THE HUMAN GENETICS COMMISSION

The UK Regulatory and Advisory Framework for Human Genetics

March 2000

CONTENTS

Introduction

This document provides brief descriptions of the main bodies in the UK regulatory and advisory framework for human genetics, including current developments in their work where this is relevant to HGC. These bodies are also listed in the Map of the UK Regulatory and Advisory Framework for Human Genetics (Annex A).

1. Human genetics bodies (non-statutory advisory)

Former Advisory Committee on Genetic Testing (ACGT)

ACGT was established in 1996 as part of the response to the 1995 Select Committee on Science and Technology report on Human Genetics. It was chaired by the Rev. Dr John Polkinghorne and considered and advised UK Health Ministers on developments in genetic testing, the ethical, social and scientific aspects, and requirements to be met by suppliers of genetic testing services. It considered the use, or potential use, of tests both within clinical practice and those supplied direct to the public. The work of this committee has now been subsumed into HGC but information on its previous activities can be found on its web pages.

Cross-membership with HGC

- Reverend Dr John Polkinghorne (former ACGT Chair)
- Professor John Durant (former ACGT Member)
- Dr Hilary Harris (former ACGT Member)
- Professor John Harris (former ACGT Member)
- Professor Alexander McCall Smith (former ACGT Member)
- Mr Philip Webb (former ACGT Member)

Gene Therapy Advisory Committee (GTAC)

Establishment of the committee

In 1989 the Government established the Committee on the Ethics of Gene Therapy (CEGT) which was tasked with drawing up ethical guidance on gene therapy. The Committee reported in 1992 and amongst its key recommendations was that a new body should be established to oversee gene therapy research in the UK and this lead to the establishment of GTAC in 1993. Before any UK gene therapy study can recruit patients the investigators must obtain approval from GTAC. GTAC is independent of, but will work closely with, the HGC.

Terms of reference

- To consider and advise on the acceptability of proposals for gene therapy research on human subjects, on ethical grounds, taking account of the scientific merits of the proposals and the potential benefits and risks.

- To work with other agencies which have responsibilities in this field, including local research ethics committees and agencies which have statutory responsibilities – the Medicines Control Agency, the Health and Safety Executive, and the Department of the Environment, Transport and the Regions.

- To provide advice to UK Health Ministers on developments in gene therapy research and their implications.

The NETS sub-group

In 1997 GTAC established a sub-group on New and Emerging Technologies (NETS) whose function is to report to GTAC on any new technologies that may have implications for gene therapy research.

Ongoing and future work

GTAC meets 5 times a year to consider proposals for gene therapy research. The Committee also receives requests to amend existing protocols throughout the year and monitors ongoing projects and maintains working relationships with outside bodies with an interest in gene therapy. Details of this work (and GTAC's wider activities) are published in their annual reports and on their web pages.

There have been two GTAC open workshops on gene therapy research. A third is planned for the summer of 2000.

NETS are currently reviewing new technologies with a view to updating their Guidance Notes. Their report should be completed by spring 2000.

GTAC are in the final stages of setting up a system for monitoring the long-term health of gene therapy patients. The project has been approved by the appropriate ethics committee and should be operational by May 2000.

Publications

- GTAC Annual Reports (1993-1999)
- Guidance on Making Proposals to Conduct Gene Therapy Research on Human Subjects (1994)
- Proceedings of workshop entitled "Gene Therapy, Myth and Reality" (1997)
- Proceedings of workshop entitled "Hitting the Target with Gene Therapy" (1998)
- Report on the Potential use of Gene Therapy In Utero (1998)
- Writing Information Leaflets for Patients Participating in Gene Therapy Research (1994)

Cross-membership with HGC

- Professor Norman Nevin (Chair GTAC)
- Professor Elizabeth Anionwu (GTAC Member)
- Professor John Burn (GTAC Member)

Genetics and Insurance Committee (GAIC)

Background

The establishment of GAIC on 12 April 1999 fulfilled the Government's commitment to establish an independent review body, to evaluate the scientific and actuarial evidence presented in support of the use of specific genetic tests for insurance products. This was made in response to the Human Genetics Advisory Commission (HGAC) report on the Implications of Genetic Testing for the Insurance Industry, issued in December 1998.

Status and terms of reference

GAIC is a non-statutory Advisory Non-Departmental Public Body and has a UK-wide remit:

- to develop and publish criteria for the evaluation of specific genetic tests, their application to particular conditions and their reliability and relevance to particular types of insurance;
- to evaluate particular tests against those criteria and promulgate its findings; and
- to report to Health, Treasury and Department of Trade and Industry Ministers, on proposals received by GAIC from insurance providers and the subsequent level of compliance by the industry with the recommendations of GAIC.

