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Genome vikings

deCODE, the Icelandic genomics company, fascinates geneticists in academia and industry. Not only is it one of the fastest growing biotech companies, deCODE also landed the largest genomics deal ever when it sold, last year, the potential rights to 12 genes associated with common complex diseases to Hoffman-La Roche for \$200 million. deCODE's competitive edge is its alliance with the Icelandic population. Promises of free drugs developed from research on the Icelandic gene pool and free genetic testing for identified susceptibility alleles, as well as a boost to Icelandic science and economy have led to wide-spread approval among the 270,000 Icelanders. The company's corporate summary reads like a gene hunter's dream, and many experts believe that deCODE's approach is one of the most promising strategies for dissecting complex diseases and traits. Consequently, the company provides an attractive scientific environment to young and ambitious researchers from Iceland and around the world.

deCODE lists five main characteristics of the Icelandic nation that make it an ideal population to study human genetics. Genetic homogeneity (1,100 years of isolation and two population bottlenecks), extensive genealogical records, which make it easy to find large families for disease-mapping through linkage and identity-by-descent methods, a large tissue bank (autopsy records and samples go back over more than 50 years), a high quality health care system whose professionals collaborate with deCODE in patient identification and recruitment, and a well-educated, cooperative population.

Based on this unique resource, deCODE is offering potential corporate partners a product portfolio that includes gene discovery through positional cloning, mutational searches of candidate genes, establishing gene function, clinical trials of drug candidates and a database for disease management and *in silico* analysis. It is the latter—or rather a parliament bill that would authorize the creation and operation of a centralized health sector database—that has caused a controversy in Iceland and abroad. The bill was first introduced last March by the Health Ministry, but subsequently withdrawn in response to protests from Icelandic scientists and physicians who also appealed to colleagues worldwide with a plea for solidarity. Their arguments concerned ethics (mainly issues of informed consent and genetic privacy), economics (creation of a monopoly for the exploitation of the national gene pool) and the question of academic freedom. After six months of public dispute, a revised version of the bill is now scheduled for parliamentary vote later this month.

While most critics agree that the revised bill is improved with regard to some of their earlier concerns, several issues remain controversial or unclear, and most pro-

Conditions for granting the operating license

- Location of the database exclusively in Iceland.
- Technical, security and organizational standards meet the requirements of the Commission for Data Protection.
- The recording and processing of health information shall be carried out by, or under the supervision of, health sector professionals.
- Detailed information shall be available on the area of activity and projects of the licensee.
- A detailed work plan from the licensee shall be available which fulfills the conditions laid down regarding working arrangements and progress.
- Icelandic health authorities shall at times have unhindered access to data from the database, so that they will be of use in the generation of health reports and other statistical processing.
- The licensee shall pay the costs of processing information for entry into the database.
- The minister might make the license subject to further conditions.

Professional organizations still oppose the idea of the database and the granting of an exclusive temporary license to a single private company. Given the complexity of the situation, more time for discussion seems justified. The interaction between deCODE and the Icelandic people is unique, but many of the issues are relevant to interactions between scientists and populations in other parts of the world, and the situation in Iceland will be an example for other ventures that use suitable populations in the search for the genetic basis of complex traits. Whether this will prove a case where things go badly wrong or a visionary arrangement that benefits all parties is uncertain.

The central database will contain encrypted medical, genealogical and genotype information of a large proportion of

the Icelandic population. The stated goal of the database is to increase knowledge in order to improve health and health services. The database will be licensed to the party that finances its creation (roughly estimated at \$100 million) for exclusive commercial exploitation (that is, the direct use of the data as well as selling access to corporate customers) for up to 12 years. This operating license will be granted by a committee comprised of a lawyer, a health care professional with a knowledge of epidemiology and an expert in information technology, and is contingent upon a number of conditions (see box). Surprisingly, no expert in human genetics is on the committee, despite the fact that the database is supposed to be used in genetic research.

