Direct-to-Consumer Genetic Testing

Report of the
Secretary's Advisory Committee on Genetics, Health, and Society

April 2010

A PDF version of this report is available at
http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_DTC_report_2010.pdf.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Secretary's Advisory Committee on
Genetics, Health, and Society
6705 Rockledge Drive
Suite 750, MSC 7985
Bethesda, MD 20892-7985
301-496-9838 (Phone)
301-496-9839 (Fax)
http://www4.od.nih.gov/oba/sacghs.htm

April 28, 2010

The Honorable Kathleen Sebelius
Secretary of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Dear Secretary Sebelius:

In keeping with our mandate to provide advice on the broad range of policy issues raised by the development and use of genetic technologies, the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) has prepared a report on *Direct-to-Consumer Genetic Testing* to highlight some concerns about genetic technologies that are being made available directly to consumers. The report outlines five steps that can be taken to reenforce the importance of providing complete, accurate, and balanced information describing the benefits, risks, and limitations of such testing and applying effective regulatory measures to maximize the benefits and minimize the harms of direct-to-consumer (DTC) genetic testing.

SACGHS identified gaps in four areas that are limiting the ability of consumers to make informed decisions about DTC genetic testing services and how DTC test results can be applied to guide health decisions. The gaps are in (1) the Federal oversight of DTC genetic testing, particularly the absence of review of DTC genetic testing claims and promotional materials by the Food and Drug Administration (FDA); (2) the evidence of clinical validity and/or clinical utility for most DTC genetic tests; (3) privacy and research protections for consumers using DTC genetic services because Federal regulations may not apply to companies offering DTC testing and State-level protections may be inadequate; and (4) knowledge about genetics among many consumers and/or inadequate training for health care providers who are queried by their patients regarding DTC test selection or interpretation of DTC test results.

To close these gaps, SACGHS recommends that the following five steps be taken, which are based on recommendations from SACGHS's prior reports on the oversight of genetic testing and the coverage and reimbursement of genetic tests and services:

- The Commissioner of FDA and the Administrator of the Centers for Medicare & Medicaid Services—with input from other Federal agencies and relevant stakeholder groups—should develop the necessary guidance and/or regulations that close gaps in the oversight of genetic tests marketed directly to consumers.
- Any Federal laboratory test registry established to address information gaps about available tests and their analytical and clinical validity should include DTC genetic tests and services.
- A joint Heath and Human Services (HHS)-Federal Trade Commission (FTC) task force should be established as soon as possible and convened as needed to provide the necessary expertise to develop guidelines for FTC to use as a basis to evaluate claims made by companies providing DTC genetic services.
- The HHS Office for Civil Rights (OCR), in conjunction with the HHS Office for Human Research Protections and other relevant HHS agencies, should identify specific gaps in State and Federal research protections and privacy protections for personal health information that may be generated through DTC genetic testing and, as needed, develop specific strategies the Federal Government should undertake consistent with its existing authority to address these gaps. OCR also should ensure that consumers are informed of potential risks to privacy.
- HHS should develop a genetics education initiative for consumers and health practitioners that includes information specific to DTC genetic testing, using existing HHS educational resources where available.

Direct-to-Consumer Genetic Testing also identifies other issues that need further study by SACGHS and/or other appropriate Federal agencies. These issues include the extent to which DTC services are being used for surreptitious genetic testing, the implications of DTC genetic testing for children, the psychosocial impact of DTC genetic testing, research use of specimens and data obtained through DTC genetic testing, the impact of DTC genetic testing on the health care system, and the potential for DTC services to exacerbate health disparities.

We appreciate the opportunity to be of service to you, and we hope that our advice regarding DTC genetic testing will prove helpful to you and the Department.

Sincerely,

Steven Teutsch, M.D., M.P.H.
Chair, SACGHS

About SACGHS

The Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) was first chartered in 2002 by the Secretary of Health and Human Services (HHS) as a public forum for deliberation on the broad range of policy issues raised by the development and use of genetic tests and, as warranted, to provide advice on these issues. The charter sets out the following specific functions of the Committee:

- Assessing how genetic and genomic technologies are being integrated into health care and public health;
- Studying the clinical, public health, ethical, economic, legal, and societal implications of genetic and genomic technologies and applications;
- Identifying opportunities and gaps in research and in data collection and analysis efforts;
- Examining the impact of current patent policy and licensing practices on access to genetic and genomic technologies;
- Analyzing uses of genetic information in education, employment, insurance, and law; and
- Serving as a public forum for discussion of issues raised by genetic and genomic technologies.

Structurally, SACGHS consists of up to 17 individuals from around the Nation who have expertise in disciplines relevant to genetics and genetic technologies. These disciplines include biomedical sciences, human genetics, health care delivery, evidence-based practice, public health, bioinformatics, behavioral sciences, social sciences, health services research, health policy, health disparities, ethics, economics, law, health care financing, consumer issues, and other relevant fields. At least two of the members are specifically selected for their knowledge of consumer issues and concerns and the views and perspectives of the general public.

Representatives of at least 19 Federal department or agencies may also sit on SACGHS in an *ex officio* (nonvoting) capacity. The departments are the Department of Commerce, Department of Defense, Department of Education, Department of Energy, Department of Justice, Department of Labor, Department of Veterans Affairs, Equal Employment Opportunity Commission, Federal Trade Commission, and the following HHS agencies: Administration for Children and Families, Agency for Healthcare Research and Quality, Centers for Disease Control and Prevention, Centers for Medicare & Medicaid Services, Food and Drug Administration, Health Resources and Services Administration, National Institutes of Health, Office for Civil Rights, Office for Human Research Protections, and Office of Public Health and Science.

SACGHS Roster*

Chair

Steven Teutsch, M.D., M.P.H. (2010)
Chief Science Officer
Los Angeles County Department of Health
Room 807
313 North Figueroa Street
Los Angeles, CA 90012

Members

Mara Aspinall, M.B.A. (2011)
President and CEO
On-Q-ity
610 Lincoln Street
Waltham, MA 02451

Sylvia Mann Au, M.S., CGC (2010)**
Hawaii State Genetics Coordinator
Genetics Program
Hawaii Department of Health
741 Sunset Avenue
Honolulu, HI 96816

Janice V. Bach, M.S.*** (2013)
State Genetics Coordinator and Manager
Genomic and Genetic Disorders Section
Michigan Department of Community Health
201 Townsend Street
Lansing, MI 48909

Paul Billings, M.D., Ph.D., FACP, FACMG (2011)
Director and Chief Scientific Officer
Genomic Medicine Institute
El Camino Hospital
2500 Grant Road
Mountain View, CA 94040

David Dale, M.D. (2012)
Professor of Medicine
University of Washington
1959 NE Pacific Street
Seattle, WA 98195

Gwen Darien (2012)
Executive Director
Samuel Waxman Cancer Research Foundation
Suite 907
1249 Fifth Avenue
New York, NY 10029

Rochelle Dreyfuss, M.S., J.D. (2011)
Pauline Newman Professor of Law
New York University School of Law
Vanderbilt Hall, Room 333
40 Washington Square South
New York, NY 10012-1099

Charis Eng, M.D., Ph.D.*** (2013)
Chair and Founding Director
Genomic Medical Institute
Cleveland Clinic Foundation
NE-50, Room NE5-314
9500 Euclid Avenue
Cleveland, OH 44195

* Terms expire in the year indicated in parentheses after the Committee Member's name.
** The appointments of these SACGHS members ended before this report on direct-to-consumer genetic testing was finalized; however, they participated in the development and deliberations of this report.
*** Appointment pending

James P. Evans, M.D., Ph.D. (2010)
Professor of Genetics and Medicine
Director of Clinical Cancer Genetics and the Bryson Program in Human Genetics
Departments of Medicine and Genetics
The University of North Carolina at Chapel Hill
Chapel Hill, NC 27599-7624

Andrea Ferreira-Gonzalez, Ph.D. (2010)
Professor of Pathology and
Director of Molecular Diagnostics Laboratory
Virginia Commonwealth University
403 North 13th Street
Clinical Support Center Room 246
Richmond, VA 23298-0248

Julio Licinio, M.D.** (2010)
Director
The John Curtin School of Medical Research
The Australian National University
Canberra, ACT 2601
Acton, Australia

Barbara Burns McGrath, R.N., Ph.D. (2010)
Research Associate Professor
School of Nursing
University of Washington
Box 357263
Seattle, WA 98195

Samuel Nussbaum, M.D. (2012)
Executive Vice President, Clinical Health Policy, and Chief Medical Officer
Wellpoint, Inc.
120 Monument Circle
Indianapolis, IN 46204

Charmaine D.M. Royal, Ph.D. (2012)
Associate Research Professor
Institute for Genome Sciences and Policy
Duke University
Box 91009
450 Research Drive
Durham, NC 27708

Sheila Walcoff, J.D (2012)
Partner
McDermott, Will & Emery, LLP
Suite 1200
600 13th Street, NW
Washington, DC 20005

Marc S. Williams, M.D., FAAP, FACMG (2010)
Director
Intermountain Healthcare
Clinical Genetics Institute
Suite 130
324 10th Avenue
Salt Lake City, UT 84103

Paul Wise, M.D., M.P.H. (2011)
Richard E. Behrman Professor of Child Health and Society
CHP/PCOR
Stanford University
117 Encina Commons
Stanford, CA 94305-6019

* Terms expire in the year indicated in parentheses after the Committee Member's name.
** The appointments of these SACGHS members ended before this report on direct-to-consumer genetic testing was finalized; however, they participated in the development and deliberations of this report.
*** Appointment pending

Ex Officio Members

Department of Commerce

Michael Amos, Ph.D.
Scientific Advisor
Chemical Science and Technology Laboratory
National Institute of Standards and Technology
100 Bureau Drive
Gaithersburg, MD 20899-8300

Department of Defense

LTC Adam Kanis, MC, USA
Department of Pediatrics
Tripler Army Medical Center
MCHK-PE
1 Jarrett White Road
Tripler AMC (Honolulu), HI 96859

Department of Energy

Daniel Drell, Ph.D.
Biologist
Life Sciences Division
Office of Biological and Environmental Research
1000 Independence Avenue, SW
Washington, DC 20585-1290

Department of Health and Human Services

Naomi Goldstein, Ph.D.
Director
Office of Planning, Research, and Evaluation
Administration for Children and Families
Seventh Floor
370 L'Enfant Promenade, SW
Washington, DC 20447

Gurvaneet Randhawa, M.D., M.P.H
Medical Officer
Center for Outcomes and Evidence
Agency for Healthcare Research & Quality
540 Gaither Road
Rockville, MD 20850

Muin J. Khoury, M.D., Ph.D.
Director
Office of Public Health Genomics
Centers for Disease Control and Prevention
Suite 1000
1825 Century Center Boulevard
Atlanta, GA 30345

Jeffrey Roche, M.D.
Medical Officer
Office of Clinical Standards and Quality
Centers for Medicare & Medicaid Services
MS S3-02-01
7500 Security Boulevard
Baltimore, MD 21244-1850

Alberto Gutierrez, Ph.D.
Director
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health
Food and Drug Administration
2098 Gaither Road
Rockville, MD 20850

Denise Geolot, Ph.D., R.N.
Director
Center for Quality
Health Resources and Services Administration
5700 Fishers Lane
Rockville, MD 20857

Eric Green, M.D., Ph.D.
Director
National Human Genome Research Institute
31 Center Drive, MSC 2152
Bethesda, MD 20892

Robinsue Frohboese, J.D., Ph.D.
Principal Deputy Director
Office for Civil Rights
Room 515F
200 Independence Avenue, SW
Washington, DC 20201

Michael A. Carome, M.D.
Associate Director for Regulatory Affairs
Office for Human Research Protections
Suite 200
1101 Wootton Parkway
Rockville, MD 20852

Department of Labor

Phyllis Borzi, J.D., M.A.
Assistant Secretary of Labor
Employee Benefits Security Administration
Suite S-2524
200 Constitution Avenue, NW
Washington, DC 20210

Department of Veterans Affairs

Ellen Fox, M.D.
Director
National Center for Ethics in Health Care
810 Vermont Avenue, NW
Washington, DC 20420

Equal Employment Opportunity Commission

Stuart Ishimaru, J.D.
Acting Chair
1801 L Street, NW
Washington, DC 20507

Federal Trade Commission

Sarah Botha, J.D.
Attorney
Division of Advertising Practices
Bureau of Consumer Protection
Room NJ-3212
600 Pennsylvania Avenue, NW
Washington, DC 20580

Acknowledgments

The Committee wishes to thank the members of the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) Task Force on Direct-to-Consumer Genetic Testing for their pivotal role in guiding the development of this report. The Task Force was chaired by Sylvia Au and composed of the following SACGHS members: Paul Billings, David Dale, Gwen Darien, James Evans, Andrea Ferreira-Gonzalez, Julio Licinio, Charmaine Royal, and Sheila Walcoff.

The Committee is also grateful for the expertise and contributions of the following Task Force *ex officio* and *ad hoc* members: Sarah Botha (Federal Trade Commission); Alberto Gutierrez and Elizabeth Mansfield (Food and Drug Administration); Penny Keller, Penelope Meyers, and Jeffrey Roche (Centers for Medicare & Medicaid Services); Muin Khoury and Katie Kolor (Centers for Disease Control and Prevention); Colleen McBride (National Institutes of Health); and Joan Scott (Genetics and Public Policy Center).

In addition, the Committee wishes to recognize the work of the SACGHS staff, particularly Cathy Fomous, who served as staff lead, and Sarah Carr for her overall guidance. The Committee is also grateful for the copyediting services of Donna Cay Tharpe.

The Committee thanks the NIH Office of Biotechnology Activities and the Office of Science Policy, under the direction of Amy Patterson, for the ongoing support and operational management of SACGHS.

Contents

Executive Summary

Technological advances have allowed increasing amounts of genetic information to be provided to patients and consumers at declining costs. At the same time, there has been a shift toward consumer-driven health care and patient empowerment. Capitalizing on these technological and social developments, commercial entities are offering an ever-widening range of direct-to-consumer (DTC) genetic services. However, the novelty of emerging genetic technologies and the speed at which these technologies are made available to consumers have raised some concerns.

In this report, the Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) highlights the importance of minimizing the harms and maximizing the benefits of DTC genetic testing. To this end, consumers need complete, accurate, and balanced information describing the benefits, risks, and limitations of such testing, along with appropriate oversight regulations that are effective and that are enforced.

For the purposes of this report, DTC genetic testing is defined as genetic tests and services that are advertised directly to consumers, that are purchased through consumer-initiated requests, and that provide test results directly to the consumer without the involvement of the consumer's health care provider. Concerns related to the use of DTC genetic testing vary according to the purpose of the test, the quality of laboratory testing, and the business model of the company offering the test. To help consumers make informed decisions about using DTC genetic testing services and apply their test results to guide health care decisions, SACGHS recommends attention to the following areas:

- Gaps in the Federal oversight of DTC genetic testing, particularly the absence of review of DTC genetic testing claims and promotional materials by the Food and Drug Administration (FDA) due to existing policies regarding premarket review and limitations under current regulatory practices;
- Lack of evidence of clinical validity and/or clinical utility for most DTC genetic tests;
- Gaps in privacy and research protections for consumers utilizing DTC genetic services because Federal regulations may not apply to companies offering DTC testing and State-level protections may be inadequate; and
- Insufficient knowledge about genetics among many consumers, limited involvement of consumers' health care providers to assist consumers in selecting genetic tests and in making health decisions based on DTC test results, and/or inadequate training for health care providers who are queried by their patients regarding test selection or interpretation of DTC test results.

Ten recommendations from prior SACGHS reports (see Appendix A) address several of the concerns outlined in this report. Although most of these recommendations speak to genetic testing or laboratory testing in general, they are also applicable to DTC genetic testing. On the basis of these previous recommendations, SACGHS proposes the following specific actions that

the Secretary of Health and Human Services (HHS) can take to address gaps and inconsistencies in Federal regulations and to accelerate the coordination of programs that facilitate comprehensive and consistent consumer and health provider genetics education:

- Direct the FDA Commissioner and the Centers for Medicare & Medicaid Services (CMS) Administrator—with input from other Federal agencies and relevant stakeholder groups—to develop the necessary guidance and/or regulations that close gaps in the oversight of genetic tests marketed directly to consumers.
- Any Federal laboratory test registry established to address information gaps about available tests and their analytical and clinical validity should include DTC genetic tests and services.
- As soon as possible, establish a joint HHS-Federal Trade Commission (FTC) task force, which will be convened as needed, to provide the necessary expertise to develop guidelines for FTC to use as a basis to evaluate claims made by companies providing DTC genetic services.
- Direct the HHS Office for Civil Rights (OCR), in conjunction with the HHS Office for Human Research Protections and other relevant HHS agencies, to identify specific gaps in State and Federal research protections and privacy protections for personal health information that may be generated through DTC genetic testing and, as needed, develop specific strategies the Federal Government can undertake consistent with its existing authority to address these gaps. OCR should also inform consumers of potential risks to privacy.
- Develop an initiative within the Office of the Assistant Secretary for Planning and Evaluation (ASPE) that focuses on genetics education for consumers and health practitioners and that includes information specific to DTC genetic testing and recognizes existing HHS educational resources. ASPE also should follow up its March 2009 report *Consumer Use of Computerized Applications to Address Health and Health Care Needs* by supporting research recommended in this report (e.g., studies to identify who uses health information technology (HIT) and who does not and obstacles to its use) and identify policies that would lower barriers to the use of HIT.

