
Average annual cost of biomarker testing	$426	$460	$488

Source: California Health Benefits Review Program, 2022.

Key: CalPERS = California Public Employees' Retirement System.

Utilization and Per-Unit Cost of Medications with Biomarkers in Drug Labels

As discussed in the *Background* section, biomarker testing can be used to inform many treatment decisions, including decisions surrounding use of medications. As an example of potential impacts of SB 912, CHBRP examined utilization of medications for which there is an FDA-approved label indication for biomarker testing or a companion diagnostic (Table 3). These medications can either be covered under the medical benefit (usually physician-administered medications) or under the pharmacy benefit (self-administered medications such as oral medications). Although SB 912 would not result in changes to benefit coverage and therefore no resulting changes in utilization of biomarker tests and related treatments, it is important to understand how use of biomarker tests may lead to other health care utilization and expenditure impacts. It should also be noted that several studies have found biomarker testing can be cost-effective, which could lead to reductions in other health care expenditures, such as emergency department utilization and in-patient hospital admission (see above discussion on *Healthcare Costs and Cost-Effectiveness of Biomarker Testing*).

For medications covered under the medical benefit with a companion diagnostic designation (meaning the biomarker test must be run in order for the medication to be prescribed/administered), there were approximately 0.4 users per 1,000 commercial/CalPERS enrollees and 0.5 users per 1,000 Medi-Cal beneficiaries. For medications covered under the medical benefit with a significant biomarker reference in the label (meaning the results of the biomarker test can provide information regarding metabolism or toxicity of the medication, and other pertinent information), there were approximately 1.0 users per 1,000 commercial/CalPERS enrollees and 1.1 users per 1,000 Medi-Cal beneficiaries.

For medications covered under the pharmacy benefit, there were approximately: 0.2 users per 1,000 commercial/CalPERS enrollees and 0.2 users per 1,000 Medi-Cal beneficiaries of medications with a companion diagnostic designation; and 33.9 users per 1,000 commercial/CalPERS enrollees and 17.3 users per 1,000 Medi-Cal beneficiaries of medications with a significant biomarker reference in the label. Biomarker testing is not required or sometimes even indicated for an enrollee to receive or be prescribed medications with a significant biomarker reference in the label.[27] As a result, there are substantially more

[27] For example, the American College of Rheumatology (ACR) conditionally recommends testing HLA–B*5801 before starting allopurinol to treat gout for individuals of Southeast-Asian descent (e.g., Han-Chinese, Korean, Thai) and Black people. For individuals who are positive for the HLA-B*58:01 variant, an alternative drug is recommended by the Clinical Pharmacogenetics Implementation Consortium (CPIC) and the Dutch Pharmacogenetics Working Group (DPWG). Only new users of the drug would be potential candidates for testing (and gout is a recurring condition so many prescriptions would not be for those with new use) and only a subset of new users (Asian and Black) would be candidates.

enrollees receiving these medications (more than 475,000 commercial/CalPERS enrollees and 165,000 Medi-Cal beneficiaries annually), than who receive biomarker tests within a single year.

As displayed in Table 3, annual per-user costs of companion diagnostic medications covered under the medical benefit average approximately $146,000 for commercial and CalPERS enrollees and $76,000 for Medi-Cal beneficiaries. Annual per-user costs of medications covered under the medical benefit with a significant biomarker reference in the label average $29,000 for commercial and CalPERS enrollees and $12,000 for Medi-Cal beneficiaries. For medications covered under the pharmacy benefit, annual per-user costs average $77,500 for companion diagnostics for commercial and CalPERS enrollees and $40,000 for Medi-Cal beneficiaries. For prescription medications with significant biomarker reference in the label, annual per-user costs are almost $4,000 for commercial and CalPERS enrollees and $3,000 for Medi-Cal beneficiaries.

As of January 1, 2022, outpatient prescription medications are covered on a fee-for-service basis by DHCS for all Medi-Cal beneficiaries.[28] To present utilization for Medi-Cal beneficiaries, CHBRP assumes utilization of medications covered under the pharmacy benefit for Medi-Cal beneficiaries in COHS and fee-for-service is similar to utilization of medications covered under the pharmacy benefit for Medi-Cal beneficiaries enrolled in DMHC-regulated Medi-Cal managed care plans. Among commercial and CalPERS enrollees, 1.8% do not have a pharmacy benefit and 2.9% have a pharmacy benefit that is not regulated by DMHC or CDI.[28] At this time, CHBRP is unable to estimate utilization of prescription medications for commercial and CalPERS enrollees whose pharmacy benefits are not regulated by DMHC or CDI.

Table 3. Projected Utilization and Costs of Medications with Companion Diagnostic or Biomarker Reference in Label, 2023

	Companion Diagnostic	Significant Biomarker Reference in Label
Commercial and CalPERS Enrollees		
Medications with biomarkers in medication label processed under the **medical benefit**		
Users per 1,000 enrollees	0.4	1.0
Average annual per user cost	$146,255	$29,302
Average annual per user cost sharing	$1,189	$478
Medication with biomarkers in medication label processed under the **pharmacy benefit** (a)		
Users per 1,000 enrollees	0.2	33.9
Average annual per user cost	$77,550	$3,725
Average annual per user cost sharing	$2,022	$177
Medi-Cal Beneficiaries (b)		
Medication with biomarkers in medication label processed under the **medical benefit**		
Users per 1,000 enrollees	0.5	1.1
Average annual per user cost	$76,150	$12,032
Medication with biomarkers in medication label processed under the **pharmacy benefit** (b)		
Users per 1,000 enrollees	0.2	17.3
Average annual per user cost (c)	$40,277	$2,914

Source: California Health Benefits Review Program, 2022.

Notes: (a) Not all commercials/CalPERS enrollees with state-regulated medical benefit coverage have pharmacy benefit coverage regulated by the state. 95.3% have a pharmacy benefit regulated by DMHC or CDI. Only commercial/CalPERS enrollees with DMHC- or CDI-regulated pharmacy benefit coverage are included in the detailed information about medications utilizing biomarkers in drug label processed under the pharmacy benefit.

(b) The Medi-Cal pharmacy benefit is carved out of managed care plans and is therefore not regulated by DMHC. Instead, the pharmacy benefit is administered by DHCS on a fee-for-service basis for all Medi-Cal beneficiaries.
(c) Nationwide Medicaid cost per drug estimates used since California specific data was not available.

