The Human Genome Project: Under an International Ethical Microscope

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At first glance, the Human Genome Project (HGP) seems ungoverned by any explicit ethical or legal norms. However, from its beginnings the HGP has spawned a myriad of international (*1–9*), regional (*10–14*), and national (*15–38*) reports and guidelines and, more recently, some legislation (*39-47*). A review of the last 5 years (December 1989 to July 1994) reveals several areas of international consensus that could serve to harmonize eventual national regulation. Five basic principles underlie this consensus: autonomy, privacy, justice, equity, and quality out of respect for human dignity. Ensuring that these international areas of "commonalty" are reinforced and adopted by the HGP is an ethical and political challenge—a unique opportunity to direct rather than react.

Autonomy. Genetic testing and the resulting information is highly personal. Because this information could be used to discriminate against individuals on socioeconomic grounds—for example, in selecting employees, immigrants, or insurance applicants—there has been a call for voluntary testing based on autonomous choice, with the participants having full information. The "right" not to know is increasingly raised as a corollary of autonomy. Most genetic information is only predictive and probabilistic—a certain gene may increase the *likelihood* of developing a disease. Indeed, it is this imprecise nature of genetic information that necessitates further protection against social pressures and a reaffirmation of informed consent procedures. Therefore, counseling has become a prerequisite to the decision to undergo testing. An exception to this principle of individual consent is newborn screening programs for immediately treatable disorders. A recent report from the United States, however, has explicitly recommended that parental consent be obtained (*34*).

There is consensus limiting genetic testing (including prenatal testing) to tests that are medically therapeutic. Which tests are considered to be therapeutic then remains to be decided by individual countries according to cultural, social, and political norms. Both France (*41, 42*) and Norway (*45*) have passed legislation centralizing the elaboration of such "therapeutic" criteria in governmental bodies. Adherence to these criteria effectively curtails the use of genetic tests for sex selection or trait enhancement.

Most genetic testing is further limited to individuals at high risk for serious disorders. Furthermore, there is consensus that predisposition testing should be limited to diseases that are treatable or preventable. Somatic cell therapy is for the most part considered experimental and thus subject to stringent limitations (used only in serious monogenic conditions) as well as to additional safeguards and oversight. Preimplantation embryo testing remains controversial and severely constrained but not totally prohibited, except in Germany (*44*).

Privacy. Respect for the privacy of the person and for the confidentiality of genetic information is crucial. Although the results of genetic tests could be considered a form of sensitive medical information, genetic testing also reveals information about other family members and is of importance to insurers and employers. Some guidelines would prohibit any communication to all third parties without consent (*8, 13, 14, 24, 30*). Most guidelines, however, advocate the communication of relevant information to family members at high risk for serious harm without the consent of the patient or of the research participant only when all attempts to elicit voluntary communication have failed. All other disclosures of information—or use of DNA samples (unless anonymous)—would require consent. Furthermore, the collection, storage, and dissemination of genetic information should be subject to special procedures of coding, of removing identifiers, and of obtaining consent for new uses.

In the areas of insurance and employment, the presence or absence of universal health insurance and social security shapes current guidelines. Little is known of the potential discriminatory or stigmatizing effects (or even benefits) of access to genetic information by insurers and employers. Even countries with universal health care recommend rejecting access to or direct testing by employers and insurers for life and disability insurance. For example, reports from both the Netherlands (*28*) and the United Kingdom (*32*) have called for a moratorium on requiring disclosure where life insurance policies are proportionate to income or of moderate size. Only Belgium has specifically included a prohibition on testing or access to genetic information by insurers in its Civil Code (*40*). The American NIH-DOE report recommends that "Information about past, present or future health status, including genetic information, should not be used to deny health care coverage or services to anyone" (*35*). Finally, genetic identity testing confirms either filial links (paternity or maternity) or presence at the scene of a crime (forensic testing) and utilizes the same techniques as medical testing [sampling, restriction fragment length polymorphisms (RFLPs), markers, and polymerase chain reaction amplification]. Similar privacy concerns arise (*38*). France has passed legislation requiring court orders for such identity testing (*41*).

Justice. The international community is united in its concern for vulnerable populations, such as incompetent adults or minors, and for future generations. Although overprotection could make research with these populations impossible, the fact that they cannot decide for themselves and are often in institutions mandates special protection—but not exclusion. Furthermore, in the absence of treatment or prevention, the presymptomatic testing of children for late onset disease has not been recommended. Where possible, both children and incompetent adults should participate in decision-making.

The continuing debate on the desirability of germline modification is sparked by a desire for justice toward future generations and prevention of eugenic uses of the technology. Although most guidelines advocate a total prohibition of germline modification, others have taken a more cautious approach, suggesting continuing discussion of its technical and ethical aspects and the development of adequate safeguards. The 1991 CIOMS Declaration of Inuyama (*8*) considered continued discussion of its technical and ethical aspects to be essential. Nevertheless, Austria (*39*), France (*41*), Germany (*44*), Norway (*45*), and Switzerland (*47*) prohibit germline alteration by statute.

Equity. Although not explicitly mentioned as a governing principle, equity is a recurring part of the ongoing discussion. How do we ensure equity of access to genetic research, testing, and information; equal costs; equal resources; and equal sharing of information? There is a potential danger and the accompanying fear of genetic testing increasing social inequality, of access to testing being linked to willingness

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to terminate a pregnancy or to financial considerations, and of denying social welfare benefits for refusal to undergo testing. There is also the possibility of creating unequal burdens for minority ethnic groups when specific genes are more prevalent in one group (*21*).

Most countries and regional and international bodies oppose attempts to patent anonymous human sequences as an affront to human dignity and in order to ensure a free flow of information between researchers. However, only in France does the Code on intellectual property declare unpatentable "... the human body, its elements and products as well as knowledge of the partial or total structure of a human gene..." (*41*).

Finally, participation in genetic testing should be based on understanding, thus mandating widespread education and training efforts as an essential foundation for the development of any public policy or legislation.

Quality. Again, although not an explicit or common principle, there is a growing realization that accredited and licensed laboratories and personnel, professional oversight and monitoring, and ethical review are critically required. Specific criteria for test sensitivity, specificity, and effectiveness have also been recommended (*12, 13, 16, 21, 29, 30, 34, 42*). Ultimately, respect for the human person begins here.

Conclusion. This overview does not do justice to the complexity of these issues, but nevertheless indicates common international positions on these extremely controversial aspects of the HGP. Considering that most national governments have not yet addressed these questions, the emergence of these common approaches is encouraging. What remains as an urgent matter, however, is the codification of their principles in an international instrument. Individual countries could then interpret them in their own domestic legislation or ensure their application through other mechanisms of review and oversight. The international bioethics committee of Unesco is moving in this direction.

Ad hoc country-by-country approaches or a later transnational harmonization of policy underestimate the universal, social importance of the HGP. Normative, international principles provide direction and signify political will to do more than pay lip service to legitimate public concerns. The accountability of the HGP is at stake. So are our present obligations of stewardship to humankind and to future generations. This unique opportunity to provide principled direction must not be lost.

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