Introduction

Purpose and Scope of This Report

The Secretary's Advisory Committee on Genetics, Health, and Society (SACGHS) has been interested in direct-to-consumer (DTC) genetic testing since its inaugural meeting in June 2003.[1] Since that time, SACGHS has written two letters to the Secretary of Health and Human Services[2] (HHS) urging action against the false and misleading DTC advertising of genetic tests, which led to a joint consumer alert[3] by the Food and Drug Administration (FDA), Federal Trade Commission (FTC), and the Centers for Disease Control and Prevention (CDC). The Committee also has held sessions focused on DTC genetic testing at its meetings,[4] heard public comment on this topic, and addressed the impact of DTC advertising in its report on the oversight of genetic testing.[5]

With the persistent emergence of new companies that offer DTC genetic testing, SACGHS continues to explore this approach to genetic services. This report highlights the importance of minimizing the harms and maximizing the benefits of DTC genetic testing and highlights issues that may help consumers make an informed decision about using DTC services and applying their genetic testing results to guide health care decisions. To this end, consumers need complete, accurate, and balanced information describing the benefits, risks, and limitations of such testing, along with appropriate oversight regulations that are effective and that are enforced.

This report also reconsiders 10 recommendations from prior SACGHS reports that addressed concerns about genetic testing regardless of the route by which it is delivered (i.e., DTC or genetic testing through a consumer's health care provider). The intent of these recommendations is to ensure that standards for DTC genetic tests harmonize with standards for provider-based genetic tests, with the recognition that deficiencies also exist in the delivery and oversight of provider-based laboratory testing.[6] Additional protections may be required for DTC genetic testing because consumers' health providers are not always involved in ordering and interpreting

---

[1] Secretary's Advisory Committee on Genetics, Health, and Society. Initial Meeting, June 11-12, 2003. See http://oba.od.nih.gov/SACGHS/sacghs_past_meeting_documents.html#jun2003. Accessed April 14, 2009.
[2] Secretary's Advisory Committee on Genetics, Health, and Society. Letters to the Secretary of Health and Human Services, 2004 and 2006. See http://oba.od.nih.gov/SACGHS/sacghs_focus_marketing.html. Accessed April 14, 2009.
[3] FTC Facts for Consumers. At-Home Genetic Tests: A Healthy Dose of Skepticism May Be the Best Prescription. July 2006. See http://www.ftc.gov/bcp/edu/pubs/consumer/health/hea02.shtm. Accessed on February 8, 2010.
[4] Secretary's Advisory Committee on Genetics, Health, and Society. Meetings with sessions on DTC genetic testing. See http://oba.od.nih.gov/SACGHS/sacghs_focus_marketing.html. Accessed April 14, 2009.
[5] Secretary's Advisory Committee on Genetics, Health, and Society. U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services. April 2008. See http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_oversight_report.pdf, p. 164-166. Accessed April 14, 2009.
[6] Secretary's Advisory Committee on Genetics, Health, and Society. U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services. April 2008. See http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_oversight_report.pdf. Accessed August 25, 2009.

these tests and because relevant Federal regulations do not always apply to entities that provide this type of testing. Therefore, concerns not adequately addressed by prior SACGHS recommendations also are discussed.

For the purposes of this report and to remain consistent with the SACGHS report on the oversight of genetic testing, a genetic or genomic test is defined as a test that involves an analysis of human chromosomes, DNA, RNA, genes, and/or gene products (e.g., enzymes and other types of proteins), which is predominantly used to detect heritable or somatic mutations, genotypes, or phenotypes related to disease and health.[7] DTC genetic testing is defined as genetic or genomic tests and services that are advertised directly to consumers, are purchased through consumer-initiated requests, and provide results to the consumer without the involvement of the consumer's health care provider.[8]

The scope of this report focuses on DTC genetic testing that provides risk assessment or diagnosis of a disease or health condition and information about drug response or other phenotypic traits. It excludes forensic analyses, paternity testing, and ancestry testing. SACGHS recognizes that there are also concerns with some types of DTC genetic tests that are outside the scope of this report (e.g., ancestry testing) and appreciates the work of other organizations such as the American Society of Human Genetics[9] that assess these concerns. This report considers a full spectrum of activities related to DTC genetic testing, including the marketing of DTC services, collection and analysis of specimens, interpretation of test results and provision of results to consumers, secondary use of specimens or data derived from the specimens for research, and the impact of DTC testing on the U.S. health care system.

Trends in Genetic Testing

Historically, genetic testing has been used to evaluate a person's risk of developing or passing on single-gene disorders, to diagnose monogenic disorders, and to enable early detection of genetic diseases or conditions (e.g., newborn screening programs). Today, in addition to these traditional uses, genetic testing is increasingly used to target treatment selection, identify and quantify treatment risks, monitor treatment effectiveness and disease prognosis, and provide probabilistic risk assessment for the future development of common conditions such as cancer and diabetes. It also is used for nonhealth-related purposes such as personal matching services.

The technologies used in genetic testing have advanced remarkably from single-gene testing to genomic sequencing. Emerging technologies provide increasingly detailed information about

---

[7] Secretary's Advisory Committee on Genetics, Health, and Society. *U.S. System of Oversight of Genetic Testing: Report of the Secretary's Advisory Committee on Genetics, Health, and Society*. April 2008. See http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_oversight_report.pdf, p. 17. Accessed April 14, 2009.

[8] Hogarth S, Javitt G, Melzer D. (2008). The current landscape for direct-to-consumer genetic testing: legal, ethical, and policy issues. *Annual Review of Genomics and Human Genetics* 9:161-182.

[9] The American Society of Human Genetics. (2008). Ancestry Testing Statement. See http://www.ashg.org/pdf/ASHGAncestryTestingStatement_FINAL.pdf and http://www.ashg.org/pdf/AncestryTesting1113.pdf. Accessed August 27, 2009.

individual and population genetic variations, but the significance of these genetic variations in assessing an individual's health is not always clear. As research continues to unravel the role of noncoding DNA sequences, epigenetic mechanisms, and environmental and behavioral factors in health and disease, the interpretation of these findings will continue to become more complex and more nuanced. In addition, the interpretation of genetic test results may change with advances in knowledge or technology.[10,11] Consumers and clinicians will need to understand that although genotypic information is static (except for somatic mutations), interpretations of genotypic information may change over time.[10] Little is known about how consumers will respond to changes in risk predictions and whether continual updates of this information will change their perception of risk.[12,13]

Emergence of Companies Offering DTC Genetic Services

Advances in genetic and genomic technologies have allowed increasing amounts of information to be provided to patients and consumers at a lower cost. At the same time, there has been a movement toward consumer-driven health care and patient empowerment.[14,15] Capitalizing on these technological and social developments, new commercial companies selling DTC genetic services have emerged.[16]

As of February 2010, more than 30 Web-based companies sell DTC genetic services[17]; however, the volume of business is unknown. These companies offer a range of services under various business models. Some companies provide a limited number of genetic tests in a particular area, such as drug response or for a particular subset of health conditions such as cancer. Other companies offer genetic tests for a large number of health conditions or traits and for different purposes such as diagnosis, carrier screening, and assessing future health risk. Companies also may provide services such as genetic counseling, collaboration with provider-based testing, DNA archiving, opportunities to participate in research, and social networking.

---

[10] Shirts BH, Parker LS. (2008). Changing interpretations, stable genes: responsibilities of patients, professionals, and policy makers in the clinical interpretation of complex genetic information. *Genetics in Medicine* 10(11):778-783.

[11] Kraft P, Hunter DJ. (2009). Genetic risk prediction—are we there yet? *New England Journal of Medicine* 360(17):1701-1703.

[12] Kuehn BM. (2008). Risks and benefits of direct-to-consumer genetic testing remain unclear. *Journal of the American Medical Association* 300(13):1503-1505.

[13] Mihaescu R, van Hoek M, Sijbrands EJ, Uitterlinden AG, Witteman JCM, Hofman A, van Duijin CM, Janssens CJW. (2009). Evaluation of risk prediction updates from commercial genome-wide scans. *Genetics in Medicine* 11(8):588-594.

[14] Robinson JC, Ginsburg PB. (2009). Consumer-driven health care: promise and performance. *Health Affairs* 28(2):272-281.

[15] Zinner MJ, Loughlin KR. (2009). The evolution of health care in America. *Urology Clinics of North America* 36:1-10.

[16] Gray SW, O'Grady C, Karp L, Smith D, Schwartz JS, Hornik RC, Armstrong K. (2009). Risk information exposure and direct-to-consumer genetic testing for BRCA mutations among women with a personal or family history of breast or ovarian cancer. *Cancer Epidemiology, Biomarkers, and Prevention* 18(4):1303-1311.

[17] Genetics and Public Policy Center. (February 26, 2010). Direct-to-consumer genetic testing companies. Available at: http://www.dnapolicy.org/resources/AlphabetizedDTCGeneticTestingCompanies.pdf. Accessed March 12, 2010.

Benefits of DTC Genetic Testing

The potential advantages of DTC genetic testing include convenience, increased access to testing,[18,19] consumer autonomy, and individual empowerment.[20] Empowered with information, consumers may take greater responsibility for their health and adopt health-promoting behaviors.[21] The DTC approach to testing also may motivate consumers to take a greater ownership in learning[22] and to be more willing to engage in medical research.[23] In addition, DTC genetic testing can provide private access to tests for consumers who are concerned about genetic discrimination. Although the Genetic Information Nondiscrimination Act of 2008[24] provides Federal protections against genetic discrimination in health insurance and employment, its scope is not comprehensive (e.g., protections do not extend to life insurance or long-term health care insurance).

Concerns About DTC Genetic Testing

Little is known about the public acceptance and use of DTC genomic tests, and little empirical evidence exists regarding the impact of DTC testing on the public.[8] The novelty of emerging genetic technologies and the speed at which these technologies are made available to consumers have raised several questions.[12]

Concerns about the use of DTC genetic testing, however, vary with the purpose of the test, the quality of laboratory testing, and the business model of the company offering the test. Tests such as cystic fibrosis carrier screening, if conducted by properly certified laboratories through companies that provide credentialed genetic professionals to explain the results to customers, raise few red flags. In contrast, companies that offer tests of questionable clinical value with little or no information about which genetic variants are analyzed and that make no provision for interaction with a qualified health professional often provoke outcries from the medical community. Concerns also vary with regard to the risk of harms that may result from DTC

---

[18] Goddard KAB, Moore C, Ottman D, Szegda KL, Bradley L, Khoury MJ. (2007). Awareness and use of direct-to-consumer nutrigenomic tests, United States, 2006. *Genetics in Medicine* 9(8):510-517.
[19] Wolfberg AJ. (2006). Genes on the Web—Direct-to-Consumer Marketing of Genetic Testing. *New England Journal of Medicine* 355(6):543-545.
[20] Howard HC, Borry P. (2008). Direct-to-consumer genetic testing: more questions than benefits? *Personalized Medicine* 5:317-320. See http://www.futuremedicine.com/doi/pdfplus/10.2217/17410541.5.4.317. Accessed March 19, 2009.
[21] Foster MW, Sharp RR. (2008). Out of sequence: how consumer genomics could displace clinical genetics. *Nature Review Genetics* 9(6):419.
[22] Foster MW, Mulvihill JJ, Sharp RR. (2009). Evaluating the utility of personal genomic information. *Genetics in Medicine* 11(8):570-574.
[23] Lee SS, Crawley L. (2009). Research 2.0: social networking and direct-to-consumer (DTC) genomics. *The American Journal of Bioethics* 9(6-7):35-44.
[24] Public Law 110-233. Genetic Information Nondiscrimination Act of 2008. See http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ233.110. Accessed July 17, 2009.

genetic testing. A federally certified laboratory conducts breast cancer (BRCA) testing to assess the risk of inherited breast cancer. However, without the guidance of a genetic counselor or other qualified health professional, consumers could misinterpret the results and take inappropriate and harmful actions (e.g., foregoing routine mammograms if results are negative). In contrast, inaccurate or misinterpreted test results for lower risk uses, such as determining hair color, are less likely to cause medical harms.

Although not all DTC genetic tests raise the same concerns, apprehensions include those listed below, which are discussed in greater detail in subsequent sections of this report.

- Gaps in regulatory oversight,[6,25,26] leading to
    - False and misleading marketing claims[26,27]
    - Incomplete or unbalanced promotional materials, which impede the ability of consumers to evaluate marketing claims and make an informed decision regarding genetic testing[28,29]
    - Questionable genetic test quality or analytical validity[8,30,31]
    - Limited evidence of clinical validity and/or clinical utility of certain genetic tests, particularly those providing risk estimates for common diseases[12,32,33]
- Lack of (1) standardized terminology for genetic variants, (2) standard procedures to select and validate genetic variants, and (3) standard criteria to assess aggregate risk[10,34,35]

---

[25] Katsanis SH, Javitt G, Hudson K. (2008). A case study of personalized medicine. *Science* 320:53-54.

[26] Javitt GH, Stanley E, Hudson K. (2004). Direct-to-consumer tests, government oversight, and the First Amendment: what the government can (and can't) do to protect the public's health. *Oklahoma Law Review* 57:251-302.

[27] Gollust SE, Hull SC, Wilfond BS. (2002). Limitations of direct-to-consumer advertising for clinical genetic testing. *Journal of the American Medical Association* 288(14):1762-1767.

[28] Geransar R, Einsiedel E. (2008). Evaluating online direct-to-consumer marketing of genetic tests: informed choices or buyer beware? *Genetic Testing* 12(1):13-24.

[29] Hudson K, Javitt G, Burke W, Byers P. (2007). ASHG statement on direct-to-consumer genetic testing in the United States. *Obstetrics and Gynecology* 110:1392-1395.

[30] Hunter DJ, Khoury MJ, Drazen JM. (2008). Letting the genome out of the bottle – will we get our wish? *New England Journal of Medicine* 358:105-107.

[31] Cho MK. (2009). Translating genomics into the clinic: moving to the post-Mendelian world. *Genome Medicine* 1(1):7.

[32] Janssens ACJW, Gwinn M, Bradley LA, Oostra BA, van Duijn CM, Khoury MJ. (2008). A critical appraisal of the scientific basis of commercial genomic profiles used to assess health risks and personalize health interventions. *The American Journal of Human Genetics* 82:593-599.

[33] Offit K. (2008). Genomic profiles for disease risk: predictive or premature? *Journal of the American Medical Association* 299(11):1351-1355.

[34] Yu W, Ned R, Wulf A, Liu T, Khoury M, Gwinn M. (2009). The need for genetic variant naming standards in published abstracts of human genetic association studies. *BMC Research Notes* 2:56. See http://www.biomedcentral.com/1756-0500/2/56. Accessed April 20, 2009.

[35] Khoury MJ, McBride C, Schully SD, Ioannidis JPA, Feero WG, Janssens AC, Gwinn M, Simons-Morton DG, Bernhardt JM, Cargill M, Chanock SJ, Church GM, Coates RJ, Collins FS, Croyle RT, Davis BR, Downing GJ, DuRoss A, Friedman S, Gail MH, Ginsburg GS, Green RC, Greene MH, Greeland P, Gulcher JR, Hsu A, Hudson KL, Kardia SL, Kimmel PL, Lauer MS, Miller AM, Offit K, Ransohoff DF, Roberts HS, Rasooly RS, Stefansson K, Terry SF, Teutsch SM, Trepanier A, Wanke KL, Witte JS, Xu J. The Scientific Foundation for Personal Genomics:

- Variable ability of consumers to understand genetic test results[8,23,28,36]
- Inadequate knowledge of health professionals to interpret genetic test results and answer patients' questions about DTC genetic test results[37,38,39,40,41,42,43,44]
- Unknown impact on the health care system[23,45,46,47]
- Unclear and inadequate privacy protections[19,48,49,50]
- Insufficient safeguards to prevent nonconsensual or unauthorized third-party testing[37,51,52]
- Inadequate protections for the research use of specimens and data derived from specimens[53]

Recommendations from a National Institutes of Health-Centers for Disease Control and Prevention Multidisciplinary Workshop. *Genetics in Medicine* 11(8):559-567.

[36] Gollust SE, Wilfond BS, Hull SC. (2003). Direct-to-consumer sales of genetic services on the Internet. *Genetics in Medicine* 5(4):332-337.

[37] Wasson K, Cook ED, Helzlsouer K. (2006). Direct-to-consumer online genetic testing and the four principles: an analysis of the ethical issues. *Ethics and Medicine* 22(2):83-91.

[38] Christianson CA, McWalter KM, Warren NS. (2005). Assessment of allied health graduates' preparation to integrate genetic knowledge and skills into clinical practice. *Journal of Allied Health* 34(3):138-144.

[39] Lapham EV, Kozma C, Weiss JO, Benkendorf JL, Wilson MA. (2000). The gap between practice and genetics education of health professionals: HuGEM survey results. *Genetics in Medicine* 2(4):226-231.

[40] Kemper AR, Uren RL, Moseley KL, Clark SJ. (2006). Primary care physicians' attitudes regarding follow-up care for children with positive newborn screening results. *Pediatrics* 118(5):1836-1841.

[41] Giardiello FM, Brensinger JD, Petersen GM, Luce MC, Hylind LM, Bacon JA, Booker SV, Parker RD, Hamilton SR. (1997). The use and interpretation of commercial APC gene testing for familial adenomatous polyposis. *New England Journal of Medicine* 336(12):823-827.

[42] Sandhaus LM, Singer ME, Dawson NV, Wiesner GL. (2001). Reporting BRCA test results to primary care physicians. *Genetics in Medicine* 3(5):327-334.