Key: CalPERS = California Public Employees' Retirement System.

[28] For more detail, see CHBRP's *Estimates of Pharmacy Benefit Coverage in California for 2023*, a resource available at http://chbrp.org/other_publications/index.php.

PUBLIC HEALTH IMPLICATIONS

As discussed in the *Policy Context* section, SB 912 would mandate coverage of biomarker testing for the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring of an enrollee's disease or condition if the test is supported by medical and scientific evidence.

This section provides an overview of public health implications related to biomarker testing including disparities and social determinants of health contributing to inequities in utilization.

Estimated Public Health Outcomes

As presented in the *Benefit Coverage, Utilization, and Cost Impacts* section, enrollees with health insurance subject to SB 912 currently have coverage, generally, for biomarker testing. For these enrollees, the passage of SB 912 would not result in a change in benefit coverage and therefore no change in utilization of biomarker tests or related therapies. As discussed, it is possible there may be some biomarker tests that are newly covered based on the implementation of SB 912, or there could be some enrollees with health insurance not surveyed by CHBRP that may gain benefit coverage. However, these estimates either can't be determined or are expected to be small. For this reason, CHBRP concludes that SB 912 would have no measurable impact on biomarker testing due to benefit coverage.

Because enrollees with health insurance subject to SB 912 currently have coverage for biomarker testing generally, there is no measurable public health impact.

Disparities[29] and Social Determinants of Health[30] in Biomarker Testing

Per statute, CHBRP includes discussion of disparities and social determinants of health (SDOH) as it relates to biomarker testing. Disparities are noticeable and preventable differences between groups of people. CHBRP found literature identifying disparities in biomarker testing by race and ethnicity, age, socio-economic status, health literacy, and geographic location.

Disparities

Race or ethnicity

It is well established that in the United States there are disparities in mortality rates for certain cancers by race or ethnicity that particularly impact African Americans disproportionately to other racial/ethnic groups (AACR, 2020). In a 2021 review article, McAlarnen et al. synthesize recent literature on the potential exacerbation of healthcare disparities as disproportionate utilization of genomic testing by race and ethnicity is observed. As biomarker testing is used increasingly in healthcare, it is being used at a lower rate by under-represented race and ethnicity groups. The authors report that several studies have found that awareness differs significantly by ethnicity, with more White participants being aware of cancer risk than Hispanic, African American, or Asian participants. Some studies found that there was a lack of trust regarding how genetic information would be used, and a lack of confidence in the validity and utilization of the results. Other themes that emerged from the reviewed studies and may contribute to persistent health

[29] Several competing definitions of "health disparities" exist. CHBRP relies on the following definition: Health disparity is defined as the differences, whether unjust or not, in health status or outcomes within a population. (Wyatt et al., 2016).

[30] CHBRP defines social determinants of health as conditions in which people are born, grow, live, work, learn, and age. These social determinants of health (economic factors, social factors, education, physical environment) are shaped by the distribution of money, power, and resources and impacted by policy (adapted from: CDC, 2014; Healthy People 2020, 2019).

disparities in genetic services for cancer were lack of provider recommendation and equal access to specialized care. The gap in genomic testing utilization by race/ethnicity will continue to be exacerbated as the lack of data gathered from representative populations limits the generalizability of current genomic research. This is particularly of concern for development of guideline recommendations which may not necessarily be reflective of the diversity of the population (Jooma et al., 2019; McAlarnen et al., 2021). These findings have been supported in other studies (Kehl et al., 2019; Lynch et al., 2018).

Age

CHBRP found evidence in the literature that differences in biomarker testing utilization exist by age. Younger patients were significantly more likely to have had biomarker testing for colorectal cancer than older patients (Greenbaum et al., 2017). Some possible reasons identified were awareness of biomarker testing, lack of provider recommendation (due to poor performance status, comorbidities, or short life expectancy), or patient refusal.

Clinical Disparities and Barriers

Many biomarker tests are relatively new clinical tools and are part of a rapidly evolving field. Because of this there may be clinical and implementation considerations involved in uptake and utilization of these tests. Studies have suggested that clinician barriers — including familiarity with guidelines and knowledge of best practices for use of biomarker testing, expertise in genomic testing, or access to a multidisciplinary specialty team — impact whether patients receive testing (Boehmer et al., 2021; Duarte et al., 2021; Wilson et al., 2018). A shortage of genetic counselors, specifically in rural areas, may also limit access to testing or delays in interpretation of results (Berninger et al., 2021; Villegas and Haga, 2019). Relatedly, studies consistently report higher rates at testing at academic medical centers compared to community sites (Boehmer et al., 2021; Wilson et al., 2018). Delays in processes of care, such as timeliness of testing in coordination with laboratories and issues with tumor sampling (i.e., appropriately characterizing and sampling tumors), are commonly reported as barriers to optimal utilization of biomarker testing in practice (Duarte et al., 2021). These disparities and barriers in clinical practice may be limiting factors in more widespread and equitable implementation of biomarker testing.

Social Determinants of Health

Social determinants of health (SDOH) include factors outside of the traditional medical care system that influence health status and health outcomes (e.g., income, education, and geography). CHBRP found literature citing differences in biomarker testing by socio-economic status, geographic location, and health literacy.

Socio-economic status

Socio-economic status is strongly associated with morbidity and mortality across the income distribution. Lower incomes are associated with lower life expectancy, higher rates of chronic disease and physical limitations, and worse self-reported health status (Khullar and Chokshi, 2018). Additionally, poor health contributes to reduced income, creating a negative feedback loop (Khullar and Chokshi, 2018).

In a 2020 systematic review and meta-analysis, Norris and colleagues examined the role of socio-economic status and utilization of predictive biomarker tests and/or precision therapies in different types of cancers. The analysis included 11 studies that reported data on predictive biomarker testing and 40 studies including data on utilization of biological and precision therapy. The authors found statistically significant differences in biological and precision therapy utilization: those with low socio-economic status were 17% less likely to be treated with precision therapies. This finding is consistent with previously published studies on cancer treatment inequalities by socio-economic status (Aarts et al., 2010; Forrest et al., 2013) and inequalities in time to screening and diagnosis of various types of cancers (Hayes et al., 2021; Lyratzopoulos et al., 2013). The overall pooled odds ratio (OR) for receipt of biological and precision therapy for patients from low socio-economic status was 0.83 (95% confidence interval [CI],

0.75–0.91). Associations with therapy utilization were strongest in lung cancer (OR 0.75; 95% CI, 0.51–1.00) and weakest in breast cancer (OR 0.93; 95% CI, 0.78–1.10).

