

**House of Lords Science and Technology Committee,
Sub-committee on Genomic Medicine**

Evidence prepared on behalf of the ESRC Centre for Social and Economic Research on Innovation in Genomics (Innogen), 18th April 2008

The Innogen Centre is part of the ESRC Genomics Network (EGN), a major investment by the Economic and Social Research Council (ESRC). The Centre was set up in 2002 and has recently had its award extended to 2012. Members of staff in the Innogen Centre who have contributed to this response include: Professor Joyce Tait, Dr. Theo Papaioannou, Dr. James Mitra, Dr. Gill Haddow, Dr. Alessandro Rosiello. Professor Graeme Laurie and Shawn Harmon, also members of the Innogen Centre, are contributing to the AHRC submission to this Inquiry.

In considering the issues below as they apply to Genomic Medicine, we have adopted a wide interpretation of the term 'genomic' to cover aspects of new life sciences that incorporate or build on genomics-related knowledge. The Innogen Centre's research programme covers:

- Science and industry strategies in promoting fundamental scientific discoveries and exploiting them for public and commercial benefit;
- Policy, regulation and governance of life science innovation;
- Public and stakeholder engagement with life science-related issues.

Our overall approach explores how interactions among these three constituencies determine which products are delivered to a public or commercial market, who develops them, and which of the many potential benefits or risks will actually materialise.

Policy Framework

Who is in charge of setting and reviewing policy in this area

Numerous government and non-government (professional) actors are involved in setting and reviewing policy. The most important are:

Government Actors

- Human Genetics Commission (HGC) advised by Advisory Committee on Genetic Testing (ACGT); Advisory Group on Scientific Advances in Genetics (AGSAG); and Human Genetics Advisory Commission (HGAC) which focuses on social and ethical issues and concerns related to genomics.
- Other important committees include: Genetics and Insurance Committee (GAIC); Gene Therapy Advisory Committee (GTAC); and Genetics Commissioning Advisory Group

(GenCAG). These committees co-ordinate policies and advise on issues of insurance and safety.

- Human Fertilisation and Embryology Authority (HFEA) licenses new genomics-based technologies.
- House of Commons Science and Technology Committee examines and makes recommendations to government on relevant topics

Non-Government Actors

- Joint Medical Genetic Services Committee (JGSC) advises the UK health departments.
- Nuffield Council on Bioethics, an independent body that examines ethical issues relevant to genomics
- British Society of Human Genetics brings together the Association of Clinical Cytogeneticists, Clinical Genetics Society and Clinical Molecular Genetics Society
- Royal College of Physicians (RCPhys) reports on clinical genetics
- Genetic Interest Group (GIG) represents patients and families and aims to raise awareness on genomics-related matters.

Who provides scientific advice on policy development? Who monitors and anticipates potential scientific developments and their relevance to future policy? How effective are these mechanisms?

The development of new genomics-related solutions for patient health care engages with a variety of areas of policy making including: science funding; support for knowledge transfer; public sector support for translation of fundamental science to new medical developments; appropriate education at all levels of scientists, medical professionals, technologists and health care workers, including increasingly a focus on interdisciplinary working; policies on stakeholder and public engagement. However, the question implies a greater degree of coherence and strategic planning than actually exists in innovation and technology policy, with significant fragmentation of powers and initiatives at both functional and regional levels.

Does the existing regulatory and advisory framework provide for optimal development and translation of new technologies? Are there any regulatory gaps?

Regulation and policy are constantly required to evolve in response to rapid scientific and technological change. Emerging regulations such as the European Advanced Therapies Regulation, and changes in the way tissues and cells, as well as clinical trials, are being regulated, show that efforts are being made to adapt policy to technological change and to facilitate innovation. but the crucial changes generally need to be made at international levels and they frequently, with hindsight, turn out not to be optimal.

A major component of the Innogen Centre research programme has focused on the interactions between innovation and regulation in genomics-related sciences^{1 2}. We have shown how regulatory decisions can have a formative influence on the structure and dynamism of an entire industry sector. This is particularly true of pharmaceuticals where the lengthy and demanding nature of the regulatory system has been a major contributor to the overall shape of the sector, including the so far unchallenged supremacy of the multinational companies in determining the innovation environment. The high costs and long delays entailed in taking a new product through the regulatory system ensure that only large multinational companies (MNCs) have the resources to operate throughout the whole innovation cycle. This barrier to entry for small companies has shaped the structure of the sector, leaving MNCs in their currently dominant position and insulating them from competitive challenges from smaller innovative companies with a high growth potential. Small companies either rely on MNCs to take their products through to market, or alternatively they need to make themselves attractive acquisition targets for MNCs. In both cases this means that they inevitably tailor their innovation strategies to

match those of the MNCs, rather than developing the radically novel applications of genomic science that were anticipated in the 1980s and 90s.