[43] Wideroff L, Vadaparampil ST, Greene MH, Taplin S, Olson L, Freedman AN. (2005). Hereditary breast/ovarian and colorectal cancer genetics knowledge in a national sample of U.S. physicians. *Journal of Medical Genetics* 42(10):749-755.

[44] Scheuner MT, Sieverding P, Shekelle PG. (2009). Delivery of genomic medicine for common chronic adult diseases. *Journal of the American Medical Association* 299(11):1320-1334.

[45] McGowan ML, Fishman JR. (2008). Using lessons learned from BRCA testing and marketing: What lies ahead for whole genome scanning services. *The American Journal of Bioethics* 8(6):18-20.

[46] Newson AJ. (2009). Personal genomics as an interactive web broadcast. *The American Journal of Bioethics* 9(6-7):27-29.

[47] Bunnik E, Janssens ACJW, Schermer M. (2009). How attitudes research contributes to overoptimistic expectations of personal genome testing. *The American Journal of Bioethics* 9(6-7):23-25.

[48] World Privacy Forum. Public Comment: Secretary's Advisory Committee on Genetics, Health, and Society Meeting, February 13, 2008. See http://oba.od.nih.gov/oba/SACGHS/meetings/feb2008/transcripts/fulldayfeb13.pdf. Accessed April 13, 2009.

[49] Gurwitz D, Bregman-Eschet Y. (2009). Personal genomics services: whose genomes? *European Journal of Human Genetics*. Advance online publication 4 March 2009; doi: 10.1038/ejhg.2008.254.

[50] Bregman-Eschet Y. (2006). Genetic databases and biobanks: who controls our genetic privacy? *Santa Clara Computer and High Technology Law Journal* 23:1-54. See http://www.chtlj.org/volumes/v23#v023.i1.Bregman.pdf. Accessed March 19, 2009.

[51] Genetics and Public Policy Center. (2009). Surreptitious DNA testing. See http://www.dnapolicy.org/policy.issue.php?action=detail&issuebrief_id=48. Accessed April 10, 2009.

[52] Aldhous P, Reilly M. (2009). Special investigation: how my genome was hacked. *New Scientist* Issue 2701. See http://www.newscientist.com/article/mg20127013.800-special-investigation-how-my-genome-was-hacked. Accessed April 2, 2009.

[53] Public Responsibility in Medicine and Research. (2007). *Report of the Public Responsibility in Medicine and Research (PRIM&R) Human Tissue/Specimen Banking Working Group: Part I Assessment and Recommendations*.

- Limited data on the psychosocial impact of DTC genetic testing[54,55,56,57,58,59]
- Unknown risks regarding DTC testing for children[60,61]
- Potential inequities in access to DTC genetic testing and services[62,63]

See http://www.primr.org/uploadedFiles/PRIMR_Site_Home/Public_Policy/Recently_Files_Comments/Tissue%20Banking%20White%20Paper%203-7-07%20final%20combined.pdf. Accessed May 22, 2009.

[54] Schwartz MD, Peshkin BN, Hughes C, Main D, Issacs C, Lerman C. (2002). Impact of BRCA1/BRCA2 mutation testing on psychologic distress in a clinic-based sample. *Journal of Clinical Oncology* 20(2):514-520.

[55] Beran TM, Stanton AL, Kwan L, Seldon J, Bower JE, Vodermaier A, Ganz PA. (2008). The trajectory of psychological impact in BRCA 1/2 genetic testing: does time heal? *Annals of Behavioral Medicine* 36(2):107-116.

[56] Schlich-Bakker KJ, ten Kroode HFJ, Ausems MGEM. (2006). A literature review of the psychological impact of genetic counseling on breast cancer patients. *Patient Education and Counseling* 62:13-20.

[57] van Dijk S, Otten W, Timmermans DR, van Asperen CJ, Meijers-Heijboer H, Tibben A, Breuning MH, Kievit J. (2005). What's the message? Interpretation of an uninformative BRCA 1/2 test result for woman at risk of familial breast cancer. *Genetics in Medicine* 7(4):239-245.

[58] Mouchawar J, Laurion S, Ritzwoller DP, Ellis J, Kulchak-Rahm A, Hensley-Alford S. (2005). Assessing controversial direct-to-consumer advertising for hereditary breast cancer testing: reactions from women and their physicians in a managed care organization. *American Journal of Managed Care* 11(10):601-608.

[59] Heshka JT, Palleschi C, Howley H, Wilson B, Wells PS. (2008). A systematic review of perceived risks, psychological and behavioral impacts on genetic testing. *Genetics in Medicine* 10(1):19-32.

[60] Tabor HK, Kelley M. (2009). Challenges in the use of direct-to-consumer personal genome testing in children. *The American Journal of Bioethics* 9(6-7):32-34.

[61] Borry P, Howard HC, Sénécal K, Avard D. (2010). Health-related direct-to-consumer genetic testing: a review of companies' policies with regard to genetic testing in minors. *Familial Cancer* 9(1):51-59.

[62] Bodie GD, Dutta MJ. (2008). Understanding health literacy for strategic health marketing: eHealth literacy, health disparities, and the digital divide. *Health Marketing Quarterly* 25(1-2):175-203.

[63] McBride CM, Alford SH, Reid RJ, Larson EB, Baxevanis AD, Brody LC. (2008). Putting science over supposition in the arena of personalized genomics. *Nature Genetics* 40(8): 939-942.

Consumer Interest in Genetic and Genomic Testing

Little is known about the consumer base for DTC genetic testing,[45] particularly the psychological and behavioral factors that motivate individuals to seek testing.[64] As a first step, several surveys have been conducted to gauge the public's interest in and use of genetic testing.

McBride et al.[64] evaluated a sample of healthy adults (age 25-40 years) for factors that predicted participants' interest in and use of a genetic susceptibility test for eight common health conditions. The test evaluated 15 polymorphisms associated with an increased risk for type 2 diabetes; lung, colon, and skin cancers; coronary heart disease; hypercholesterolemia; hypertension; and osteoporosis. The study sample of 527 individuals who considered testing was drawn from commercially insured members of a large Midwestern health maintenance organization. From this study sample, 266 had genetic testing and 261 did not. Participants who underwent testing received a report of their results in the mail, a phone call from a research educator to discuss the results, a followup survey 3 months later, and a genetic consultation if they requested one. The study findings suggested that when provided with balanced information, participants recognized the limitations and utility of receiving personal genetic profiles. There was no evidence that those who considered or sought testing were inclined to overestimate the contribution of genetics to common health conditions. Factors that predicted the use of genetic susceptibility testing included a perception of health habits in need of change (e.g., diet, smoking), considering it important to learn about genetics, and participant confidence to understand genetics. Perceiving the tested-for health conditions as severe reduced the likelihood of being tested.

Two 2008 national surveys—HealthStyles and DocStyles—assessed awareness and use of DTC personal genomic tests.[65] For the surveys, personal genomic tests were defined as "genetic tests marketed directly to consumers that scan a person's entire genetic makeup for potential health risks." Of the 5,399 respondents to the consumer HealthStyles survey, 68 percent were white, 12 percent Black, 12 percent Hispanic, and 7 percent "other." The majority of respondents (88 percent) were age 35 years or older. Among the respondents, 22 percent were aware of personal genomic tests, and 0.3 percent (about 16 people) had used these tests. Two-thirds of the users reported sharing the tests results with a health care provider. Of the 1,880 respondents to the DocStyles survey, 1,750 were physicians, and 130 were registered dieticians; 42 percent of respondents were aware of DTC personal genomic tests. The majority of health care providers who were aware of DTC testing (75 percent) had learned about personal genomic tests from a media or Internet source, and 22 percent had read about these tests in a medical or scientific

[64] McBride CM, Alford SH, Reid RJ, Larson EB, Baxevanis AD, Brody LC. (2009). Characteristics of users of online personalized genomic risk assessments: implications for physician-patient interactions. *Genetics in Medicine* 11(8):582-587.
[65] Kolor K, Liu T, St. Pierre J, Khoury MJ. (2009). Health care provider and consumer awareness, perceptions, and use of direct-to-consumer personal genomic tests, United States, 2008. *Genetics in Medicine* 11(8):595.

journal. Among health care providers aware of this type of testing, 42 percent had at least one patient who had asked questions in the past year about personal genomic testing, and 15 percent had at least one patient who had brought test results to them in the past year. Personal genomic test results appear to influence clinical decisionmaking: 75 percent of health care providers who reviewed their patients' test results reported changing some aspect of the patient's care (e.g., type or dose of medication, screening tests offered, frequency of followup appointments).

The 2006 HealthStyles and DocStyles surveys assessed awareness and use of DTC nutrigenomic tests.[18] This type of testing generally involves evaluating multiple variants associated with common disorders, such as heart disease and diabetes, along with consumer-provided information on diet and lifestyle habits, to assess potential health risks. The HealthStyles survey received responses from 5,250 adults, and 14 percent were aware of DTC nutrigenomic tests compared with 50 percent who were aware of conventional forms of genomic testing (e.g., tests to diagnose disease). Of those aware of DTC nutrigenomic testing, only 4 percent (0.6 percent of the entire sample) had made use such a test. Among those who had used the test, only 10 percent discussed the results of DTC nutrigenomic testing with their physicians. The DocStyles survey found that 44 percent of physicians were aware of DTC nutrigenomic testing. Both surveys revealed that the media are the primary sources of information on DTC nutrigenomic testing for consumers and physicians.

In a 2008 survey, McGuire et al.[66] explored consumer attitudes toward DTC testing and provides a genomic profile. The investigators were challenged by the difficulty of identifying people who had purchased genomic tests and of predicting who would be among the early adopters of these services. Because DTC genomic testing services are offered primarily through the Internet and because some DTC testing companies provide an optional social networking component, the researchers reasoned that social networkers would likely be aware of genomic testing. Therefore, the survey was conducted among users of Facebook.com, a social networking Web site, and 1,087 surveys were completed. The survey was voluntary, anonymous, and confidential and requested demographic information and information about awareness of and attitudes toward DTC genomic testing companies and perceptions of genomic test results. The age of the respondents ranged from 18 to 81 years (mean 35 years, standard deviation 12 years). Most of the survey participants were Caucasian (83 percent) and college educated (59 percent) and reported having health insurance (85 percent). The researchers acknowledged that the respondents were not representative of the U.S. population, but the demographics were consistent with those of Internet and users of social networks.

Nearly half of the survey participants (47 percent) had heard of DTC genomic testing companies prior to the survey, 6 percent reported having used the services of these companies, and 64 percent indicated interest in using these services. (The survey participants had not been informed about the cost of genomic testing, and assumptions about cost could have influenced reported interest in testing.) Among those who had used or were interested in using DTC genomic testing

[66] McGuire AL, Diaz CM, Wang T, Hilsenbeck SG. (2009). Social networkers' attitudes towards direct-to-consumer personal genome testing. *The American Journal of Bioethics* 9(6-7):3-10.

services, 81 percent reported that they were curious about their genetic makeup as their reason for their interest, 74 percent reported that they would consider testing for someone else (e.g., child, spouse), and 65 percent said that test results would influence their future health care decisions. Among participants who underwent genomic testing, 60 percent considered their results as a medical diagnosis, even though many companies claim only to provide information for educational purposes and not medical diagnoses, and 53 percent had discussed their results with their physician. Among the respondents not interested in DTC genomic testing, 53 percent thought that the information would not be useful. Other concerns expressed by this group were the cost of testing (40 percent), privacy (39 percent), reliability of results (21 percent), and receipt of potentially unwanted information (21 percent).

Among all respondents, the researchers found that less than half (42 percent) expressed confidence in understanding the risks and benefits of genomic testing, and 46 percent reported that they knew enough about genetics to understand the results. Additionally, 61 percent agreed that physicians have a professional obligation to help individuals understand genetic testing results, although only 47 percent agreed that physicians have enough knowledge to help patients. When asked whether genomic testing companies provide enough information for consumers to make informed decision about using the testing services, only 30 percent agreed. Half of respondents (51 percent) supported Federal regulation of companies providing genomic testing.

Wilde et al.[67] evaluated public attitudes toward genetic risk prediction of major depression through four structured focus groups. Of the 36 participants, 24 indicated interest in genetic susceptibility testing for major depression if it were available. However, following a discussion of perceived positive and negative implications of predictive genetic testing, 9 of the 24 participants interested in testing changed their minds. Privacy issues and fear of genetic discrimination were the predominant reasons for the changes in attitude. Participants with a remaining interest in predictive genetic testing for the risk of depression said they would arrange for testing through a trusted medical professional; they were not interested in DTC genetic testing. However, some stated they would consider DTC testing if there were adequate protections against discrimination and misuse of their DNA samples.

The 2008 Life Sciences Survey conducted by Virginia Commonwealth University[68] questioned 1,005 adults. One question stated: "Genetic testing is being used to identify people at risk for diseases such as cancer, heart disease, Alzheimer's, and others. Overall, how much would you favor or oppose making genetic testing easily available to all who want it—do you strongly favor, somewhat favor, somewhat oppose, or strongly oppose this?" In response, 80 percent of participants said they were strongly or somewhat in favor. However, 53 percent of respondents said they disagreed or strongly disagreed with the statement "Rules set by government will keep us safe from any risks linked to modern genetic science."

---

[67] Wilde A, Meiser B, Mitchell PB, Schofield PR. (2010). Public interest in predictive genetic testing, including direct-to-consumer testing, for susceptibility to major depression: preliminary findings. *European Journal of Human Genetics* 18(1):47-51.

[68] Virginia Commonwealth University. (2008). Life Sciences Survey 2008. See http://www.news.vcu.edu/doc/VCU-Life-Sciences-Report-2008.pdf. Accessed March 20, 2009.

A 2008 Web survey of 1,000 adults by Cogent Research[69] found that 91 percent of respondents would be willing to undergo a genetic test for at least one disease condition (from a list of 40 conditions that included cancer, stroke, diabetes, Parkinson disease, and Alzheimer disease). The majority of respondents (88 percent) also said they would talk with their doctors if they received a test result that indicated they were at risk for a particular disease. Approximately 55 percent of respondents said they would make health care choices (e.g., the frequency of checkups) based on genetic test results, and 45 percent claimed they would make lifestyle changes. Only 12 percent of survey respondents were aware of DTC genetic testing.

The 2008 Personalized Medicine and Wellness Survey conducted by Burrill & Company and ChangeWave Research[70] found that "consumers are worried about developing genetic-based disease but remain reluctant to use genetic tests that will provide early warning signs." This survey questioned 550 "upscale business professionals," and responses indicated that "while consumers are warming to the availability of genetic tests, they still need to be convinced of the value of the information these new tools provide." Only 20 percent of survey participants said they would be likely or very likely to undergo a test in the next few years to measure their genetic risk for certain diseases. Other key findings from this survey include the following:

- The benefits of genetic tests need to be made clear. Companies need to make a case that genetic testing provides consumers with actionable information (e.g., use of preventive interventions) and is not just a source of dire news to come.
- Privacy issues remain a barrier to the use of new genetic tests. Despite the recent passage of new privacy laws protecting an individual's genetic "fingerprint," consumers remain concerned about who will have access to their information and how it will be used.
- Lower cost will become a primary motivator for people to undergo genetic testing, but concerns about family history of a specific disease also will drive use of genetic tests.
- Doctors are the gatekeepers for the use of genetic tests. Despite the proliferation of information through the Internet, doctors remain the most likely place consumers will turn to for information. A doctor's recommendation is the most likely reason someone will obtain a genetic test.
- New legal protection under the Genetic Information Nondiscrimination Act has increased consumers' comfort level with genetic testing, but consumers still want additional issues to be addressed (e.g., extending protections to life and disability insurance).

[69] Cogent Research. (2008). Cogent Genomics Attitudes & Trends. See http://oba.od.nih.gov/oba/SACGHS/meetings/March2009/White_slides.pdf. Accessed March 19, 2009.
[70] Burrill & Company and ChangeWave Research. (2008). *Personalized Medicine and Wellness Survey: Executive Summary*. See http://www.burrillandco.com/content/CWSurvey_61708.pdf. Accessed March 19, 2009.

In 2007 the consumer research firm Yankelovich[71] conducted a study of tens of thousands of consumers in 17 countries. Analysis of survey responses led to segmentation of consumers into the following six groups: (1) leading the way: generally healthy consumers who organize their lives around health and are avid information-seekers, (2) in it for fun: consumers who practice healthy behaviors but are interested in health from the perspective of what it means to their social lives, (3) value independence: do-it-yourselfers who are tired of science and medical messages creating confusion in their lives and are determined to figure it out on their own, (4) I need a plan: undisciplined consumers who are well informed but need structure and help them apply the information they have, (5) not right now: relatively healthy but disinterested consumers who are not likely to engage in health information, and (6) get through the day: consumers with poor health for whom nothing they have tried has produced a meaningful result.

The Yankelovich study found that consumers have some familiarity with genomics but a very limited understanding. Their curiosity is piqued, but they do not necessarily know about genetic testing companies. The biggest concerns of consumers related to the accuracy of test results, and they were not particularly concerned about privacy. For certain conditions, consumers today turn more and more to blogs for an empathetic ear, and they trust people in social networks as much, if not more, than their physicians. Because consumers are not a homogeneous group, health messages should be targeted. To communicate with consumers effectively, it is important to remember that a single message does not fit all.

