

Defining the spectrum of genome policy

Susanne B. Haga and Huntington F. Willard.

Abstract | Many achievements in the genome sciences have been facilitated by policies that have prioritized genome research, secured funding and raised public and health-professional awareness. Such policies should address ethical, legal and social concerns, and are as important to the scientific and commercial development of the field as the science itself. On occasion, policy issues take precedence over science, particularly when impasses are encountered or when public health or money is at stake. Here we discuss the spectrum of current issues and debates in genome policy, and how to actively engage all affected stakeholders to promote effective policy making.

Genomics, the science of whole genomes, differs in approach, breadth and emphasis from genetics, which focuses on the roles and inheritance of individual genes and their variants. Genomics encompasses the development and application of technologies for the comprehensive study of the biology of cells, tissues, whole organisms and even populations. It includes genome sequence analysis, as well as studies of gene expression, protein products and metabolites. The data from such studies have advanced such diverse areas as evolution, developmental biology, drug development and clinical diagnosis. Examples of applications are as diverse as comparative sequence analysis, tumour microarray expression profiling, whole-genome analysis for disease-association studies and hand-held sensors that identify airborne pathogens.

Although policy issues can be categorized in different ways, we consider five main areas of genome policy (BOX 1): research issues; legal issues; economic issues; educational issues; and acceptance and implementation. The natural history of any genome advance or application, from the discovery stage through to translation, production and both professional and public acceptance, can be considered in terms of these broad categories. Many policy issues have arisen in response to genetic advances and applications, but the broader scale of genome sciences expands and potentially exacerbates them, and gives rise to new issues. Although presented here in discrete categories (BOX 1), genome policy is actually a complex network of issues, whereby one issue can influence or be dependent on another.

Various approaches have been taken to address genome policy issues (BOX 2). Although some issues are amenable to a measured and deliberate approach, others require a more rapid response. The approaches that are taken are influenced not only by the issue itself, but by different governments, levels of scientific understanding, cultural attitudes to science and technology and health-care systems. Given the diversity of factors, there is no right or wrong approach to addressing a particular policy issue. However, in reviewing the different approaches that can be taken, two important themes emerge: the involvement of multiple stakeholders and the need for solid scientific and (where applicable) clinical data.

Expert opinion or authority has traditionally served as the backbone for policy decision making. As public opinion is not generally formed on the basis of expert knowledge, their perspectives can be marginalized. The association between the concerns of the public and low scientific literacy is known as the 'knowledge deficit' model^{1,2}. In recent years, however, this model has come under heavy criticism. Studies have revealed conflicting data regarding the relationship between scientific knowledge and attitudes, showing that it is more complex than is frequently appreciated³⁻⁸. An alternative view holds that scientific knowledge is but one facet of public understanding of science. 'Institutional knowledge' (that is, the political processes that are relevant to science policy) and 'social knowledge' (the relevance of scientific applications to local or personal circumstances) also inform public understanding of science⁹.

In some settings, dependence on expert opinion is giving way to a more inclusive policy-making process, reflecting both a growing distrust of government and industry and a greater awareness of the broad social and ethical implications of genetics and genomics¹⁰. It has even been suggested that it is the experts who have a knowledge deficit in understanding the views of the lay public¹¹. Whereas past efforts focused on enhancing public science literacy, current efforts have moved towards increased public consultation and engagement¹². Indeed, an inverse relationship between science literacy and trust was documented during the human cloning debate¹³.

In this Perspective, from our complementary viewpoints of scientific and policy research, we provide an overview of some of the issues that exist within each category of genome policy (BOX 1), describe various approaches that are used to address these issues, and highlight the importance of the engagement of stakeholders in policy-making decisions.

Research policy issues

Over the past 20 years, several organizations have been established to advance genome research, including **Genome Canada**, the US **National Human Genome Research Institute** (NHGRI), **Genoma España**, **Instituto Nacional de Medicina Genómica** (Mexico), the **Riken Genomic Sciences Center** (Japan) and the **Sanger Institute** (United Kingdom). Their accomplishments have been facilitated by policies that are related to the planning and conduct of genome research. Research policy issues include prioritization of research, allocation of funds and access to research data.

Research prioritization and allocation.

Research prioritization and allocation are crucial to the development of a balanced research portfolio, whether private or public. Priorities are often decided by the scientific elite, in their positions as members of national advisory councils of scientific funding agencies. In the United States, every research institute within the **National Institutes of Health** (NIH) has its own advisory council, and at least one seat on each is reserved for a member of the public. Each council can solicit feedback from the general scientific community if desired; the current NHGRI vision for genomics research, for example, was informed by extramural as well as intramural scientists, administrators and advisors¹⁴.

Box 1 | Policy issues in the genome sciences

Research issues

- Prioritization of research areas (basic, applied and technology development)
- Allocation of funds
- Provision of the necessary facilities
- Access to tools and research samples

Legal issues

- Protection of human subjects
- Regulatory oversight (product and manufacturing review, labelling, laboratory quality and environmental impact)
- Intellectual property and licensing practices
- Genetic discrimination
- Trade agreements
- Privacy and confidentiality

Economic issues

- Cost-effectiveness
- Reimbursement of health-care providers by insurers and governments
- Market value and pricing
- Supply and demand
- Commercialization of public-sector initiatives

Education issues

- Education of health professionals
- Development of clinical guidelines
- Classroom education
- Public education
- Risk communication

Acceptance and implementation issues

- Public adoption of genomic technology
- Behaviour modification in response to genomic results
- Cultural respect

Collaboration between patient organizations and researchers has led to patient representatives being named as co-inventors on patent applications³¹. These potentially overlooked stakeholders have collaborated not only in the collection and provision of often difficult-to-collect samples (as described above in the case of CFC and PXE), but also in data collection and analysis. The recognition of these contributions has resulted in the redistribution of financial benefits, and has potentially strengthened the partnership between investigator and patient groups. In any future changes to the patent system it is crucial to consider the views of and effects on such groups, as well as government, industry, professional organizations, academia and the public³².

Budget allocation is a high-stakes affair that involves government agencies, legislative bodies, lobbyists, special interest groups, professional organizations and industry. As the genome sciences become a large component of other areas in life sciences and biomedical research, it will be important to avoid a duplication of efforts through resource sharing and coordination of research priorities by multiple agencies or councils. In the United Kingdom, for example, the importance of continued genome research following the completion of the Human Genome Project was recognized by several research councils as a top priority.