Health literacy

Health literacy — a person's capacity to access, understand, appraise, and apply information for healthcare decisions — may impact how patients utilize healthcare and biomarker testing. Health literacy plays a role in awareness, access, and interpretation of biomarker testing results (Rostamzadeh et al., 2020; Williams et al., 2018). In a study of familiarity with precision medicine concepts and values associated with getting genetic testing (e.g., cost, privacy, trust, counseling) across health literacy levels, Williams found that most patients reported low familiarity with precision medicine concepts, but those with higher health literacy gave significantly greater importance to provider trust than those with lower levels ($p \leq .008$). It was concluded that culturally sensitive efforts tailored to health literacy level should be implemented to enhance equitable utilization of precision medicine as a healthcare tool.

Geographic location

Rural-urban disparities exist for time to diagnosis and treatment of certain cancers (Bergin et al., 2018). Because clinical guidelines for biomarker testing exist for many types of cancer, among other diseases/conditions, this disparity is carried forward to biomarker testing (Greenbaum et al., 2017).

Because there is no measurable impact from SB 912, there is also no projected impact on disparities identified in biomarker testing.

However, as discussed in the *Benefit Coverage, Utilization, and Cost Impacts* section, utilization of biomarker testing differs between commercial and CalPERS enrollees and for beneficiaries in DMHC-regulated Medi-Cal managed care plans, despite coverage. There is also literature indicating that the disparities identified could widen inequities in utilization of biomarker testing if not specifically addressed.

LONG-TERM IMPLICATIONS

In this section, CHBRP estimates the long-term impact of SB 912, which CHBRP defines as impacts occurring beyond the first 12 months after implementation. These estimates are qualitative and based on the existing evidence available in the literature. CHBRP does not provide quantitative estimates of long-term impacts because of unknown improvements in clinical care, changes in prices, implementation of other complementary or conflicting policies, and other unexpected factors.

As discussed previously, a changing landscape exists for biomarker testing as new biomarkers are identified, tested, and approved for use in clinical care. However, health plans and policies currently cover biomarker testing as supported by scientific and medical evidence. CHBRP assumes it is likely that plans and policies will continue to incorporate new clinical guidelines as they become available in future years. While not directly related to SB 912, there are implications for health plans and policies, including Medi-Cal, as new biomarker tests become available and new therapies indicated by biomarker testing become available. As shown the *Benefit Coverage, Utilization, and Cost Impacts* section, some medications cost more than $100,000 annually. Although utilization of these medications is low, should utilization increase, related health care expenditures would increase as well. As noted previously, evidence supports cost-effectiveness of several biomarker tests, which could contribute to offsets in health care expenditures or improved quality of life for enrollees.

APPENDIX A TEXT OF BILL ANALYZED

On February 10, 2022, the California Senate Committee on Health requested that CHBRP analyze SB 912.

SENATE BILL **NO. 912**

Introduced by Senator Limón

February 02, 2022

An act to add Section 1367.667 to the Health and Safety Code, to add Section 10123.209 to the Insurance Code, and to amend Section 14132 of the Welfare and Institutions Code, relating to health care coverage.

LEGISLATIVE COUNSEL'S DIGEST

SB 912, as introduced, Limón. Biomarker testing.

(1) Existing law, the Knox-Keene Health Care Service Plan Act of 1975, provides for the licensure and regulation of health care service plans by the Department of Managed Health Care, and makes a willful violation of the act a crime. Existing law provides for the regulation of health insurers by the Department of Insurance. Existing law requires health care service plan contract or health insurance policy issued, amended, delivered, or renewed on or after July 1, 2000, to provide coverage for all generally medically accepted cancer screening tests, and prohibits that contract or policy issued, amended, delivered, or renewed on or after July 1, 2022, from requiring prior authorization for biomarker testing for certain enrollees or insureds. Existing law applies the provisions relating to biomarker testing to Medi-Cal managed care plans, as prescribed.

This bill would require a health care service plan contract or health insurance policy issued, amended, or renewed on or after July 1, 2023, to provide coverage for biomarker testing, including whole genome sequencing, for the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring of an enrollee’s or insured’s disease or condition if the test is supported by medical and scientific evidence, as prescribed. This bill would apply these provisions relating to biomarker testing to the Medi-Cal program, including Medi-Cal managed care plans, as specified. Because a willful violation of these provisions by a health care service plan would be a crime, the bill would impose a state-mandated local program.

(2) Existing law provides for the Medi-Cal program, administered by the State Department of Health Care Services and under which qualified low-income individuals receive health care services pursuant to a schedule of benefits. The Medi-Cal program is, in part, governed and funded by federal Medicaid program provisions. Existing law includes Rapid Whole Genome Sequencing

as a covered benefit for any Medi-Cal beneficiary who is one year of age or younger and is receiving inpatient hospital services in an intensive care unit.

Subject to the extent that federal financial participation is available and not otherwise jeopardized, and any necessary federal approvals have been obtained, this bill would expand the Medi-Cal schedule of benefits to include biomarker testing for the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring of a Medi-Cal beneficiary's disease or condition if the test is supported by medical and scientific evidence, as prescribed. The bill would authorize the department to implement this provision by various means without taking regulatory action.

(3) The California Constitution requires the state to reimburse local agencies and school districts for certain costs mandated by the state. Statutory provisions establish procedures for making that reimbursement.

This bill would provide that no reimbursement is required by this act for a specified reason.

Vote: majority Appropriation: no Fiscal Committee: yes Local Program: yes

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THE PEOPLE OF THE STATE OF CALIFORNIA DO ENACT AS FOLLOWS:

SECTION 1. Section 1367.667 is added to the Health and Safety Code, immediately following Section 1367.665, to read:

1367.667. (a) A health care service plan contract, except for a specialized health care service plan contract, that is issued, amended, delivered, or renewed on or after July 1, 2023, shall cover biomarker testing pursuant to this section. Biomarker testing shall be covered for the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring of an enrollee's disease or condition only if the test is supported by medical and scientific evidence, including, but not limited to, any of the following:

(1) A labeled indication for a test that has been approved or cleared by the United States Food and Drug Administration (FDA) or is an indicated test for an FDA-approved drug.