Surveys also were conducted in Michigan, Oregon, and Utah as part of CDC's 2006 Behavioral Risk Factor Surveillance System (BRFSS) to assess the public's knowledge of and interest in DTC nutrigenomic testing.[72] Among respondents, awareness was 24.4 percent in Oregon, 19.7 percent in Utah, and 7.6 percent in Michigan. Less than 1 percent of respondents had used this type of test. Four States—Michigan, Oregon, Utah, and Connecticut—have included questions on awareness and use of DTC personal genome scans in their 2009 BRFSS State surveys. Data will be available for analysis in spring 2010.

Between 2003 and 2004 the Washington State Department of Health conducted a series of 15 community focus groups to discuss genetic issues such as genetic discrimination and equity of genetic services.[73] The topic of direct-access genetic testing arose several times. Some participants thought that these tests would ensure privacy of results, provide useful information, and help improve access to genetic testing. Others were concerned about contamination, test accuracy, regulation, and availability of help to interpret results.

---

[71] Yankelovich. (2008). Consumer interest in health and genomic information. Personalized Health Care Initiative Workshop: Understanding the Needs of Consumers in the Use of Genome-based Health Information Services. See http://www.webconferences.com/hhs/. Accessed April 13, 2009.

[72] Goodard KAB, Duquette D, Zlot A, Johnson J, Annis-Emeott A, Lee PW, Bland MP, Edwards KL, Oehlke K, Giles RL, Rafferty A, Cook ML, Khoury MJ. (2009). Public awareness and use of direct-to-consumer genetic tests: results from 3 state population-based surveys, 2006. *American Journal of Public Health* 99(3):442-445.

[73] Washington State Department of Health. (2008). *Genetic Services Policy Project, Final Report*. See http://depts.washington.edu/genpol/finalreport/. Accessed March 19, 2009.

In summary, survey findings indicate that consumers have an interest in genetic testing, but awareness and use of DTC testing is not widespread. Consumers expressed concerns about test accuracy[66,71,73] and privacy,[67,70,73] and increasingly, they are turning to social networks as sources of information about certain health conditions.[71] Future research on the consumer use of DTC testing will be necessary to understand the impact and implications of DTC genetic testing services.

DTC Genetic Testing Concerns

When consumers pay for genetic tests with uncertain or questionable analytical validity, clinical validity, and/or clinical utility, they spend money on tests that are of unclear value and that could put them at risk for harm.[36,74] Erroneous or misinterpreted test results could influence consumers to alter their behaviors, with adverse consequences, such as inappropriately changing medications or foregoing recommended screenings (e.g., mammograms). Test results also could cause consumer confusion, particularly if results are voluminous, reveal variants of unknown significance, or have nuanced risk interpretations, as with analyses of thousands of single-nucleotide polymorphisms (SNPs).

SACGHS has identified several issues with various aspects of DTC genetic testing that may impede consumers in making informed decisions about using DTC genetic testing services, selecting the appropriate test, understanding the test results, and applying the results to guide health care decisions.

Gaps in the Oversight of DTC Genetic Testing

Although an increasing range of DTC genetic tests is becoming available, policies and regulations that ensure test quality have lagged behind. There are significant gaps in government oversight of DTC genetic testing and of genetic testing generally. FDA has authority under the Food, Drug, and Cosmetic Act[75] to regulate commercial laboratory tests as devices if they are used in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease. FDA reviews device safety and effectiveness, which generally are in the form of analytical and clinical performance data[76] and labeling information before devices are marketed, and it requires postmarket reporting of adverse events if there are problems with a device. Many DTC genetic tests, however, may fall into the category of laboratory-developed tests (LDTs), and FDA historically has exercised "enforcement discretion" with respect to LDTs. As a result, there has been no premarket review of most DTC genetic tests to ensure that these tests meet FDA standards for demonstrating adequate evidence of safety and effectiveness before

---

[74] Hudson K, Javitt G, Burke W, Byers P, with the ASHG Social Issues Committee. (2007). ASHG statement on direct-to-consumer genetic testing in the United States. *American Journal of Human Genetics* 81:635-637.

[75] Food, Drug, and Cosmetic Act, section 201(h). See http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/FDCActChaptersIandIIShortTitleandDefinitions/ucm086297.htm. Accessed August 28, 2009.

[76] Class III/high-risk devices that pose a significant risk of illness or injury require FDA premarket approval (PMAs), as do devices found not substantially equivalent to Class I and II predicate through the 510(k) process. The PMA process is more involved that the 510(k) process and includes the submission of clinical data to support claims made for the device. PMA approval is based on a determination by FDA that there is sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s). Code of Federal Regulations, Title 21, Part 814, premarket approval of medical devices. See http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=814. Accessed September 4, 2009.

they are made available to consumers, and there is no postmarket surveillance.[25] Thus, DTC companies that use LDTs face few regulatory barriers to marketing.[8]

The Centers for Medicare & Medicaid Services (CMS) has regulatory responsibilities for the oversight of laboratory testing, including genetic testing, under the Clinical Laboratory Improvement Amendments of 1988 (CLIA).[77] However, only analytical validity requirements are enforced under CLIA, as CMS does not have authority to enforce requirements for clinical validity. In addition, some companies that offer DTC genetic tests are not required to be CLIA certified. Certain tests, such as those for fetal gender, provide information that does not fit the CLIA definition of "laboratory,"[78] which CMS uses as the decisive factor in regulating laboratories under CLIA.[6,8] Other DTC genetic testing companies that may not meet the definition of "laboratory" are those that serve only as a mailing service and do not perform testing or those that provide an interpretation service to clarify results from a CLIA-certified laboratory.

Therefore, at least some of the activities of DTC genetic testing companies are not federally regulated because companies may use LDTs, for which FDA exercises enforcement discretion, and/or the tests are performed in or the interpretation of test results is provided by laboratories or other entities that may not require CLIA certification. An additional oversight hurdle is that CMS cannot directly impose enforcement actions against laboratories that meet the CLIA definition of "laboratory" but that are not CLIA certified. If CLIA-applicable laboratories do not comply with CLIA regulations or if they do not cease testing, they are reported to the HHS Office of Inspector General for enforcement action.

Two States—New York and Washington—have opted out of the CLIA program in favor of a State-supervised program that is equally as or more stringent than CLIA. For example, New York requires evidence of the clinical validity of laboratory tests, including DTC genetic tests, before tests are made available to patients and consumers. Other States have regulations that augment CLIA requirements. California, for example, uses a broader definition for laboratory than CLIA and also recognizes genetics as a specialty.[79] As a result, some California companies, such as entities that interpret raw genetic data provided by a CLIA-certified laboratory, may not

---

[77] Centers for Medicare & Medicaid Services. Clinical Laboratory Improvement Amendments. See http://www.cms.hhs.gov/clia/. Accessed April 14, 2009.

[78] Centers for Medicare & Medicaid Services. Clinical Laboratory Improvement Amendments, 42 CFR 493.2. Laboratory means a facility for the biological, microbiological, serological, chemical, immunohematological, hematological, biophysical, cytological, pathological, or other examination of materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of, human beings. These examinations also use procedures to determine, measure, or otherwise describe the presence or absence of various substances or organisms in the body. Facilities only collecting or preparing specimens (or both) or only serving as a mailing service and not performing testing are not considered laboratories.
See http://www.cms.hhs.gov/CLIA/downloads/apcindex.pdf. Accessed July 10, 2009.

[79] Business and Professions Code §1206. See http://www.aacc.org/members/loc_sections/scalifornia/resourcectr/Documents/GeneticTestiing_CLTACHandout.pdf. Accessed July 10, 2009.

be subject to certain Federal regulations under CLIA but must adhere to State regulations for clinical laboratories. Legislation has been introduced in the California State Senate (SB 482)[80] that would define a new category of business—one that provides "post-CLIA bioinformatics services"—which is described as the "postproduction interpretation, by means of an algorithm, of biological data" (e.g., interpretation of genomic SNP analyses). Under the proposed bill, these entities would be exempt from requirements applicable to clinical laboratories but would have to meet new requirements for specified experts (e.g., bioinformaticians), privacy, recordkeeping, disclosure, and audits. According to a 2007 analysis by the Genetics and Public Policy Center (GPPC),[81] 25 States limit or forbid the practice of DTC testing as a violation of State laws that require the involvement of a licensed physician or authorized person when ordering laboratory tests or providing medical information. These States may have difficulty prohibiting the sale of DTC tests, however, when sales are mediated via the Internet.[8]

In addition to and because of regulatory gaps in oversight, data supporting the analytical validity, clinical validity, clinical utility, and evidentiary basis for claims of DTC genetic tests are rarely publicly accessible. Enhancing the transparency of this information, which also would highlight where data are lacking or insufficient, is critical for enabling consumers to make informed decisions in selecting and ordering DTC genetic tests. The CMS Web site provides contact information for CLIA-certified laboratories, the type of CLIA certification, and expiration date,[82] but it does not include analytical validity data. Making such data transparent is difficult if the data are proprietary, and the effort would require steadily available resources to develop and maintain an up-to-date registry. In its 2008 report on the oversight of genetic testing, SACGHS recommended the establishment of a mandatory registry for all laboratory tests.[83] Many stakeholders—including test manufacturers, laboratories, patient advocacy groups, and professional societies representing health care providers—support the development of a test registry.[84,85]

Claims

Gollust et al.[36] suggest that premarket and postmarket regulatory attention to clinical genetic tests, including an assessment of Internet Web sites, is needed to protect consumers from

---

[80] California Senate Bill No. 482. See http://www.leginfo.ca.gov/pub/09-10/bill/sen/sb_0451-0500/sb_482_bill_20090414_amended_sen_v98.pdf. Accessed July 10, 2009.
[81] Genetics and Public Policy Center. (2007). Survey of direct-to-consumer testing statutes and regulations. See http://www.dnapolicy.org/resources/DTCStateLawChart.pdf. Accessed March 19, 2009.
[82] Centers for Medicare &Medicaid. Laboratory Demographics Lookup. See http://www.cms.hhs.gov/CLIA/20_CLIA_Laboratory_Demographic_Information.asp. Accessed February 8, 2010.
[83] Secretary's Advisory Committee on Genetics, Health, and Society. U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services. April 2008. See http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_oversight_report.pdf, pp. 8-9. Accessed November 18, 2009.
[84] Javitt G, Katsanis S, Scott J, Hudson K. (2009). Developing the blueprint for a genetic testing registry. *Public Health Genomics* 13(2):95-105.
[85] Genetics and Public Policy Center. (February 12, 2008). Analysis of Public Comments on the SACGHS Genetic Testing Oversight Draft Report. See http://www.dnapolicy.org/resources/SACGHSCommentanalysis02.12.08.pdf. Accessed November 18, 2009.

exaggerated claims and from tests with little evidence of clinical value. However, DTC LDTs offered under enforcement discretion are not subject to FDA premarket review or consumer protection regulations related to disclosure of information about a test's limitations or risks.

Also disconcerting are claims that understate the services provided by DTC genetic testing companies. Many companies that offer DTC genetic tests declare that their services should not be used as a basis for making medical decisions or that they are for informational purposes only and not intended for use to assess health.[61] Yet, some of these same companies offer tests for high-penetrance susceptibility mutations such as BRCA, which provide information that is clinically useful and clinically actionable.[86] Also, given the pleiotropic nature of genetic variations, testing that is marketed by DTC companies as "informational" could be recast as clinically significant as research advances the understanding of the genetic basis of health.[46] In these cases, claims that DTC tests are not intended for the diagnosis, cure, treatment, mitigation, or prevention of disease, other impairments, or conditions, or for health assessment are misleading.

FTC has broad statutory authority under section 5 of the Federal Trade Commission Act to take action against unfair and deceptive acts and practices that affect consumers[87] and specific authority under section 12 of the Act to take action against false advertising for health care products.[88] FTC has used its authority to investigate claims made by DTC companies. For example, FTC sent letters in August 2009 that closed the investigation of two nutrigenetics companies—Sciona and Genelex Corporation—that manufactured and/or marketed the MyCellf™ program.[89,90] Consumers who purchased MyCellf™ answered a lifestyle questionnaire and provided a cheek swab for the analysis of about two dozen SNPs purportedly related to five health areas, including heart health, bone health, and inflammation. Consumers received a report containing recommendations for diet and lifestyle changes based on the DNA analysis and questionnaire. FTC took action because it determined—after consulting with experts—that the scientific evidence did not support the companies' claims that diet and lifestyle recommendations could significantly impact health outcomes. Since the letters were sent to these companies, Sciona has ceased operations, and Genelex Corporation has stopped marketing nutrigenetic tests, including MyCellf™. In addition, FTC, together with FDA and CDC, issued a consumer alert in 2006 that provided advice on the use of DTC genetic tests.[3]

---

[86] Angrist M. (2009). We are the genes we've been waiting for: rational responses to the gathering storm of personal genomics. *The American Journal of Bioethics* 9(6-7):30-31.
[87] Federal Trade Commission Act (15 U.S.C. §§ 45). See http://www.law.cornell.edu/uscode/html/uscode15/usc_sec_15_00000045----000-.html. Accessed November 18, 2009.
[88] Federal Trade Commission Act (15 U.S.C. §§ 52). See http://www.law.cornell.edu/uscode/html/uscode15/usc_sec_15_00000052----000-.html. Accessed on November 18, 2009.
[89] Federal Trade Commission. Letter to Sciona, Inc., August 14, 2009. See http://www.ftc.gov/os/closings/090814scionaclosingletter.pdf. Accessed November 18, 2009.
[90] Federal Trade Commission. Letter to Genelex Corporation, August 14, 2009. See http://www.ftc.gov/os/closings/090814genelexclosingletter.pdf. Accessed on November 18, 2009.

Although FTC has the authority to take action against DTC companies, the lack of agreed-on standards for demonstrating clinical validity and clinical utility for DTC genetic testing complicates FTC's investigations, which examine whether advertisers possess competent and reliable scientific evidence (i.e., evidence agreed on by experts in the field) to substantiate claims.[91]

In addition to FTC oversight, State laws may provide protection against unfair and deceptive trade practices such as false and misleading claims, but these laws are largely untested. A 2009 survey of State laws commissioned by GPPC[92] revealed that all States have general consumer protection statutes, but no State laws directly address genetic testing. The most relevant State laws were those in California and Nevada, which specifically prohibit false or misleading scientific or clinical assertions, and laws in Pennsylvania and Nebraska, which explicitly prohibit false or misleading statements about privacy policies. Moreover, 20 States have adopted the Uniform Deceptive Trade Practices Act,[93] which defines a deceptive trade practice as any representation "that goods or services have sponsorship, approval, characteristics, ingredients, uses, benefits, or quantities that they do not have." In addition, the survey found that 14 States have laws prohibiting companies from failing to declare a "material fact" about a product or service, and 28 States prohibit misleading practices or misrepresentation of goods.

GPPC concluded that these State laws are broad enough to encompass DTC genetic testing products and services but underscored the challenge of applying such laws due to the complexity of DTC genetic testing products and services. Furthermore, the survey found that, on the basis of these laws, no actions have been taken against DTC genetic testing companies, although, one State's attorney general has investigated a company advertising genetic testing directly to the public.

Promotional Materials

Providing accurate and balanced information is a key concept in the regulation of DTC advertising.[26] In a study of 24 commercial Web sites that offer DTC genetic testing, Geransar and Einsiedel[28] found that although the majority of companies provided background information on basic genetics and the disease being tested, this information was not always complete, pertinent, or accurate. They also found that companies offering tests with little or no professionally recognized clinical utility were most likely to present misleading or irrelevant information.

---

[91] Secretary's Advisory Committee on Genetics, Health, and Society. Verbatim transcript of the Twentieth Meeting, October 9, 2009. Session on direct-to-consumer genetic testing. See http://oba.od.nih.gov/oba/SACGHS/meetings/October2009/1009SACG-v2.pdf, p.153. Accessed November 18, 2009.

[92] Genetics and Public Policy Center. (2009). Survey of state false advertising laws. See http://www.dnapolicy.org/resources/Prince_StateFalseAdvertisingLaws.pdf. Accessed August 27, 2009.

[93] National Conference of Commissioners on Uniform State Laws, (1966). *Revised Uniform Deceptive Trade Practices Act.* See http://www.law.upenn.edu/bll/archives/ulc/fnact99/1920_69/rudtpa66.htm. Accessed September 11, 2009.

Many of the Web sites of companies that provide DTC genetic testing services or DTC advertising materials lack information on the risks or limitations of genetic testing and the accuracy of test results.[36,94,95] With only limited risk disclosure as well as the exaggerated benefits described on some sites, consumers may not have the necessary information to make informed decisions about genetic testing.[36]

Geransar and Einsiedel[28] also provided a review of some analyses of DTC advertising content that have been conducted in the United States and Canada. A study of DTC advertisements for genetic tests in U.S. print media outlets (e.g., cancer-support magazines, Jewish community newspapers, pregnancy magazines) found that several advertisements overstated the value of genetic testing for clinical care, and some presented exaggerated claims or distorted information about disease risk. The advertisements also failed to include risk information to balance claims of effectiveness.[27] An analysis of BRCA advertisements in the Canadian media found that the value of BRCA testing frequently was misrepresented and that the portrayal of risk was problematic for advertisements targeted to high- and low-risk populations (Ashkenazi Jewish and general Canadian populations, respectively).[96] Mouchawar et al.,[58] however, found that DTC advertising may not be problematic. They reported that during a BRCA advertisement campaign, women generally did not report anxiety or confusion, except for Hispanic women and women with a higher self-perceived risk of breast and ovarian cancer. Mouchawar et al. suggest that the lack of anxiety or confusion may reflect efforts to pretest and refine the advertisements prior to launching the advertising campaign.