Public dialogue about research prioritization will inevitably reveal a range of stakeholder perspectives. Dissatisfaction with current funding policies and/or personal interest in a specific disease or research area has led to an increase in the number of private foundations as an alternative source of funding. For example, advocates for breast cancer research have educated themselves not only about science, but also about the policy-making process, and have been extremely vocal and persuasive in increasing support for breast cancer research.

Access to research data and materials. One of the most notable aspects of research in the genome sciences is the sheer size and complexity of the data sets that are produced. Genomic data are collected and stored in a digital format, which enables rapid data sharing and the development of public databases. One of the significant policy decisions of the early genome era was to provide open access to basic research data^{15,16}, which promises to lessen what would otherwise be substantial differences in research capacities between different laboratories, in both developed and developing nations. The successful implementation of open-access policies was contingent on active participation by data producers, users and funding agencies. In recent years, however, the threat of bioterrorism has raised concerns regarding the potential 'dual use' of genomic data¹⁷. Although open access to basic genomic information has accelerated research, widespread debate has ensued about data sharing of genome sequences and other data related to pathogens. As a result, advisory committees such as the US **National Science Advisory Board for Biosecurity** were formed.

In contrast to data-access policies, which are typically decided by small groups of experts and policy makers, sample-access policies have been increasingly influenced by patient groups and advocacy organizations.

For example, the identification of the genes that cause cardiofaciocutaneous (CFC) syndrome and pseudoxanthoma elasticum (PXE) was made using samples collected by CFC International and PXE International, respectively REFS 18,19. Without these organizations, researchers would probably not have been able to collect sufficient patient samples, nor would they have had the workforce to achieve their study goals in a reasonable time frame.

Legal issues

As new genome technologies are developed, several legal issues have emerged, including regulatory oversight of applications such as microarray-based diagnostics, intellectual property, genetic discrimination, privacy and protection of research subjects. In particular, intellectual property and genetic discrimination have dominated the legal landscape in genomics. Many legal issues are addressed through new or revised government regulations, legislation and court rulings.

Intellectual property. The early patenting successes of recombinant DNA technology, followed by favourable court rulings and legislation encouraging the patenting of government-supported research innovations, led to a biotechnology industry that is dependent, in part, on a strong intellectual property portfolio²⁰. However, over the past decade, intellectual property laws and licensing practices of genes and genetic material have been controversial^{21–25}. Concerns have been raised about the under-utilization of patented resources due to limited access and benefit sharing ("...fair and equitable sharing of the benefits arising out of the utilization of genetic resources"²⁶), and the effects on research, innovation and clinical services^{27,28}. Furthermore, new challenges are posed by discoveries that involve the analysis of large numbers of genes or even entire genomes (BOX 3).

Various mechanisms have been used to address intellectual property issues, including revisions to regulations, case law and development of guidance documents. For example, in response to public concerns about the overly broad nature of patenting and the lack of demonstrated utility of many genetic patents, the US examination guidelines have been revised to require that a technology has a more specific use in order to be patentable²⁹. In Europe, a decade-long debate led to the adoption of an **EU Biotechnology Directive**, which was then incorporated into the patenting criteria of the European Patent Office³⁰.

Box 2 | Approaches to addressing genome policy issues

Legislative approach

Genetic discrimination: more than 20 bills have been introduced in the United States to prohibit genetic discrimination by health insurers and/or employers.

Regulatory approach

Genetic testing: the proposal to revise the US **Clinical Laboratory Improvement Amendments** regulations to add the quality of genetic testing as a specialty.

Guidelines approach

Gene patenting: revisions to the utility criteria of the US patent examination guidelines.

Licensing: the US National Institutes of Health have published best practices for the licensing of genomic inventions⁷⁴.

Voluntary approach

Genetic discrimination: the Association of British Insurers **Concordat and Moratorium on Genetics and Insurance**.

Genetic testing: the establishment of **EuroGenTest** Network to ensure quality of tests.

Public Consultation approach

Genetic discrimination: an 18-month public consultation carried out by the Australian Law Reform Commission⁷⁵⁻⁷⁷.

GM foods: the **GM Nation**⁵² public dialogue in the United Kingdom.

Genetic discrimination. The use of genetic information in decisions regarding health insurance, life insurance and employment has been a global concern of patients, families, health professionals and research participants alike. In 1997, the United Nations Educational, Scientific and Cultural Organisation (UNESCO) declared that "...no one shall be subjected to discrimination based on genetic information..."³³, a policy that was reiterated in its 2003 report on human genetic data³⁴. Despite such universal statements, implementing protections against discrimination has been a challenge for many countries. Several approaches, including legislation, moratoria and public consultation, have been used to define the extent of and protect against genetic discrimination³⁵.

In the United States, at least 20 bills on genetic discrimination have been introduced in Congress since 1995. However, only the **Health Insurance Portability and Accountability Act** has passed, providing protection against genetic discrimination for group health plans. More than 30 US states have enacted legislation providing a patchwork of protections against the use of genetic information by health insurers and/or employers. In the United Kingdom, a moratorium on using genetic testing information for insurance underwriting is in effect until 2011 (REF. 36). In 1999, the **Genetics and Insurance Committee** was formed to review the use of genetic tests for insurance underwriting purposes. Of the 17 applications that were submitted by the Association of British Insurers, only one has been approved — the test for **Huntington disease** for life insurance

policies over UK£500,000 (REF. 37). Some have recently called for legislation against genetic discrimination in employment in the United Kingdom, citing evidence of this in the United States and Australia³⁸.

The highly publicized first case of alleged genetic discrimination was filed by the US Equal Employment Opportunity Commission (EEOC) against the US railway company Burlington Northern Santa Fe (BNSF). EEOC alleged that the company

tested a group of employees who had filed for worker's compensation for a rare genetic condition without their consent, a violation of the Americans with Disabilities Act. The company reached a US\$2.2 million settlement with the EEOC³⁹.

