



# The Economic and Functional Impacts of Genetic and Genomic Clinical Laboratory Testing in the United States

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# The Economic and Functional Impacts of Genetic and Genomic Clinical Laboratory Testing in the United States

Simon Tripp, Martin Grueber and Deborah Cummings

Battelle Technology Partnership Practice

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The **American Clinical Laboratory Association (ACLA)** is a not-for-profit organization which offers members the benefits of representation, education, information and research. Its primary purpose is to:

- Advocate for laws and regulations that recognize the essential role that laboratory services play in delivering cost-effective health care;
- Encourage the highest standards of quality, service and ethical conduct among its members; and
- Promote public awareness about the value of laboratory services in preventing illness, diagnosing disease, and monitoring medical treatment.

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## Executive Summary

Accurate diagnosis is the foundation for choosing the right treatments for patients, and clinical laboratory tests provide critical information that health care providers use in about 70 percent of their decisions<sup>1</sup>. Modern advances in research have recently prompted an expansion in genetic and genomic testing, and these types of tests represent a fast-growing component of the clinical laboratory marketplace.

While there is currently no standard definition of genetic and genomic tests, Battelle and the American Clinical Laboratory Association used the following definition for the purposes of this study:

*A genetic or genomic test involves an analysis of human chromosomes, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), genes, and/or gene products (e.g., enzymes, metabolites and other types of proteins), which is predominately used to detect heritable or somatic mutations, genotypes, or phenotypes related to disease, health or identity. The purpose of genetic tests includes predicting risk of disease, screening newborns, directing clinical management, identifying carriers, and establishing prenatal or clinical diagnoses or prognoses in individuals, families, or population, as well as use for forensic and identity purposes.*

This definition actually serves to highlight some of the key areas of biomedical application for genetic and genomic testing:

- **Diagnosis of Disease:** Whereby genetic or genomic tests are used to screen a patient with a suspected disease (usually a hereditary genetic disease) to positively identify the disease. This is genetic or genomic testing applied to a symptomatic individual.
- **Predictive Medicine:** The presymptomatic testing of individuals to determine the risk of developing adult onset diseases and disorders (such as for Huntington's disease or breast cancer.)
- **Genotyping of Specific Disease:** Such as the genotyping of a patient's specific HIV strain or cancer tumor to guide therapeutic approaches. In many respects this is closely linked to pharmacogenomics.
- **Pharmacogenomics:** Whereby genetic or genomic testing is used to optimize drug therapies based on the patient's genotype and known genetic linkages to drug efficacy or toxicity.
- **Identity testing:** Whereby genetic testing assists in confidently establishing identity, providing individual genetic identification profiles. These profiles can be used to establish biological relatedness.
- **Forensic testing:** Whereby genetic testing is used to establish the identity of individuals based upon a specimen of blood, urine, or other tissue.
- **Carrier Screening:** This involves testing unaffected individuals who carry one copy of a gene for a disease that requires two copies for the disease to be expressed.
- **Newborn Screening:** Whereby newborns are screened shortly after birth for disorders that are treatable, but difficult to otherwise detect clinically.

Genetic and genomic testing can thus be seen to be at the heart of a new paradigm of medicine that is evidence-based and rooted in quantitative science. It is facilitating a move towards personalized, predictive and preventive medicine, and away from a more reactive medicine that only responds to

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<sup>1</sup> UK Department of Health Pathology Modernisation Team. Modernising Pathology Services, 2004. Available at [www.dh.gov.uk](http://www.dh.gov.uk). 60-70% of NHS patients' diagnoses depend on laboratory tests, p. 7.

emergent symptoms, or provides general, one-size fits all therapies without an understanding of the underlying individualized response that may occur (positively or negatively) to such a trial-and-error approach.

Genetic and genomic testing makes possible what Leroy Hood at the Institute for Systems Biology has termed P4 medicine—medicine that is personalized, predictive, preventive and participatory. The benefits of this approach to medicine are highlighted by Hood and Galas as being able to:<sup>2</sup>

- *Detect disease at an earlier stage, when it is easier and less expensive to treat effectively;*
- *Stratify patients into groups that enable the selection of optimal therapy;*
- *Reduce adverse drug reactions by more effective early assessment of individual drug responses;*
- *Improve the selection of new biochemical targets for drug discovery;*
- *Reduce the time, cost, and failure rate of clinical trials for new therapies; and*
- *Shift the emphasis in medicine from reaction to prevention and from disease to wellness.*

It is clear that genetic and genomic testing provides a new suite of quantitative test tools for diagnosing disease—tools that hold promise for enhancing the accuracy of a diagnosis for symptomatic patients, predicting the risk of disease in asymptomatic individuals, guiding safer therapeutic approaches, and preventing diseases from occurring in the first place.

Tests rooted in genetic and genomic advancements have emerged as accurate tools for diagnosing monogenic and polygenic diseases and disorders, and as predictive tools for enhancing public health and personal health decisions. Genetic and genomic testing is also able to characterize specific cancers, definitively identify infectious organisms and organismal strains, and guide the prescription and dosing of appropriate therapeutic approaches.

From an economic standpoint, genetics and genomics tests and diagnostics development represent an expanding industry for the United States. Built upon biomedical research programs, such as the Human Genome Project (HGP), and subsequent genomics research and development (R&D), the U.S. is a global leader in this advanced field of science and is home to many successful and growing companies leveraging genetic and genomic advancements to produce new diagnostic tests and technologies. Likewise, the growth of genetic and genomic testing is providing new job and economic growth opportunities within clinical laboratories (both freestanding commercial laboratories and within other laboratory settings, such as in hospitals).

The genetic and genomic clinical laboratory testing industry is an R&D-driven, innovative sector that is important to the U.S. economy not only for the economic benefits it generates, but also the health care enhancements provided by the application of its testing products. Using input/output analysis, Battelle has quantified both the direct economic impact of the U.S. genetic and genomic clinical laboratory testing industry, and the total impact of the industry generated in the economy via direct, indirect and induced economic impacts (also known as multiplier-effect impacts)<sup>3</sup>. As Table ES-1 illustrates, the results of the input/output analysis show that while genetic and genomic testing is still in the relatively

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<sup>2</sup> Leroy E. Hood and David J. Galas. December 2008. "P4 Medicine: Personalized, Predictive, Preventive, Participatory: A Change of View that Changes Everything." Version 6: December 12, 2008. Accessed online at [http://www.cra.org/ccc/docs/init/P4\\_Medicine.pdf](http://www.cra.org/ccc/docs/init/P4_Medicine.pdf)

<sup>3</sup> There is currently no specific NAICS code solely for genetics and genomics clinical laboratory testing, and data for industry work in this regard is captured within other existing NAICS codes along with data for traditional laboratory testing tools and activities. As such, Battelle had to perform primary research, including a survey of major clinical laboratory organizations, and reference published market research reports, in order to derive estimates of the current percentage of laboratory test volumes, revenues and employment that are focused in the genetics and genomics testing space.

early stages of its development, and much future growth is expected to occur, **the genetic and genomic testing industry is responsible for generating:**

- **More than 116,000 U.S. jobs;**
- **Nearly \$6 billion in personal income for U.S. workers;**
- **\$9.2 billion in value-added<sup>4</sup> activity; and**
- **\$16.5 billion in national economic output.**

In addition, state and local governments across the U.S. receive an estimated \$657 million in annual tax revenues allocable to the genetic and genomic clinical laboratory testing industry, while the federal government receives nearly \$1.2 billion in related taxes annually.

**Table ES-1: Economic Impacts of U.S. Genetic and Genomic Clinical Laboratory Testing on the U.S. (\$Millions)**

Category of Impact	Jobs	Personal Income	Value-Added	Output (Business Volume)	State/Local Tax Revenue	Federal Tax Revenue
Direct Impacts	43,563	\$2,504	\$3,221	\$5,890	\$98	\$448
Indirect Impacts	27,397	\$1,417	\$2,360	\$4,118	\$189	\$290
Induced Impacts	45,326	\$2,035	\$3,614	\$6,518	\$370	\$437
Total Impacts	116,286	\$5,956	\$9,195	\$16,526	\$657	\$1,175
Impact Multiplier	2.7	2.4	2.9	2.8	6.7	2.6

Source: Battelle analysis; IMPLAN U.S. 2009 Model

*Personal Income: Measures cash, benefits and non-cash payments received by individuals in the economy.*

*Value-Added: Represents the difference between an industry's or an establishment's total output and the cost of its intermediate inputs.*

*Output: Is the dollar value of production (i.e., sales).*

The expenditure-based economic impacts, while notable and substantial, represent only part of the overall beneficial impact of genetic and genomic testing. As a result of the industry's focus, genetic and genomic testing is bringing new capabilities and enhanced accuracy to the diagnosis of diseases and disorders in symptomatic and asymptomatic individuals. As the universe of genetic and genomic tests grows, their ability to improve human health, longevity and quality of life is the primary purpose of their development and deployment, and ultimately results in the industry's functional impacts on society. Functional impacts, also known as forward linkage impacts, are the benefits generated by the industry's products and services. In the case of the genetic and genomic clinical testing industry, the products and services make possible multiple desirable societal benefits, both economic and non-economic:

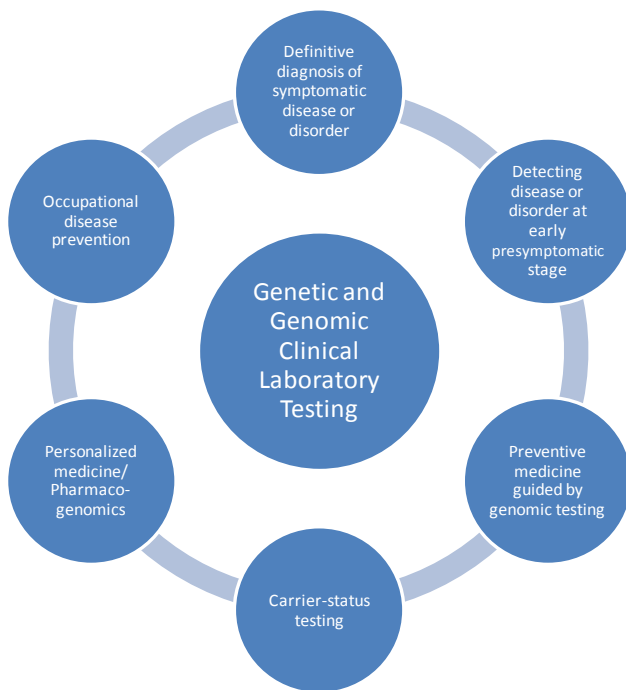
- Providing a definitive, accurate diagnosis of a disease or disorder, thereby helping to avoid misdiagnoses and the associated stress on patients and healthcare spending on unnecessary or ineffective treatments.
- Detecting a disease or disorder at an early stage, or even a pre-symptomatic stage, when it is easier and less expensive to treat effectively, thereby saving healthcare costs and increasing labor force productivity.
- Providing information on disease susceptibility associated with specific genes or genomic characteristics, thereby facilitating preventive measures and appropriate life planning.

<sup>4</sup> Value-added represents the difference between an industry's or an establishments total output and the cost of its intermediate inputs. It equates to the difference between the total sales of an industry less the costs of each step in the production of products sold.