Other studies indicate that interest in clinical genetic tests decreases after educational interventions[97,98] and also may occur when more thorough information is provided prior to ordering DTC genetic tests. Gray et al.[16] found that women's beliefs about DTC genetic testing, intention to get BRCA testing, and preference for where they get tested are altered by provision of information on the possible risks of online BRCA testing. They also found that women who receive information on some of the possible risks of DTC BRCA testing have more negative beliefs about such testing than women in the control group and were more likely to prefer clinic-based testing rather than Internet-based testing. The findings also suggest that inclusion of information on possible risks of Internet-based BRCA testing through commercial Web sites may lower women's intentions to get any type of BRCA testing. If an effort to optimize

---

[94] Goddard KAB, Robitaille J, Dowling NF, Parrado AR, Fishman J, Bradley LA, Moore CA, Khoury MJ. (2009). Health-related direct-to-consumer genetic tests: a public health assessment and analysis of practices related to Internet-based tests for risk of thrombosis. *Public Health Genomics* 12:92-104.

[95] Bowen DJ, Battuello KM, Raats M. (2005). Marketing genetic tests: empowerment or snake oil? *Health Education & Behavior* 32(5):676-685.

[96] Donelle L, Hoffman-Goetz L, Clark JN. (2004). Portrayal of genetic risk for breast cancer in ethnic and non-ethnic newspapers. *Women and Health*. 40:93-111.

[97] Schwartz MD, Benkendorf J, Lerman C, Issacs C, Ryan-Robertson A, Johnson L. (2001). Impact of educational print materials on knowledge, attitudes, and interest in BRCA1/BRCA2: testing among Ashkenazi Jewish women. *Cancer* 92(4):932-940.

[98] Green MJ, Biesecker BB, McInerney AM, Mauger D, Fost N. (2001). An interactive computer program can effectively educate patients about genetic testing for breast cancer susceptibility. *American Journal of Medical Genetics* 103(1):16-23.

informed consent in the area of DTC BRCA testing inadvertently discourages at-risk women from obtaining a BRCA test, then more harm may be done than good. It is important to understand the potential impact of regulating claims and information on consumers' beliefs and intentions.

Analytical Validity

In the context of genetic testing, analytical validity means the ability to measure the genotype of interest accurately and reliably. Concerns about the analytical validity of DTC genetic tests include pretest errors (e.g., sample contamination, improper storage of specimens) and nontransparent quality-control measures during the testing phase.[30] CLIA-certified laboratories, however, must establish procedures that meet preanalytical requirements for the submission, handling,[99] and maintenance of the integrity of specimens[100] and assessment of these procedures.[101] In addition, CLIA requires the establishment of performance specifications (e.g., accuracy, precision, reportable range of test results, sensitivity, specificity, reference interval) for any modified FDA-cleared or -approved test kit and/or LDT used in the laboratory.[102] CLIA-certified laboratories also must participate successfully in performance assessment programs, using either proficiency testing programs[103] or alternative methods of assessment.[104]

Some trouble spots, however, cause concern. It is difficult for consumers to assess a laboratory's performance because the public cannot readily access data from CLIA inspections. In addition, for many genetic tests, there is an insufficient supply of standard reference materials for laboratories to perform proficiency testing and alternate assessment.[105] Also, minimal standards of analytical validity have not been established for many genetic tests, particularly as new analytical platforms are developed.[31] Furthermore, DTC testing entities that do not meet the

---

[99] Centers for Medicare & Medicaid Services. Clinical Laboratory Improvement Amendments, 42 CFR Sec. 493.1242. Standard: Specimen submission, handling, and referral. See http://wwwn.cdc.gov/clia/regs/subpart_k.aspx#493.1242. Accessed August 27, 2009.

[100] Centers for Medicare & Medicaid Services. Clinical Laboratory Improvement Amendments, 42 CFR Sec. 493.1232. Standard: Specimen identification and integrity. See http://wwwn.cdc.gov/clia/regs/subpart_k.aspx#493.1232. Accessed August 27, 2009.

[101] Centers for Medicare & Medicaid Services. Clinical Laboratory Improvement Amendments, 42 CFR Sec. 493.1249. Standard: Preanalytic systems assessment. See http://wwwn.cdc.gov/clia/regs/subpart_k.aspx#493.1249. Accessed August 27, 2009.

[102] Centers for Medicare & Medicaid Services. Clinical Laboratory Improvement Amendments, 42 CFR Sec. 493.1253. Standard: Establishment and verification of performance specifications. See http://wwwn.cdc.gov/clia/regs/subpart_k.aspx#493.1253. Accessed August 27, 2009.

[103] Centers for Medicare & Medicaid Services. Clinical Laboratory Improvement Amendments, 42 CFR Sec. 493, subpart H. Participation in proficiency testing for laboratories performing nonwaived testing. See http://wwwn.cdc.gov/clia/regs/subpart_h.aspx. Accessed August 27, 2009.

[104] Centers for Medicare & Medicaid Services. Clinical Laboratory Improvement Amendments, 42 CFR Sec. 493.1236(c). Evaluation of proficiency testing performance. See http://wwwn.cdc.gov/clia/regs/subpart_k.aspx#493.1236. Accessed August 27, 2009.

[105] Secretary's Advisory Committee on Genetics, Health, and Society. U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services. April 2008. See http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_oversight_report.pdf, p. 83-84. Accessed August 25, 2009.

CLIA definition of "laboratory" are not required to be CLIA certified and, therefore, would not be held to CLIA requirements.

Standards for Terminology and Risk Assessment

Providing standardized genetic information that can be interpreted and confirmed at a later date by a third party is vitally important, and current guidelines for genetic testing emphasize the importance of utilizing standardized terminology from established databases.[10,34,106] For SNP analysis, however, there is no standard terminology for raw genetic data or for documentation of risk assessment models. Appropriate standards for terminology might include reporting the National Library of Medicine's National Center for Biotechnology Information (NCBI) dbSNP build,[107] reference SNP accession identification number (rs number),[108] and strand direction for each variant or location of variants within reference sequence from the NCBI reference sequence (refseq) database.[109] In addition, scientific standards are needed to select and validate genetic variants that are used to evaluate disease risk, to assess aggregate risk when multiple variants are considered, and to determine the appropriate measures to calculate the predictive value of genomic profiles based on SNP analyses.[31,35,110,111]

Shirts and Parker[10] explain that standards are important because, even though individuals being tested may not be able to interpret the results themselves, the genetic information is theirs, and they should be able to take the information to obtain a second opinion, as they might do with any other test. At this time, however, the business model of some companies offering SNP analyses is a locked-in service model that requires customers to subscribe to an interpretation service from the same company, and they are charged for updated risk estimates. This model leaves consumers without access to sufficient genetic data to enable them to seek outside analysis. Shirts and Parker recommended that companies strive to retain clients by providing transparent risk calculations and understandable reports that clearly explain the test interpretation and for how long the information is valid.

---

[106] Richards CS, Bale S, Bellissimo DB, Das S, Grody W, Hegde MR, Lyon E, Ward BE, Molecular Subcommittee of the ACMG; Laboratory Quality Assurance Committee. (2008). ACMG recommendations for standards for interpretation and reporting of sequence variations: revisions 2007. *Genetics in Medicine* 10:294-300.
[107] National Center for Biotechnology Information. dbSNP. See http://www.ncbi.nlm.nih.gov/projects/SNP/. Accessed July 2, 2009.
[108] National Center for Biotechnology Information. Reference SNP reports and submitter reports have different identifiers in dbSNP. See http://www.ncbi.nlm.nih.gov/SNP/get_html.cgi?whichHtml=how_to_submit#REFSNP. Accessed July 2, 2009.
[109] National Center for Biotechnology Information. Reference sequences. See http://www.ncbi.nlm.nih.gov/RefSeq/. Accessed July 2, 2009.
[110] Kraft P, Wacholder S, Cornelis MC, Hu FB, Hayes RB, Thomas G, Hoover R, Hunter DJ, Chanock S. (2009). Beyond odds ratios—communicating disease risk based on genetic profiles. *Nature Reviews Genetics* 10:264-269.
[111] Ray, T. (April 15, 2009). More work needed to standardize consumer genomics offerings, top U.S. health official says. *Pharmacogenomics Reporter*.

Clinical Validity

The clinical validity of a genetic test refers to the test's accuracy in detecting the presence of, or predicting the future risk for, a health condition or phenotype. An analysis of 24 companies offering DTC genetic testing[28] found that claims for the clinical validity of tests were supported by a range of sources, including unpublished company findings, information from professional and patient organizations, and peer-reviewed research (mostly observational studies). More than one-third of companies provided no references to outside sources of information.

Several DTC genetic services companies offer testing that uses microarray technology to screen for hundreds to a million SNPs. These tests do not identify genetic variants that are diagnostic; SNPs are surrogate genetic markers that have been associated with an increased risk of developing a disease.[12] Although much scientific progress has been made in identifying genetic variants associated with disease,[112] for the most part their clinical relevance remains unclear.[113] In most cases—other than for Mendelian disorders—only a small proportion of the genetic contribution to a disease or condition has been identified; disease variants account for marginal increases in risk, with odds ratios of 1.5 or less.[11,30,114,115] Thus, genetic variant-disease associations can be valid, but the variant accounts for a very small part of the disease etiology. Even when variants that are associated with modest increased risks are combined, they generally have low discriminatory and predictive ability.[116,117] For common, multifactorial diseases, interactions among multiple genes and between genetic variants and environmental factors also must be considered. In addition, DTC companies may use only a subset of all known genetic variants associated with a particular disease. Different companies may select different variants to assess the same condition. A full accounting of disease susceptibility requires the identification of multiple genetic variants and their interactions with environmental, behavioral, and other genetic factors through well-designed studies.[30]

Clinical Utility

In addition to concerns about the analytical and clinical validity of DTC genetic tests, few or no data exist on clinical utility—the balance of risks and benefits of a test. Hunter et al.[30] found few

---

[112] National Human Genome Research Institute. A Catalog of Published Genome-Wide Association Studies. See http://www.genome.gov/26525384. Accessed April 8, 2009.

[113] Melzer D, Hogarth S, Liddell K, Ling T, Sanderson S, Zimmern RL. (2008). Genetic tests for common diseases: new insights, old concerns. *British Medical Journal* 336:590-593.

[114] Manolio T. (July 8, 2008). State of the science of genomic associations: current and future directions. Secretary's Advisory Committee on Genetics, Health, and Society. See http://oba.od.nih.gov/oba/SACGHS/meetings/july2008/manolio.pdf. Accessed April 14, 2009.

[115] Manolio T, Brooks LD, Collins FS. (2008). A HapMap harvest of insights into the genetics of common disease. *Journal of Clinical Investigations* 118:1590-1605.

[116] Janssens AC, van Duijn CM. (2008). Genome-based prediction of common disease: advances and prospects. *Human Molecular Genetics* 17:R166-R173.

[117] Jakobsdottir J, Gorin MB, Conley YP, Ferrell RE, Weeks DE. (2009). Interpretation of genetic association studies: markers with replicated highly significant odds ratios may be poor classifiers. *PLoS Genetics* 5(2):e1000337.

observational studies and no clinical trials that demonstrate the risks and benefits associated with screening for individual gene variants or genome-wide variants. Proponents of susceptibility testing argue that knowledge of increased risk to a disease for which there are protective interventions (e.g., diabetes) will motivate patients to comply with these interventions, but evidence is scanty. Hall and Gartner[118] stated that there is no evidence that people who act on advice provided by genome-wide susceptibility testing would be any better off than those acting on generic health advice in the absence of genetic testing (e.g., do not smoke, use alcohol in moderation, exercise regularly, and eat a balanced diet).

Another issue, particularly for analyses involving multiple SNPs or genes, is incomplete reporting of genotypic information due to patents for particular genes or DNA sequences. Fear of patent infringement liability could limit the return of genotypic information,[119] which in turn could limit clinical utility and undermine the validity of testing.

In evaluating the clinical utility of a genetic test, the types of outcomes that are considered depend on the purpose of the test and the audience of decisionmakers.[22,120,121] For public health programs, the impact on morbidity and mortality is probably a critical factor. Third-party payers likely consider whether the test is useful for timely and accurate diagnosis and clinical management. In the DTC context, the consumer ultimately makes the decision about whether testing will be useful, and this process may include personal and nonclinical considerations. (Determining whether information may be useful to an individual is sometimes referred to as "personal utility.") For example, genetic information about a disease that cannot be treated or prevented may provide opportunities for personal actions such as informing family members, supporting research, or augmenting insurance coverage (e.g., purchasing long-term care insurance).[22,121,122] Such decisions, however, may be flawed if the information provided by a DTC company is incomplete, inaccurate, or misleading.[8]

Consumer and Provider Understanding of Test Results

The 2004 Institute of Medicine (IOM) report on health literacy revealed that half of U.S. adults lack the skills needed to evaluate the risks and benefits of health-related technologies.[123] This

[118] Hall W, Gartner C. (2009). Direct-to-consumer genome-wide scans: astrologicogenomics or simple scams? *The American Journal of Bioethics* 9(6-7):54-55.
[119] Secretary's Advisory Committee on Genetics, Health, and Society. (2009). Public Consultation Draft Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests. See http://oba.od.nih.gov/oba/SACGHS/SACGHS%20Patents%20Consultation%20Draft%203%209%202009.pdf. Accessed April 20, 2009.
[120] Grosse SD, Khoury MJ. (2009). What is the clinical utility of genetic testing? *Genetics in Medicine* 8(7):448-450.
[121] Grosse SD, McBride CM, Evans J, Khoury MJ. (2009). Personal utility and genomic information: look before you leap. *Genetics in Medicine* 11(8):575-576.
[122] Hsu AR, Mountain JL, Wojcicki A, Avey L. (2009). A pragmatic consideration of ethical issues relating to personal genomics. *The American Journal of Bioethics* 9(6-7):1-2.
[123] Institute of Medicine. (2004). Health literacy: a prescription to end confusion. See http://www.iom.edu/Reports/2004/Health-Literacy-A-Prescription-to-End-Confusion.aspx. Accessed April 14, 2009.

finding—together with the complexity of concepts such as gene penetrance, relative and absolute risk, validity, and gene-environment interactions—may increase the likelihood of misunderstanding genetic test results.[23] Genetic information, particularly from tests with low or uncertain clinical validity that are provided directly to consumers without adequate interpretation, may be applied inappropriately as consumers make decisions regarding the management of their health.[28,36] For example, consumers could misinterpret a negative genetic test result for colon cancer as zero risk and be less motivated to comply with screening guidelines for preventive care.[8]

Regardless of the limited evidence for the clinical validity and utility of certain DTC genetic tests, consumers who are curious about their genome or are early adopters of new technologies will buy these services. Consumers who bring their tests results to their health care provider create a teachable opportunity.[64,124] It is assumed that providers can help their patients understand their test results and translate this information into appropriate clinical or preventive care, although health care providers may lack the genetic competencies that their patients need.

Several studies indicate that many physicians do not have sufficient knowledge to guide patients appropriately in the use of genetic tests. For example, the Menasha et al.[125] analysis of survey responses from 89 physicians found that 71 percent of physicians rated their knowledge of genetics and genetic testing as fair to poor. A National Cancer Institute study of a random sample of 1,251 physicians from 8 specialties found that only 40 percent of primary care physicians and 57 percent of tertiary care physicians felt qualified to recommend genetic testing for cancer susceptibility to their patients.[126] Giardiello et al.[41] reported that only 68.4 percent of medical professionals with no specialty training in genetics correctly interpreted genetic test results for familial adenomatous polyposis. Sandhaus et al.[42] found that many physicians are unprepared to interpret genetic risk information relevant to results reported for BRCA mutations.

In a review of research on the delivery of genomic medicine for common, adult-onset diseases by Scheuner et al.,[44] the most consistent finding was that primary care providers reported being underprepared to integrate genomics into the practice of medicine. The authors reported that health professionals lack basic knowledge about genetics and the confidence to interpret familial patterns of disease. These deficiencies limit providers' abilities to order tests, interpret test results accurately, and refer their patients for genetic consultation. Many primary care physicians report an inability to discuss the details of a condition or management of that condition with their patients even for relatively routine test such as newborn screening.[40] If health providers are not equipped to provide adequate genetic counseling for tests involving single genes, how can they be expected to interpret whole-genome scans?[45]

---

[124] Haga S, Willard HF. (2008). Letter to the editor: letting the genome out of the bottle. *New England Journal of Medicine* 358(20):2184.

[125] Menasha JD, Schechter C, Willner J. (2000). Genetic testing: a physician's perspective. *The Mount Sinai Journal of Medicine* 67(2):144-151.

[126] Freedman AN, Wideroff L, Olson L, Davis W, Klabunde C, Srinath KP, Reeve BB, Croyle RT, Ballard-Barbash R. (2003). US physicians' attitudes toward genetic testing for cancer susceptibility. *American Journal of Medical Genetics Part A* 120(1):63-71.

Studies that include other health professionals report experiences similar to those of physicians in terms of genetics knowledge, skills, and abilities surrounding genetic testing for their patients.[39] In a survey of individuals graduating from six allied health care training programs, 78 percent reported that the genetics knowledge and skills covered in their training programs were marginal to none.[38]

Impact on the Health Care System

The DTC model, by definition, bypasses a consumer's personal health care provider; however, providers may be approached by their patients after DTC testing for interpretation of results or other followup services.[46,65] McGuire et al.[66] found that 78 percent of potential users of DTC testing for personal genomic information probably would turn to their physicians for help in interpreting test results. For example, consumers may ask about test results indicating an increased risk for cancer or heart disease, even if the increase is small, and physicians may feel obligated to offer tests such as computerized tomography (CT) scans, colonoscopies, or other procedures.