Despite the well-documented fears of genetic discrimination^{40,41} and the BNSF case, testimony before United States legislators by members of the public and scientific communities has not resulted in protections. Opponents of such protections cite the lack of available empirical data about the practice of genetic discrimination^{42,43}, or about its effect on research⁴⁴, clinical practice⁴⁵ or insurance-purchasing behaviour^{46,47} and the threat of increased litigation. The continuing debate was possibly prolonged by an initial 'deficit' in knowledge of stakeholder perspectives and a perceived lack of urgency, highlighting the importance of gathering stakeholder opinions at an early stage.

Oversight. As the number of gene-targeted drugs and diagnostic applications rises, regulatory agencies face the task of assessing their safety and efficacy. Achieving a balance between ensuring safety and effectiveness and allowing innovation is a challenging goal. Therefore, it is important that all parties are involved in the policy-making process — the developers of targeted drugs and diagnostic tests, reference laboratories,

Box 3 | Genome patenting and licensing

The patent system provides a valuable incentive to share new innovations and promote research and development. However, it can also create impediments to research and increase the costs that are associated with commercial development and marketing. Recently, attention has expanded beyond the scope of patent claims to licensing practices. In particular, the practice of exclusive licensing has been of substantial concern as it affects research, education, quality assessment, pricing and access.

Although there are several examples of patenting debates from genetics (for example, **BRCA1** and **BRCA2**), patents resulting from genomic advances cover more genes and genetic sequences, and can extend to whole genomes. At least 10 patents for whole genomes of prokaryotic organisms have been granted by the US Patent and Trademark Office⁷⁸. Patent applications have also been filed for the genome of the coronavirus that is associated with severe acute respiratory syndrome (SARS).

The assignees of the 11 genomes with pending or granted patent approval include two universities, six non-profit research institutes, one technology transfer company on behalf of a university, seven private companies and three public research organizations. At least two of the patent applicants of the SARS genome indicated that their actions were intended to secure public access to downstream products such as vaccines⁷⁹. Although some for-profit groups might seek and license patents to bolster revenue and market value, other companies might opt to support academic research in hopes of preventing the patenting of potentially valuable information by competitors⁸⁰.

The need to secure licences from multiple patent holders for a single application can lead to royalty stacking and patent thickets. As little regulation exists, some groups have taken steps to encourage fair licensing practices⁷⁴. The creation of patent pools (an agreement between patent owners to cross-license their patents for applications with shared properties) has also been proposed as a solution^{81,82}.

The evidence of the effects of genetic patents and licensing practices is conflicting^{28,83}. Any new regulation must have a basis in solid evidence that the problems of the current system are outweighing the benefits, resulting in public harms. Patients, industry, government and academia all have a stake in the outcome of this debate.

government regulatory officials and professional and consumer organizations.

Pharmacogenetic testing is considered one of the most promising clinical applications of genomics research. Tests have the potential to reduce adverse drug responses and the associated costs, and to improve outcomes over a shorter treatment period, by identifying the most appropriate drug and dose. Although, as with any medical innovation, the introduction of pharmacogenetic testing into clinical practice requires evidence of a favourable ratio of benefits and risks. In 2005, on the basis of two public stakeholder meetings, the US Food and Drug Administration (FDA) released a guidance policy on the voluntary submission of pharmacogenomic data⁴⁸. More recently, the recognition of the need for harmonization in this new field has led to guidelines on the joint processing of voluntary data submissions to the FDA and the European Medicines Agency^{49,50}.

Economic policy issues

Economics is an influential driver of any new field, and economic and trade policy affects public demand, pricing and reimbursement for genomic technology. For example, the successful translation of advances into clinical practice will depend, in part, on the coverage and reimbursement policies of health insurers and health plans (BOX 4). Economic policies can affect or be affected by other policy arenas, such as research prioritization, intellectual property and acceptance. For example, much of the growth of the biotechnology and genomics industries has depended on a strong intellectual property portfolio to establish market value, particularly in the absence of revenue-generating products.

An important economic issue is trade policies for genetically modified (GM) products. The GM debate has been dominated by highly publicized fears about the unknown risks that are associated with these crops and related products⁵¹, and scientists and other supporters have not been equally vocal about the potential benefits. The public concern regarding the safety of these products for health and the environment has affected national and international policies. However, the World Trade Organization recently upheld a ruling that the European Union moratorium between 1998 and 2004 violated international trade rules. Changes in EU trade policy on labelling and traceability of GM foods and the recent approval of GM corn represent strong steps towards the creation of new markets.

In 2003, a national dialogue was launched in the United Kingdom by an independent steering board to ascertain public views about GM issues⁵². Despite criticisms that the consultation was limited by funds and time, and that the survey methodologies were flawed, the fact that 37,000 people participated is significant. The report concluded that the overwhelming majority of Britons opposed GM food products and the growing of GM crops. Despite this near consensus against GM crops, the government granted approval of GM maize the following year, raising questions about the legitimacy of the public-consultation process.

Educational policy issues

The successful introduction of genomic applications will greatly depend on the ability of the public to comprehend the purposes, benefits and risks of these products, particularly in health, but also in agriculture, nutrition and other fields. Approaches to enhancing knowledge of genetics and genomics include courses at all levels — secondary school, undergraduate and postgraduate degrees, professional courses (for example, in medical schools and licensing examinations), within university faculties, informal public education campaigns, and through continuing education⁵³. In many areas, changes to

public school curricula and content require approval by a school board that consists of elected officials, the significance of which is underscored by the ongoing debates in the United States concerning the teaching of evolutionary theory⁵⁴. In 2003, the NHGRI created the **Education and Community Involvement Branch** to help inform the public about genomics research and provide educational resources to teachers, students and consumers. Furthermore, many centre-based grants are required to devote a portion of the budget for training and educational activities.

The importance of education in genetics gained attention in the United Kingdom in a 2003 White Paper⁵⁵. The report proposed a £50 million 3-year plan to improve education of health professionals in genetics. New uses for genetic and genomic tools, particularly in medicine⁵⁶, will warrant even broader education initiatives to avoid potential harms such as the misinterpretation of genetic test results⁵⁷. One of the more prominent recommendations to be implemented was the creation of the **National Genetics Education and Development Centre** to provide a central training resource in the National Health Service.