(2) A national coverage determination made by the federal Centers for Medicare and Medicaid Services or a local coverage determination made by a Medicare Administrative Contractor.

(3) Nationally recognized clinical practice guidelines and consensus statements.

(b) A health care service plan that is subject to this section shall ensure that biomarker testing is provided in a manner that limits disruptions in care, including the need for multiple biopsies or biospecimen samples.

(c) When coverage of biomarker testing for the purpose of diagnosis, treatment, or ongoing monitoring of any medical condition is restricted for use by a health care service plan, the enrollee and their prescribing health care practitioner shall have access to clear, readily accessible, and

convenient processes to request an exception. That process shall be made readily accessible on the health care service plan's internet website.

(d) This section shall apply to any health care service plan contract and Medi-Cal managed care plan contract with the State Department of Health Care Services pursuant to Chapter 7 (commencing with Section 14000) or Chapter 8 (commencing with Section 14200) of Part 3 of Division 9 of the Welfare and Institutions Code.

(e) For purposes of this section, the following definitions apply:

(1) "Biomarker" means a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacological responses to a specific therapeutic intervention. A biomarker includes, but is not limited to, gene mutations or protein expression.

(2) "Biomarker testing" means the analysis of an individual's tissue, blood, or other biospecimen for the presence of a biomarker. Biomarker testing includes, but is not limited to, single-analyte tests, multiplex panel tests, and whole genome sequencing.

(3) "Consensus statements" means statements developed by an independent, multidisciplinary panel of experts who utilize a transparent methodology and reporting structure, and are subject to a conflict of interest policy. These statements are aimed at specific clinical circumstances and are based on the best available evidence to optimize the outcomes of clinical care.

(4) "Nationally recognized clinical practice guidelines" means evidence-based clinical practice guidelines developed by independent organizations or medical professional societies utilizing a transparent methodology and reporting structure, and are subject to a conflict-of-interest policy. Clinical practice guidelines establish standards of care informed by a systematic review of evidence and an assessment of the benefits and costs of alternative care options, and those guidelines include recommendations intended to optimize clinical care.

(f) This section is subject to the provisions of Section 1367.665 as amended by Chapter 605 of the Statutes of 2021 for an enrollee with advanced or metastatic stage three or four cancer.

SEC. 2. Section 10123.209 is added to the Insurance Code, to read:

10123.209. (a) A health insurance policy that is issued, amended, delivered, or renewed on or after July 1, 2023, shall include coverage for biomarker testing pursuant to this section. Biomarker testing shall be covered for the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring of an insured's disease or condition only if the test is supported by medical and scientific evidence, including, but not limited to, any of the following:

(1) A labeled indication for a test that has been approved or cleared by the United States Food and Drug Administration (FDA) or is an indicated test for an FDA-approved drug.

(2) A national coverage determination made by the federal Centers for Medicare and Medicaid Services or a local coverage determination made by a Medicare Administrative Contractor.

(3) Nationally recognized clinical practice guidelines and consensus statements.

(b) A health insurance policy that is subject to this section shall ensure that biomarker testing is provided in a manner that limits disruptions in care, including the need for multiple biopsies or biospecimen samples.

(c) When coverage of biomarker testing for the purpose of diagnosis, treatment, or ongoing monitoring of any medical condition is restricted for use by a health insurer, the insured and their prescribing health care practitioner shall have access to clear, readily accessible, and convenient processes to request an exception. That process shall be made readily accessible on the health insurer's internet website.

(d) This section shall apply to an insurance policy issued, sold, renewed, or offered for health care services or coverage provided in the Medi-Cal program pursuant to Chapter 7 (commencing with Section 14000) or Chapter 8 (commencing with Section 14200) of Part 3 of Division 9 of the Welfare and Institutions Code.

(e) This section shall not apply to vision-only, dental-only, accident-only, specified disease, hospital indemnity, Medicare supplement, long-term care, or disability income insurance, except that for accident-only, specified disease, or hospital indemnity insurance, coverage for benefits under this section shall apply to the extent that the benefits are covered under the general terms and conditions that apply to all other benefits under the policy or contract. This section shall not impose a new benefit mandate on accident-only, specified disease, or hospital indemnity insurance.

(f) For purposes of this section, the following definitions apply:

(1) "Biomarker" means a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacological responses to a specific therapeutic intervention. A biomarker includes, but is not limited to, gene mutations or protein expression.

(2) "Biomarker testing" means the analysis of an individual's tissue, blood, or other biospecimen for the presence of a biomarker. Biomarker testing includes, but is not limited to, single-analyte tests, multiplex panel tests, and whole genome sequencing.

(3) "Consensus statements" means statements developed by an independent, multidisciplinary panel of experts who utilize a transparent methodology and reporting structure, and are subject to a conflict of interest policy. These statements are aimed at specific clinical circumstances and are based on the best available evidence to optimize the outcomes of clinical care.

(4) "Nationally recognized clinical practice guidelines" means evidence-based clinical practice guidelines developed by independent organizations or medical professional societies utilizing a transparent methodology and reporting structure, and are subject to a conflict-of-interest policy. Clinical practice guidelines establish standards of care informed by a systematic review of

evidence and an assessment of the benefits and costs of alternative care options, and those guidelines include recommendations intended to optimize clinical care.

(g) This section is subject to the provisions of Section 10123.20 as amended by Chapter 605 of the Statutes of 2021 for an insured with advanced or metastatic stage three or four cancer.

SEC. 3. Section 14132 of the Welfare and Institutions Code is amended to read:

14132. The following is the schedule of benefits under this chapter:

[No substantial changes were made to sections (a)-(af) of this code section]

(ag) (1) By July 1, 2023, biomarker testing, as specified in this subdivision, is a covered benefit, subject to utilization controls. Biomarker testing shall be covered for the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring of a Medi-Cal beneficiary's disease or condition only if the test is supported by medical and scientific evidence, including, but not limited to, any of the following:

(A) A labeled indication for a test that has been approved or cleared by the United States Food and Drug Administration (FDA) or is an indicated test for an FDA-approved drug.

(B) A national coverage determination made by the federal Centers for Medicare and Medicaid Services or a local coverage determination made by a Medicare Administrative Contractor.

(C) Nationally recognized clinical practice guidelines and consensus statements.

(2) The department shall ensure that biomarker testing is provided in a manner that limits disruptions in care, including the need for multiple biopsies or biospecimen samples.