Current work

GAIC have developed an application form for use by the insurance industry to seek approval to use genetic test results for insurance risk assessment. The accompanying notes set out the criteria they will use to evaluate the use of specific genetic test results for specific insurance purposes. GAIC is carrying out a public consultation on the documents to ensure that the criteria are acceptable to all relevant stakeholders (patient's associations, genetics practitioners and academics, insurers and actuaries etc). The consultation ends on 17 March 2000.

Future work

GAIC will review comments from the Consultation at their meeting on 17 April 2000. They aim to evaluate all ten tests (covering seven conditions) currently being used by insurance companies (endorsed by the Association of British Insurers) by the end of 2000. Thereafter GAIC will evaluate the genetic tests that the insurance industry would like to use as they come on line. GAIC are to develop a system to monitor the use of genetic test results and compliance with their recommendations.

Cross-membership with HGC

- Professor John Durant (Chair of GAIC)

Former Advisory Group on Scientific Advances in Genetics (AGSAG)

The former AGSAG (a joint venture between the Department of Health and the Medical Research Council) met twice in 1998/99 before being subsumed into HGC.

AGSAG has now been dissolved and will not take on further work. However, laboratory services for testing for genetic disorders had been identified as an important issue for discussion and a paper was commissioned from Professor Veronica van Heyningen. The NHS Executive Board discussed genetics as a strategic issue at its meeting in April 1999. An expert working group, the Working Group on Laboratory Services for Genetics, was convened to scope the short and long-term issues and make recommendations for resolving current problems in service delivery and planning for anticipated future pressures.

The working group on laboratory services met for the first time in July 1999 and aims to report to HGC within one year.

Terms of reference (of the working group)

- To document the current extent of genetic testing (biochemical, cyto and molecular) within the NHS, in terms of activity and cost within mainstream services and research projects, as applied to patient diagnosis and management.

- To identify those tests and technologies likely to become available within the next 5, 10 and 20 years and to consider the potential organisational and financial implications for NHS services of the introduction of these technologies.

- To advise where barriers to testing exist, including technical, organisational, education and training needs and resource constraints. To consider the impact of biotechnology patents on service provision.

- To develop models of service delivery in the context of health needs for NHS genetic testing.

- To report with recommendations for action to the NHS Executive Board and the Human Genetics Commission.

Ongoing work

The working group will meet about five times in the year. Three subgroups have been established to take forward the detailed aspects of the work in the following areas:

- **Monogenic disorders**
  To consider barriers to testing, need for testing and possible models for service delivery testing for rare genetic disorders.

- **Technical issues**
  To think about the evolving technologies and how the NHS is to deal with them. This includes work to list and describe the capabilities and advantages/disadvantages of new technologies in existence and on the way in relation to high throughput testing for genetics (both testing for known mutations and screening for unknown mutations). A small workshop for invited experts (NHS, academic and commercial) took place in November 1999.

- **Future scope of tests**
  The two most likely situations for expanding the scope and volume of genetic testing are predispositional screening and targeted drug therapy. This group will work on:
  - defining the type of tests that may be available;
  - assessing the usefulness of the tests (positive predictive power);
  - how services for tests might be planned and delivered; and
  - the impact on lifestyle of these tests – the requirements for influencing behaviour and the research gaps in knowing how to achieve this.

Former Human Genetics Advisory Commission (HGAC)

The former HGAC was established in December 1996 in response to a House of Commons Select Committee report. It provided independent advice to UK health and industry ministers on issues arising from developments in human genetics that have social, ethical and/or economic consequences. It also advised on ways to build public understanding of the new genetics. HGAC has now closed and its responsibilities have passed to the Human Genetics Commission.

HGAC's role was facilitative and advisory. The topics it addressed and produced reports on were insurance and genetic testing, employment and genetic testing, and cloning (jointly with the Human Fertilisation and Embryology Authority). HGAC held consultations on these topics and also held a national conference and local consultations.

Information about HGAC and its reports are still available on its website.