Despite the increased recognition of the importance of genetics and genomics education, the proportion of public funds

Box 4 | Demonstrating the cost-effectiveness of genomic medicine

Genomic medicine is one of the most eagerly anticipated consequences of the sequencing of the human genome. In contrast to medical genetics — which has a basis in the study of inherited characteristics, most often single genes — genomic medicine is comprehensive, and includes the interactions of multiple genes and environmental factors as they relate to disease status, prognosis and treatment response. However, irrespective of the health-care system, demonstration of the clinical use of genomic testing is crucial to its uptake.

Several genomic profiles have recently been developed, enabling more precise disease diagnosis or prediction of treatment mode and/or response. For example, the **Oncotype DX** assay (Genomic Health), a 21-gene expression test, estimates the likelihood of breast cancer recurrence and the benefit from certain chemotherapy regimens. An economic analysis has shown the test to be superior to current clinical practice, and appropriate use could result in increased survival and cost savings⁸⁴. Another genome profile is the **AlloMap Test** (XDx Expression Diagnostics), which is used to predict cardiac allograft rejection⁸⁵. By providing a non-invasive method to ascertain the risk of rejection, which was previously monitored through the expensive procedure of endomyocardial biopsy, this test has been shown to be cost-effective⁸⁶.

Demonstration of the clinical utility of new genomic tests will be an important component of cost-effectiveness studies, technology assessment reports and professional clinical guidelines in determining coverage and reimbursement decisions⁸⁷. In January 2006, a reimbursement coverage policy decision by a Medicare contractor was established for **Oncotype DX**⁸⁸. The test was deemed "...safe and effective and reasonable and necessary to contribute to breast cancer diagnosis and major treatment decisions." By contrast, a technology assessment by a major private insurer concluded that "insufficient evidence" was available to determine whether the test improved outcomes⁸⁹.

Other challenges that affect the economic influence of genome technologies include lack of oversight, limited uptake due to fears of genetic discrimination, determination of medical necessity and who should be tested, and the absence of immediate benefit. The high costs of some tests that might benefit only a small group will create a difficult dilemma for health-care and insurance administrators, given the rapidly rising health-care expenditures.

Box 5 | **Direct to consumer marketing: caveat emptor**

Direct to consumer (DTC) marketing of genetic and genomic applications is an increasingly popular commercial strategy. Products ranging from ancestry testing to medical testing to genetically tailored cosmetics and diets are available for purchase, priced from US\$50 to more than \$1000. For some tests, approval by a health professional is not required — tests can be ordered by and results returned directly to the consumer. Although DTC marketing strategies can raise awareness and perhaps encourage consumers to discuss the appropriateness of tests with physicians, they could mislead vulnerable individuals⁹⁰. As a result, education becomes vitally important to ensure that consumers are equipped with the knowledge to understand the benefits, risks and limitations of testing.

Nutrigenomics is the study of the interaction between genes and diet. Many nutrigenomic tests are available DTC. For example, **Genelex** offers a nutrition profile of 19 genes with the option of a consultation with a nutritionist and tailored diet plan⁹¹. **Sciona** also offers a DNA assessment of 19 genes related to bone health, heart health and inflammation⁹². Information regarding the clinical validity of the 19 genes or evidence of improved outcomes on the basis of the recommended lifestyle or diet is not provided.

Outside of health care, **Genetic Technologies Limited** offers a test to determine one's "...ability to excel in either sprint/power events, or in endurance events."⁹³ The α -actinin 3 (ACTN3) Sports Gene Test is based on the findings of one study that describes the association between a single polymorphism and athletic performance in Caucasian individuals⁹⁴. No independent validation studies or functional studies to demonstrate the biological significance of the polymorphism have been conducted, nor has it been shown whether special training programmes result in different outcomes on the basis of a person's ACTN3 genotype.

Purchasers of DTC tests might choose not to share the results with their practitioner out of fear of genetic discrimination. Therefore, public education must ensure that there is an understanding of the information that is obtained from genetics and genomics and its bearing on their health, lifestyle or environment. Concern about DTC tests prompted the UK Health and Science Ministers to request an investigation by the **Human Genetics Commission**. The commission recommended stricter controls be established for tests that are offered directly to the public, and that predictive genetic tests should not be available for direct purchase⁹⁵.

that is devoted to educational efforts is likely to be quite small compared with that devoted to research. In 2002 alone, the **Medical Research Council** was allocated £54.3 million for post-genome research initiatives, but what proportion of this would be adequate for education, and how should 'adequacy' be measured? It will be crucial for any educational initiative to include an external evaluation component to determine the success of the project in meeting its stated goals, as is required by educational projects that are supported by the US **National Science Foundation**.

The ability of patients to make informed decisions about their health depends on a clear understanding of both disease risk and options that are available to reduce risk or severity. Therefore, health professionals and manufacturers have an important role through verbal or written communication during the informed consent process, or through printed labels and advertisements⁵⁸. Currently, however, products that are marketed directly to consumers are not required to disclose detailed information such as outcomes of clinical studies or the specific genes that were tested (BOX 5). Although policy changes could improve the

information-disclosure requirements, the understanding of such information might still be limited. Consumer fact sheets and talking points have been developed to raise consumer awareness and to highlight important issues to be considered during the decision-making process⁵⁹.

Acceptance and implementation

The acceptance of genome applications, by both professionals and the public, depends primarily on the perceived benefits and risk. The adoption of new genomics applications will therefore depend on two factors: demonstration of safety and effectiveness; and successful communication of this evidence to the people who will influence the acceptance of the technology. Although the absence of such safety and effectiveness data does not preclude policy decision making, changing initial policies and attitudes after data become available could be extremely challenging.

To outline this point, the acceptance of GM food products has been substantially influenced by the public perception of the risks and benefits to human health and the environment. Although the safety studies that are needed are costly, long and

complex, this research is crucial to answering the concerns of the public. But even if safety concerns could be addressed, would demand for these products increase? Policy decisions that are based only on expert data without successful communication to the public are unlikely to satisfy all stakeholders, and therefore acceptance will be limited¹¹.