The 2008 DocStyles survey[65] found that about 790 health care providers (42 percent of 1,880 respondents) were aware of DTC personal genomic testing. Of this group, about 120 providers had at least 1 patient who brought personal genomic test results to them in the past year; 75 percent reported changing some aspect of the patient's care. Among providers who were aware of personal genomic testing, 52 percent responded that the test results would be somewhat or very likely to influence their care of a patient; 15 percent were uncertain.

Giovanni et al.[127] reported on 24 cases of patients entering the health care system following DTC testing. Cases were identified through a survey of genetics professionals. The patients ranged in age from 21 to 60 years (mean age 42 years), and most were Caucasian. The DTC testing used by these patients included whole-genome SNP analysis, single-gene sequencing, analysis of single-gene variants, and paternity testing. About 52 percent of patients self-referred to genetics professionals, and others were referred by a primary care provider. The reasons that patients conferred with a genetics professional included interpretation or reinterpretation of test results and questions about personal risk. Out-of-pocket costs to the patients ranged from $20 to $5,565. The estimated cost to the health care system—on the basis of Medicare reimbursement standards using national averages—ranged from $40 to $20,604. Followup tests and interventions included CT scans, magnetic resonance imaging (MRI), mammograms, cancer antigen 125 (CA125) and prostate-specific antigen (PSA) testing, and prophylactic mastectomy.

Current public and private health insurance systems are not designed to compensate physicians for the time it takes to educate patients about DTC genetic and genomic test results, order

[127] Giovanni M, Fickie M, Lehmann L, Meckley L, Murray M. (2009). Patients entering the healthcare system following direct-to-consumer testing. The American Society of Human Genetics Annual Meeting, October 20-24, 2009, program number 236. See http://www.ashg.org/cgi-bin/2009/ashg09s. Accessed on November 18, 2009.

confirmatory diagnostic testing, or provide treatment and care on the basis of information obtained from DTC services.[66] Ambiguous, incidental, or false-positive results from DTC genetic testing could lead to additional testing that increases medical costs and exposes patients to unnecessary procedures that may have adverse effects.[128] Providing followup services to DTC testing could further strain an already overburdened medical system and limit the resources available for established health care interventions.[45,47,121,129]

Privacy Protections

The consequences of DTC genetic testing extend beyond the risk of adverse patient outcomes and cost implications for the health care system.[48] Unlike genetic testing provided through a hospital, clinic, or physician office, companies that offer DTC genetic testing generally are not covered entities under the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule.[19] Therefore, these companies are not subject to the Federal privacy protections that limit the use and disclosure of individually identifiable protected health information.

In some circumstances, a DTC company may be a business associate of a covered entity, dependent on the specifics of the service it provides to the HIPAA-covered entity. In the case that a DTC company is a business associate of a covered entity (e.g., Navigenics has partnered with the MDVIP network,[130] and 23andMe has partnered with Palomar Pomerado Health[131]), an agreement between the covered entity and the business associate would stipulate the permitted uses and disclosures of protected health information by the DTC company. In addition, new "breach notification" regulations mandated by the Health Information Technology for Economic and Clinical Health (HITECH) Act[132] require business associates to notify the covered entity of breaches of protected health information at or by the business associate and to identify the affected individuals.

Genetic databases and biorepositories must be secured from unauthorized access. Appropriate security measures should restrict not only external access to the information by hackers but also the number of internal personnel who have access to personal information, particularly to identifiable or potentially identifiable information.[50] Few DTC genetic testing Web sites, however, describe whether there are protections for sample storage, withdrawal of specimens or data derived from specimens from the database or biorepository, and future use of specimens or

---

[128] McGuire AL, Burke W. (2008). An unwelcome side effect of direct-to-consumer personal genome testing: raiding the medical commons. *Journal of the American Medical Association* 300(22):2669-2671.
[129] Caulfield T. (2009). Direct-to-consumer genetics and health policy: a worst-case scenario? *The American Journal of Bioethics* 9(6-7):48-49.
[130] National physician group MDVIP partners with Navigenics. See http://blog.navigenics.com/articles/comments/national_physician_group_mdvip_partners_with_navigenics/. Accessed November 19, 2009.
[131] 23andMe and Palomar Pomerado Health Partner to Give PPH Members Access to Their Genetic Information. See https://www.23andme.com/about/press/20090427/. Accessed November 19, 2009.
[132] American Recovery and Reinvestment Act of 2009. Title XIII, Health Information Technology for Economic and Clinical Health Act. Subtitle D, Privacy. See http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=111_cong_bills&docid=f%3Ah1enr.txt.pdf. Accessed November 19, 2009.

data derived from specimens.[36] Bregman-Eschet[50] has offered several actions to protect consumer specimens and data, including policies on informed consent, access, security, confidentiality, ownership, information transfer, information sharing, and accountability.

Gurwitz and Bregman-Eschet[49] explain that privacy interests also can be compromised if a genetic testing company decides to sell its database containing the genotypic and phenotypic information of its customers to a third party. For commercial biotechnology companies, databases that contain genetic information are some of their most valuable assets. A company might sell its database in case of financial difficulty or simply for the sake of making a profit, just as it might do with any other valuable asset. Many consumers may be unaware of this possibility. In the absence of a Federal law prohibiting the sale of personal genetic information and in view of previous court decisions allowing the transfer of personal information from one entity to another, the unrestricted sale or transfer of genetic information to a third party may be a real possibility. In such cases, personal information might be transferred to a company with less strict privacy protection mechanisms. This issue also raises the question of ownership of genotypic and phenotypic information stored in the database. Who owns the information? The company that retrieved the information or the individual who wished to explore and investigate his or her genetic makeup? Five States explicitly define genetic information as personal property, and one State—Alaska—extends personal property rights to DNA samples.

If a specimen and information retrieved from it are considered the property of the company collecting and storing it, then the company is free to treat it as any other commodity, including selling or transferring the information to a third party. One possible solution, as described by Winickoff and Winickoff,[133] is to define the holder of genetic information as the "trustee" of the information it holds. This model would apply restrictions and responsibilities to the safekeeping of genetic information collected and stored by companies offering DTC genetic tests. For example, it would place restrictions on the transferability of information collected and future disclosures in the absence of consent from the customer.

The World Privacy Forum noted in its remarks to SACGHS[48] that companies providing goods and services to consumers have a vast appetite for consumer information, especially for information about health conditions. A large industry of consumer profilers and other commercial data brokers satisfy that appetite. Existing enterprises that collect and sell consumer information tend to seek and sell genetic information in the same way that they seek and sell other health and consumer information. Genetic information is another potential profit center for sellers of consumer lists and consumer profiles. DTC advertising of genetic tests and consumer-initiated genetic testing likely will be sources of genetic information for marketing uses. These activities are significantly unregulated for privacy, so the possibility of data leakage is high. Indeed, it is expected that some genetic testing activities may develop principally for the purpose of obtaining information for sale to marketers and others. Data profilers may find that they can make a profit by offering free or low-cost genetic testing for consumers; the profits come from

[133] Winickoff DE, Winickoff RN. (2003). The charitable trust as a model for genomic biobanks. *New England Journal of Medicine* 349:1180-1184.

the sale of a consumer's genetic profile to marketers. Most genetic findings likely would be relevant for the consumer's entire life and would have some relevance for relatives of a consumer. The stream of income from data sales over many years may support a significant upfront cost to acquire the core data. If testing is sufficiently inexpensive, a barber could sweep up and sell the hair samples of customers to data profilers. Even a consumer in possession of a wholly confidential genetic test result may find that hidden tracking of Internet usage exposes the results indirectly to advertisers and profilers as a result of the consumer searching for related materials.[134]

Some consumers choose to share their genetic information with large social networks, and the consequences of this sharing are difficult to predict. Consumers who share their genetic information in this manner may not understand that they risk their confidentiality as well as the that of their family members.[135] For example, a woman who shares information about her breast cancer risk is also sharing her children's (or future children's) risk of breast cancer.[23] Consumers also could share genetic data that are meaningless today but that later reveal an elevated risk for a serious disease.[136] Without a process analogous to informed consent, there is no mechanism to ensure that such consumers consider the effects or ramifications of sharing such data.[23]

Nonconsensual Testing

As noted by GPPC,[51] the combination of technologies that permit the analysis of small amounts of DNA, increased availability of testing services, and lack of regulations to protect genetic privacy creates an environment that is ripe for surreptitious testing, that is, the collection and analysis of DNA without consumer consent and the disclosure of information derived from such analysis without consumer permission. Most States do not have laws restricting surreptitious DNA testing, and those that do generally place restrictions only on nonconsensual health-related testing. Ten States have laws that broadly restrict surreptitious DNA testing for both health- and nonhealth-related purposes, such as parentage determination or ancestry. Even where State laws expressly prohibit surreptitious testing, it is unclear that these laws have ever been enforced.

A *New Scientist* investigation demonstrated how surreptitious genomic testing could be carried out with a credit card and a private e-mail account.[52] It showed that an unauthorized third party could use an item with another person's DNA (e.g., a drinking glass) to obtain a sample that could be used for genomic analysis. Thwarting surreptitious genomic testing may require new laws to protect privacy by making it a crime to possess someone else's DNA with the intent to analyze it without consent. For example, the U.K. Human Tissue Act 2004 created a new offense

---

[134] Federal Trade Commission. Behavioral Advertising: Tracking, Targeting, & Technology. See http://www.ftc.gov/bcp/workshops/ehavioral/index.shtml. Accessed April 14, 2009.
[135] Resnik DB. (2009). Direct-to-consumer genomics, social networking, and confidentiality. *The American Journal of Bioethics* 9(6-7):45-46.
[136] Stanford University School of Medicine. Press Release June 5, 2009. Risks of sharing personal genetic information online need more study, Stanford bioethicists say. See http://med.stanford.edu/news_releases/2009/june/networking.html. Accessed July 13, 2009.

for DNA theft, punishable by up to 3 years in prison and/or a fine.[137] According to this Act, it is unlawful in the United Kingdom to possess human tissue with the intention of analyzing its DNA without the consent of the person from whom the DNA came. Such laws, however, may be difficult to enforce.

Commercial genomic testing companies do not explicitly warn potential customers of the possible legal consequences of submitting another person's DNA without consent. Gurwitz and Bregman-Eschet[49] explored measures that can ensure that customers submit and have access to only their own DNA samples (or samples of individuals in their legal custody) and not to the DNA of third parties about whom they would like to gain genetic information. A simple way to increase customer awareness against sending another person's DNA sample may be to require a signed statement—to be sent with the DNA sample—confirming that the sample is his or her own or from a person in their custody. An analysis by the National Conference of State Legislatures found that laws in 17 States require informed consent for a third party to perform or require a genetic test or to obtain genetic information, and 27 States require consent to disclose genetic information. In addition, 19 States have established specific civil and/or criminal penalties for violating State privacy laws.[138]

Research Use of Consumer Specimens or Data

Several companies that offer DTC genetic testing services are actively engaged in research and support projects such as defining genetic, environmental, and behavioral factors in disease and health; refining risk prediction models; and learning how consumers utilize their test results. These efforts are commendable, but they also raise questions as to whether the informed consent process is sufficient and whether studies are appropriate if they are not approved by an institutional review board (IRB). Do individuals who purchase DTC genetic testing services understand that companies may conduct internal research with their specimens (or data derived from the specimen) or may share specimens and data with external investigators? In addition, consumers may not fully understand the significance of sharing genetic material with third parties, even if the sample or data are delinked from personal account information.[139]

Another concern is that, because DTC companies in most cases do not use Federal funds to conduct human subjects research and are not regulated by FDA, they are not legally bound to comply with the requirements of Federal regulations that protect human research subjects. There are three major regulatory regimes relevant to the banking and research use of human specimens and/or associated data: the Federal Policy for the Protection of Human Subjects, also widely

[137] Human Tissue Act 2004. Non-consensual analysis of DNA (part 3, section 45). See http://www.opsi.gov.uk/acts/acts2004/ukpga_20040030_en_5#pt3-pb1-l1g45. Accessed November 19, 2009.
[138] National Conference of State Legislatures. (2008). Genetic Information: Legal Issues Relating to Discrimination and Privacy. See http://www.ncsl.org/programs/health/genetics/prt.htm. Accessed April 10, 2009.
[139] Wasson K. (2009). Direct-to-consumer genomics and research ethics: should a more robust informed consent process be included? *The American Journal of Bioethics* 9(6-7):56-57.

known as the Common Rule,[140] FDA regulations,[141] and the HIPAA Privacy Rule.[142,143] In addition, research programs within DTC genetic testing companies may not adhere to HHS regulations that provide additional protections for vulnerable populations such as pregnant women[144] and children.[145] For example, in studies involving children, HHS rules require that adequate provisions be made to solicit the assent of children who are capable of providing assent, except in limited circumstances.

Although some companies voluntarily abide by parts of these Federal regulations, barriers in nontraditional research settings preclude wider adoption of the protections and/or irregular compliance over time (i.e., companies may adopt research regulations and later cease compliance). Moreover, inconsistent regulations and lack of clear guidance pose challenges to researchers using human specimens and data. For example, the level of regulatory oversight is related to the degree of identifiability of specimens or data (i.e., the extent to which biological material can be linked to the person from whom it was obtained), and the Common Rule and the HIPAA Privacy Rule use different definitions for "individually identifiable." Under the Common Rule, specimens are individually identifiable if the identity of the individual to whom the specimen pertains is or may be readily ascertained by the investigator associated with the specimen. The HIPAA Privacy Rule has a different definition of "individually identifiable"[146] and delineates—under the Privacy Rule's safe-harbor standard—18 identifiers that must be removed to render the health information not individually identifiable.[147] Determining which regulations apply can be confusing, particularly because of the inconsistent terminology used in

---

[140] Code of Federal Regulations. Title 45, Part 46: Protection of Human Subjects. See http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm. Accessed May 22, 2009.
[141] Code of Federal Regulations. Title 21, Part 50: Protection of Human Subjects. See https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?CFRPart=50. Accessed May 27, 2009.
[142] Code of Federal Regulations. Title 45, Parts 160, 162, 164. Health Insurance Portability and Accountability Act. See http://www.hhs.gov/ocr/privacy/hipaa/administrative/combined/index.html. Accessed May 27, 2009.
[143] Although the HIPAA Privacy Rule does not apply to specimens per se, it may apply to information associated with the specimens.
[144] Code of Federal Regulations. Title 45, Part 46, Subpart B: Additional Protections for Pregnant Women, Human Fetuses, and Neonates Involved in Research. See http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#subpartb. Accessed July 29, 2009.
[145] Code of Federal Regulations. Title 45, Part 46, Subpart D: Additional Protections for Children Involved as Subjects in Research. See http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#subpartd. Accessed July 29, 2009.
[146] Code of Federal Regulations. Title 45, Part 160.103. Health Insurance Portability and Accountability Act, Definitions. See http://edocket.access.gpo.gov/cfr_2007/octqtr/pdf/45cfr160.103.pdf. Accessed September 17, 2009. The Privacy Rule defines *individually identifiable health information* as information that is a subset of health information, including demographic information collected from an individual, and (1) is created or received by a health care provider, health plan, employer, or health care clearinghouse; and (2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual; and (a) that identifies the individual; or (b) with respect to which there is a reasonable basis to believe the information can be used to identify the individual.
[147] Code of Federal Regulations. Title 45, Part 164.514(b)(2). Health Insurance Portability and Accountability Act, Implementation specifications: requirements for de-identification of protected health information. See http://edocket.access.gpo.gov/cfr_2007/octqtr/pdf/45cfr164.514.pdf. Accessed September 17, 2009.

regulations.[53] In addition, advancements in genomic technologies make increasingly real the possibility that anonymized sequenced DNA can be readily linked to an individual.[148,149]

The Public Responsibility in Medicine and Research (PRIM&R) Human Tissue/Specimen Banking Working Group developed a white paper that addresses challenges related to the collection, storage, distribution, and use of human specimens and associated data for research purposes.[53] As noted in the PRIM&R white paper, the predominant risks from the research use of identifiable human specimens—and data obtained from these specimens—are psychosocial, primarily the loss of privacy and/or confidentiality of health information. Such harms can occur if specimens or data are not adequately protected or are used inappropriately for nonresearch purposes. Another possibility is that these materials could be transferred or sold to third parties that do not protect the privacy or welfare of or respect the rights of specimen donors.

The PRIM&R white paper offers strategies to address some of the ethical challenges associated with the use of human specimens and data for research, including a toolkit for IRBs and researchers.[150] Chief among the issues addressed in the PRIM&R white paper are informed consent (including informed consent for future unspecified research and waivers of informed consent); operating procedures for overseeing specimen collections, biorepositories, and databanks; and approaches to ensure the protection of privacy and confidentiality. The toolkit also includes a discussion of State law requirements for the use of specimens. For example, several States have enacted statutes that extend the scope of Federal requirements to all research, regardless of the funding source. Virginia, Maryland, and New York require IRB review of all human subjects' research and prior informed consent of subjects. California has passed a law that requires researchers to obtain the informed consent of subjects or their legally authorized representatives prior to conducting human subjects research. A database of State genetic privacy laws is maintained by the National Conference of State Legislatures.[151]

Some researchers have challenged traditional perspectives about privacy protections. For example, Malm has questioned what she refers to as the "obsession with genetic privacy."[152] She asks, if society at large is likely to benefit from the sharing of genetic information, might

---

[148] McGuire AL, Gibbs RA. (2006). No longer de-identified. *Science* 312:370-371.