Cross-membership with HGC

- Professor Norman Nevin (former HGAC Member)
- Revd Dr John Polkinghorne (former HGAC Member)

2. Principal health-related bodies in the advisory and regulatory framework

2.1 Statutory bodies

Human Fertilisation and Embryology Authority (HFEA)

Background

The HFEA was established by the Human Fertilisation and Embryology Act 1990 following the Warnock Report's recommendations. Its principal tasks are to license and monitor clinics that carry out *in vitro* fertilisation (IVF), donor insemination (DI) and human embryo research. The HFEA also regulates the storage of gametes (sperm and eggs) and embryos. In addition, the HFEA produces a Code of Practice that gives guidance to licensed clinics; keeps a register about donors, treatments and children born from those treatments; provides advice and information to patients, donors and clinics; and keeps under review information about human embryos, the provision of treatment services and other activities governed by the 1990 Act. It advises the Secretary of State if asked about such matters. The Authority's 21 Members are appointed by UK Health Ministers.

Current activities

The HFEA keeps scientific developments in its area under close and continual review, and considers these both in terms of safety and ethics. Of relevance to HGC is the current consultation on pre-implantation genetic diagnosis A consultation document was published jointly with ACGT in November 1999 and responses are due by 31 March 2000.

Cross-membership with HGC

- Ruth Deech (HFEA Chair)

Committee on Safety of Medicines (CSM)

The CSM is an independent statutory advisory body established under the Medicines Act (Section 4) which advises the UK Licensing Authority (Government Health Ministers) on the quality, efficacy and safety of medicines in order to ensure that appropriate public health standards are met and maintained.

An External Advisory Panel established by the CSM and the Medicines Control Agency (MCA) jointly, provides additional expertise in areas not represented on the main committee. A sub-committee (one of three), the Biological Sub-Committee, advises the main committee on the quality (in relation to efficacy) of medicines of biological origin including vaccines, blood products and products derived from biotechnological sources.

Terms of reference

- To provide advice to the Licensing Authority on whether new products (new active substances) submitted to the UK MCA should be granted a marketing authorisation. These responsibilities require close collaboration with the MCA's Licensing Division:
  - on applications for a Marketing Authorisation for generic biological products;
  - on application for Clinical Trials Certificates.

- To monitor the safety of marketed medicines, in close association with the MCA's Post-Licensing Division to ensure that medicines meet acceptable standards of safety and efficacy.

2.2 Interim non-statutory body

The UK Xenotransplantation Interim Regulatory Authority (UKXIRA)

UKXIRA acts as the focal point for xenotransplantation (animal to human transplants) activity in the UK. The Authority acts on a non-statutory basis, offering advice to Government on all aspects of xenotransplantation including the acceptability of specific applications to undertake clinical trials involving xenotransplant procedures.

The main link to genetics is the genetic modification of source animals. Pigs are currently considered the most likely source animal for organs and tissue. The modification involves adding an extra gene to the genetic make-up of the pigs that allows them to produce a human protein on the surface of their organs. This ensures that, post-transplant, the recipients' immune system will not automatically reject the organ as foreign. Applications to the UKXIRA may (depending on the procedure involved) also require approval from GTAC.

2.3 Non-statutory advisory bodies

UK National Screening Committee (NSC)

The UK NSC was set up to address the uncontrolled introduction of screening programmes that were of variable quality, questionable clinical and cost effectiveness and which showed variations across the country. The NSC advises Ministers, the devolved Assemblies and the Scottish Parliament on the case for implementing new programmes and the case for continuing, modifying or withdrawing existing ones. New programmes are assessed against a set of internationally recognised criteria covering the test, clinical and cost effectiveness, treatment options and programme management.

The NSC has two specialist sub-groups dealing with antenatal and childhood screening.

The NSC will be considering genetic screening in the context of its population screening programmes. It will be considering the contribution that family history or genetic tests can make to increasing the sensitivity and specificity of screening for particular diseases. Its findings will be reported to HGC.

Managing Clinical Interventions Group (MCIG)

An internal cross-DH/NHS body which advises UK Health Ministers through the NHS Executive Board.

Terms of reference

- To identify, in consultation with all relevant parties, the requirements of the NHS for research and evidence-based guidance to inform and guide clinical practice, in particular but not exclusively those arising out of clinical innovation.

- To advise Ministers through the Executive Board and the National Assembly for Wales on the most appropriate means of meeting those requirements in each case, including referral to the NHS R&D programme and/or the National Institute for Clinical Excellence.

- In determining the relative priority to be given to individual topics, to bear in mind:
  - Ministerial priorities as set out in National Service Frameworks, the NHS priorities guidance and other places; and
  - the intrinsic significance of particular conditions and health needs.

The UK Foresight Programme

The UK Foresight Programme is about developing visions of the future – identifying market drivers, threats and opportunities that can be used to inform the decisions that need to be taken today. Foresight brings panels of people together who understand the possibilities opened up by advances in science, engineering and technology with people who understand markets, consumer needs and delivery.