(3) A Medi-Cal beneficiary and their prescribing health care practitioner shall have access to a clear, readily accessible, and convenient process to request an exception to the biomarker testing benefit. That process shall be made readily accessible on the department's internet website.

(4) This subdivision shall be implemented only to the extent that federal financial participation is available and not otherwise jeopardized, and any necessary federal approvals have been obtained.

(5) Notwithstanding Chapter 3.5 (commencing with Section 11340) of Part 1 of Division 3 of Title 2 of the Government Code, the department may implement this subdivision by means of all-county letters, plan letters, plan or provider bulletins, or similar instructions, without taking any further regulatory action.

(6) For purposes of this subdivision, the following definitions apply:

(A) "Biomarker" means a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a specific therapeutic intervention. A biomarker includes, but is not limited to, gene mutations or protein expression.

(B) "Biomarker testing" is the analysis of an individual's tissue, blood, or other biospecimen for the presence of a biomarker. Biomarker testing includes, but is not limited to, single-analyte tests, multiplex panel tests, and whole genome sequencing.

(C) "Consensus statements" are statements developed by an independent, multidisciplinary panel of experts who utilize a transparent methodology and reporting structure, and are subject to a conflict of interest policy. These statements are aimed at specific clinical circumstances and are based on the best available evidence to optimize the outcomes of clinical care.

(D) "Nationally recognized clinical practice guidelines" are evidence-based clinical practice guidelines developed by independent organizations or medical professional societies utilizing a transparent methodology and reporting structure, and are subject to a conflict of interest policy. Clinical practice guidelines establish standards of care informed by a systematic review of evidence and an assessment of the benefits and costs of alternative care options, and those guidelines include recommendations intended to optimize clinical care.

(7) This subdivision is subject to the provisions of Section 1367.665 of the Health and Safety Code and Section 10123.20 of the Insurance Code as amended by Chapter 605 of the Statutes of 2021 for a Medi-Cal beneficiary with advanced or metastatic stage three or four cancer.

SEC. 4. No reimbursement is required by this act pursuant to Section 6 of Article XIII B of the California Constitution because the only costs that may be incurred by a local agency or school district will be incurred because this act creates a new crime or infraction, eliminates a crime or infraction, or changes the penalty for a crime or infraction, within the meaning of Section 17556 of the Government Code, or changes the definition of a crime within the meaning of Section 6 of Article XIII B of the California Constitution.

APPENDIX B COST IMPACT ANALYSIS: DATA SOURCES, CAVEATS, AND ASSUMPTIONS

With the assistance of CHBRP's contracted actuarial firm, Milliman, Inc, the cost analysis presented in this report was prepared by the faculty and researchers connected to CHBRP's Task Force with expertise in health economics.[31] Information on the generally used data sources and estimation methods, as well as caveats and assumptions generally applicable to CHBRP's cost impacts analyses are available at CHBRP's website.[32]

This appendix describes analysis-specific data sources, estimation methods, caveats, and assumptions used in preparing this cost impact analysis.

Analysis-Specific Data Sources

Current coverage of biomarker testing for commercial and Medi-Cal enrollees was determined by a survey of the largest (by enrollment) providers of health insurance in California. Responses to this survey represented 66% of commercial enrollees with health insurance that can be subject to state benefit mandates. Responses to this survey represented 39% of Medi-Cal enrollees with health insurance that can be subject to state benefit mandates. In addition, CalPERS and DHCS were queried regarding related benefit coverage.

For this analysis, CHBRP relied on CPT® codes to identify services related to SB 912. CPT copyright 2022 American Medical Association. All rights reserved. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. CPT is a registered trademark of the American Medical Association.

Analysis-Specific Caveats and Assumptions

The analytic approach and key assumptions are determined by the subject matter and language of the bill being analyzed by CHBRP. As a result, analytic approaches may differ between topically similar analyses, and therefore the approach and findings may not be directly comparable.

Methodology for Identifying Biomarker Tests

- CHBRP identified procedure codes specific to biomarker tests that were medically effective and available in 2019, since claims data were identified using Milliman's 2019 Consolidated Health Cost Guidelines Sources Database (CHSD).
- CHBRP is unable to distinguish within claims data the reason for biomarker testing. Additionally, claims data does not include the reason for the biomarker test, unless the test results in a diagnosis or is used in the treatment of, appropriate management of, or ongoing monitoring of an existing disease or condition. Some claims with biomarker testing do not have a diagnosis because the biomarker test did not identify a suspected condition or disease (a negative result of the test).
- Biomarker test procedure codes specific to prenatal testing were excluded from the list of test codes used in the analysis. These codes describe tests covered under California's statewide program for the prenatal testing for genetic disorders and birth defects, where some genetic

[31] CHBRP's authorizing statute, available at https://chbrp.org/about_chbrp/index.php, requires that CHBRP use a certified actuary or "other person with relevant knowledge and expertise" to determine financial impact.
[32] See method documents posted at http://chbrp.com/analysis_methodology/cost_impact_analysis.php; in particular, see *2023 Cost Analyses: Data Sources, Caveats, and Assumptions*.

testing is standard for California pregnancies and additional genetic testing is recommended and already covered for high-risk pregnancies.

- Biomarker test procedure codes specific to other genetic screening were excluded as screening uses of biomarkers were not specified in the bill language. CHBRP also excluded biomarker test procedures that are included in "common blood biomarker tests," as described in the *Background* section, since these tests are already covered by insurance plans and policies.
- Some of the tests reported by certain biomarker test procedure codes could be provided for prenatal testing or screening of asymptomatic individuals for genetic mutations, which are uses not specified by bill language, as well as for other reasons stated by the bill language, such as cancer diagnosis and treatment selection. Therefore, the principal diagnosis codes on all claims for the biomarker test codes in Milliman's 2019 Consolidated Health Cost Guidelines Sources Database (CHSD) were identified. Biomarker tests reported with a principal diagnosis code assigned to one of the following AHRQ Clinical Classifications Software Refined (CCSR)[33] categories were removed in order to exclude biomarker tests for indications not assumed to be covered by SB 912. These include:
    - Contraceptive and procreative management
    - Other pregnancy and delivery including normal
    - Residual codes; unclassified
    - Other complications of pregnancy
- The biomarker tests remaining after these steps were those used to develop unit cost and utilization and can be found in Table 4**.**