- Minimizing the impact of devastating childhood diseases through testing of potential parents for carrier-status of genetic disorders.
- Directing the application and dosing of therapeutics most likely to be safe and effective given the patient’s genotype, thereby avoiding adverse drug reactions and the healthcare costs associated with treating them.
- Using genetic and genomic testing applications in occupational health practices to determine the effects of worker exposure to hazardous agents, and to determine individual hyper-susceptibility to the diseases that exposure may cause.

With the reference human genome sequence only completed a decade ago, and the Human Genome Project unveiling a far more complex genetic structure than previously thought, the development of commercially available genetic and genomic testing tools and techniques is still in a relatively early stage. That said, in each of the bulleted categories of societal benefits shown above and illustrated in Figure ES-1, genetic and genomic testing is being applied *today* to improve the care and prognosis of patients. Furthermore, each area holds significant future promise for far more wide-ranging application and subsequent benefits.

**Figure ES-1: Functional Applications of Genetic and Genomic Clinical Laboratory testing**



The platform of knowledge and the technologies resulting from human genome sequencing have formed the basis of nothing less than a medical revolution. The primary impacts of this revolution may not yet be felt in every daily clinical practice, but that day is accelerating towards us. Writing in *Nature*, Eric Lander notes that:

*“Medical revolutions require many decades to achieve their full promise. Genomics has only just begun to permeate biomedical research: advances must proceed through fundamental tools, basic discoveries, medical studies, candidate interventions, clinical trials, regulatory approval and widespread adoption. We must be scrupulous not to promise the public a pharmacopoeia of quick pay-offs. At the same time, we should remain unabashed about the ultimate impact of*

*genomic medicine, which will be to transform the health of our children and our children's children.”<sup>5</sup>*

This medical revolution will in turn lead to significant global economic opportunities. For these economic opportunities to be captured within the United States, however, the genetic and genomic clinical testing industry needs to be able to operate in a business environment that encourages continued R&D investment and facilitates profitable business operations (generating profits for reinvestment in the innovation cycle). Sustaining U.S. industrial leadership as the innovative genetic and genomic clinical testing sector continues to grow and prosper carries the promise of significant future economic and societal benefits.

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<sup>5</sup> Eric S. Lander. 2011. “Initial impact of the sequencing of the human genome.” *Nature*. Volume 470, February 10, 2011.



## I. Introduction

Accurate diagnosis is the foundation for choosing the right treatments for patients, and clinical laboratory tests provide critical information that health care providers use in about 70 percent of their decisions.<sup>6</sup> Modern advances in research have recently prompted an expansion in genetic and genomic testing, and these types of tests represent a fast-growing component of the clinical laboratory marketplace. Tests rooted in genetic and genomic advancements have emerged as highly accurate tools for diagnosing monogenic and polygenic diseases and disorders, and as predictive tools for enhancing public health. Genetic and genomic testing is also able to characterize specific cancers, definitively identify infectious organisms and organismal strains, and guide the prescription and dosing of appropriate therapeutic approaches.

Genetic and genomic testing can thus be seen to be at the heart of a new paradigm of medicine that is evidence-based and rooted in quantitative science. It is facilitating a move towards personalized, predictive and preventive medicine, and away from a more reactive medicine that only responds to emergent symptoms, or that provides general, one-size fits all therapies without an understanding of the underlying individualized response that may occur (positively or negatively) to such a trial-and-error approach.

From an economic standpoint, genetic and genomic tests and diagnostics development represent an expanding industry for the United States. Built upon biomedical research programs, such as the Human Genome Project (HGP), and subsequent genomics R&D, the U.S. is a global leader in this advanced field of science, and is home to many successful and growing companies leveraging genetic and genomic advancements to produce new diagnostic tests and technologies. Likewise, the growth of genetic and genomic testing is providing new job and economic growth opportunities within clinical laboratories (both freestanding commercial laboratories and within other laboratory settings, such as in hospitals). These laboratory jobs are good-paying jobs requiring skills and specialized technical know-how—the type of jobs needed to sustain a high standard of living for American workers. In the longer term, jobs and economic growth are also likely to occur in the custom formulation and preparation of personalized therapeutics based on the implementation of personalized medicine—pairing medicines with companion diagnostics.

Genetic and genomics tests provide a means to very desirable ends. Medicine that can be predictive and preventive, which is personalized to a patient's genomic profile, will help to keep us healthier and reduce the costs associated with chronic conditions and disease that may otherwise emerge without preventive action. Medicine will also be more targeted, using genetic and genomic tests to identify which therapy will be most effective given the patient's genomic profile. Such tests, and the promise of personalized medicine, provide a new level of precision to clinical care—reducing the costs and suffering associated with misdiagnosis, the prescription of drugs unlikely to work for a particular patient, and the potential for adverse drug reactions.

### A Need to Quantify Genetic and Genomic Testing Impacts

Up until now, there has not been a thorough analysis of the specific impacts likely to be generated by the genetic and genomic testing industry. Recent work by Battelle examining impacts associated with

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<sup>6</sup> UK Department of Health Pathology Modernisation Team. Modernising Pathology Services, 2004. Available at [www.dh.gov.uk](http://www.dh.gov.uk). 60–70% of NHS patients' diagnoses depend on laboratory tests, p. 7.

the Human Genome Project<sup>7</sup> suggests that the genomic and related testing sector has experienced a high rate of growth in recent years, but a customized impact analysis is required to quantify the clinical laboratory sector's impact and the prospects for the growth of this industry built upon progress in genetics and genomics moving forward. Recognizing the importance and promise of the emerging genetics and genomics laboratory testing market, the American Clinical Laboratory Association (ACLA) approached the Battelle Memorial Institute's Technology Partnership Practice (authors of the HGP report) to request a study be performed specifically measuring impacts associated with the emerging genetics and genomics clinical testing market.

The time is right to conduct this report. Genome sequencing is now more affordable than ever, with costs rapidly approaching a level that will enable whole patient genome sequencing to be a routine clinical activity. The political environment is also highly dynamic at present, and decision makers need to have information regarding innovative, potentially high-growth economic sectors with which to guide their decision making. Bioscience, biomedicine, and biotechnology is a key target for national and individual state economic development efforts, and information regarding the genetic and genomic clinical laboratory testing sector, and its prospects for growth, will help guide strategic economic development efforts.

### Impact Analysis Methodology

The Battelle report, herein, provides detailed estimates of the current economic impacts of genetics and genomics testing—performed both by independent clinical laboratories and by hospitals (primarily academic medical centers and children's hospitals)—quantifying current direct, indirect and induced economic impacts associated with genetics and genomics testing within the United States. This economic segment will be referred to throughout the remainder of this report as the **genetic and genomic clinical laboratory testing sector** of the economy.

The Battelle economic impact analysis uses a custom economic input/output (I/O) model that quantifies the interrelationships between economic sectors in the economy of the United States. I/O data matrices track the flow of commodities to industries from producers and institutional consumers within the nation. These data also show expenditure and consumption activities by workers, owners of capital, and imports. The trade flows built into the model permit estimating the impacts of one sector on all other sectors with which it interacts.

The measured economic impacts consist of three types: **direct impacts** (the specific impact of genetic and genomic clinical laboratory testing expenditures in the first round of spending), **indirect impacts** (the impact of expenditures by suppliers to the genetic and genomic clinical laboratory testing sector), and **induced impacts** (the additional economic impacts of the spending of genetic and genomic clinical laboratory testing sector employees and suppliers' employees in the overall economy that can be specifically attributed to the direct genetic and genomic clinical laboratory expenditures). I/O analysis thus models the flow of funds that originate from direct genetic and genomic clinical laboratory testing expenditures in the economy and the ongoing ripple (multiplier) effect of these expenditures. In other words, economic impact models are based on the concept of "a multiplier"—i.e., every dollar spent in the economy may be partially re-spent (or recirculated) in the local economy, thereby generating additional economic activity and impact. I/O analysis represents the generally accepted standard methodology for measurement of economic impacts.

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<sup>7</sup> Simon Tripp and Martin Grueber. 2011. "Economic Impact of the Human Genome Project. Battelle Memorial Institute, Technology Partnership Practice.

The current estimated impacts of the genetic and genomic clinical laboratory testing sector were calculated using a 2009 U.S. IMPLAN I/O model (the most current available) generated by MIG, Inc. (one of two major developers of nationally and regionally-specific I/O tables and analytical systems). The analysis is structured upon a foundation of employment data included within the IMPLAN model that is built primarily from the United States Department of Labor's Quarterly Census of Employment and Wages (QCEW, tied to unemployment insurance reporting), collected in 2010 for the year 2009. These data, which are the latest data for the IMPLAN model, provide detailed intelligence on the number of establishments, monthly employment, and quarterly wages, by North American Industry Classification System (NAICS) industry, by county geography, by ownership sector, and for the entire U.S. The IMPLAN model employment data is further enhanced by U.S. Bureau of Economic Analysis data to account for sole proprietorships and other very small firms that fall outside of the QCEW data collection protocols.

Battelle acquired the necessary data files for use with the IMPLAN system and developed a customized model to quantify the direct, indirect and induced impacts of the genetic and genomics clinical testing sector. The model incorporates detail of the sector and its interrelationships with more than 430 other individual sectors that cover the entire national economy. With these data, the analysis is able to show not only the overall impact on the U.S. economy, but impacts on specific sub-sectors of the economy that are strongly dependent on economic activity generated by the genetic and genomic clinical laboratory sector.

There is currently no specific NAICS code solely for genetics and genomics clinical laboratory testing, and data for industry work in this regard is captured within other existing NAICS codes along with data for traditional laboratory testing tools and activities. As such, Battelle had to perform primary research, including a survey of major clinical laboratory organizations, in order to derive estimates of the current percentage of laboratory test volumes, revenues and employment that are focused in the genetics and genomics testing space. ACLA facilitated distribution of a Battelle-designed web-based survey to its membership, and follow-up was performed by both Battelle and ACLA to secure the required data.

### **Functional Impacts of Genetic and Genomic Clinical Testing**

The direct and indirect economic impacts generated by the output of business sectors within the U.S. economy quantify an important component of the genetic and genomic clinical laboratory testing sector's impacts. The impacts quantified by the input/output modeling, however, only tell part of the full genetic and genomic testing impact story (just covering what economists term "backward linkage" or expenditure-based impacts).

It is important that Battelle's analysis also go further, examining the broader functional impacts (also known as forward linkage impacts) associated with genetic and genomic-based clinical testing. An industry should not be solely judged on its spending impacts and multiplier effects on the national economy, rather the "functional" impacts of the actual products or services of an industry must also be considered—especially when they are important products in securing human health and wellbeing.

The genetic and genomic clinical laboratory testing sector is bringing new capabilities and enhanced accuracy to the diagnosis of diseases and disorders in symptomatic and asymptomatic individuals. As the universe of genetic and genomic tests grows, these modern biomedical diagnostic tools are being used to:

- *Provide accurate diagnosis of patient specific diseases and disorders.*
- *Provide information on disease susceptibility associated with specific genes or genomic characteristics, thereby facilitating preventive measures.*

- *Develop refined treatment regimes and protocols based on the patient's genome.*
- *Avoid misdiagnoses and the costs associated with such.*
- *Avoid adverse drug reactions, or delayed treatment benefits, associated with the prescription of drugs unlikely to work appropriately given the patient's genome.*

These, and other, functional benefits of genetic and genomic testing are facilitating significant advancements in the practice of clinical medicine. They are also important for developing new approaches to disease treatment and as tools for identification of targets for therapeutics. Currently in its early stages, these tests are also bringing about the era of personalized medicine—a new paradigm of medicine in which therapies are tailored to the specific genome of the patient with the net result being more effective and safer approaches to treatment.