In medicine, the desire of the public for genome-based tests will be influenced by policies including reimbursement by insurers or the state (and therefore cost-effectiveness) and privacy and discrimination protections. However, demand has not always matched the anticipation for testing^{60,61}, and the demonstration of clinical utility and cost-effectiveness depends, in part, on the implementation of behavioural changes that might be recommended on the basis of such tests. For example, levels of compliance with general public health recommendations, such as recommended dietary allowances⁶², smoking cessation⁶³ or colon cancer screening⁶⁴, make it unclear if the addition of genomic information will further motivate individuals. Because genomic information is more individualized, albeit more complex, it is hoped that the public response to this information might be better than it has been to general health recommendations. Data from the few studies that have been carried out so far have been inconsistent about how genomic information will affect behavioural response⁶⁵⁻⁶⁷. Results from genomic testing will mostly be in the form of risk probabilities rather than absolute (yes or no) outcomes. Therefore, understanding the likelihood of behaviour modification on the basis of risk probabilities should be prioritized as an important research issue.

Formulating genome policies

Given the dependence of policy making on research, scientists and policy makers should have a fundamental understanding of each other's work. In particular, scientists should be made aware of policy issues, the various approaches that are used to address them, and effective methods to communicate scientific data to non-expert audiences. Other stakeholders, such as disease advocacy groups, have recognized the importance of understanding political processes, educating their members and providing opportunities to engage with policy makers⁶⁸. In turn, policy makers must understand the scientific process in order to assess scientific evidence in areas such as appropriations, environmental policy and biodefense. We acknowledge,

however, that the effectiveness of this suggestion has yet to be demonstrated.

One example of a successful programme to allow scientists to engage in the political process is the American Association for the Advancement of Science's **Science & Technology Policy Fellowship Program**⁶⁹. In operation for more than 30 years, this programme started with the placement of 7 scientists in Congressional offices and has expanded to almost a dozen federal agencies, with sponsorship from more than 30 professional societies and more than 100 fellows annually. After completion of the 12-month fellowship, about one-third of the scientists move on to work in the policy sector. However, as this highly competitive programme is limited to a few scientists each year, wider awareness of policy issues might alternatively be achieved with interdisciplinary training programs.

The input of stakeholders is important to the development of effective research policies, particularly for large-scale studies. The **International HapMap Project** is a successful model of the joint efforts of ethicists, lawyers, scientists, government officials, industry and community representatives in the development of a study design as well as policies on issues such as informed consent and community consultation⁷⁰. In particular, ethicists were involved alongside scientists in scientific planning phases from the beginning of the project.

Other large-scale studies, such as national biobanks that include samples from up to a million citizens, raise ethical issues that would benefit from input from multiple stakeholders, particularly the public. Given that biobanks depend on public participation, engaging the public remains a crucial step to their success^{71,72}. In Iceland, a brief public consultation was conducted through radio and television programs, town hall meetings and public surveys. By contrast, the United Kingdom embarked on an ambitious 3-year public-consultation campaign through town hall meetings, focus groups, interactive workshops, key informant interviews and calls for comments on draft reports. Although the exchange of information helped to inform policy making, it also sought to raise public awareness about these projects. However, the distinction between a public-relations campaign and a public-consultation or education initiative is an important one to make, as public relations veiled as public consultation can lead to skepticism and mistrust⁷³.

Conclusion

Policy considerations are tightly interwoven throughout all aspects of genome research and applications (BOX 1). Just as genomics is enabling medicine to take a more prospective approach, policy making will similarly need to anticipate the likely consequences of the genome sciences as they affect science, health and society. To be effective, those that are involved in policy research and deliberations must connect with other stakeholders in academia, government, industry and the public. The regular exchange of information between stakeholders and policy makers will hopefully lead to policies that are well informed and have a basis in sound scientific data. Ultimately, we all share the goal of advancing scientific knowledge and improving health and well-being. A consensus among stakeholders, including the general public, will greatly help genomic advances to achieve these ends.

Susanne B. Haga and Huntington F. Willard are at the Institute for Genome Sciences & Policy, Duke University, 101 Science Drive, Box 3382, Durham, North Carolina 27708, USA.