Similar degrees of restriction on innovation pathways are beginning to emerge in new areas of medical innovation. In the case of stem cell therapies, for example, the evolving regulatory system is mirroring the structure currently applied to pharmaceuticals, and the more policy and regulatory barriers that are erected along the development path, the more likely it is that only very large multinational companies will be able to develop the technology. For stem cell-based innovations, multinational companies will be interested in applications that can contribute to evaluation of new drug candidates but they are unlikely to embrace stem cell based therapies as these will not fit with their current profit models or their production, distribution and marketing strategies. This will not mean that no therapeutic applications will arise from stem cell developments but there may be many fewer of them than would be the case under a different regulatory regime.

Because of their influence on these questions, regulatory agencies have a particularly important role in shaping the genomics-related innovation sectors of the future³. International agencies are beginning to discuss structural reforms of regulatory systems to develop smarter, more targeted regulation to match the potentially more varied innovation landscape of the 21st Century. It would be in the UK's interests to encourage and support such initiatives.

One concern related to research governance is whether the patent regimes as they apply to DNA continue to be conducive to life science innovation. For example in the patenting of a DNA sequence that has use in research but no immediate therapeutic or diagnostic value, the Nuffield Council on Bioethics has noted that there has been an increase in the number of patents asserting rights over DNA sequences in this category. Since the 1990's, researchers have used partial DNA sequence or expressed sequence tags (ESTs) as an aid to identifying genes. Granting patents over parts of genes means that these can be privately owned as research tools, excluding others from research to identify the genes themselves.

One component of the shift to more bottom-up, 'governance' based approaches to regulation and the provision of advice⁴ at regional levels, as shown by recent Innogen research is the importance of public-private collaborations and partnerships in Cambridge and Scotland for innovation and economic growth. These collaborations play an important role in building firm-based and policy-making capabilities and public policy can help to facilitate their formation and expansion⁵.

In what way is science and clinical policy decision making informed by social, ethical and legal considerations?

Social, ethical and legal considerations (advanced through consultations and advisory committees) reflect, and to some extent also determine, the balance of power between Publics (citizens and stakeholders), Policy-Makers (governance, regulation and the state) and Innovators (science and industry). Considerations such as human rights, informed consent, ownership, accessibility and confidentiality, contribute increasingly to the policy agenda for regulation of genomics/post-genomics research and innovation, alongside the need to ensure safety, quality and efficacy of new products and processes.

Thus, although scientific advice provides the main basis for legitimacy of policy decision making, there is also an increasingly important role for public consultation and engagement in informing such decisions. There are unresolved tensions between these two sources of authority for decision making, with outstanding questions about the quality of public consultations and the extent of use of their results. Such questions include: the appropriate timing, topic and format for a consultation; the expectations raised among those being consulted; how to deal with irreconcilable differences of opinion among those being consulted; and the extent to which the outcomes of a consultation should be allowed to over-ride scientific advice.

The Innogen Centre is making an important contribution to elaboration and evaluation of public engagement techniques, for example in relation to development of genetic databases, stem cell science and the development of related therapies, and in identifying, understanding and dealing with conflicting interests and values in decision making related to genomics and medicine. We are also working on risk governance of stem cell based therapies and synthetic biology research. Insights that have emerged so far from this research include:

- The need for different engagement approaches to deal with debates and discussion based on potentially conflicting interests (as in the case of patient groups) and those based on conflicting values or ideology (as for example with religious objections to human embryonic stem cell research and applications);
- The need to consider the circumstances under which it is democratically justified to allow the interests or values of one societal group to over-ride those of others.

Research and Scientific Development

Who is taking the lead in the consideration and co-ordination of research and the development of new technologies?

Research is mainly led by the research councils, at the UK level. Likewise regulatory and some financial matters are dealt by the UK Government. However, for the *development* of new technologies, regional innovation system thinking tends to dominate over national planning so that innovation and technology policies are increasingly developed and implemented at a regional level, based on local endowments. The promotion of entrepreneurial activities, private-public partnerships, public provision, intellectual property licensing, scientific training etc, are achieved by a mix of sometimes overlapping schemes promoted by both regional and national entities.

How does research in the UK compare internationally? How much collaboration is there?

The UK research base is one of the most effective worldwide, based on the number of published and cited papers per pound invested in fundamental research.

There are numerous international collaborations for research in genomics and biotechnology. For example, the Biotechnology and Biological Sciences Research Council (BBSRC) collaborates with scientists around the world, promoting international links at both policy and scientific levels to make the most of new scientific opportunities and to explore ways of sharing knowledge and technology. Also the International Science and Innovation Network (SIN) of the Foreign and Commonwealth Office collaborates with a number of public and private actors, ensuring that the UK retains its position at the cutting edge of world science.

The Economic and Social Research Council (ESRC) has supported the largest co-ordinated research investment internationally, that studies socio-economic aspects of genomics-related development. It also supports international collaborations, for example with a similar initiative in the Netherlands, as well as with Canada, the USA, Africa, India, China and Argentina.

Data Use and Interpretation

Is genomic information published etc in a useful way? Should there be a common public database? If so, who should fund and have responsibility?