### **Report Format**

To-date, no detailed study has been made of the economic impacts of genetic and genomic testing and the promise of these tools for reshaping medicine. Battelle's research is directed towards estimating the current size of the genetic and genomic clinical testing sector in the U.S. and then modeling the quantitative economic impacts being generated by the sector. Battelle also discusses and provides perspective on many of the functional benefits associated with the rise of genetic and genomic clinical testing.

In Chapter II, Battelle first discusses the clinical testing marketplace in general (based on existing market research reports) and discusses the genetic and genomic testing component within this overall market. In order to identify the size of the genetic and genomic component of the testing market, Battelle deployed a survey to leading clinical reference laboratories across the U.S. (ACLA members) and conducted interviews with ACLA member organizations, diagnostic kit manufacturers, and several academic medical center clinical laboratory leaders.

In Chapter III, market estimates are deployed in quantifying the current economic impact of genetic and genomic clinical laboratory testing on the U.S. The generally accepted econometric technique of input/output (I/O) analysis is used to model and quantify the direct and indirect impacts of this test sector on business volume (economic output), jobs, personal income, and government revenues.

In Chapter IV, consideration is given to the functional impacts of genetic and genomic testing and their promise for the future in advancing the accuracy and effectiveness of clinical care. Finally in Chapter V, a brief discussion of the industry's future outlook is undertaken.

## II. The Clinical Laboratory Testing Marketplace

Diagnostics represent an extremely high-value/high-return tool for health care, providing their critically important health care decision support function for just 1.6 percent of Medicare spending.<sup>8</sup>

Despite representing a small percentage of overall health care costs, the huge scale of health care in the U.S. still means that diagnostics and clinical laboratory tests represent a very large market. Recent market research analysis, for example, places the size of the clinical laboratory testing market in the United States at \$62 billion for 2010.<sup>9</sup>

With more than 68,000 classified medical diseases, disorders and diagnostic codes,<sup>10</sup> and multiple sub-types for many diseases, the demand for accurate clinical diagnostic tests is intense. The majority of tests are routine high-volume tests that the majority of laboratories are equipped to perform (e.g. urinalysis, fecal blood tests, direct antigen strep tests, etc.). However, as test complexity and sophistication increases, the number of labs able to perform these tests diminishes significantly (by virtue of the required investment in specially trained personnel and specialized equipment). The sophisticated realms of esoteric testing, advanced molecular diagnostics, and genetic and genomic testing are primarily reserved for specialized independent commercial clinical laboratories serving a diverse set of health care provider customers, and for major research-oriented/academic medical center and children's hospitals. Very little genetic and genomic testing is taking place outside of the independent clinical laboratory and major academic medical center space (i.e., very little is done in physician office laboratories or in community hospital laboratories). Given the focus of this report on the impact of genetic and genomic testing, it is this subset of specialized test providers that is of primary relevance and interest. Battelle has thus concentrated research on the reference labs, academic medical center and specialized children's hospital labs in order to quantify the current impact of these advanced diagnostic tools.

### The Overall Clinical Testing Market

As noted above, recent research suggests that clinical laboratory testing is a \$62 billion industry in the United States. Within this testing marketplace, tests take place in a diversity of laboratory types. Analysis of Centers for Medicare Services (CMS) Clinical Laboratory Improvement Amendments (CLIA) data for 2009, performed by G2 Intelligence, indicates that hospitals perform the highest volume of tests (53.7 percent), while independent clinical testing laboratories perform 33.1 percent, physicians offices 9.4 percent and "other" labs (including settings such as public health labs, prisons, nursing homes, etc.) account for 3.9 percent.

In 2009, CMS data indicate there were 8,690 CLIA-certified hospital laboratories, with a median hospital test volume of 571,335 tests. In the same year there were 5,346 CLIA-certified independent laboratories in the U.S., and 110,925 physicians' office labs. In total CMS recorded 214,875 CLIA-certified labs across the U.S. in 2009.

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<sup>8</sup> Medicare Payment Advisory Commission (MedPAC). A Data Book: Health Care Spending and the Medicare Program, June 2011. 1.6% of Medicare spending on clinical laboratory services, page 203.

<sup>9</sup> G2 Intelligence. 2011. "Lab Industry Strategic Outlook 2011: Market Trends and Analysis."

<sup>10</sup> World Health Organization. International Classification of Diseases 2012. See discussion at the U.S. Centers for Disease Control at <http://www.cdc.gov/nchs/icd/icd10cm.htm>

While the overall clinical laboratory testing market is large and diverse, when it comes to high complexity and lower volume specialty tests (a.k.a. esoteric tests) the number of laboratories engaged reduces substantially. Most physicians' office labs, for example, only perform relatively simple routine tests, and likewise most community hospital laboratories would outsource their more sophisticated tests to independent specialty commercial laboratories or the labs of large academic medical center hospitals and health systems.

While only a subset of the total clinical lab testing market, the world of specialized, highly sophisticated clinical tests is growing considerably faster than the average for all clinical testing. G2 Intelligence identified "esoteric testing" as experiencing growth from \$7 billion in 2006 to \$14.3 billion in 2010.

### Genetic and Genomic Clinical Testing

Identifying the current market size of the genetic and genomic clinical laboratory testing component is difficult. Genetic and genomic molecular diagnostic tests are part of multiple sectors tracked in the frequently cited G2 report. Genetic and genomic tests are, for example, included within, but not exclusive to, the categories of "esoteric tests," "anatomical pathology tests" and "cytology tests". Molecular pathology, for example, is a subcomponent of the anatomic pathology category and is an emerging discipline focused on the use of nucleic-acid based techniques such as in-situ hybridization, PCR and microarrays for specialized study of disease in tissues and cells. The majority of tests for hereditary genetic disorders would be considered sub-components of the esoteric testing market. The emerging area of pharmacogenomics includes genetic and genomic tests designed to identify patient genes as they specifically relate to effectiveness, dosing and potential side effects of specific therapeutic compounds.

The challenge of measuring the current market is echoed by Results for Life in their document *Genetic Test Primer*. Here it is noted that:

*A concise definition of genetic testing remains elusive because it can include testing on virtually all elements of the human gene—DNA, RNA, chromosomes, human proteins, and certain metabolites used to detect inherited or acquired diseases and conditions. Such techniques are often characterized in different ways—cytogenetics for detecting abnormalities of chromosomes within a cell; molecular genetics for detecting changes at the level of genes or DNA; and biochemical techniques to detect changes in human proteins.*

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The National Library of Medicine (NLM), in lead-in narrative to its GeneTests site, notes that:

*A genetic test is the analysis of human DNA, RNA, chromosomes, proteins, or certain metabolites in order to detect alterations related to a heritable disorder. This can be accomplished by directly examining the DNA or RNA that makes up a gene (direct testing), looking at markers co-inherited with a disease-causing gene (linkage testing), assaying certain metabolites (biochemical testing), or examining the chromosomes (cytogenetic testing).*

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However, NLM's GeneTests site is only focused on hereditary diseases, and thus their definition excludes many other important applications of genetic and genomic testing relating to acquired diseases (such as cancer), infectious diseases, and pharmacogenomic testing.

What there does seem to be agreement on is that genetic and genomic testing comprises three major categories: *molecular genetics* applications (focused on the identification of single or multiple-genes associated with a disease, disorder or potential drug response); *cytogenetics* applications examining chromosomes and chromosomal abnormalities, and *biochemical techniques* detecting markers of changes to proteins and certain metabolites linked to genetic function.

While there is currently no standard definition of genetic and genomic tests, Battelle and the American Clinical Laboratory Association used the following definition for the purposes of this study:

*A genetic or genomic test involves an analysis of human chromosomes, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), genes, and/or gene products (e.g., enzymes, metabolites and other types of proteins), which is predominately used to detect heritable or somatic mutations, genotypes, or phenotypes related to disease, health or identity. The purpose of genetic tests includes predicting risk of disease, screening newborns, directing clinical management, identifying carriers, and establishing prenatal or clinical diagnoses or prognoses in individuals, families, or population, as well as use for forensic and identity purposes.*

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This definition actually serves to highlight some of the key areas of biomedical application for genetic and genomic testing:

- **Diagnosis of Disease:** Whereby genetic or genomic tests are used to screen a patient with a suspected disease (usually a hereditary genetic disease) to positively identify the disease. This is genetic or genomic testing applied to a symptomatic individual.
- **Predictive Medicine:** The presymptomatic testing of individuals to determine the risk of developing adult onset diseases and disorders (such as Huntington's disease, certain cancers, etc.).
- **Genotyping of Specific Disease:** Such as the genotyping of a patient's specific HIV strain or cancer to guide therapeutic approaches. In many respects this is closely linked to pharmacogenomics.
- **Pharmacogenomics:** Whereby genetic or genomic testing is used to optimize drug therapies based on the patient's genotype and known genetic linkages to drug efficacy or toxicity.
- **Identity testing:** Whereby genetic testing assists in confidently establishing identity, providing individual genetic identification profiles. These profiles can be used to establish biological relatedness.
- **Forensic testing:** Whereby genetic testing is used to establish the identity of individuals based upon a specimen of blood, urine, or other tissue.
- **Carrier Screening:** This involves testing unaffected individuals who carry one copy of a gene for a disease that requires two copies for the disease to be expressed.
- **Newborn Screening:** Whereby newborns are screened shortly after birth for disorders that are treatable, but difficult to otherwise detect clinically.

Genetic and genomic testing can thus be seen to be at the heart of a new paradigm of medicine that is evidence-based and rooted in quantitative science. It is facilitating a move towards personalized, predictive and preventive medicine, and away from a more reactive medicine that only responds to emergent symptoms, or provides general, one-size fits all therapies without an understanding of the underlying individualized response that may occur (positively or negatively) to such a trial-and-error approach.

Genetic and genomic testing makes possible what Leroy Hood at the Institute for Systems Biology has termed P4 medicine—medicine that is personalized, predictive, preventive and participatory. The benefits of this approach to medicine are highlighted by Hood and Galas as being able to:<sup>11</sup>

- *Detect disease at an earlier stage, when it is easier and less expensive to treat effectively.*
- *Stratify patients into groups that enable the selection of optimal therapy.*
- *Reduce adverse drug reactions by more effective early assessment of individual drug responses.*
- *Improve the selection of new biochemical targets for drug discovery.*
- *Reduce the time, cost, and failure rate of clinical trials for new therapies.*
- *Shift the emphasis in medicine from reaction to prevention and from disease to wellness.*

It is clear that genetic and genomic testing provides a new suite of quantitative test tools for the diagnostician—tools that hold promise for enhancing the accuracy of a diagnosis for symptomatic and asymptomatic individuals and a tool to guide more effective and safer therapeutic approaches for both the treatment of emergent diseases and disorders and for prevention.