Correspondence to S.B.H.
e-mail: susanne.haga@duke.edu

doi:10.1038/nrg2003

- Ziman, J. Public understanding of science. *Sci. Technol. Human Values* **16**, 99–91 (1991).
- Sturgis, P. & Allum, N. Science in society: re-evaluating the deficit model of public attitudes. *Public Underst. Sci.* **13**, 55–74 (2004).
- Gaskell, G., Allum, N. & Stares, S. *Europeans and biotechnology 2002. A report to the EC Directorate General for Research from the project 'Life Sciences in European Society'* [online], <http://ec.europa.eu/public_opinion/archives/ebs/ebs_177_en.pdf> (2003).
- Pardo, R., Midden, C. & Miller, J. D. Attitudes towards biotechnology in the European Union. *J. Biotechnol.* **98**, 9–24 (2002).
- Hampel, J., Pfennig, U. & Peter, H. Attitudes toward genetic engineering. *New Genet. Soc.* **19**, 233–249 (2000).
- Sturgis, P., Cooper, H. & Fife-Shaw, C. Attitudes to biotechnology: opinions of a better-informed public. *New Genet. Soc.* **24**, 31–56 (2005).
- Pfister, H., Bohm, G. & Jungermann, H. The cognitive representation of genetic engineering: knowledge and evaluations. *New Genet. Soc.* **19**, 296–316 (2000).
- Wellcome Trust. *Public perspectives on human cloning* [online], <http://www.wellcome.ac.uk/doc%5Fwtd003422.html> (1998).
- Wynne, B. Knowledge in context. *Sci. Technol. Human Values* **16**, 111–121 (1991).
- Jones, M. & Salter, B. The governance of human genetics: policy discourse and constructions of public trust. *New Genet. Soc.* **22**, 21–41 (2003).
- Brunk, C. G. Public knowledge, public trust: understanding the 'knowledge deficit'. *Community Genet.* **9**, 178–183 (2006).
- Irwin, A. Constructing the scientific citizen: science and democracy in the biosciences. *Public Underst. Sci.* **10**, 1–18 (2001).
- Franklin, S. Culturing biology: cell lines for the second millennium. *Health* **5**, 335–354 (2001).
- Collins F. S., Green E. D., Guttmacher A. E. & Guyer M. S. US National Human Genome Research Institute. A vision for the future of genomics research. *Nature* **422**, 835–847 (2003).
- DOE-NIH Joint Subcommittee. NIH, DOE Guidelines Encourage Sharing of Data, Resources. *Human Genome News* **4** [online], <http://www.ornl.gov/sci/techresources/Human_Genome/publicat/hgn/v4n5/04share.shtml> (1993).
- The Wellcome Trust. *Summary of principles agreed at the International Strategy Meeting on Human Genome Sequencing* [online], <http://www.gene.ucl.ac.uk/hugo/bermuda.htm> (1996).
- National Research Council, Committee on Genomics Databases for Bioterrorism Threat Agents. *Seeking Security: Pathogens, Open Access, and Genome Databases* (National Academies, Washington, 2004).
- Le Saux, O. *et al.* Mutations in a gene encoding an ABC transporter cause pseudoxanthoma elasticum. *Nature Genet.* **25**, 223–227 (2000).
- Rodriguez-Viciana, P. *et al.* Germline mutations in genes within the MAPK pathway cause cardio-facio-cutaneous syndrome. *Science* **311**, 1287–1290 (2006).
- Brody, B. Intellectual property and biotechnology: the US internal experience — part I. *Kennedy Inst. Ethics J.* **16**, 1–37 (2006).
- World Health Organization. *Genetics, genomics and the patenting of DNA: review of potential implications for health in developing countries* [online], <http://www.who.int/genomics/FullReport.pdf> (2005).
- Canadian Biotechnology Advisory Committee. *Human Genetic Materials, Intellectual Property and the Health Sector* [online], <http://strategies.ic.gc.ca/epic/internet/incbac-cccbs.nsf/en/ah00578e.html> (2006).
- Nuffield Council. *The ethics of patenting DNA* [online], <http://www.nuffieldbioethics.org/go/ourwork/patentingdna/introduction> (2002).
- Commission on Intellectual Property Rights. *Integrating intellectual property rights and development policy* [online], <http://www.iprcommission.org/papers/pdfs/final_report/CIPRfinal.pdf> (2002).
- The HUGO Intellectual Property Committee. *Statement on the scope of gene patents, research exemption and licensing of patented gene sequences for diagnostics* [online], <http://www.hugo-international.org/PDFs/Statement%20on%20the%20Scope%20of%20Gene%20Patents,%20Research%20Exemption.pdf> (2003).
- Convention on Biological Diversity. *Article 1. Objectives* [online], <http://www.biodiv.org/convention/articles.shtml?lg=0&a=cbd-01> (1992).
- Heller, M. A. & Eisenberg, R. S. Can patents deter innovation? The anticommons in biomedical research. *Science* **280**, 698–701 (1998).
- Cho, M. K., Illangasekare, S., Weaver, M. A., Leonard, D. G. & Merz, J. F. Effects of patents and licenses on the provision of clinical genetic testing services. *J. Mol. Diagn.* **5**, 3–8 (2003).
- US Department of Commerce. Patent and Trademark Office. *Utility Examination Guidelines. Fed. Reg.* **66**, 1092–1099 (2001).
- European Parliament. *Texts adopted by Parliament: patents on biotechnological inventions* [online], <http://www.europarl.europa.eu/sides/getDoc.do?language=EN&pubRef=-//EP//TEXT+TA+20051026+ITEMS+DOC+XML+V0//EN/sdocta8> (2005).
- Marshall, E. Patient advocate named co-inventor on patent for the PXE disease gene. *Science* **305**, 1226 (2004).
- Malakoff, D. Intellectual property. NIH roils academe with advice on licensing DNA patents. *Science* **303**, 1757–1758 (2004).
- United Nations Educational, Scientific and Cultural Organization (UNESCO). *Universal Declaration on the Human Genome and Human Rights* [online], <http://portal.unesco.org/shs/en/ev.php-URL_ID=1881&URL_DO=DO_TOPIC&URL_SECTION=201.html> (1997).
- United Nations Educational, Scientific and Cultural Organization (UNESCO). *A declaration on human genetic data* [online], <http://portal.unesco.org/shs/en/ev.php-URL_ID=1882&URL_DO=DO_TOPIC&URL_SECTION=201.html> (2003).
- Lemmons, T., Joly, Y. & Knoppers, B. M. Genetics and life insurance: a comparative analysis. *GenEdit* **2**, 1–14 [online], <http://www.humgen.umontreal.ca/int/genedit.cfm?idisel=1267> (2004).
- HM Government and Association of British Insurers. *Concordat and Moratorium Genetics and Insurance* [online], <http://www.dh.gov.uk/assetRoot/04/10/60/50/04106050.pdf> (2005).
- Genetics and Insurance Committee. *October 2000: Huntington's Disease (GAIC/01.1)* [online], <http://www.advisorybodies.doh.gov.uk/genetics/gaic/huntingtons-oct00.pdf> (2000).
- GeneWatch UK. *Joint Statement of Concern Regarding Genetic Testing in the Workplace* [online], <http://www.genewatch.org> (2006).