[149] Homer N, Szelinger S, Redman M, Duggan D, Tembe W, Muehling J, Pearson JV, Stephan DA, Nelson SF, Craig DW. (2008). Resolving individuals contributing trace amounts of DNA to highly complex mixtures using high-density SNP genotyping microarrays. *PLoS Genetics* 4(8):e1000167. See http://www.plosgenetics.org/article/info%3Adoi%2F10.1371%2Fjournal.pgen.1000167. Accessed July 13, 2009.

[150] Public Responsibility in Medicine and Research. (March 2007). *Report of the Public Responsibility in Medicine and Research (PRIM&R) Human Tissue/Specimen Banking Working Group; Part II Tools for Investigators, IRBs, and Repository Managers.* See http://www.primr.org/uploadedFiles/PRIMR_Site_Home/Public_Policy/Recently_Files_Comments/Tissue%20Banking%20White%20Paper%20final%20Part%20II.pdf. Accessed May 22, 2009.

[151] National Conference of State Legislatures. State Genetic Privacy Laws. See http://www.ncsl.org/programs/health/genetics/prt.htm. Accessed May 27, 2009.

[152] Malm H. (2009). Genetic privacy: might there be a moral duty to share one's genetic information? *The American Journal of Bioethics* 9(6-7):52-54.

individuals have a duty to share that information, as opposed to merely a consent-based right to do so? Should policies and regulations be developed in ways that facilitate and encourage this sharing even, perhaps, at the cost of a reduction in confidentiality? IOM takes a similar view in its report *Beyond the HIPAA Privacy Rule: Enhancing Privacy, Improving Health Through Research.* [153] The report suggests that obligations to implement comprehensive privacy protections are independent of patient consent and that if society seeks to derive the benefits of medical research in the form of improved health, information should be shared to achieve the greater good, with regulations and oversight to support the use of such information.

Psychosocial Impact

Many unanswered questions remain about consumer understanding of DTC genetic testing results and what consumers will do with the information resulting from such tests. For example, could genetic testing cause distress for consumers who receive ambiguous results?[12] Studies of the impact of clinic-based genetic testing may help provide some answers.

A study that examined the psychological impact of BRCA testing found that testing and genetic counseling led to psychological benefit for patients with negative results and no increased distress for those who already had received positive or inconclusive test results.[54] Another study of women who underwent BRCA testing found that women with BRCA mutations had significantly more depressive symptoms and negative mood at 1 month and 6 months after receiving the test results compared with women without BRCA mutations. At 12 months, however, negative mood and depressive symptoms returned to baseline.[55]

A literature review by Schlich-Bakker et al.[56] of the psychological impact of genetic testing on breast cancer patients indicated that patient receipt of inconclusive tests results was followed by a range of emotional reactions, from relief to uncertainty, and sometimes the results were misinterpreted as an absence of genetic predisposition. In a later study that examined interpretation of inconclusive BRCA test results, van Dijk et al.[57] found that few women (12 of 183) with an inconclusive result believed that the risk of carrying a BRCA mutation was nonexistent. More importantly, the intention to obtain mammograms did not change among women with inconclusive results. A study that assessed the impact of DTC advertising for BRCA testing on patients and physicians at a managed care organization found little apparent negative impact (e.g., anxiety or confusion) on patients, and 84 percent of physicians reported no strain on the doctor-patient relationship.[58]

A systematic review of predispositional genetic testing by Heshka et al.[59] evaluated 30 studies involving hereditary nonpolyposis colorectal cancer, hereditary breast and ovarian cancers, and Alzheimer disease. Most of the studies provided standard genetic counseling that included an explanation of the benefits, risks, and limitations of genetic testing. The authors found that

[153] Institute of Medicine. (2009). *Beyond the HIPAA Privacy Rule: Enhancing Privacy, Improving Health Through Research*. Washington, DC: The National Academies Press. See http://www.iom.edu/Reports/2009/Beyond-the-HIPAA-Privacy-Rule-Enhancing-Privacy-Improving-Health-Through-Research.aspx . Accessed September 17, 2009.

predispositional genetic testing had no significant effect on psychological outcomes (e.g., distress, anxiety, depression) and did not change perceived risk. Also, there was little effect on behavior (e.g., surveillance, screening uptake, lifestyle changes). Breast cancer screening rates were similar among carriers and noncarriers of BRCA mutations. However, the screening rates of ovarian and colorectal cancers seemed to be higher among mutation carriers compared with noncarriers.

In a prospective, randomized, controlled trial, Green et al.[154] examined the effect of disclosing the apolipoprotein E (APOE) genotype to asymptomatic adults who had a parent with Alzheimer disease. (The ε4 allele of the APOE gene is associated with an increased susceptibility to this disease.) For the study, 162 participants were randomly assigned to receive their APOE genotype (disclosure group) or not to receive genotypic results (nondisclosure group). Study participants learned about the limitations of APOE testing and the absence of a medical benefit of such testing in a 90-minute, semiscripted group session led by a genetic counselor. Symptoms of anxiety, depression, and test-related distress were measured at 6 weeks, 6 months, and 1 year after disclosure or nondisclosure. There were no significant differences between the disclosure and nondisclosure groups in anxiety, depression, or test-related distress. However, a subgroup analysis of the disclosure group revealed that the subgroup negative for the APOE ε4 allele had a significantly lower level of test-related stress than the ε4-positive subgroup at 6 weeks and 6 months after disclosure and was marginally significant at 12 months. The authors point out that if the APOE genotypic information had been provided without genetic counseling or to subjects who had no family history of Alzheimer disease, the results might have been different. In addition, the exclusion of participants with low neurocognitive scores and high depression scores may have influenced the results.

There are several limitations to the studies described above. None of the studies examined DTC genetic testing services, and the participants interacted with health care providers. The studies also lacked diversity; most participants were Caucasian and well educated. Several studies that assessed behavioral impacts noted that participants were highly motivated, were likely to adhere to screening recommendations, and may have had a higher ability to cope with test results.[59] Additional research will provide a better understanding of the psychosocial impact of DTC genetic testing.

DTC Genetic Testing for Children

The survey of social networkers by McGuire et al.[66] revealed that 63 percent of respondents agreed that parents should be able to have their children tested. Several companies provide DTC genetic testing for children, but such companies may not assume the same kinds of responsibilities as clinicians, such as adhering to professional standards and guidelines.[61] For example, DTC genetic testing companies may not require the assent of the child, and there may

[154] Green RC, Roberts JS, Cupples LA, Relkin NR, Whitehouse PJ, Brown T, Eckert SL, Butson M, Sadovnick AD, Quaid KA, Chen C, Cook-Deegan R, Farrer LA for the REVEAL Study Group. (2009). Disclosure of APOE genotype for risk of Alzheimer's disease. *New England Journal of Medicine* 361:245-254.

be no provision for information about the risks and benefits of testing in children.[60] Moreover, individuals who are tested as children are denied the right to choose whether they want to share their genetic information with family members (e.g., parents)[155] or others, if test results have been shared through social networking.[23] The impact of DTC genetic testing in minors is unclear because there are no empirical data on harms, including whether harms in a DTC delivery model differ from those in a medical delivery model or if harms differ across populations or by reasons for seeking testing.[60]

In the context of a discussion about the use of biomarkers to predict behavioral and psychiatric disorders, Singh and Rose[156] raised several questions about the consequences of testing children through DTC genetic testing services. Will biomarker information that provides a cognitive-behavioral risk profile for a child affect how parents view their child and how they act on behalf of the child? In what circumstances might this have positive consequences, and when might this information do harm? Some of these questions apply more broadly, for example, to what extent and at what age do children have the right to know their personal biomarker profile? Do children have the right to refuse to submit to genetic screenings that are not clinically indicated? Conversely, should children have the right to submit their own samples to such companies? Singh and Rose suggest that the regulations of children's rights, capacity, and consent in other contexts—such as birth control and cosmetic surgery—could inform thinking about children's access to personal biomarker information.

Disparities

There is a growing divide, driven in part by education and socioeconomic status, between consumers who utilize genetic information in their health care and those who do not.[63,157] Bodie and Dutta[62] note that health-related disparities are likely to increase in the future, due in part to a growing reliance on Internet-based technologies to disseminate health information and services. Several studies document the language, cultural, and socioeconomic barriers that prevent ethnic and racial minorities from gaining access to and using health care information and services.[158,159,160,161,162,163,164]

---

[155] Borry P, Howard HC, Sénécal K, Avard D. (2009). Direct-to-consumer genome scanning services. Also for children? *Nature Review Genetics* 10(1):8.

[156] Singh I, Rose N. (2009). Biomarkers in psychiatry. *Nature* 460:202-207.

[157] Chung, WK. (2007). Implementation of genetics to personalize medicine. *Genetics in Medicine* 4(3):248-265.

[158] Ngo-Metzger Q, Massagli MP, Clarridge BR, Manocchia M, Davis RB, Iezzoni LI, Phillips RS. (2003). Linguistic and cultural barriers to care. *Journal of General Internal Medicine*18(1):44-52.

[159] Kelly PA, Haidet P. (2007). Physician overestimation of patient literacy: a potential source of health care disparities. *Patient Education and Counseling* 66(1):119-122.

[160] Safeer RS, Cooke CE, Keenan J.(2006). The impact of health literacy on cardiovascular disease. *Vascular Health and Risk Management* 2(4):457-464.

[161] Sanders TV, Cavazos-Rehg P, Jupka K, Caito N, Gratzke J, Tate K, Deshpande A, Kreuter M. (2008). Evidential preferences: cultural appropriateness strategies in health communications. *Health Education Research* 23(3):549-559.

[162] Torke AM, Corbie-Smith GM, Branch WT Jr. (2004). African American patients' perspectives on medical decision making. *Archives of Internal Medicine* 164(5):525-530.

It is unknown whether DTC genetic testing will be an exception to these findings, but the problems identified in these publications may be exacerbated by the interpretation of test results in minority populations. For example, variants of unknown significance in BRCA2 are reported more commonly in minority populations, in part because of inadequate knowledge of the spectrum of normal variation in nonwhite populations.[157] Typically, genetic association studies have not been validated in populations of non-European ancestry. Genetic variants associated with disease may not be the same across different populations, and allele frequencies or linkage disequilibrium patterns also may differ.[165] For minorities to gain health benefits from genetic and genomic tests, data for disease-associated variants must be available for specific subpopulations.

---

[163] Ray-Mazumder S. (2001). Role of gender, insurance status and culture in attitudes and health behaviors in a US Chinese student population. *Ethnicity and Health* 6(3-4):197-209.

[164] Nguyen GT, Bowman MA. (2007). Culture, language, and health literacy: communicating about health with Asians and Pacific Islanders. *Family Medicine* 39(3):208-210.

[165] Ng PC, Murray SS, Levy S, Venter JC. (2009). An agenda for personalized medicine. *Nature* 461:724-726.

Recommendations and Action Steps

Ten recommendations from prior SACGHS reports address several of the concerns outlined in this report (see Appendix A). Although most of these recommendations speak to genetic testing or laboratory testing in general, they are also applicable to DTC genetic testing.

Based on these 10 prior recommendations, SACGHS proposes 5 specific actions that the HHS Secretary can take to address gaps and inconsistencies in Federal regulations and to accelerate the coordination of programs that facilitate comprehensive and consistent consumer and health provider genetics education.

Oversight Gaps, Analytical Validity, Standardization, Clinical Validity, Clinical Utility, and Promotional Materials

In its 2008 report on the oversight of genetic testing, SACGHS identified several gaps in the regulation of genetic tests—including DTC genetic tests—and of laboratories offering these tests. In brief, the Committee made the following recommendations to address these gaps (see Appendix A, recommendations 1-5, for the complete text of each recommendation):

- SACGHS is concerned about certain types of health-related tests that are marketed directly to consumers and that fall outside the scope of the Clinical Laboratory Improvement Amendments (CLIA). SACGHS recommended that CLIA regulations and, if necessary, CLIA's statutory authority, along with the Food and Drug Administration's (FDA) risk-based regulatory authority and processes, should be expanded to encompass the full range of health-related tests, including those offered directly to consumers.

- SACGHS also identified gaps in the enforcement of existing regulations. For example, the CLIA program has an array of enforcement actions available, but those actions cannot be directly imposed on uncertified laboratories. Instead, the Centers for Medicare & Medicaid Services (CMS) must report the laboratory to HHS Office of Inspector General for action. To prevent laboratories from performing tests without appropriate CLIA certification, CMS should establish and exercise its regulatory authority to take direct enforcement actions against laboratories that perform tests for clinical purposes without proper CLIA certification.

- Currently, there are gaps in the extent to which analytical validity data and clinical validity data can be generated and evaluated for genetic tests. HHS should ensure funding for (1) the development and characterization of reference materials, methods, and samples for assay, analyte, and platform validation; for quality control and performance assessment; and for standardization; (2) the sharing of information regarding method validation, quality control, and performance issues; (3) the creation of public reference databases to enable more effective and efficient collection of mutation and polymorphism data; and (4) the establishment of standards and guidelines for applying genetic tests in clinical practice.

- The Committee is concerned about the gap in oversight related to the clinical validity of laboratory-developed tests (LDTs) and recommended that FDA address all LDTs in a manner that takes advantage of its current experience in evaluating LDTs.

- SACGHS found a paucity of information on the clinical utility of genetic testing. More fundamentally, there has been insufficient analysis of the standard of evidence on which the clinical utility of genetic tests should be evaluated. To fulfill these needs, SACGHS recommended that HHS create and fund a sustainable public/private entity of stakeholders to assess the clinical utility of genetic tests (e.g., building on the Centers for Disease Control and Prevention's Evaluation of Genomic Applications in Practice and Prevention initiative).

Action step to address DTC genetic testing based on these recommendations:

> *The HHS Secretary should direct the FDA Commissioner and the CMS Administrator—with input from other Federal agencies and relevant stakeholder groups—to develop necessary guidance and/or regulations that close gaps in the oversight of genetic tests marketed directly to consumers.*

Transparency

The SACGHS oversight report also noted that there are considerable information gaps about the number and identity of laboratories performing genetic tests and the specific genetic tests being performed. To enhance the transparency in this field, the Committee decided that a mandatory, publicly available, Web-based registry would offer the best approach to address these information gaps and recommended that HHS appoint and fund a lead agency to develop and maintain the mandatory registry for laboratory tests. The lead agency should work collaboratively with its sister agencies to create a comprehensive registry and minimize duplicative collection of registry information.[166] (See Appendix A, recommendation 6, for full text.)

Action step to address DTC genetic testing based on this recommendation:

> *Any Federal laboratory test registry established to address information gaps about available tests and their analytical and clinical validity should include DTC genetic tests and services.*

Claims

[166] On March 18, 2010—subsequent to SACGHS's approval of this report—the National Institutes of Health announced its plan to develop a voluntary genetic testing registry. The announcement is available at http://www.nih.gov/news/health/mar2010/od-18.htm (accessed March 24, 2010).

A recommendation from the SACGHS report on the oversight of genetic testing—specific to DTC tests—addresses the Committee's concern about marketing claims. This recommendation calls for Federal agencies such as the Federal Trade Commission (FTC) and FDA to strengthen their monitoring and enforcement efforts against laboratories and companies that make false and misleading claims about laboratory tests, including DTC tests. (See Appendix A, recommendation 7, for full text.)

Action step to address DTC genetic testing based on this recommendation:

> *As soon as possible, the HHS Secretary should establish a joint HHS-Federal Trade Commission (FTC) task force, which will be convened as needed, to provide the necessary expertise to develop guidelines for FTC to use as a basis to evaluate claims made by companies providing DTC genetic services.*

Privacy

Another recommendation from the SACGHS oversight report that is specific to DTC genetic tests addresses privacy issues and is directly applicable to the concerns outlined in this report. SACGHS recommended that relevant Federal agencies, including the HHS Office for Civil Rights, along with other State agencies and consumer groups, should propose strategies to protect consumers from potential harm and from unanticipated and unwanted compromises in privacy that may lead to harm. (See Appendix A, recommendation 2, for full text.)

Action step to address DTC genetic testing based on this recommendation:

> *The HHS Secretary should direct the HHS Office for Civil Rights (OCR), in conjunction with the HHS Office for Human Research Protections and other relevant HHS agencies, to identify specific gaps in State and Federal research protections and privacy protections for personal health information that may be generated through DTC genetic testing and, as needed, develop specific strategies the Federal Government can undertake consistent with its existing authority to address these gaps. OCR should also inform consumers of potential risks to privacy.*

Genetics Education

Three prior SACGHS recommendations from its reports on the oversight of genetic testing and coverage and reimbursement of genetic tests and services apply to concerns about consumers' and providers' understanding of DTC test results. In brief, these recommendations noted the following education needs (see Appendix A, recommendations 8-10, for full text):

- There are documented deficiencies in genetic knowledge in all relevant stakeholder groups. SACGHS recommended that HHS should work with all relevant government agencies and interested private parties to identify and address deficiencies in knowledge about appropriate genetic and genomic test applications in practice and to educate key groups such as health

care practitioners, public health workers, public and private payers, and consumers of health care. Sufficient resources should be provided to translate research knowledge regarding analytical validity, clinical validity, and clinical utility into evidence-based clinical practice guidelines that enhance the quality of clinical health care and public health care outcomes.