### **Battelle’s Analysis of the Genetic and Genomic Clinical Testing Space**

Battelle’s primary task with this research project is to determine the current economic impact of the genetic and genomic clinical laboratory testing sector using input/output (I/O) analysis. The fundamental input data for the I/O analysis is a current estimate of employment in genetic and genomic testing in the United States. To derive this estimate, Battelle designed a secure online survey (with the hyperlink delivered by ACLA via e-mail to its membership). The survey captures information from clinical laboratories regarding the current portion of their employment and test activity focused on the performance of genetic and genomic tests (with the definition of the tests being as shown on the previous page).

In addition to performing the survey, Battelle also interviewed several knowledgeable individuals in the laboratory sector, academic medical center clinical laboratories and the advanced diagnostics manufacturing industry to gain their perspective on the relative distribution of genetic and genomic testing between the independent clinical laboratory and major research hospital/academic medical center laboratory spaces.

As a result of this research, Battelle’s best estimates of the size of the genetic and genomic testing space are as follows:

#### **Projections of Market Size**

Two existing, and recently published, research reports on the clinical laboratory test sector have been produced by G2 Intelligence<sup>12</sup> and by IBISWorld<sup>13</sup> (who also cite industry size research conducted by LabCorp). These reports differ moderately in their size estimates for the total market for all clinical laboratory testing, with the G2 report estimating the size of the market at \$62 billion and IBISWorld citing a LabCorp quantification of \$55 billion.

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<sup>11</sup> Leroy E. Hood and David J. Galas. December 2008. “P4 Medicine: Personalized, Predictive, Preventive, Participatory: A Change of View that Changes Everything.” Version 6: December 12, 2008. Accessed online at [http://www.cra.org/ccc/docs/init/P4\\_Medicine.pdf](http://www.cra.org/ccc/docs/init/P4_Medicine.pdf)

<sup>12</sup> G2 Intelligence. 2011. “Lab Industry Strategic Outlook 2011: Market Trends and Analysis.”

<sup>13</sup> Sophia Snyder. IBISWorld. October 2011. “Healthy prognosis: New technologies and greater insurance coverage will strengthen demand.” IBISWorld Industry Report 62151 – Diagnostic and Medical Laboratories in the U.S.

In terms of the size of just the genetic and genomic component of the testing market, the IBISWorld report estimates it to be \$2.5 billion, or 4.54 percent of the total clinical laboratory testing market (and equivalent to 45.5 percent of their estimated \$5.5 billion for the esoteric testing space). The G2 study does not specifically call out genetic and genomic testing, but highlights esoteric testing as being a \$14.3 billion sector (23 percent of the total clinical lab space). If we apply the “45.5 percent of esoteric testing” market figure from the IBISWorld numbers to the G2 numbers, we arrive at an estimate of the size of the genetic and genomic test market being \$6.5 billion (or 10.5 percent of the total G2 estimated clinical laboratory testing market). Based then, on analysis of these two market research reports it is reasonable to assume that the genetic and genomic market space will currently fall somewhere within a range of 4.5 percent to 10.5 percent of the total clinical laboratory market.

As noted above, Battelle administered a survey to ACLA member clinical laboratories, with the survey being completed by both LabCorp and Quest (covering a large component of market share) and seven other major clinical labs. The survey asked the laboratories to specify their annual revenues from all tests, and their revenues only from genetic and genomic tests. The survey results indicate that 9.5 percent of the clinical laboratory revenues are currently derived from genetic and genomic testing—an amount that falls within the 4.5–10.5 percent range predicted by the aforementioned market research reports.

**Using the recent G2 estimate of \$62 billion for the total size of the clinical laboratory testing marketplace, and applying 9.5 percent being in genetic and genomic testing from the Battelle/ACLA Member survey, results in an estimated current genetic and genomic testing market size of \$5.89 billion.**

Interviews with laboratory industry leaders and individuals familiar with genetic and genomic testing across various laboratory settings indicate that currently approximately 50 percent of the market is served by independent clinical laboratory companies and 50 percent served by the specialized labs of academic medical centers and major children’s hospital systems. Based on this, Battelle considers it prudent to conclude that the current genetic and genomic testing revenue for independent clinical laboratories will stand at circa \$2.95 billion, with academic medical center/children’s hospital labs likewise doing a similar business volume in tests. These total market size estimates are used to drive the impact analysis modeling.

### III. The Economic Impact of Genetic and Genomic Clinical Laboratory Testing Services

#### Direct, Indirect and Induced Impacts of U.S. Genetic and Genomic Clinical Laboratory Testing

The economic impact analysis measures the impacts that business activities in genetic and genomic clinical laboratory testing have on the United States economy. The analysis makes use of a custom economic input/output (I/O) model quantifying the national interrelationships between economic sectors. I/O data matrices track the flow of commodities to industries from producers and institutional consumers within the nation. The data also show consumption activities by workers, owners of capital, and imports. These trade flows built into the model permit estimating the impacts of the genetic and genomic clinical laboratory testing sector on all other sectors with which it interacts.

The current estimated impacts of the sector were calculated using the most recently published (2009) U.S. specific I/O models generated by MIG, Inc. (one of two major developers of regionally and nationally specific I/O tables). IMPLAN provides a specialized software platform for impact analysis and highly detailed data tables at the national and individual state levels. Battelle acquired the necessary data files for use with the IMPLAN system and developed a customized model to quantify the direct, indirect and induced impacts of genetic and genomic clinical laboratory testing (see text box).

The model incorporates detail of the sector and its interrelationships with more than 430 other individual sectors that cover the entire national economy. With these data, the analysis is able to show not only the overall impact on the U.S. economy, but impacts on specific sub-sectors of the economy that are strongly dependent on economic activity generated by genetic and genomic clinical testing services.

Table 1 presents the findings from Battelle's I/O analysis of the U.S. genetic and genomic clinical laboratory testing sector. **The overall economic impact of the sector on the U.S. economy (as measured by "output") totals more than \$16.5 billion on an annual basis.** This impact comprises nearly \$5.9 billion in direct impact of clinical laboratories and \$10.6 billion in indirect and induced impacts (an output multiplier of 2.8—meaning that **every \$1 dollar in output generated by genetic and genomic clinical laboratory testing generates another \$1.8 in output in other sectors of the economy**).

Genetic and genomic testing is still in the relatively early stages of its development, and much future growth is expected to occur. Still, even in this early stage of development **the U.S. genetic and genomic clinical laboratory testing sector is responsible for supporting more than 116,000 jobs in the U.S. economy** (45,563 direct jobs and an additional 72,723 indirect and induced jobs) in 2009. Together, this genetic and genomic clinical laboratory testing sector-related workforce received nearly \$6 billion in wages and benefits in 2009. In addition, the sector is also an important generator of government

Impacts consist of three general types: **direct impacts** (the specific impact or effect of genetic and genomic clinical laboratory testing expenditures in the first round of spending), **indirect impacts** (the impact of expenditures by suppliers to laboratories performing genetic and genomic testing), and **induced impacts** (the additional economic impact of the spending of genetic and genomic clinical laboratory testing employees and suppliers' employees in the overall economy that can be attributed to the direct testing sector expenditures).

In other words, I/O analysis models the flow of funds that originate from direct genetic and genomic clinical laboratory testing sector expenditures in the economy and the ongoing ripple (multiplier) effect of these expenditures. I/O analysis represents the generally accepted standard for measurement of economic impacts.

revenues for state and local jurisdictions and for the federal government. The analysis shows that genetic and genomic clinical laboratory testing business volume, directly and through the multiplier effect, generated nearly \$657 million in estimated state and local tax revenue and nearly \$1.2 billion in federal tax revenues in 2009.

**Table 1: Economic Impacts of U.S. Genetic and Genomic Clinical Laboratory Testing on the U.S. (\$Millions)**

Category of Impact	Jobs	Personal Income	Value-Added	Output (Business Volume)	State/Local Tax Revenue	Federal Tax Revenue
Direct Impacts	43,563	\$2,504	\$3,221	\$5,890	\$98	\$448
Indirect Impacts	27,397	\$1,417	\$2,360	\$4,118	\$189	\$290
Induced Impacts	45,326	\$2,035	\$3,614	\$6,518	\$370	\$437
<b>Total Impacts</b>	<b>116,286</b>	<b>\$5,956</b>	<b>\$9,195</b>	<b>\$16,526</b>	<b>\$657</b>	<b>\$1,175</b>
Impact Multiplier	2.7	2.4	2.9	2.8	6.7	2.6

Source: Battelle analysis; IMPLAN U.S. 2009 Model

*Personal Income: Measures cash, benefits and non-cash payments received by individuals in the economy.*

*Value-Added: The difference between an industry's or an establishment's total output and the cost of its intermediate inputs.*

*Output: The dollar value of production (i.e., sales).*

I/O analysis illuminates the supply chain related to genetic and genomic clinical laboratory testing activities and measures the economic impacts on related-sectors of the economy. Table 2 shows the sectors of the economy that have the highest volumes of employment and output associated with genetic and genomic clinical laboratory testing business activity.

**Table 2: Total Genetic and Genomic Clinical Laboratory Testing Sector Impacts on Key Supplier Industries and on the Rest of the U.S. Economy**

<b>NAICS Industry Sector Title</b>	<b>2009 Employment</b>	<b>2009 Output (\$Millions)</b>
<b>Genetic and Genomic Clinical Laboratory Testing (Direct Impacts)</b>	<b>43,563</b>	<b>\$5,890</b>
<b>Key (Top 20 based on Indirect Impacts) Industry Supplier Sectors</b>		
<i>Real estate establishments</i>	5,332	\$770
<i>Medical/diagnostic labs and outpatient/ ambulatory care services</i>	2,001	\$271
<i>Management of companies and enterprises</i>	1,383	\$285
<i>Management- scientific- and technical consulting</i>	1,737	\$233
<i>Wholesale trade businesses</i>	2,324	\$460
<i>Telecommunications</i>	662	\$296
<i>Employment services</i>	4,639	\$199
<i>Insurance carriers</i>	1,134	\$363
<i>Petroleum refineries</i>	28	\$257
<i>Legal services</i>	1,116	\$187
<i>Pharmaceutical preparation manufacturing</i>	138	\$178
<i>Food services and drinking places</i>	5,492	\$319
<i>Nondepository credit intermediation</i>	505	\$229
<i>Monetary authorities and depository credit intermediation</i>	916	\$254
<i>Office administrative services</i>	757	\$87
<i>Services to buildings and dwellings</i>	1,903	\$115
<i>Insurance agencies and brokerages</i>	904	\$133
<i>Accounting, tax preparation, bookkeeping</i>	1,055	\$101
<i>Electric power generation and transmission</i>	220	\$144
<i>Surgical and medical instrument manufacturing</i>	182	\$57
<b>Total of Key Supplier Sectors (Indirect &amp; Induced Effects)</b>	<b>32,425</b>	<b>\$4,937</b>
<b>Remaining Sectors of Economy (Indirect &amp; Induced Effects)</b>	<b>40,298</b>	<b>\$5,699</b>
<b>Total Genetic and Genomic Clinical Laboratory Testing Impacts (Direct, Indirect &amp; Induced Effects)</b>	<b>116,286</b>	<b>\$16,526</b>

Source: Battelle analysis; IMPLAN U.S. 2009 Model

### **Additional Economic Benefits Associated with Genetic and Genomic Clinical Laboratory Testing**

The life sciences have proven to be a key economic development engine for the U.S. economy in recent decades. Built upon U.S. investment in basic science and translational biomedical research, U.S. industry has produced a broad range of high-value biomedical technologies and products that create high-paying jobs and sustain America’s leadership in the modern innovation economy.