39. Equal Employment Opportunity Commission. *Press Release: EEOC and BNSF settle genetic testing case under Americans with Disabilities Act* [online]. < <http://www.eeoc.gov/press/5-8-02.html> > (2002).
40. Hall, M. *et al.* Concerns in a primary care population about genetic discrimination by insurers. *Genet. Med.* **7**, 311–316 (2005).
41. Apse, K. A., Biesecker, B. B., Giardiello, F. M., Fuller, B. P. & Bernhardt, B. A. Perceptions of genetic discrimination among at-risk relatives of colorectal cancer patients. *Genet. Med.* **6**, 510–516 (2004).
42. Otlowski, M. F., Taylor, S. D., Barlow-Stewart, K. K. Genetic discrimination: too few data. *Eur. J. Hum. Genet.* **11**, 1–2 (2003).
43. Wong, J. G. & Lih-Mak, F. Genetic discrimination and mental illness: a case report. *J. Med. Ethics* **27**, 393–397 (2001).
44. Hamvas, A. *et al.* Informed consent for genetic research. *Arch. Pediatr. Adolesc. Med.* **158**, 551–555 (2004).
45. Nedelcu, R. *et al.* Genetic discrimination: the clinician perspective. *Clin. Genet.* **66**, 311–317 (2004).
46. Zick, C. D. *et al.* Genetic testing for Alzheimer's disease and its impact on insurance purchasing behavior. *Health Aff. (Millwood)* **24**, 483–490 (2005).
47. Aktan-Collan, K., Haukkala, A. & Kaariainen, H. Life and health insurance behaviour of individuals having undergone a predictive genetic testing programme for hereditary non-polyposis colorectal cancer. *Community Genet.* **4**, 219–224 (2001).
48. US Food and Drug Administration. *Guidance for Industry: Pharmacogenomic Data Submissions* [online]. < <http://www.fda.gov/cder/guidance/6400fnl.pdf> > (2005).
49. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. *Final Concept Paper E15: Terminology in Pharmacogenomics* [online]. < <http://www.ich.org/LOB/media/MEDIA3099.pdf> > (2006).
50. European Medicines Agency. *Guiding Principles: Processing Joint FDA EMEA Voluntary Genomic Data Submissions (VGDSs) within the framework of the Confidentiality Arrangement* [online]. < <http://www.emea.eu.int/pdfs/general/direct/pr/FDAEMEA.pdf> > (2006).
51. Tencalla, F. Science, politics, and the GM debate in Europe. *Regul. Toxicol. Pharmacol.* **44**, 43–48 (2006).
52. GM Nation. *The Findings of the Public Debate* [online]. < http://www.gmnation.org.uk/docs/gmnation_finalreport.pdf > (2003).
53. Haga, S. B. Teaching resources in genetics. *Nature Rev. Genet.* **7**, 223–229 (2006).
54. Mervis, J. The Dover ID decision. Judge Jones defines science — and why intelligent design isn't. *Science* **311**, 34 (2006).
55. Department of Health. *Our inheritance, our future — realising the power of genetics in the NHS* [online]. < <http://www.dh.gov.uk/assetRoot/04/01/92/39/04019239.pdf> > (2003).
56. Guttmacher, A. E., Jenkins, J. & Uhlmann, W. R. Genomic medicine: who will practice it? A call to open arms. *Am. J. Med. Genet.* **106**, 216–222 (2001).
57. Giardiello, F. M. *et al.* The use and interpretation of commercial APC gene testing for familial adenomatous polyposis. *N. Engl. J. Med.* **336**, 823–827 (1997).
58. Khoury, M. J. *et al.* Challenges in communicating genetics: a public health approach. *Genet. Med.* **2**, 198–202 (2000).
59. Federal Trade Commission. *Facts for Consumers: At-Home Genetic Tests: A Healthy Dose of Skepticism May Be the Best Prescription* [online]. < <http://www.ftc.gov/bcp/edu/pubs/consumer/health/hea02.htm> > (2006).
60. Kessler, S., Field, T., Worth, L. & Mosbarger, H. Attitudes of persons at risk for Huntington disease toward predictive testing. *Am. J. Med. Genet.* **26**, 259–270 (1987).
61. Craufurd, D., Dodge, A., Kerzin-Storarr, L. & Harris, R. Uptake of presymptomatic predictive testing for Huntington's disease. *Lancet* **2**, 603–605 (1989).
62. Auld, G. W. *et al.* Reported adoption of dietary fat and fiber recommendations among consumers. *J. Am. Diet. Assoc.* **100**, 52–58 (2000).
63. Watt, R. G. *et al.* Public health aspects of tobacco control: setting the agenda for action by oral health professions across Europe. *Oral Health Prev. Dent.* **4**, 19–26 (2006).
64. Thorpe, L. E. *et al.* Colon cancer screening practices in New York City, 2003: results of a large random-digit dialed telephone survey. *Cancer* **104**, 1075–1082 (2005).
65. Botkin, J. R. *et al.* Genetic testing for *BRCA1* mutation: prophylactic surgery and screening behavior in women 2 years post testing. *Am. J. Med. Genet.* **118**, 201–209 (2003).
66. Hadley, D. W. *et al.* Colon cancer screening practices after genetic counseling and testing for hereditary nonpolyposis colorectal cancer. *J. Clin. Oncol.* **22**, 39–44 (2004).
67. Senior, V., Marteau, T. M. & Peters, T. J. Will genetic testing for predisposition to disease result in fatalism? A qualitative study of parents responses to neonatal screening for familial hypercholesterolemia. *Soc. Sci. Med.* **45**, 1857–1860 (1999).
68. Genetic Alliance. *Genetics Day on the Hill and Strategies for Success Teleconference Series* [online]. < http://www.geneticalliance.org/ws_display.asp?filter=gadvocacy.bonus06 > (2006).
69. American Association for the Advancement of Science. *Science & Technology Policy Fellowship Program* [online]. < <http://fellowships.aaas.org> > (2006).
70. The International HapMap Consortium. Integrating ethics and science in the International HapMap Project. *Nature Rev. Genet.* **5**, 467–475 (2004).
71. Godard, B., Marshall, J., Laberge, C. & Knoppers, B. M. Strategies for Consulting with the Community: The cases of four large-scale genetic databases. *Sci. Eng. Ethics.* **10**, 457–477 (2004).
72. Deschenes, M. & Sallee, C. Accountability in population biobanking: comparative approaches. *J. Law Med. Ethics.* **33**, 40–53 (2005).
73. Office of Science and Technology and the Wellcome Trust. Science and the public: a review of science communication and public attitudes toward science in Britain. *Public Underst. Sci.* **10**, 315–330 (2001).
74. Department of Health and Human Services. National Institutes of Health. Best practices for the licensing of genomic inventions: Final Notice. *Fed. Regist.* **70**, 18413–18415 (2005).
75. Australian Law Reform Commission and Australian Health Ethics Committee of the National Health and Medical Research Council. *Protection of Human Genetic Information (IP 26)* [online]. < <http://www.austlii.edu.au/au/other/alrc/publications/issues/26> > (2001).
76. Australian Law Reform Commission and Australian Health Ethics Committee of the National Health and Medical Research Council. *Protection of Human Genetic Information (Discussion paper 66)*. [online]. < <http://www.austlii.edu.au/au/other/alrc/publications/dp/66> > (2002).
77. Australian Law Reform Commission and Australian Health Ethics Committee of the National Health and Medical Research Council. *Essentially Yours: The Protection of Human Genetic Information in Australia (ALRC 96)* [online]. < <http://www.austlii.edu.au/au/other/alrc/publications/reports/96> > (2003).
78. O'Malley, M. A., Bostanci, A. & Calvert, J. Whole-genome patenting. *Nature Rev. Genet.* **6**, 502–506 (2005).
79. Gold, E. R. SARS genome patent: symptom or disease? *Lancet* **361**, 2002–2003 (2003).
80. Angrist, M. & Cook-Deegan, R. M. Who owns the genome? *New Atlantis* **11**, 87–96 (2006).
81. US Patent and Trademark Office. *Patent Pools: A Solution to the Problem of Access in Biotechnology Patents?* [online]. < <http://www.uspto.gov/web/offices/pac/dapp/opa/patentpool.pdf> > (2000).
82. Simon, J. *et al.* Managing severe acute respiratory syndrome (SARS) intellectual property rights: the possible role of patent pooling. *Bull. World Health Organ.* **83**, 707–710 (2005).
83. Stott, M. & Valentine, J. Gene patenting and medical research: a view from a pharmaceutical company. *Nature Rev. Drug Discov.* **3**, 364–368 (2004).
84. Hornberger, J., Cosler, L. E. & Lyman, G. H. Economic analysis of targeting chemotherapy using a 21-gene RT-PCR assay in lymph-node-negative, estrogen-receptor-positive, early-stage breast cancer. *Am. J. Manag. Care.* **11**, 313–324 (2005).
85. Deng, M. C. *et al.* Noninvasive discrimination of rejection in cardiac allograft recipients using gene expression profiling. *Am. J. Transplant.* **6**, 150–160 (2006).
86. Evans, R. W. *et al.* The economic implications of noninvasive molecular testing for cardiac allograft rejection. *Am. J. Transplant.* **5**, 1553–1558 (2005).
87. Ramsey, S. D. *et al.* Toward evidence-based assessment for coverage and reimbursement of laboratory-based diagnostic and genetic tests. *Am. J. Manag. Care* **12**, 197–202 (2006).
88. Center for Medicaid and Medicare Services. *LCD for Oncotype DX Test — Breast Cancer Prognosis (L20634)* [online]. < http://www.cms.hhs.gov/mcd/viewcd.asp?lcd_id=20634&lcd_version=14&show=all > (2006).
89. Technology Evaluation Center. Blue Cross Blue Shield Association. *Gene Expression Profiling for Managing Breast Cancer Treatment. Assessment Program 20* [online]. < http://www.bcbs.com/tec/Vol20/20_03.pdf > (2005).
90. Gollust, S. E., Hull, S. C. & Wilfond, B. S. Limitations of direct-to-consumer advertising for clinical genetic testing. *JAMA* **288**, 1762–1767 (2002).
91. Genelex. *Nutritional Genetic Testing*. [online]. < <http://www.healthanddna.com/professional/nutrigenetics.html> > (2006).
92. Sciona, Inc. *Discover your Cell — Which Cell is Right for Me? — Comprehensive* [online]. < <http://www.mycell.com/comprehensive.html> > (2006).
93. Genetic Technologies Limited. *Sports Performance — ACTN3 Sports Gene Test* [online]. < <http://www.gtg.com.au/HumanDNATesting/index.asp?menuid=070.110.020> > (2006).
94. Yang, N. *et al.* *ACTN3* genotype is associated with human elite athletic performance. *Am. J. Hum. Genet.* **73**, 627–631 (2003).
95. Human Genetics Commission. *Genes Direct: ensuring the effective oversight of tests supplied directly to the public* [online]. < http://www.hgc.gov.uk/UploadDocs/DocPub/Document/genesdirect_full.pdf > (2003).