The bill's authors list four main benefits of the database. The first is to gain new knowledge on the nature of health and disease. Second, higher quality and more economy in health services. Third, the development of high-technology industry in Iceland and thus employment for highly educated people. Fourth, the potential to attract enterprises relating to the database to Iceland. The authors see the main risk associated with the database in the potential of abuse of data, and thus the revised bill emphasizes the safety of personal information.

The revised version of the bill stipulates that the staff of the licensee work only with encrypted information. Medical and genealogical information will be attached to an identifier code under the supervision of the Commission for Data Protection, and genetic information will only be linked to that code. Critics argue, however, that encrypted data are not anonymous, and that in a small population like Iceland, it would be easy to infer an individual's identity. The new bill spells out a patient's right to request that his/her information not be entered into the database. It also addresses the issue of access of the database by Icelandic academics for research purposes (even though it is not clear exactly who can apply): a committee of three representatives—one nominated by the University of Iceland's Faculty of Medicine, one by the licensee, and one appointed by the minister of health—shall grant such access unless the research is expected to have an adverse effect upon the licensee's commercial interests.

Seen from the outside, several important questions remain unanswered. What status will deCODE have in the Icelandic society, economy and scientific community? Already, one of every thousand Icelanders works at deCODE—and the company is growing. The bill specifies that one party be granted an exclusive license for

commercial exploitation of the database, so the licensee (with deCODE being the only plausible candidate) would have a monopoly for a period of up to 12 years. Is that a healthy socio-economical situation? Should the Icelandic government become concerned about the licensee's conduct, how easy will it be to impose regulations? There is no indication that deCODE intends to abuse its position of power, but it is wise to consider safeguards at an early stage.

What is the value of the data in the database? Are they for sale by the licensee to the highest bidder for any purpose? According to the bill, the annual fee for the license is determined mainly by the costs for the various committees and the Commission for Data Protection (with the fact that the licensee directly pays for these 'independent' committees in itself problematic). It is clear that the Icelandic economy profits from deCODE, but one wonders whether the annual fees should also be dependent on the company's profits, or even whether individuals who contribute information to the database should become shareholders in the company. Is there a way to redistribute some of the profits to the people who provide the resource in the first place?

Given the complexity of the issues, one wonders whether there has been enough time and discussion to permit authentic 'informed consent' from the Icelandic people. Is it appropriate to rely on a patient's initiative not to give consent and make presumed consent the default stage? There is no obvious mechanism that allows individuals to withdraw consent at a later stage. Twelve years is a long time, and no-one can foresee what deCODE or any of its corporate partners who buy access to the database will use the data for. It seems plausible that people would be happy to support some projects but not others. It is stated in the bill that detailed information must be available on the licensee's area of activity and projects before a license can be granted, but given the nature of genetic research, it is impossible to foresee what kind of projects potential corporate customers will be interested in over the next twelve years, nor does it seem likely that these customers themselves will know.

With respect to Icelandic academic research, the database potentially represents a powerful new resource, but academic access is restricted to projects that do not interfere with the commercial interests of the licensee. It is unclear what will happen when these interests change, and scientists are concerned that they will have to discuss their ideas in front of a committee member affiliated with deCODE. As before, Icelandic scientists will have unrestricted access to medical information and patients, but deCODE's appearance has changed the scientific landscape in Iceland dramatically. Many academics have been offered collaborations with the company, but those who have declined will not have an easy time conducting research independently of deCODE. Are there ways by which deCODE could support genetic and biomedical research in Iceland that would present an alternative to the 'collaborate-or-die' situation academics are faced with now?

As deCODE is becoming a major economical force in Iceland, the future of the company is of national interest. deCODE's business plan does not stop at gene discovery, and, at least in the areas of clinical trials and pharmacogenomics, continued support of the population will be essential. Updating the people about progress and projects and making it clear that they have a choice regarding further participation will be crucial. From a scientific perspective, deCODE has the potential to become a major player in the international effort to understand and combat complex diseases. All things considered, the future implications of the health database bill as well as deCODE's presence in the Icelandic academic and economical landscapes could do with further discussion to ensure that scientific promise is realized without compromising the welfare of 'non-aligned' scientists, the Icelandic economy and those who make deCODE's initiative possible — the Icelandic population.