#### **Genetic and Genomic Clinical Laboratory Testing and High Quality Job Creation**

Requiring a well-educated, skilled and technologically trained workforce, the performance of genetic and genomic clinical laboratory testing generates good quality, high-wage, and family sustaining jobs.

Comparatively high levels of wages and salaries are provided within the industry, as are family-sustaining benefits packages—helping to support a high quality of life for an estimated 46,563 persons

directly employed in genetic and genomic clinical laboratory testing. Battelle’s analysis indicates that the annual average personal income of a worker in this sector was \$57,475 in 2009—a significant wage premium as compared to \$45,320 in the overall economy.

### **Genetic and Genomic Tests and the U.S. Innovation Economy**

It takes significant levels of R&D to produce new genetic and genomic clinical laboratory tests. Innovation and new test development takes place within the laboratory industry (both independent labs and in academic medical research centers) and within specialized diagnostics development companies.

Within the clinical laboratory industry both commercial laboratories and academic-based clinical laboratories are playing an important role in the development of new genetic and genomic tests—and earning income from their use and licensing. The development of proprietary genetic and genomic tests has also been the basis for the formation of new, innovative diagnostics companies and expansion of the innovative product offerings of established diagnostics production companies that produce reagents, gene chips, test kits and associated products. Likewise the expanding demand for genetics and genomics analysis is driving expansion of a genomic analysis technology industry—with companies manufacturing gene sequencers and other sophisticated analytical systems and sample processing technologies required by the industry.

A recent analysis by Battelle of the economic impact of the total genomics industry in the United States found it to already be generating total economic impacts across the U.S. economy of \$67 billion in economic output and more than 310,000 jobs<sup>14</sup>. The clinical diagnostics sector has been one of the first movers in applying the findings of advanced biomedical research programs, such as the Human Genome Project, in bringing new technologies and tools to market and making direct use of U.S. R&D discoveries and innovations in genomics and associated science.

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<sup>14</sup> Simon Tripp and Martin Grueber. 2011. “Economic Impact of the Human Genome Project. Battelle Memorial Institute, Technology Partnership Practice.

## IV. The Functional Societal Benefits of Genetic and Genomic Clinical Laboratory Testing

The expenditure-based economic impacts discussed in the previous chapter, while substantial, represent only a fraction of the overall beneficial impact of genetic and genomic testing. As a result of the industry's focus, genetic and genomic testing is bringing new capabilities and enhanced accuracy to the diagnosis of diseases and disorders in symptomatic and asymptomatic individuals. As the universe of genetic and genomic tests grows, these modern biomedical diagnostic tools are being used to:

- *Provide accurate diagnosis of patient specific diseases and disorders.*
- *Provide information on disease susceptibility associated with specific genes or genomic characteristics, thereby facilitating preventive measures.*
- *Develop refined treatment regimes and protocols based on the patient's genome.*
- *Avoid misdiagnoses and the costs associated with such.*
- *Avoid adverse drug reactions, or delayed treatment benefits, associated with the prescription of drugs unlikely to work appropriately given the patient's genome.*

In other words, the application of genetic and genomic tests to improve human health, longevity and quality of life is the primary purpose of their development and deployment, and ultimately result in the industry's functional impacts on society. Functional impacts, also known as forward linkage impacts, are the benefits generated by the industry's products and services.

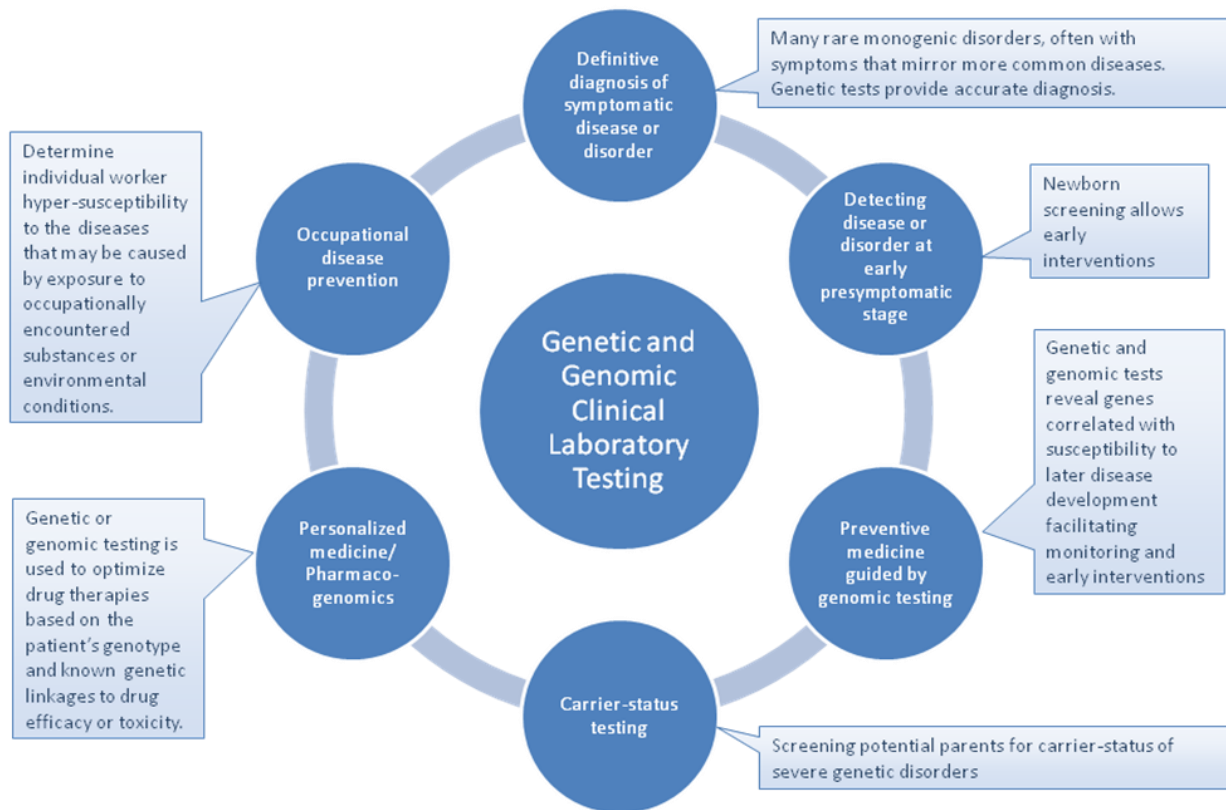
In the case of the genetic and genomic clinical testing industry, the products and services make possible multiple desirable societal benefits, both economic and non-economic:

- Providing a definitive, accurate diagnosis of a disease or disorder, thereby helping to avoid misdiagnoses and the associated stress on patients and healthcare spending on unnecessary or ineffective treatments.
- Detecting a disease or disorder at an early stage, or even a pre-symptomatic stage, when it is easier and less expensive to treat effectively, thereby saving healthcare costs and increasing labor force productivity.
- Providing information on disease susceptibility associated with specific genes or genomic characteristics, thereby facilitating preventive measures and appropriate life planning.
- Minimizing the impact of devastating childhood diseases through testing of potential parents for carrier-status of genetic disorders.
- Directing the application and dosing of therapeutics most likely to be safe and effective given the patient's genotype, thereby avoiding adverse drug reactions and the healthcare costs associated with treating them.
- Using genetic and genomic testing applications in occupational health practices to determine the effects of worker exposure to hazardous agents, and to determine individual hyper-susceptibility to the diseases that exposure may cause.
- Using genetic tests assists in confidently establishing identity, providing individual genetic identification profiles. These profiles can be used to establish biological relatedness.

- Using genetic tests for forensic analysis, which is used to establish the identity of individuals based upon a specimen of blood, urine, or other tissue.

With the reference human genome sequence only completed a decade ago, and the Human Genome Project unveiling a far more complex genetic structure than previously thought, the development of commercially available genetic and genomic testing tools and techniques is still in a relatively early stage. That said, in each of the bulleted categories of health care benefits shown above and illustrated in Figure 1, genetic and genomic testing is being applied *today* to improve the care and prognosis of patients. Furthermore, each area holds significant future promise for far more wide-ranging application and subsequent benefits.

**Figure 1: Functional Applications of Genetic and Genomic Clinical Laboratory testing**



Below, each of these categories of functional health care benefit is discussed, and some examples of current applications are presented to illustrate the scope and promise of genetic and genomic clinical laboratory testing both today and in the future.

**Providing a definitive, accurate diagnosis of a disease or disorder, thereby helping to avoid misdiagnoses and the associated costs and negative health impacts that result from them.**

The ability to diagnose a patient's disease or disorder accurately and quickly has been a longstanding struggle within the healthcare industry. A study of autopsies published in *Mayo Clinic Proceedings* comparing clinical diagnoses with postmortem diagnoses revealed that in 26 percent of cases, the clinical diagnosis was inaccurate. Furthermore, the study revealed that if the true diagnosis had been

known prior to death, it more than likely would have resulted in a change in treatment and prolonged survival rate.<sup>15</sup>

Misdiagnoses have serious impact on the quality of care patients receive. Individuals who receive a false positive diagnosis often endure unnecessary treatments, with both medical as well as financial ramifications, before the misdiagnosis is discovered. At the same time, when an individual receives a false negative diagnosis, the undetected illness can cause the patient's condition to deteriorate to the point where more extensive medical intervention becomes necessary, which in turn has both medical and financial ramifications. Furthermore, when a diagnosis is simply unable to be reached, equivocal interpretations lead to additional testing which results in a delay in definitive treatment for the patient as well as additional financial costs. Finally, in addition to the medical symptoms and the increased financial costs, misdiagnoses also cause individuals to suffer increased anxiety and stress.

Genetic and genomic testing is bringing new capabilities and enhanced accuracy to the diagnosis of diseases and disorders in symptomatic and asymptomatic individuals that are resulting in more accurate diagnosis of patient specific diseases and disorders that in turn help to avoid misdiagnoses and the costs associated with such. Some of the functional benefits of genetic and genomic diagnostic testing include:

- The ability to confirm or rule out a known or suspected genetic disorder in a symptomatic individual.
- The capability to provide diagnostic information at a lower cost and with less risk than other procedures.
- The ability to perform testing in symptomatic individuals of any age.
- The ability to alter medical management for the individual upon confirmation of the diagnosis.

**The ability to diagnose diseases more precisely by using genetic and genomic testing leads to more effective treatment. For example:**

- **Childhood Leukemia:** The ability to effectively treat childhood leukemia requires that the subtype of the disease be accurately diagnosed. By utilizing genetic testing to identify the disease subtype, physicians are then able to choose drugs and treatment protocols that are most effective for the diagnosis. As a result of genetic testing, today's cure-rate for children exceeds 80 percent compared to 4 percent in the 1960's.
- **Cervical Cancer:** Certain high-risk strains of the Human Papilloma Virus (HPV), which causes cervical cancer, are difficult to diagnose. Genetic tests are able to identify the high-risk HPV strains, which in turn allows for earlier decisions about treatment and frequency of follow-up monitoring.