The reluctance to publish negative results contributes to a perception of secrecy rather than transparency and openness and more needs to be done to encourage the sharing of negative as well as positive results, e.g. of clinical trials.

In the context of a common public database, the centralisation of electronic medical records is currently under way and we should consider what lessons can be learned from this that are relevant to public trust and understanding. Funding should come from a centralised impartial source and control should be by a national independent organisation, given recent breaches of

security of government held data and the possible effect on public perception of the security of a government controlled public DNA database. A body akin to the National Blood Transfusion Service has been proposed as a trustworthy institution to take on this role.

Considering the international implications of sharing of data and samples, there is a lack of harmonisation in the way collections are procured, held and used, but the governance mechanisms for sharing information from large-scale collections have not yet been developed. Organisations such as Public Population Project in Genomics (P3G) are attempting to find solutions for this problem.

What are the implications of the generation and storage of genome data on personal data security and privacy, and on its potential use or abuse in employment and insurance? How should these be addressed?

In the context of insurance, procedures are already in place to prevent individuals who participate in clinical research from being discriminated against by insurance companies, as part of the voluntary moratorium agreed by the companies. Insurers have stated that applicants do not have to divulge genetic information derived from a clinical study so that denial of coverage or loading of the premium are not yet valid concerns. However the moratorium will end in 2011 and this protection may not continue. Genomic information does have implications for data security and privacy and these need to be addressed by policymakers and regulators to ensure sufficient public safeguards without inhibiting scientific advance.

Translation

Who is responsible for translation to clinical practice?

For many areas of genomic medicine, industry is crucial to the successful translation of new therapies and discoveries to clinical practice, and cross sectoral collaboration is increasingly taking place, between universities/public sector research organisations, commercial companies and health services. In the past the perception has been that commercial organisations received the majority of the benefit from public sector alliances, but this is beginning to change. New large scale collaborations are being developed where the public sector is a key investor, such as the Scottish Translational Medicine Research Collaboration (TMRC) and here the challenge is to ensure that benefits accrue to all partners. Because translational medicine, by definition, involves many areas of science, and a range of institutions and commercial organisations, a variety of different policy and investment initiatives is needed to extract maximum value.

Regulators and policymakers also have a key role to ensure that translation to clinical practice is supported, where necessary, by enabling and well-conceived regulation, for example making it easier to set up a clinical trial (single rather than multiple site licenses, as is being developed in Scotland) would facilitate translation.

Given the pace of technological advance, how “future-proof” is healthcare investment in this area?

No investment is future proof, especially in such a complex area as genomics, where regulation, investment and success can be capricious. The key is to balance or share the risk, partly through the involvement of the commercial sector. Furthermore, investment, policy and regulation must be adaptive to changes in scientific knowledge, technological advance and unforeseen changes in the socio-political environment. Investment in broad based initiatives and fostering adaptive institutional change are likely to be more ‘future-proof’ than investment in a single technology or therapy area.

The increasing use of Foresight techniques in policy and government circles arises in part from an attempt to ‘future-proof’ public investments in genomic technologies. However, long experience should have made our human limitations in such areas abundantly clear⁶. Predictions about the speed of development of an innovation are generally wrong: some take

much longer than predicted, some happen surprisingly fast, and others never materialise. However, in a medical context regulatory requirements will usually mean a 10-15 year development time scale and this adds greatly to uncertainty about the economic environment and future public and stakeholder attitudes and needs. Thus, attempting to predict future public desires and needs, alongside attempting to predict health technology outcomes multiplies the scale of uncertainty.

Predictions based on a sound understanding of the *interactions* between science/innovation, regulation/governance and public needs and desires, are likely to be less uncertain than those based on any one of those areas in isolation. However, a more robust long term strategy is likely to be one that ensures an open science and innovation environment and avoids fore-closing on any one area of innovation based on simplistic interpretations of what is likely in future to be possible technologically or desirable from the public point of view.

Biomarkers and Epidemiology

What impact will genomic data have on data emerging from projects such as UK Biobank, GS and other biobanks?

This question is complex and multi-faceted. Results from research based DNA databases are not yet in a position to give individual, or even group-based, feedback about genetic propensity to inherit a disease.

There is an increasing need for regulation to ensure that public confidence in these databases is safeguarded, rather than relying on volunteers' acceptance of consent conditions. Current DNA database policy is based on open consent whereby any use of the contribution cannot be precisely stated but will be medically and ethically approved. However, the ethical safeguard providing the option for withdrawal of a sample can only apply while the donor of the sample is alive. Greater clarity is needed to safeguard both the scientific potential of the database and the requirements of individual donors.

There is some concern in medical and scientific circles that commercial involvement in developing DNA databases and in using the insights they provide to develop products will lead to public opposition to the databases themselves. However, our research has shown that accommodation can be achieved by mobilisation of a grass-roots solution known as 'benefit-sharing' or 'profit pay-off', backed up by a pragmatic legal framework which responds seriously to public concerns⁷.

References

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