Methodology for Identifying Therapeutic Products Influenced by Biomarker Tests

- Medications and biologicals included in the analysis were drawn from two FDA categories:
    - First, all medications and biologicals indicated by a companion diagnostic device (i.e., a diagnostic biomarker test) that provides information that is essential for the safe and effective use of a corresponding therapeutic product were included.
        - Note that the use of a companion diagnostic device is stipulated in the instructions for use in the labeling of the diagnostic device, either including a specific therapeutic product(s) or, if approved for oncology products, a specific group of oncology therapeutic products. In addition, the use of a companion diagnostic device is stipulated in the labeling of the therapeutic product, as well as in the labeling of any generic equivalents and biosimilar equivalents of the therapeutic product.
    - Second, medications and biologicals with significant pharmacogenomic information found in the drug labeling that includes specific actions to be taken based on the biomarker information were included. In the case of these medications and biologicals, pharmacogenomics plays an important role in identifying responders and nonresponders to medications, avoiding adverse events, and optimizing medication dose.
- The list of medications and biologicals can be found in Table 5**.**

Methodology and Assumptions for Utilization and cost

- The utilization rates for biomarker tests, medications processed under the medical benefit, and medications processed under the pharmacy benefit are based on the 2019 CHSD. The data was limited to California enrollees.
- The commercial allowed costs for biomarker tests, medications processed under the medical benefit, and medications processed under the pharmacy benefit are based on the 2019 CHSD.

[33] Clinical Classifications Software Refined (CCSR) for ICD-10-CM Diagnoses. Healthcare Cost and Utilization Project (HCUP). March 2021. Agency for Healthcare Research and Quality, Rockville, MD. www.hcup-us.ahrq.gov/toolssoftware/ccsr/dxccsr.jsp

- The Medi-Cal allowed costs for biomarker tests and medications processed under the medical benefit are based on the February 2022 Medi-Cal fee-for-service reimbursement rates. For services where a fee-for-service rate is not available, the Medi-Cal rate is calculated as 70% of the commercial rate. This discount was determined by comparing the commercial and Medi-Cal rates of the biomarker tests and related services where fee-for-service rates were available.
- Medi-Cal allowed costs for medications processed under the pharmacy benefit are based on nationwide allowed costs for the Medicaid population from 2019 CHSD.
- Biomarker tests were identified as 'single-analyte, 'multiplex panel tests', or 'whole exome or genome' tests using procedure codes. The procedure codes used to identify biomarker tests are in Table 4.
- Medications processed under the medical or pharmacy benefit were identified as 'companion diagnostic' or as having 'significant biomarker reference in label'. The included medications are listed in Table 5**.**
- Commercial utilization for biomarker tests, medications processed under the medical benefit, and medications processed under the pharmacy benefit were trended from 2019 to 2023 using 2.0%, 1.5%, and 3.0% trend, respectively. Allowed costs per unit were trended using 4.0%, 6.5%, and 4.0%, respectively. All trends are based on trend guidance in the Milliman Health Cost Guidelines. The medical trends reflect typical medical service trends and do not consider the rapid advancements in biomarker testing.
- Medicaid utilization for biomarker tests and medications were trended from 2019 to 2023 using 1% trend. Allowed costs per unit for biomarker tests and medications processed under the medical benefit were trended from 2019 to 2023 using 0% trend. Drug costs processed under the pharmacy benefit were trended using a 4% annual trend based on Kaiser Family Foundation report on Utilization and spending trends in Medicaid outpatient prescription medications from 2015 to 2019 (KFF, 2021).
- The trends applied reflect typical medical service trends and do not consider the rapid growth in this area.

Methodology and Assumptions for Cost Sharing

- The paid-to-allowed ratios for biomarker tests, medications processed under the medical benefit, and medications processed under the pharmacy benefit for commercial claims using the CHSD database and used to calculate cost sharing for commercial members.
- Medicaid members were assumed to not have cost sharing.

Table 4. Biomarker Procedure Codes

Category	List of CPT/HCPCS
Single Gene	81105 - 81112, 81120 - 81121, 81161 - 81168, 81170 - 81194, 81200 - 81210, 81214 - 81227, 81230 - 81256, 81260 - 81264, 81269 - 81276, 81278 - 81279, 81283 - 81300, 81302 - 81348, 81350 - 81353, 81355, 81357, 81360 - 81364, 81373 - 81374, 81376 - 81377, 81380 - 81383, 81400 - 81405, 83890 - 83894, 83896 - 83898, 83902 - 83909, 83912 - 83914, 83950 - 83951, 88182, 88184 - 88185, 88261, 88264, 88271, 88280, 88283, 88285, 88289, 88291, 88341 - 88343, 88346 - 88350, 88360 - 88361, 88364 - 88365, 88367 - 88369, 88373, 88384 - 88388, 0009U, 0023U, 0026U, 0027U, 0028U, 0029U, 0030U, 0031U, 0032U, 0033U, 0034U, 0035U, 0040U, 0046U, 0058U, 0059U, 0067U, 0070U, 0071U, 0072U, 0073U, 0074U, 0075U, 0076U, 0136U, 0137U, 0154U, 0155U, 0156U, 0157U, 0158U, 0159U, 0160U, 0161U, 0177U, 0180U, 0181U, 0182U, 0183U, 0184U, 0185U, 0186U, 0187U, 0188U, 0189U, 0190U, 0191U, 0192U, 0193U, 0194U, 0195U, 0196U, 0197U, 0198U, 0199U, 0200U, 0201U, 0206U, 0207U, 0218U, 0221U, 0222U, 0229U, 0230U, 0231U, 0232U, 0233U, 0234U, 0235U, 0236U, S3800, S3840 - S3842, S3844 - S3846, S3849 - S3850, S3852 - S3853, S3855, S3861, S3865 - S3866