For patients with extremely rare disorders, diagnosis has historically been very difficult. Primary care physicians and pediatricians may never have encountered a specific type of monogenic disorder that presents in a patient. Unfamiliarity with a rare disorder can lead to an incorrect diagnosis, the wrong treatment, negative side effects from the wrong treatment, and ongoing suffering from the disorder or disease. It is particularly difficult for a physician to diagnose a rare disease when its symptoms may mirror another more common disease. Without definitive genomic tests, physicians are often running practically blind; having to use a sub-optimal one-size fits all approach to their diagnoses and treatments.

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<sup>15</sup> Roosen J, Frans E, Wilmer A, et al. Comparison of premortem clinical diagnoses in critically ill patients and subsequent autopsy findings. *Mayo Clinic Proceedings* 2000; 75:562-567.

Finally, in addition to the functional benefits related to the accurate diagnosis of diseases and disorders that are resulting in better healthcare and a reduction in financial costs, the technology that is enabling more effective and efficient diagnostic and treatment techniques is also spurring further innovation in other fields as well. Specifically, great strides are being made in the field of health informatics as research and genomic databases are designed to manage and protect the vast amount of information being collected.<sup>16</sup> One example is the Electronic Medical Records and Genomics (eMerge) Network, which is charged with integrating scientific and medical records databases. The project, which began in 2007, has shown that data about disease characteristics in electronic medical records and patient's genetic information can be used in large genetic studies. Organized by the National Human Genome Research Institute (NHGRI), the eMERGE Network is a national consortium formed to develop, disseminate, and apply approaches to research that combine DNA biorepositories with electronic medical record (EMR) systems for large-scale, high-throughput genetic research. The consortium is exploring the ability (and feasibility) of using EMR systems to investigate gene-disease relationships. More than a dozen phenotypes are currently being investigated.<sup>17</sup>

### Detecting a disease or disorder at an early stage, or even a pre-symptomatic stage, when it is easier and less expensive to treat effectively.

The ability to detect a disease or disorder at a relatively early stage in its progression, even at a pre-symptomatic stage, often results in less invasive and less costly medical treatments in the long-run. For instance, a study of the overall expenditures of breast cancer patients found that the four-year mean cumulative costs for treating stage III and IV cancer patients was approximately two to three times higher than cancer patients with stage 0 and I of the disease.<sup>18</sup>

According to the U.S. Centers for Disease Control and Prevention's Report on Chronic Disease Overview, treating diabetes, heart disease, Alzheimer's, and cancer comprises 75 percent of U.S. health care costs.<sup>19</sup> The ability to detect and better treat these chronic conditions at an earlier stage in their development would greatly reduce both the medical and financial costs of treatment, thus greatly reducing their burden on both the individual patient as well as the economy overall.

**The ability to detect diseases before symptoms even occur, by using genetic and genomic testing, allows for earlier and often more effective treatment. For example:**

- **Heart Disease:** A number of gene variations increase an individual's susceptibility to heart disease and heart attacks. Genetic tests are able to identify the genetic variations allowing for earlier detection and subsequent treatment by increasing the dosage of statin drugs. This has resulted in significantly reducing the risk of heart attacks and coronary heart diseases among this patient set.
- **Emphysema:** Gene variations increase the likelihood of liver cancer in patients with emphysema. Genetic tests are able to identify the variation, which in turn allows for an early diagnosis without a biopsy that in turn enables

The early detection of diseases is being greatly aided by genetic and genomic testing. By utilizing genetic and genomic testing, diseases can be detected and therefore diagnosed earlier, thereby allowing for

<sup>16</sup> Michael Rugnetta, Whitney Kramer: "Paving the Way for Personalized Medicine-Facilitating Inter-Agency Coordination for the Integration of Personalized Medicine into Our Health Care System" *Science Progress*, September 2009.

<sup>17</sup> eMerge web site: <http://www.genome.gov/27540473>

<sup>18</sup> Logorreta AP, Brooks RJ, Leibowitz AN, Solin LJ. Cost of breast cancer treatment: A 4-year longitudinal study. *Arch Intern MED* 1996; 156:2197-2201.

<sup>19</sup> Centers for Disease Control and Prevention, "Chronic Disease Overview" available at <http://www.cdc.gov/NCCdphp/overview.htm>

targeted medical treatment at the onset of the disease, saving the costs of treatment of more advanced disease states. The refined testing techniques use genetic factors to adjust a patient's response when individual metabolic characteristics may cause false positive as well as false negative results.<sup>20</sup>

Therefore, a significant functional benefit of genetic and genomic testing includes the ability to detect at an early stage, or even a pre-symptomatic stage, individuals who have a specific genetic disorder so that treatment can be started as soon as possible. This creates an environment in which the medical condition can be treated most effectively and very often at a reduced financial cost.

One specific area in which genetic and genomic testing are used to detect a disease or disorder at a pre-symptomatic stage is the field of newborn screening. Newborn screening is the systematic screening of newborn babies to identify individuals at increased risk for certain disorders. The purpose of newborn screening is to identify babies with certain congenital genetic, metabolic, or infectious disorders early, in an effort to improve their long term health. Early detection of these abnormalities can prevent severe disability, mental retardation or even death, and may also save states and families money by avoiding financially burdensome medical costs and state institutional services. For example, in a recent study conducted in the United Kingdom, the costs associated with newborn screening for cystic fibrosis were analyzed. The study found that the cost of therapy for patients diagnosed by newborn screening was significantly lower than equivalent therapies for clinically diagnosed patients, on average 40 percent less.<sup>21</sup> The study concluded that the clinical, social, and economic evidence suggests that universal newborn screening programs for cystic fibrosis should be adopted internationally.

Within the U.S., newborn screening programs are public health programs operated by each individual state. It is estimated that 4.1 million infants in the U.S. are screened annually for genetic and metabolic disorders.<sup>22</sup> The particular disorders screened vary from state to state. National standards for newborn screening were adopted in May of 2010, and the current goal of advocates is to ensure that each individual state adopts the national standards so that every newborn in the U.S. is screened for the same panel of disorders, regardless of the state in which they are born.

### **Providing information on disease susceptibility associated with specific genes or genomic characteristics, thereby facilitating preventive measures.**

Genetic and genomic testing is providing information on disease susceptibility associated with specific genes or genomic characteristics, often referred to as predictive testing, thereby facilitating preventive measures. Predictive testing is offered to asymptomatic individuals with a family history of a genetic disorder. Predictive testing is of two types: presymptomatic (eventual development of symptoms is certain when the gene mutation is present, e.g., Huntington's disease) and predispositional (eventual development of symptoms is likely but not certain when the gene mutation is present, e.g., breast cancer). Some of the functional benefits of genetic and genomic predictive testing include:

- Capability through early diagnosis to allow for medical intervention that either prevents or slows the onset of the condition and promotes well-being.
- Ability for individual to alter his or her lifestyle to manage the disease or disorder.

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<sup>20</sup> Ibid.

<sup>21</sup> Sims, E.J., et.al., Economic implications of newborn screening for cystic fibrosis: a cost of illness retrospective cohort study. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/17416263>

<sup>22</sup> National Conference of State Legislatures available at: <http://www.ncsl.org/IssuesResearch/Health/NewbornGeneticandMetabolicScreeningLaws/tabid/14416/Default.aspx>

- If a genetic characteristic is discovered that indicates disease susceptibility, it can allow time to plan for future health care, making more realistic life choices or employment decisions, and informed reproductive decisions.
- Regardless of the result, testing can end the uncertainty surrounding the chance of developing the condition. If an individual doesn't carry the genetic characteristic, a huge burden may be lifted and a less stressful life may be led.

By determining who falls into at-risk groups through genetic testing, individuals who are susceptible to certain diseases or disorders can be targeted earlier with preventative measures which in turn improves the quality of lives. Tests are currently available that identify people at high risk for conditions that may be preventable. For example, aggressive monitoring for and removal of colon growths in individuals inheriting a gene for familial adenomatous polyposis (a precursor to colon cancer development) has saved many lives. Also in development is a gene test that will provide doctors with a simple diagnostic test for a common iron-storage disease, transforming it from a usually fatal condition to a treatable one.

However, it is important to note that predictive testing has become somewhat controversial over the years since it first became available. Commercialized gene tests for adult-onset disorders such as Alzheimer's disease and some cancers are the subject of most of the debate over genetic testing. These tests are targeted to healthy (presymptomatic) individuals who are identified as being at high risk because of a strong family medical history for the disease or disorder. However, the tests can only provide a probability for developing the condition. One of the most serious limitations of these predictive tests (at the present time) is the difficulty in interpreting a positive result since some people who carry a disease-associated mutation never develop the disease. Scientists believe that these mutations may work together with other, unknown mutations or with environmental factors to cause disease. Therefore, some in the medical establishment feel that uncertainties surrounding test interpretation, the current lack of available medical options for these diseases, the tests' potential for provoking anxiety, and risks for discrimination and social stigmatization could outweigh the benefits of testing in those specific applications.

**The ability to provide information on disease susceptibility associated with certain genes or genomic characteristics by using genetic and genomic testing facilitates preventative measures. For example:**

- **Breast and Ovarian Cancer:** Genetic tests can identify variations in the BRCA1 and BRCA2 genes that increase the risks for breast and ovarian cancer, which in turn allows preventive measures such as closer monitoring and preventive surgery.
- **Blood Clotting:** Individuals with a variation in the Factor V gene and other genes have a five times greater risk of developing blood clots. Genetic tests can identify the unique variations that increase this risk, which enables individuals to take preventive strategies and medication to manage clotting.
- **Melanoma:** Genetic tests can identify increased susceptibility to the disease by identifying gene variations that lead to 40 percent of melanoma cases. The tests allow preventive steps such as surgery on suspicious lesions, as well as lifestyle choices such as less exposure to the sun.

## Minimizing the impact of devastating childhood diseases through testing of potential parents for carrier-status of genetic disorders.

Carrier testing is a form of genetic testing that identifies individuals who carry one copy of a gene mutation that, when present in two copies, causes a genetic disorder. This type of testing is offered to individuals who have a family history of a genetic disorder and to people in ethnic groups with an increased risk of specific genetic conditions. If both potential parents are tested, the test can provide information about a couple's risk of having a child with a genetic condition.