- Because providers have an important role in ensuring the appropriate use of and access to genetic tests and services among diverse populations, there is a critical need for programs to educate and train health care providers and payers in genetics and genomics. The HHS Secretary should (1) develop a plan for HHS agencies to work collaboratively with Federal, State, and private organizations to develop, catalog, and disseminate case studies and practice models that demonstrate the relevance of genetics and genomics; (2) provide financial support to assess the impact of genetics education and training on health outcomes; and (3) strive to incorporate genetics and genomics into relevant HHS initiatives.

- Public awareness of new health care tests and treatments can create consumer demand. For patients and consumers to ably evaluate health plan benefits and health care providers and make the most appropriate decisions for themselves and their families, they need reliable and trustworthy information about family history, genetics, and genetic technologies. The HHS Secretary should ensure that educational resources are widely available through Federal Government Web sites and other appropriate public information mechanisms to inform decisions about genetic tests and services.

Action step to address DTC genetic testing based on these recommendations:

> *The HHS Secretary should direct the Office of the Assistant Secretary for Planning and Evaluation (ASPE) to develop an initiative that focuses on genetics education for consumers and health practitioners, including information specific to DTC genetic testing, and that recognizes existing HHS educational resources. ASPE also should follow up its March 2009 report* Consumer Use of Computerized Applications to Address Health and Health Care Needs *by supporting research recommended in this report (e.g., studies to identify who uses health information technology (HIT), who does not, and obstacles to its use) and identify policies that would lower barriers to the use of HIT.*

Conclusions

DTC genetic testing companies face few regulatory barriers to marketing their services.[8] CMS enforces regulatory requirements for analytical validity under CLIA, but it does not have the authority to enforce requirements for clinical validity. In addition, some companies that offer DTC genetic tests are not required to be CLIA-certified because their services do not fit the CLIA definition of "laboratory." Furthermore, FDA generally exercises enforcement discretion for most LDTs, including DTC genetic tests developed as LDTs. Thus, there is no requirement for evidence of clinical validity before these tests are made available to consumers,[25] no requirement for public information on test performance, and no FDA enforcement of regulations for promotional materials, which requires disclosure of information about a test's limitations or risks.[8] Also, DTC genetic testing companies are not subject to HIPAA or the Common Rule, which provide privacy and research protections. Therefore, as an increasing range of DTC genetic tests are offered to consumers, policies that ensure DTC test quality and safety lag behind.

In addition to oversight gaps, deficiencies in consumers' and providers' knowledge of genetics cause concern. Genetic information, particularly from tests with low or uncertain clinical validity, which is provided directly to consumers with inadequate or ambiguous interpretation, may be applied inappropriately as consumers make decisions regarding the management of their health.[28,36] Consumers who ask their personal health care provider for help in understanding their test results may find their provider lacks the knowledge and skill to interpret genetic information.[38,39,40,41,42,44,125]

To minimize the harms and maximize the benefits of DTC genetic testing, consumers need complete, accurate, and balanced information describing the benefits, risks, and limitations of testing, along with appropriate oversight regulations that are effective and enforced. Previous recommendations by SACGHS, if implemented, would address issues related to oversight; the analytical validity, clinical validity, and clinical utility of DTC tests; standardization; promotional materials; marketing claims; privacy; and the educational needs of consumers and health professionals. Some concerns, however, would benefit from additional evaluation by SACGHS and/or other appropriate Federal agencies. These concerns include nonconsensual testing, the impact of DTC genetic testing in children, limited data on the psychosocial impact of DTC genetic testing, inadequate protections for the research use of specimens and data derived from specimens obtained through DTC genetic testing, the impact of DTC testing on the health care system, and the potential exacerbation of health disparities

APPENDIX A

Prior SACGHS Recommendations Relevant to Direct-to-Consumer Genetic Testing

The following recommendations from prior SACGHS reports address some of the concerns related to direct-to-consumer genetic testing.

Oversight Gaps and Privacy

From the SACGHS report on the oversight of genetic testing:[6]

1. SACGHS is concerned about certain types of health-related tests that are marketed directly to consumers and apparently fall outside the scope of CLIA. Some nutrigenomic tests (e.g., a test for caffeine metabolism) and tests that determine the gender of a fetus are examples of health-related tests that skirt the boundaries of CLIA's authority. There is insufficient oversight of laboratories offering such tests, and their potential impact on the public health is an increasing concern. Direct-to-consumer marketing of laboratory tests and consumer-initiated testing has the potential for adverse patient outcomes, social stigmatization, privacy concerns, and cost implications for the health care system. SACGHS recommends that:

   > CLIA regulations and, if necessary, CLIA's statutory authority, along with FDA's risk-based regulatory authority and regulatory processes, should be expanded to encompass the full range of health-related tests, including those offered directly to consumers. Relevant Federal agencies (e.g., CMS, CDC, FDA, and FTC) should collaborate to develop an appropriate definition of health-related tests that FDA and CMS could use as a basis for expanding their scope. Additionally, these Federal agencies, including the HHS Office for Civil Rights, along with other State agencies and consumer groups should propose strategies to protect consumers from potential harm and from unanticipated and unwanted compromises in privacy that may lead to harm. Additional oversight strategies that might be established should be balanced against the benefits that consumers may gain from wider access to genetic tests and potential cost savings.

2. Factfinding by SACGHS also identified gaps in the enforcement of existing regulations. For example, the CLIA program has an array of enforcement actions available, but those actions cannot be directly imposed on uncertified laboratories. Instead, CMS must report the laboratory to the HHS Inspector General for action. Neither Medicare nor Medicaid can reimburse laboratories without CLIA certificates, but this restriction has no consequence for laboratories that perform direct-to-consumer (DTC) testing. To address enforcement gaps, SACGHS recommends the following actions:

   > To prevent laboratories from performing tests without appropriate CLIA certification, CMS should establish and exercise its regulatory authority to take direct enforcement actions against laboratories that perform tests for clinical purposes without proper

CLIA certification. CMS should step up its efforts to make publicly available a list of laboratories that have been cited by CLIA for condition-level deficiencies.

Analytical Validity

From the SACGHS report on the oversight of genetic testing:

3. Currently, there are gaps in the extent to which analytical validity and clinical validity data can be generated and evaluated for genetic tests. To address these gaps, SACGHS recommends devoting public resources for genetic testing through the following actions:

    A. In consultation with relevant agencies, HHS should ensure funding for the development and characterization of reference materials, methods, and samples (e.g., positive and negative controls and samples from different ethnic/geographic populations) for assay, analyte, and platform validation; for quality control and performance assessment; and for standardization.

    B. HHS should ensure funding for the development of a mechanism to establish and support a laboratory-oriented consortium to provide a forum for sharing information regarding method validation, quality control, and performance issues.

    C. HHS agencies, including NIH and CDC, should continue to work with public and private partners to support, develop, and enhance public reference databases to enable more effective and efficient collection of mutation and polymorphism data, expand clinical reference sequence databases, and provide summary data on gene-disease associations to inform clinical validity assessments (e.g., RefSeqGene, HuGENet). Such initiatives should be structured to encourage robust participation; for example, there is a need to consider mechanisms for anonymous reporting and/or protections from liability to encourage information sharing among members.

    D. HHS should provide the necessary support for professional organizations to develop and disseminate additional standards and guidelines for applying genetic tests in clinical practice. CMS should work with professional organizations to develop interpretative guidelines to enhance inspector training and laboratory compliance.

Clinical Validity

From the SACGHS report on the oversight of genetic testing:

4. The Committee is concerned by the gap in oversight related to clinical validity and believes that it is imperative to close this gap as expeditiously as possible. To this end, the Committee makes the following recommendations:

A. FDA should address all laboratory tests in a manner that takes advantage of its current experience in evaluating laboratory tests.

B. This step by FDA will require the commitment of significance resources to optimize the time and cost of review without compromising the quality of assessment.

C. The Committee recommends that HHS convene a multistakeholder public and private sector group to determine the criteria for risk stratification and a process for systematically applying these criteria. This group should consider new and existing regulatory models and data sources (e.g., New York State Department of Health Clinical Laboratory Evaluation Program). The multistakeholder group should also explicitly address and eliminate duplicative oversight procedures.

D. To expedite and facilitate the review process, the Committee recommends the establishment of a mandatory test registry.

Clinical Utility

From the SACGHS report on the oversight of genetic testing:

5. Information on clinical utility is critical for managing patients, developing professional guidelines, and making coverage decisions. SACGHS found a paucity of information on the clinical utility of genetic testing. There are inadequate data on which to base utility assessments, and only a few studies have been done of the clinical utility of specific genetic tests. More fundamentally, there has been insufficient analysis of the standard of evidence on which the clinical utility of genetic tests should be evaluated and on which evidence-based methods applicable to genetic testing should be developed. Further policy analysis is also needed to define the process by which clinical utility assessments will be applied. To fill these needs SACGHS recommends the following:

   A. HHS should create and fund a sustainable public/private entity of stakeholders to assess the clinical utility of genetic tests (e.g., building on CDC's Evaluation of Genomic Applications in Practice and Prevention (EGAPP) initiative). This entity would:
      - Identify major evidentiary needs
      - Establish evidentiary standards and level of certainty required for different situations such as coverage, reimbursement, quality improvement, and clinical management
      - Establish priorities for research and development
      - Augment existing methods for assessing clinical utility as well as analytical and clinical validity, such as those used by EGAPP and the U.S. Preventive Services Task Force, with relevant modeling tools
      - Identify sources of data and mechanisms for making them usable for research, including the use of data from electronic medical records
      - Recommend additional studies to assess clinical effectiveness

- Achieve consensus on minimal evidence criteria to facilitate the conduct of focused, quick-turnaround systematic reviews
- Increase the number of systematic evidence reviews and make recommendations based on their results
- Facilitate the development and dissemination of evidence-based clinical practice guidelines and clinical decision support tools for genetic/genomic tests
- Establish priorities for implementation in routine clinical practice
- Publish the results of these assessments or otherwise make them available to the public via a designated HHS or other publicly supported Web site (e.g., GeneTests)

B. To fill gaps in the knowledge of the analytical validity, clinical validity, clinical utility, utilization, economic value, and population health impact of genetic tests, a Federal or public/private initiative should:
   - Develop and fund a research agenda to fill those gaps, including the initial development and thorough evaluation of genetic tests and the development of evidence-based clinical practice guidelines for the use of those tests
   - Disseminate these findings to the public via a designated HHS or other publicly supported Web site (e.g., GeneTests)

Laboratory Test Registry

From the SACGHS report on the oversight of genetic testing:

6. There are considerable information gaps about the number and identity of laboratories performing genetic tests and the specific genetic tests being performed. To gain a better understanding of the genetic tests being offered as laboratory-developed tests and to enhance the transparency in this field, SACGHS reviewed proposals for a voluntary or mandatory test registry and considered the benefits and burdens of each type of system. The Committee decided that a mandatory, publicly available, Web-based registry that is well staffed to maintain an accurate and current database would offer the best approach to addressing these information gaps in the availability of tests and their analytical and clinical validity. Since genetic tests are not different from other laboratory tests for oversight purposes, the registry should include all laboratory tests. The Committee also discussed whether such a database should reside at CDC, CMS, or FDA, but recognized that unresolved issues, including practical and legal questions, require further analysis before a final decision can be made about how and where to implement the registry. In concluding that a mandatory registry should be established, SACGHS recommends the following course of action:

   A. HHS should appoint and fund a lead agency to develop and maintain the mandatory registry for laboratory tests. The lead agency should work collaboratively with its sister agencies to create a comprehensive registry and minimize duplicative collection of registry information. For this purpose, the lead agency should be staffed with qualified

personnel who are experienced in developing and updating large databases in a timely and accurate manner.

B. The lead agency, in collaboration with its sister agencies, should convene a stakeholders meeting by September 2008 to determine the data elements associated with analytical validity, clinical validity, clinical utility, and accessibility that should be included in the test registry. The lead agency should cast a wide net for broad stakeholder representation, including individuals from the private sector who can represent a role for public-private partnerships in developing a registry. The lead agency, through this stakeholder effort, should assess the level of effort, as well as the burden on the laboratory and the impact on other key stakeholders such as patients, physicians, and payers, necessary to obtain each data element, including linking to reliable sources of existing information.

C. While awaiting completion of the above processes, HHS should use short-term voluntary approaches such as incentivizing laboratories to register with GeneTests and encouraging laboratories to make their test menus and analytical and clinical validity data for these tests publicly available on laboratory Web sites.

Claims

From the SACGHS report on the oversight of genetic testing:

7. Appropriate Federal agencies, including CDC, CMS, FDA, and FTC, should strengthen monitoring and enforcement efforts against laboratories and companies that make false and misleading claims about laboratory tests, including direct-to-consumer tests.

Education

From the SACGHS report on the oversight of genetic testing:

8. There are documented deficiencies in genetic knowledge in all relevant stakeholder groups. In addition to the creation of the SACGHS education task force, SACGHS recommends the following strategies to address these deficiencies:

   A. HHS should work with all relevant government agencies and interested private parties to identify and address deficiencies in knowledge about appropriate genetic and genomic test applications in practice and to educate key groups such as health care practitioners, public health workers, public and private payers, and consumers of health care. These educational efforts should take into account differences in language, culture, ethnicity, and perspectives on health and disability as well as issues of medical literacy, access to electronic information sources such as the Internet, and deficiencies in public infrastructures (e.g., libraries) that can affect the use and understanding of genetic information.

B. Based on increased research regarding analytical validity, clinical validity, and clinical utility, sufficient resources should be provided to translate this knowledge into evidence-based clinical practice guidelines that enhance the quality of clinical health care and public health care outcomes.

From the SACGHS report on the coverage and reimbursement of genetic tests and services:[167]

9. Genetic tests are being marketed to health care providers and directly to consumers. If providers are not adequately trained in the use and interpretation of genetic tests, they may provide inappropriate services to their patients and expect to be reimbursed for them. Providers need adequate genetics education and training to know when genetic tests are appropriate and to help their patients make decisions about when to be tested. A working knowledge of genetics also is important for health payers because it will help them make informed and appropriate coverage decisions.

   Since genetic tests and services are being integrated into all areas of health care and since providers have an important role in ensuring appropriate use of and access to genetic tests and services among diverse populations, there is a critical need for programs to educate and train health care providers and payers in genetics and genomics. Health care providers should be able to meet established genetic competencies and, thereby, integrate genetics effectively into their practices. The HHS Secretary should develop a plan for HHS agencies to work collaboratively with Federal, State, and private organizations to develop, catalog, and disseminate case studies and practice models that demonstrate the relevance of genetics and genomics.

   The HHS Secretary should provide financial support to assess the impact of genetics education and training on health outcomes.

   The HHS Secretary should strive to incorporate genetics and genomics into relevant initiatives of HHS, including the National Health Information Infrastructure.

10. Public awareness of new health care tests and treatments can create consumer demand. Although greater public awareness and demand can facilitate coverage for new, safe, efficacious, and appropriate genetic tests and services, because of the complexity of genetic tests, they also can result in misinformation and inappropriate demand for genetic tests and services.

    For patients and consumers to evaluate health plan benefits and health care providers and to make the most appropriate decisions for themselves and their families, they need reliable and trustworthy information about family history, genetics, and genetic

[167] Secretary's Advisory Committee on Genetics, Health, and Society. Coverage and Reimbursement of Genetic Tests and Services. February 2006. See http://oba.od.nih.gov/oba/sacghs/reports/CR_report.pdf. Accessed April 15, 2009.

technologies. The HHS Secretary should ensure that educational resources are widely available through Federal Government Web sites and other appropriate public information mechanisms to inform decisions about genetic tests and services.

APPENDIX B

List of Abbreviations and Acronyms

AHRQ	Agency for Healthcare Research and Quality
APOE	apolipoprotein E
APOE ε4 allele	a variant of the APOE gene
ASPE	Office of the Assistant Secretary for Planning and Evaluation
BRCA	breast cancer
BRCA2	breast cancer 2, early-onset gene
BRFSS	2006 Behavioral Risk Factor Surveillance System
CA125	cancer antigen 125
caBIG®	cancer Biomedical Informatics Grid®
CDC	Centers for Disease Control and Prevention
CLIA	Clinical Laboratory Improvement Amendments of 1988
CMS	Centers for Medicare & Medicaid Services
CT	computerized tomography
dbSNP	single-nucleotide polymorphism database
DNA	deoxyribonucleic acid
DocStyles	a CDC survey
DTC	direct-to-consumer
EGAPP	Evaluation of Genomic Applications in Practice and Prevention
FDA	Food and Drug Administration
FTC	Federal Trade Commission
GPPC	Genetics and Public Policy Center
GWAS	genome-wide association study
HealthStyles	a CDC survey
HHS	U.S. Department of Health and Human Services
HITECH Act	Health Information Technology for Economic and Clinical Health Act
HIPAA	Health Insurance Portability and Accountability Act
HIT	health information technology
HRSA	Health Resources and Services Administration
IOM	Institute of Medicine
IRB	institutional review board
LDT	laboratory-developed test

MRI	magnetic resonance imaging
NCBI	National Center for Biotechnology Information
NCI	National Cancer Institute (HHS/NIH)
NIH	National Institutes of Health
OCR	Office for Civil Rights
OHRP	Office for Human Research Protections
PRIM&R	Public Responsibility in Medicine and Research
PSA	prostate-specific antigen
refseq	reference sequence
RNA	ribonucleic acid
rs	refSNP accession identification number
SACGHS	Secretary's Advisory Committee on Genetics, Health, and Society
SB	senate bill
SNP	single-nucleotide polymorphism