Multiple Genes	81211 - 81213, 81280 - 81282, 81301, 81370 - 81372, 81375, 81378 - 81379, 81406 - 81408, 81410 - 81411, 81413 - 81414, 81419, 81430 - 81440, 81442, 81445, 81448, 81450, 81455, 81470 - 81471, 81490, 81493, 81500, 81503 - 81504, 81518 - 81522, 81525, 81529, 81535 - 81536, 81538 - 81542, 81545 - 81546, 81551 - 81552, 81554, 81595, 83900 - 83901, 88187 - 88189, 88262 - 88263, 88272 - 88275, 88344, 88366, 88374, 88377, 0001U, 0002U, 0003U, 0004U, 0005U, 0015U, 0016U, 0017U, 0018U, 0021U, 0022U, 0037U, 0045U, 0047U, 0048U, 0050U, 0053U, 0055U, 0057U, 0062U, 0063U, 0069U, 0078U, 0080U, 0081U, 0083U, 0084U, 0087U, 0088U, 0089U, 0090U, 0092U, 0095U, 0101U, 0102U, 0103U, 0104U, 0105U, 0108U, 0111U, 0113U, 0114U, 0120U, 0129U, 0130U, 0131U, 0132U, 0133U, 0134U, 0135U, 0138U, 0139U, 0153U, 0162U, 0169U, 0170U, 0171U, 0172U, 0173U, 0174U, 0175U, 0179U, 0203U, 0204U, 0205U, 0208U, 0216U, 0217U, 0219U, 0220U, 0228U, 0237U, 0238U, 0239U, 0239U , 0242U, 0244U, 0245U, 0246U, 0001M, 0002M, 0003M, 0004M, 0006M, 0007M, 0011M, 0012M, 0013M, 0014M, 0015M, 0016M, 0017M, 0018M, S3854
Whole Exome or Genome	81228 - 81229, 81257 - 81259, 81265 - 81268, 81277, 81415 - 81417, 81425 - 81427, 81460, 81465, 0012U, 0013U, 0014U, 0019U, 0036U, 0056U, 0094U, 0209U, 0211U, 0212U, 0213U, 0214U, 0215U, S3870

Source: California Health Benefits Review Pogram, 2022.

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Table 5. Medications Influenced by Biomarker Tests

Category	Generic Name
Significant Biomarker Reference in Label	Abacavir, Aducanumab-avwa, Alglucosidase Alfa, Allopurinol, Amifampridine, Anakinra, Anastrozole, Arsenic Trioxide, Avapritinib , Avelumab, Azathioprine , Belinostat, Blinatumomab , Boceprevir, Bosutinib, Brentuximab Vedotin , Busulfan, Cabotegravir and Rilpivirine , Cabozantinib, Capecitabine, Carbamazepine , Carglumic Acid, Casimersen, Cerliponase Alfa, Cholic Acid, Cisplatin, Crizanlizumab-tmca, Daclatasvir, Dasabuvir, Ombitasvir, Paritaprevir, and Ritonavir, Dasatinib, Denileukin Diftitox, Dinutuximab, Docetaxel, Dolutegravir, Durvalumab, Duvelisib, Eculizumab , Elagolix, Elbasvir and Grazoprevir, Elexacaftor, Ivacaftor, and Tezacaftor, Elosulfase, Eltrombopag , Emapalumab-lzsg, Enfortumab Vedotin-ejfv, Entrectinib , Eribulin , Eteplirsen, Everolimus , Exemestane, Fam-Trastuzumab Deruxtecan-nxki, Fluorouracil , Fosdenopterin, Fosphenytoin , Fulvestrant , Gemtuzumab Ozogamicin, Givosiran, Golodirsen, Goserelin, Ibrutinib , Inebilizumab-cdon, Inotersen, Inotuzumab Ozogamicin, Irinotecan, Isatuximab- irfc , Ivacaftor, Ivacaftor and Lumacaftor, Ixabepilone , Lapatinib , Ledipasvir and Sofosbuvir, Lenalidomide, Lenvatinib, Letrozole, Lonafarnib , Lumasiran, Luspatercept–aamt, Lusutrombopag , Lutetium Dotatate Lu-177, Margetuximab-cmkb , Mercaptopurine , Metreleptin, Migalastat, Mycophenolic Acid, Natalizumab, Neratinib , Nusinersen, Obinutuzumab, Olaratumab, Omacetaxine, Ombitasvir, Paritaprevir, and Ritonavir, Osimertinib, Oxcarbazepine, Palbociclib, Patisiran, Pazopanib , Peginterferon Alfa-2b, Phenytoin , Ponatinib, Raloxifene, Raltegravir, Ramucirumab , Regorafenib, Ribociclib, Risdiplam, Rituximab, Rivaroxaban, Rosuvastatin, Sacituzumab Govitecan-hziy, Satralizumab-mwge, Selpercatinib, Setmelanotide , Simeprevir, Sodium Oxybate, Sodium Phenylbutyrate, Sofosbuvir, Sofosbuvir and Velpatasvir, Sofosbuvir, Velpatasvir, and Voxilaprevir, Tafamidis, Tamoxifen , Telaprevir, Tepotinib , Thioguanine , Tipiracil and Trifluridine , Toremifene, Tretinoin, Triheptanoin, Tucatinib, Ustekinumab, Valproic Acid , Viltolarsen, Vincristine
Companion	Abemaciclib, Ado-trastuzumab emtansine, Afatinib, Alectinib, Alpelisib, Amivantamab-vmjw, Atezolizumab, Binimetinib, Brigatinib, Capmatinib, Cemiplimab-rwlc, Ceritinib, Cetuximab, Cobimetinib, Crizotinib, Dabrafenib, Dacomitinib, Deferasirox, Dostarlimab-gxly, Enasidenib, Encorafenib, Erdafitinib, Erlotinib, Gefitinib, Gilteritinib, Imatinib mesylate, Infigratinib, Ipilimumab , Ivosidenib, Larotrectinib, Lorlatinib, Midostaurin, Mobocertinib, Nilotinib, Niraparib, Nivolumab, Olaparib, Panitumumab, Pembrolizumab, Pemigatinib, Pertuzumab, Pralsetinib, Rucaparib, Sotorasib, Talazoparib, Tazemetostat, Trametinib , Trastuzumab, Vemurafenib, Venetoclax

Source: California Health Benefits Review Program, 2022.

Determining Public Demand for the Proposed Mandate

CHBRP reviews public demand for benefits relevant to a proposed mandate in two ways. CHBRP:

- Considers the bargaining history of organized labor; and
- Compares the benefits provided by self-insured health plans or policies (which are not regulated by the DMHC or CDI and therefore not subject to state-level mandates) with the benefits that are provided by plans or policies that would be subject to the mandate.

On the basis of conversations with the largest collective bargaining agents in California, CHBRP concluded that in general, unions negotiate for broader contract provisions such as coverage for dependents, premiums, deductibles, and broad coinsurance levels.