Carrier testing can improve risk assessment for members of certain racial and ethnic groups more likely to carry mutations for certain genetic conditions. Some autosomal recessive diseases occur more commonly in particular ethnic groups. In these situations, carrier testing may be offered to individuals who do not have a family history. For instance, Tay-Sachs is a neurological disease that is more common in Ashkenazi, or Eastern European Jews. Children with the disease lack a key enzyme, and as a result lose mental and physical abilities and usually die by the age of four. In the last decade, only about a dozen new cases of Tay-Sachs occurred each year in the United States. The predominant reason for the decline in the rate of the disease is attributed to genetic carrier testing, often facilitated through ethnically-based groups that promote testing. For instance, Dor Yeshorim, a Brooklyn-based group that recruits Jews to be tested, has over 300,000 members and tests for nine diseases, including Tay-Sachs. The organization claims that "in the Orthodox Ashkenazi community around the world, we virtually have wiped out the diseases we screen for."<sup>23</sup>

Examples of Ethnicity-Based Carrier Testing

Disease	Ethnic Group	Carrier Frequency
Canavan disease	Ashkenazi Jewish	1/40
Cystic fibrosis	Caucasian	1/25
Sickle cell anemia	African-American	1/14
Tay-Sachs disease	Ashkenazi Jewish	1/30

Source: National Center for Biotechnology Information

In the future, gene therapy techniques may permit clinicians to treat genetic defects after birth. While gene therapy is still in the research phase, a number of therapies are being sought for genetic conditions such as congenital blindness, hemophilia, cystic fibrosis, and muscular dystrophy.<sup>24</sup>

## Directing the application and dosing of therapeutics most likely to be safe and effective given the patient's genotype, thereby avoiding adverse drug reactions and the healthcare costs associated with treating them.

It is widely recognized by the health care industry that the ability to determine an individual's responsiveness to drug therapies is extremely beneficial across a myriad of factors, including the ability to save treatment time, avoid inappropriate or ineffective treatments, and avoid potentially adverse reactions. Genomic variations lead to different ways in which individuals metabolize drugs. Individuals are already known to have different abilities to absorb drugs, such that normal doses can lead to unexpectedly low or high drug concentrations in the blood, causing ineffective therapy or severe toxicity. For example, genetic mutations in liver enzymes associated with the cytochrome P-450 system have been found to determine how the body will metabolize or break down drugs. The use of a simple

<sup>23</sup> Available at: <http://www.msnbc.msn.com/id/35430449/ns/health-pregnancy/t/dreaded-diseases-dwindle-gene-testing/>

<sup>24</sup> N Engl J Med 2009; 361:725-727 August 13, 2009

test for cytochrome P-450 enzymes is already in use to prescribe the level of antidepressants like Prozac and Zoloft for individuals.<sup>25</sup>

The development of what has been termed personalized medicine (or targeted medicine) is expected to lead to more effective, safer medicines prescribed in accurate dosages; better, safer drugs at first try; and improvements in the drug discovery and approval process—all of which have the potential to lead to a decrease in the overall cost of health care.<sup>26</sup>

One of the first applications of personalized medicine already advancing health care treatments is the use of genomic information to more precisely prescribe medications based on an individual's genetic ability to metabolize drugs, a growing field referred to as "pharmacogenomics." Over time, pharmaceutical and biotechnology companies will be able to develop drugs that are more specific to the genomic variations in diseases found across sub-population groups. And with improved understanding of genetic variation and the interaction of genes and the environment, it is expected that individualized wellness treatments involving exercise, diet and lifestyle will be commonplace based on an individual's risk profile.

There are well-recognized and documented benefits that personalized medicine, particularly involving the first wave of pharmacogenomics, can deliver, particularly:

- **Improved patient safety** – It is estimated that underdosing, overdosing and misdosing of medications cost more than \$100 billion dollars annually, and can be considered a leading cause of death in America.<sup>27</sup> Annually, approximately 3.1 billion prescriptions are issued in the United States, of which approximately 2.1 million result in an adverse reaction. One million prescriptions from this latter group may result in hospitalization, and of these, more than 100,000 patients may die.<sup>28</sup> The problem is that prescribing medications today is based on a trial-and-error approach. Often, doctors will have a choice of drugs to treat patients and will try to apply one after another until they find the one that works best for their particular patients. The point of pharmacogenomics is to get the prescription right the first time. The use of genetic and genomic testing to identify

**Genetic and genomic testing has created the ability to select the specific medication that will best treat the disease. For example:**

- **HIV:** Currently, viral genetic variations make the HIV virus resistant to some anti-retroviral drugs. Genetic testing can determine the genetic makeup and rapid mutation of an individual's virus and pinpoint the most effective drug. This can dramatically improve the individual's quality and length of life, which is now often measured in decades rather than months or a few short years.
- **Cardiovascular Disease:** Genetic variations in an individual's ability to metabolize warfarin, a common blood-thinning drug, often lead to clotting or bleeding. Genetic testing can now identify the variation allowing for more precise and individualized dosing. Studies have indicated that broad use of the genetic testing could reduce strokes by 17,000 annually and costs by \$1 billion annually.
- **Colon Cancer:** Due to a gene variation, patients can experience life-threatening side-effects from certain colon cancer drugs. Genetic testing can now identify the variation allowing for physicians to choose other drugs to address the cancer.

<sup>25</sup> See Schimpf, pages 19 to 21 for a good discussion of how cytochrome P-450 enzymes work.

<sup>26</sup> Marcia Van Riper, Jim Evans, Jay Kaufman; Howard McLeod, UNC Center for Genomics and Society: Knowledge and Attitudes about Pharmacogenetic Testing Among Clinicians & Patients, report on research activities, November 2011. [http://genomics.unc.edu/genomicsandsociety/html/knowledge\\_and\\_attitudes\\_about\\_.html](http://genomics.unc.edu/genomicsandsociety/html/knowledge_and_attitudes_about_.html) accessed 24 October 2011

<sup>27</sup> Roland Valdes, "Introduction to Pharmacogenetics in Patient Care Conference by American Association of Clinical Chemistry, Nov. 6, 1998.

<sup>28</sup> Mancinelli et al., "Pharmacogenomics: The Promise of Personalized Medicine," AAPS PharmSci, March 7, 2000, page 10.

biomarkers that can warn against adverse reactions and drug ineffectiveness, and thus has the potential to significantly improve health care.

- **Increased effectiveness and cost efficiency of treatments** in light of the varying response rates to drug treatments based on genetic variations. Studies have shown that of 14 major drug classes, seven have shown less than 50 percent effective-patient-response rates<sup>29</sup> suggesting significant gains are to be made by diagnosing which patients will respond effectively to what drug dosages.
- **More cost-effective development of drugs** – Through the use of pharmacogenomics tools, it will be possible to target new investigational therapeutic agents to patient subgroups and so reduce the risk of failures in clinical research. Without a doubt, the fact that a clinical trial includes individuals predisposed not to respond to the drug—either because of the genetic variation of their disease or their ability to metabolize the therapeutic treatment—adds cost, delays and even the risk of failing to demonstrate efficacy.

It is important to note that there is some ethical disagreement surrounding the use of direct-to-consumer genetic tests. However, many practitioners in the medical field feel that these tests are an important component of the “collaborative care,” or “patient-centered care,” model of health care that is gaining ground as the U.S. health care system is re-evaluated and reforms are considered. Many in the health care field consider the leading direct-to-consumer (DTC) genetic testing companies scientifically sound information resources and platforms for conversation between patient and doctor, bridging the divide between traditional medicine and “open-access” trend.<sup>30</sup> In a 2009 study by Drs. James P. Evans and Robert C. Green published in *Genetics in Medicine*, 15 percent of doctors surveyed had a patient who discussed a DTC test, and 75 percent of those doctors adjusted their approach to their patient’s care as a result. DTC testing is a disruptive element in the medical field, to be sure, and it is therefore controversial, but DTC tests also introduce a new element of collaboration into healthcare. The study finds that the goal of better preventing, diagnosing, and treating conditions is the same.<sup>31</sup> “Co-practitioners,” as some describe the relationship, may be taken as an affront to traditional practitioners, but many in the health care field feel that the challenge of integrating better patient knowledge into their care will be worth the effort in improved care.<sup>32</sup>

### **Using genetic and genomic testing applications in occupational health practices to determine the effects of worker exposure to hazardous agents, and to determine individual hyper-susceptibility to the diseases that exposure may cause.**

Genetic and genomic testing is being used in occupational health research to determine the hyper-susceptibility of individuals to various hazardous chemical and biological materials.<sup>33</sup> This involves the genetic monitoring of exposed populations over time to track any genetic changes that may occur due

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<sup>29</sup> See DHHS, page 16 cites Garrison LP Jr. Austin MJ. Linking pharmacogenetics-based diagnostics and drugs for personalized medicine. *Health Affairs* 2006;25(5), 1281-1290 and Spear BB, Health-Chiozzi M, Fugg J. Clinical application of pharmacogenetics. *Trends Mol Med* 2001;7(5);201-204

<sup>30</sup> James P. Evans, MD, PhD, and Robert C. Green, MD, MPH: “Direct to consumer genetic testing: Avoiding a culture war” *Genetics in Medicine* Volume 11, Number 8, August 2009

<sup>31</sup> Ibid.

<sup>32</sup> Morris W. Foster, PhD, John J. Mulvihill, MD, and Richard R. Sharp, PhD: “Evaluating the utility of personal genomic information,” *Genet Med* 2009;11(8):570–574.

<sup>33</sup> “Read My Genes” Issues in Ethics, “Ethical Issues in Use of Genetic Information in the Workplace (Current Opinions in Psychiatry 2005; 18:518–524

to the exposure to the agents in question.<sup>34</sup> These tests can detect the presence of genetic abnormalities in healthy individuals that may place those individuals at increased risk for developing certain diseases. In the workplace, such tests can be used to screen job applicants and employees who, because of their genetic makeup, may be more likely to develop diseases if exposed to certain worksite substances, such as chemicals or radiation.

Research to date has identified about fifty genetic disorders thought to increase a person's susceptibility to the toxic or carcinogenic effects of environmental agents. For example, individuals with the sickle cell trait may be at increased risk for sickle cell anemia if exposed to carbon monoxide or cyanide. Exposure to lead or benzene can be especially hazardous to the health of people with the thalassaemia gene.<sup>35</sup>

Advocates for genetic screening view it as a means to significantly reduce the incidence of occupational disease. Employees can use the information obtained from genetic testing to ensure that they do not place themselves in environments that might cause them harm. According to one report, 390,000 workers contract disabling occupational diseases each year, and 100,000 of these workers die.<sup>36</sup> With the information obtained through genetic screening, employees have the potential to avoid work environments that would be hazardous to their health, sparing workers and their families the physical, emotional, and financial costs of disabling diseases and premature death.

Employers too would benefit from genetic screening. The U.S. Bureau of Labor Statistics reports that occupational illness costs private sector employers 850,000 lost workdays annually.<sup>37</sup> Litigation over illnesses associated with hazardous worksite substances also imposes heavy costs on employers. By reducing occupational disease, genetic screening could reduce the costs of lowered productivity, excess absenteeism, and high employee turnover, as well as the cost associated with workers' compensation payments, health insurance, and liability for occupational disease. Finally, the lowered incidence of work-related diseases could also benefit society as a whole by reducing the health care costs covered by Medicare and Medicaid, public assistance, and social security payments.

But critics of this emerging technology have maintained that screening violates workers privacy rights and increases racial and ethnic discrimination in the workplace since a predisposition to genetically-based disease is often associated with race or ethnic background. For example, the sickle cell trait is found in 1 out of 14 African-Americans, but only in 1 out of 1,000 Caucasians. As a result, critics have argued that genetic screening could have a disproportionate impact on racial groups that have already been victims of past discrimination. These concerns led to the enactment of the Genetic Information Non-Discrimination Act (GINA), which prohibits employers from using the genetic information of employees for discriminatory purposes. It will be important to the genetic testing field as occupational testing moves forward to monitor the effectiveness of GINA in addressing concerns regarding employee privacy and the potential for employers to discriminate.