Three thematic and ten sectoral Foresight panels pool knowledge and ideas about future possibilities, needs and requirements, matching these visions to UK circumstances, strengths and potential capabilities.

Thematic panels

- Ageing population
- Crime prevention
- Manufacturing 2020

Sectoral panels

- Built environment and transport
- Chemicals
- Defence, aerospace and systems
- Energy and natural environment
- Financial services
- Food chain and crops for industry
- Healthcare
- Information, communications and media
- Materials
- Retail and consumer services

Healthcare panel

The Healthcare panel is considering, with a 20-year perspective, the future evolution of health care. This includes exploring the potential of new technologies and their likely impact on competitiveness and healthcare delivery, integrating public expectations, healthcare organisation and SET issues. The panel has established a series of task forces, grouped under three inter-related headings:

People
- Public and patients
- National, European and global milieu
- Older people (with Ageing Population Panel)

Organisation
- Organisation and delivery of healthcare
- Information

Technology
- Delivering the promise of the human genome
- Pharmaceuticals, biotechnology and medical devices
- Neuropsychiatric health
- Transplantation

The Foresight website has more information about the work of the Healthcare Panel and within this, the Foresight Knowledge Pool allows you to contribute your views and link to related sites.

2.4 Special Health Authority

National Institute for Clinical Excellence (NICE)

NICE is a Special Health Authority, which was brought into being on 1 April 1999. Working with the NHS, NICE will systematically appraise the clinical benefits and costs of selected new and established health interventions. It will offer clinicians and managers clear guidance on which treatments work best for patients and which do not. This guidance will support everyone in the NHS and will be available for patients and the public.

NICE will assess the evidence of all the clinical benefits of an intervention in the broadest sense. This will include the impact on quality of life as well as likely effects on mortality and estimates of the associated costs. In the light of the evidence, NICE will reach a judgement as to whether, on balance, the intervention can be recommended as a cost-effective use of NHS resources in general, or for specific indications, or for defined subgroups of patients. Where there is already an intervention for a condition, NICE will estimate the net impact on both costs and benefits of the new intervention.

NICE's scope includes:

- pharmaceuticals;
- medical devices;
- diagnostic techniques;
- procedures; and
- health promotion.

The Department of Health and the National Assembly for Wales will select technologies for appraisal based on one or more of the following criteria:

- Is the technology likely to result in a significant health benefit, taken across the NHS as a whole, if given to all patients for whom it is indicated?
- Is the technology likely to result in a significant impact on other health-related government policies (eg reduction in health inequalities)?

- Is the technology likely to have a significant impact on NHS resources (financial or other) if given to all patients for whom it is indicated?

- Is NICE likely to be able to add value by issuing national guidance?

For new technologies under development, manufacturers or sponsors may normally expect advance warning (two years or longer) that their technologies are likely to be referred to NICE. For new technologies, formal notice of referral will usually occur one year before anticipated use by the NHS.

NICE has issued a forward work plan up to July 2000. None of the technologies proposed for appraisal in this period are human genetics/biotechnological ones.

2.5 Agencies

Medicines Control Agency (MCA)

The primary objective of the Medicines Control Agency (MCA) is to safeguard public health in relation to medicines administered to humans. This is achieved largely through a system of licensing and inspection followed by monitoring of medicines after they have been licensed. The MCA is the executive body for the Licensing Authority (LA) and has delegated power from it to administer licensing, inspection and post-licensing procedures. These activities have a statutory basis in UK[1] and European[2] law. Within the EU, Marketing Authorisations may be granted either by the national competent authority (UK LA) or by the European Commission, according to the nature of the product.

Genetic material for therapeutic use

Genetic material for therapeutic use is a medicinal product and is therefore regulated by legislation that applies to medicines. Any medicine, (i) derived from DNA, (ii) produced by hybridoma technology or (iii) that is a monoclonal antibody, which includes any gene therapy product, requires a marketing authorisation via the European licensing procedure; no national licences for this type of product are allowed in the European Union. The manufacturer of the product must have a manufacturing authorisation or, if outside the EU, must be approved or the marketing authorisation and the product imported through an authorisation holder in the EU. So far no gene therapy product has been granted a marketing authorisation. Guidance notes[3] on the development of these products have been prepared by the Committee on Proprietary Medicinal Products (CPMP) of the European Agency for the Evaluation of Medicinal Products(EMEA).