Among publicly funded self-insured health insurance policies, the preferred provider organization (PPO) plans offered by CalPERS have the largest number of enrollees. The CalPERS PPOs currently provide benefit coverage similar to what is available through group health insurance plans and policies that would be subject to the mandate.

To further investigate public demand, CHBRP used the bill-specific coverage survey to ask carriers who act as third-party administrators for (non-CalPERS) self-insured group health insurance programs whether the relevant benefit coverage differed from what is offered in group market plans or policies that would be subject to the mandate. The responses indicated that there were no substantive differences.

APPENDIX C INFORMATION SUBMITTED BY OUTSIDE PARTIES

In accordance with the California Health Benefits Review Program (CHBRP) policy to analyze information submitted by outside parties during the first 2 weeks of the CHBRP review, the following parties chose to submit information.

> Invitae submitted multiple pieces of information to CHBRP in March 2022. These items include background information, studies on the effectiveness and cost-effectiveness of biomarker testing, information types of tests, and information on potential cost savings due to increased benefit coverage and utilization.

Submitted information is available upon request. For information on the processes for submitting information to CHBRP for review and consideration please visit: www.chbrp.org/requests.html

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ABOUT CHBRP

The California Health Benefits Review Program (CHBRP) was established in 2002. As per its authorizing statute, CHBRP provides the California Legislature with independent analysis of the medical, financial, and public health impacts of proposed health insurance benefit-related legislation. The state funds CHBRP through an annual assessment on health plans and insurers in California.

A group of faculty, researchers, and staff complete the analysis that informs California Health Benefits Review Program (CHBRP) reports. The CHBRP **Faculty Task Force** comprises rotating senior faculty from University of California (UC) campuses. In addition to these representatives, there are other ongoing researchers and analysts who are **Task Force Contributors** to CHBRP from UC that conduct much of the analysis. The **CHBRP staff** works with Task Force members in preparing parts of the analysis, and manages external communications, including those with the California Legislature. As required by CHBRP's authorizing legislation, UC contracts with a certified actuary, **Milliman**, to assist in assessing the financial impact of each legislative proposal mandating or repealing a health insurance benefit. 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. Information on CHBRP's analysis methodology, authorizing statute, as well as all CHBRP reports and other publications, are available at www.chbrp.org.

CHBRP Staff

Garen Corbett, MS, Director
John Lewis, MPA, Associate Director
Adara Citron, MPH, Principal Policy Analyst
Sabrina Woll, Policy Associate
Karen Shore, **PhD,** Contractor*
An-Chi Tsou, PhD, Contractor*
*Independent Contractor working with CHBRP to support analyses and other projects.

Faculty Task Force

Paul Brown, PhD, University of California, Merced
Timothy T. Brown, PhD, University of California, Berkeley
Janet Coffman, MA, MPP, PhD, *Vice Chair for Medical Effectiveness,* University of California, San Francisco
Todd Gilmer, PhD, University of California, San Diego
Sylvia Guendelman, PhD, LCSW, University of California, Berkeley
Elizabeth Magnan, MD, PhD, *Co-Vice Chair for Public Health*, University of California, Davis
Sara McMenamin, PhD, *Vice Chair for Medical Effectiveness and Public Health*, University of California, San Diego
Joy Melnikow, MD, MPH, *Co-Vice Chair for Public Health*, University of California, Davis
Aimee Moulin, MD, University of California, Davis
Jack Needleman, PhD, University of California, Los Angeles
Mark A. Peterson, PhD, University of California, Los Angeles
Nadereh Pourat, PhD, *Vice Chair for Cost*, University of California, Los Angeles
Dylan Roby, PhD, University of California, Irvine
Marilyn Stebbins, PharmD, University of California, San Francisco

Task Force Contributors

Bethney Bonilla, MA, University of California, Davis
Danielle Casteel, MA, University of California, San Diego
Shana Charles, PhD, MPP, University of California, Los Angeles, and California State University, Fullerton
Margaret Fix, MPH, University of California, San Francisco
Naomi Hillery, MPH, University of California, San Diego
Jeffrey Hoch, PhD, University of California, Davis
Julia Huerta, MPH, University of California, Davis
Michelle Keller, PhD, MPH, University of California, Los Angeles
Jacqueline Miller, University of California, San Francisco
Marykate Miller, MS, University of California, Davis
Amy Quan, University of California, San Francisco
Dominique Ritley, MPH, University of California, Davis
Emily Shen, University of California, Los Angeles
Riti Shimkhada, PhD, University of California, Los Angeles
Meghan Soulsby Weyrich, MPH, University of California, Davis
Steven Tally, PhD, University of California, San Diego
Sara Yoeun, MPH, University of California, San Diego

National Advisory Council

Lauren LeRoy, PhD, Strategic Advisor, L. LeRoy Strategies, Chair
Stuart H. Altman, PhD, Professor of National Health Policy, Brandeis University, Waltham, MA
Deborah Chollet, PhD, Senior Fellow, Mathematica Policy Research, Washington, DC
Allen D. Feezor, Former Deputy Secretary for Health Services, North Carolina Department of Health and Human Services, Raleigh, NC
Charles "Chip" Kahn, MPH, President and CEO, Federation of American Hospitals, Washington, DC
Jeffrey Lerner, PhD, President Emeritus, ECRI Institute Headquarters, Plymouth Meeting, PA; Adjunct Senior Fellow, Leonard Davis Institute of Health Economics, University of Pennsylvania
Donald E. Metz, Executive Editor, *Health Affairs,* Bethesda, MD
Dolores Mitchell, (Retired) Executive Director, Group Insurance Commission, Boston, MA
Marilyn Moon, PhD, Senior Fellow, Retired, American Institutes for Research, Washington, DC
Carolyn Pare, (Retired) President and CEO, Minnesota Health Action Group, Bloomington, MN
Richard Roberts, MD, JD, Professor Emeritus of Family Medicine, University of Wisconsin-Madison, Madison, WI
Alan Weil, JD, MPP, Editor-in-Chief, *Health Affairs,* Bethesda, MD

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CHBRP assumes full responsibility for the report and the accuracy of its contents. All CHBRP bill analyses and other publications are available at www.chbrp.org.

Garen Corbett, MS
Director

Please direct any questions concerning this document to: California Health Benefits Review Program; MC 3116; Berkeley, CA 94720-3116, info@chbrp.org, or www.chbrp.org

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