### **Using genetic tests assists in confidently establishing identity, providing individual genetic identification profiles.**

DNA testing methods can assist in confidently establishing identity, providing individual genetic identification profiles. These profiles can be used to establish biological relatedness. For example, the

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<sup>34</sup> CDC/NIOSH: Genetics in the Workplace, November 2010.

<sup>35</sup> Claire Andre and Manuel Velasquez, "Read My Genes: Genetic Screening in the Workplace," *Issues in Ethics*, 4(2), Santa Clara University, available at: <http://www.scu.edu/ethics/publications/iie/v4n2/genes.html>

<sup>36</sup> Ibid.

<sup>37</sup> Ibid.

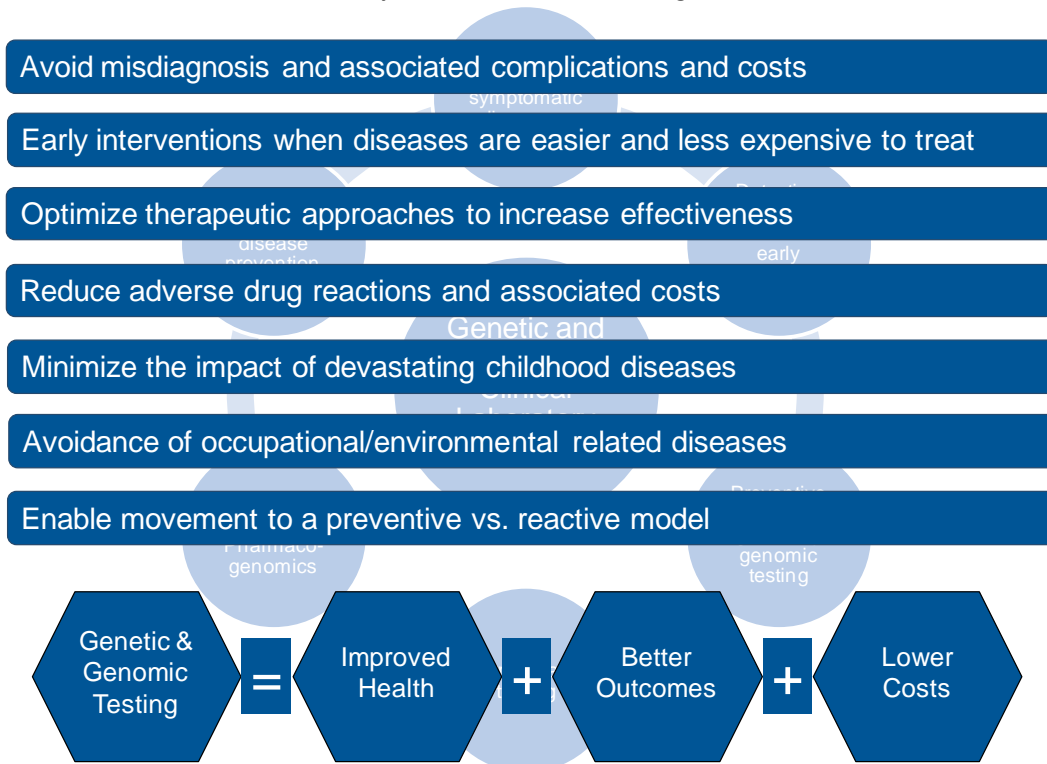
DNA paternity test is generally used to determine whether a man could be the biological father of a child. These tests are highly accurate, excluding, on average, more than 99.999% of non-parents, thereby providing a high probability of paternity. DNA tests are also used to identify newborns, to provide information to the US Citizenship and Immigration Services (USCIS) for persons seeking to immigrate to the US, and assist in confirming genetic relatedness for enrollment as a member of a federally recognized American Indian tribe. A common requirement for tribal membership is lineal descendancy (genealogical documentation) to a member of a tribe’s base roll or someone descended from a member on the base roll. (A base roll is the original list of members as designated in a tribal constitution.)

**Using genetic tests for forensic analysis, which is used to establish the identity of individuals based upon a specimen of blood, urine, or other tissue.**

Forensic DNA testing is used to establish the identity of individuals based upon a specimen of blood, urine, or other tissue. Typical specimen matching cases include a urine drug screen that has been reported as positive for a substance of abuse, or biopsy samples from a physician’s office or hospital to verify that the sample has been taken from a particular patient. In criminal cases, forensic DNA analyses are used when biological evidence has been left at the scene or transferred from one item and/or person to another and needs to be connected to an individual for whom no reference sample is available. These may be the result of homicide cases in which no body has been recovered, but blood stains have been located at the crime scene. In these cases, a reference sample from at least one parent can be used to perform a reverse paternity test for purposes of linking identity.

**In Summary: Functional Benefits Generated by Genetic and Genomic Testing**

**Figure 2: Functional Benefits Generated by Genetic and Genomic Testing**



The genetics and genomics testing industry is creating significant global benefits to not only the economy but to society as a whole, and fortunately represents an expanding industry in which the United States is a global leader. In addition to the new jobs and economic growth being created by clinical laboratories, the industry's focus is bringing new capabilities and enhanced accuracy to the health care field, thereby helping to improve human health, longevity and the quality of life. Genetic and genomic clinical testing is resulting in:

- *Avoidance of misdiagnoses and associated complications and costs.*
- *Early disease intervention when treatments can be more effective and less expensive.*
- *Optimization of therapeutic approaches to increase drug effectiveness.*
- *Elimination of adverse drug reactions and associated costs.*
- *Reduction of severe genetic disorders in newborns.*
- *Avoidance of occupational/environmental related diseases.*
- *Overall movement of the healthcare system from a reactive model to a preventative model.*

Today, genetic and genomic testing is leading to improved individual health and a better health care system at a lower cost. And it is important to remember that the development of commercially available genetic and genomic testing tools and techniques is still in its infancy. The health care benefits described above and illustrated in Figure 2 will only continue to grow and expand in the future, with each underlying functional benefit holding significant future promise for a far more wide-ranging application and subsequent positive impact.

## V. Into the Future

Modern advances in genetics and genomics have recently prompted an expansion in diagnostics capabilities, and these types of tests are being applied today to quantitatively diagnose diseases and disorders, to develop optimized treatment regimens for patients based on their genomic profile, and to develop gene therapies to correct disease-causing genetic variants. Tests rooted in genetics and genomics advances have emerged as highly accurate tools for diagnosing monogenic and polygenic diseases and disorders and as predictive tools for enhancing public health. Genetic and genomic testing is also able to characterize specific cancers, definitively identify infectious organisms and organismal strains, and guide the prescription and dosing of appropriate therapeutic approaches.

The platform of knowledge and the technologies resulting from human genome sequencing have formed the basis of nothing less than a medical revolution. The primary impacts of this revolution may not yet be felt in every daily clinical practice, but that day is accelerating towards us. Writing in *Nature*, Eric Lander notes that:

*“Medical revolutions require many decades to achieve their full promise. Genomics has only just begun to permeate biomedical research: advances must proceed through fundamental tools, basic discoveries, medical studies, candidate interventions, clinical trials, regulatory approval and widespread adoption. We must be scrupulous not to promise the public a pharmacopoeia of quick pay-offs. At the same time, we should remain unabashed about the ultimate impact of genomic medicine, which will be to transform the health of our children and our children’s children.”*<sup>38</sup>

Into the future, genetics and genomics tests make possible the emergence of “personalized and predictive medicine”. Within this space, pharmacogenomics is a new and developing field that will allow clinicians to prescribe the right drug in the right dose—therapeutics customized to the genomic profile of the patient. Such personalized medicine will bring many advantages: allowing physicians to prescribe a medicine that is proven to work for the specific genomic profile of the patient (thereby avoiding

### **The Future of Genomics in Medicine**

**Diagnostics** – Appropriate treatment of a disease can only begin once an accurate diagnosis is made. Genomics will increasingly drive advanced, highly accurate diagnostics development by:

- Identification of variant genes and their impact on monogenic and multigenic diseases.
- Sub classification of diseases by genome analysis to direct personalized medicine approaches (as is already occurring in certain cancers).
- Methods for real-time pathogen detection and identification.

**Therapeutics** – Genomics will significantly increase in utility across a range of therapeutic R&D and application areas, including:

- Identification of specific disease-relevant targets.
- Rational drug design to produce drugs specifically aimed at the characteristics of the identified targets.
- Repurposing of existing drugs for application to newly identified genomic targets and signatures
- Previously failed drugs “rescued” for application to genomic sub-populations
- Clinical trials improved through genomic stratification of participants
- Significantly reduced adverse drug events, and associated costs, driven by genotype-guided drug prescription.
- Increasing application of gene therapies
- Therapeutic strategies developed for genotype-environment interactions and for adaptation to behavioral and lifestyle characteristics.

*Eric Green and Mark Guyer. 2011. “Charting a course for genomic medicine from base pairs to bedside.” Nature. Volume 470. February 10th 2011.Pp:204–213.*

<sup>38</sup> Eric S. Lander. 2011. “Initial impact of the sequencing of the human genome.” *Nature*. Volume 470, February 10, 2011.

the costs, harm and treatment delay associated with providing a drug unlikely to work); significantly reduce adverse drug reactions, and potentially providing a pathway to reduced healthcare costs by providing highly accurate, targeted treatments instead of the more wasteful “scatter-gun” or the “try, wait, change and try something else” approach that too often has to be employed.

As a result, in the future genetic and genomic clinical testing is expected to result in:

- ***P4 Medicine—personalized, predictive, preventive, and participatory;***
- ***Large-scale increases in available tests;***
- ***Clinical applications of whole genome sequencing;***
- ***Significantly lowered disease burden;***
- ***A healthier workforce that has higher productivity;***
- ***Genetic, data-rich environment that identifies targets for drug discovery; and***
- ***A reduction in time, cost, and failure rates of clinical trials.***

This medical revolution will in turn lead to significant global economic opportunities. For these opportunities to be captured within the United States, however, the genetic and genomic clinical testing industry needs to be able to operate in a business environment that encourages continued R&D investment and facilitates profitable business operations (generating profits for reinvestment in the innovation cycle). Sustaining U.S. industrial leadership as the innovative genetic and genomic clinical testing sector continues to grow and prosper carries the promise of significant future economic benefits.

#### ***The Future Cost of Sequencing – Dramatic Cost Reductions lead to Widespread Application***

*“It is now possible to order your personal genome sequenced today for a retail cost of under ~\$20,000. This cost will likely fall to less than \$1,000 by 2012, and to \$100 by 2013.*

*At costs below \$1,000 per genome, a number of intriguing applications of DNA sequencing become cost effective. For example, researchers will have access to thousands or even millions of human genomes to seek correlations between genotypes and phenotypes. Medical doctors will be able to order genome sequencing along with standard laboratory tests, and will likely do so if they believe that knowledge of the DNA sequence will facilitate patient diagnosis and/or treatment. Even web-based genetic testing service companies will exploit full genome sequences to gather and dispense medical and ancestry information, and provide genetic counseling.”*

***JASON Program***

***“The \$100 Genome: Implications for the DoD”***

***December 2010. JASON, The MITRE Corporation. McLean, VA***