Acknowledgements

The authors would like to thank B. Cook-Deegan and M. Garfinkel for their helpful comments on the manuscript.

Competing interests statement

The authors declare no competing financial interests.

DATABASES

The following terms in this article are linked online to:
Entrez Gene: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene>
BRCA1 | *BRCA2*
OMIM: <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM>
 CFC | Huntington disease | PXE

FURTHER INFORMATION

AlloMap Test: <http://www.allomap.com/index.html>
Clinical Laboratory Improvement Amendments: <http://www.cms.hhs.gov/clia>
Concordat and Moratorium on Genetics and Insurance: http://www.abi.org.uk/Display/File/Child/106/Concordat_and_Moratorium.pdf
Duke Institute for Genome Sciences and Policy: <http://www.genome.duke.edu>
Education and Community Involvement Branch: <http://www.genome.gov/11008538>
EU Biotechnology Directive: <http://eurlex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31998L0044:EN:HTML>
EuroGenTest: <http://www.eurogenest.org>
Genelex: <http://www.genelex.com>
Genetic Technologies Limited: <http://www.gtg.com.au>
Genetics and Insurance Committee: <http://www.advisorybodies.doh.gov.uk/genetics/gaic/index.htm>
Genome Canada: <http://www.genomecanada.ca>
Genoma España: <http://www.gen-es.org>
GM Nation: <http://www.gmnation.org.uk>
Health Insurance Portability and Accountability Act: <http://www.cms.hhs.gov/HIPAAgenInfo>
Human Genetics Commission: <http://www.hgc.gov.uk/Client/index.asp?ContentId=1>
Instituto Nacional de Medicina Genómica: <http://www.inmegen.gob.mx>
International HapMap Project: www.hapmap.org
Medical Research Council: <http://www.mrc.ac.uk/index.htm>
National Genetics Education and Development Centre: <http://www.geneticseducation.nhs.uk>
National Human Genome Research Institute: <http://www.genome.gov>
National Institutes of Health: <http://www.nih.gov>
National Science Advisory Board for Biosecurity: <http://www.biossecurityboard.gov>
National Science Foundation: <http://www.nsf.gov>
Oncotype DX: <http://www.genomichealth.com/oncotype/default.aspx>
Riken Genomic Sciences Center: <http://www.gsc.riken.go.jp/indexE.html>
Sanger Institute: <http://www.sanger.ac.uk>
Science & Technology Policy Fellowship Program: <http://fellowships.aaas.org>
Sciona: <http://www.sciona.com>
Access to this links box is available online.