Clinical trials of gene therapy products require statutory[4] approval, which is obtained from the MCA and no manufacturing authorisation is required. Clinical trials of medicines are regulated nationally; however there is an EC directive on clinical trials[5] under discussion. Applications that require difficult risk/benefit evaluations are submitted to the Committee on Safety of Medicines (CSM) for advice.

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[1] The Medicines Act 1968, The Medicines (Application for Grant of Product Licenses – Products for Human Use) Regulations 1993 S.I. 1999/2538, The Medicines (Standard Provisions for Licenses and Certificates) Amendment (No2 Regulations 1993 SI 1993/2539.

[2] Directive 65/65 EEC, 75/318/EEC, 75/319/EEC, and Regulations (EEC) 2309/93, 540/95, 541/95 and 542/95.

[3] Note for Guidance on the quality, pre-clinical and clinical aspects of gene therapy transfer medicinal products: CPMP/5863/93 (draft out for consultation).

[4] In accordance with the Medicines Act 1968.

[5] Amended proposal for a Directive of the European Parliament and of the Council on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use. COM(99) 193 final (COD 97/0197).

In granting permission to conduct a clinical trial for a medicine the Licensing Authority makes it a condition that the sponsor must report adverse drug reactions (ADRs) to the MCA. By monitoring and analysing these reports assessors can identify safety signals that may suggest the need to change the design of the clinical trial protocol or even to stop the clinical trial. ADR reports from clinical trials are entered onto the Adverse Drug Reaction On-line Information Tracking (ADROIT) database, access to which is strictly controlled. The data is assessed and can be analysed for safety signals using database searches.

Good clinical practice in clinical trials

Good Clinical Practice (GCP) is a set of internationally recognised ethical and scientific quality requirements that must be observed for designing, conducting, recording and reporting clinical trials to support a marketing authorisation (licence). These standards are agreed internationally[6]. Based on this guideline the MCA established an inspectorate for Good Clinical Practice (GCP) in 1996 and started voluntary inspections for compliance with GCP in 1997. The draft European Directive[6], which is currently under discussion would bring compliance with GCP within UK legislation and provide the legal basis for mandatory inspections.

Outside clinical trials legislation, EC Directives and UK Regulations allow supply of an unlicensed medicine to a doctor or dentist, (or for use in a registered pharmacy, hospital or health centre under the supervision of a pharmacist). This is in response to the doctor or dentist's order and for use by their individual patients on their direct personal responsibility. A doctor prescribing an unlicensed product or a product outside its licensed indications does so entirely on his own responsibility.

Other regulatory bodies

The MCA works closely with Public Health Division, which has responsibility for research ethics and for the Gene Therapy Advisory Committee (GTAC), and with the Health Services Directorate, which has responsibility for the UK Xenotransplantation Interim Regulatory Authority (UKXIRA). The timing of the decisions of these specialist ethics committees and the MCA are usually co-ordinated because the MCA has responsibility for statutory approval of clinical trials in the UK.

Medical Devices Agency (MDA)

The MDA is an executive agency of the Department of Health with responsibility, on behalf of the Secretary of State for Health, for ensuring that medical devices meet appropriate standards of safety, quality and performance. In vitro diagnostic medical devices (IVDs) fall within the definition of a medical device[7]. Genetic testing devices are a category of IVDs.

At present in the UK there are no statutory controls dealing specifically with IVDs, including genetic testing devices. MDA operates an Adverse Incident reporting system in which users of IVDs, including genetic testing devices, are encouraged to report to MDA problems they encounter in the performance of a device. Where appropriate, MDA carries out an investigation in collaboration with the user and the supplier. If necessary an advisory notice may be issued to the Health Service and the device may be removed from the market.

[6] Published in an International Conference on Harmonisation guideline: 'Note for guidance on Good Clinical Practice' (ICH E6)(CPMP/ICH/135/95), which came into operation in the EU in January 1997.

[7] The Medical Device Directive (93/42/EEC) L169, 12 July 1993.

A recently agreed European Directive on IVDs[8] will for the first time impose statutory controls on IVDs being marketed within the European Union. This will begin to be implemented throughout the Europe Union during the coming year. The Directive lays down harmonising rules designed to ensure the safety and performance of IVDs. It will become illegal not to comply with the requirements of the IVD Directive towards the end of 2003. MDA will have responsibility for ensuring that the essential requirements of this Directive are complied with in the UK. Genetic testing devices that are sold or supplied anywhere within the European Union will be regulated under the IVD Directive.

2.6 Non-Governmental

Medical Research Council (MRC)

Background

The Medical Research Council is a UK national body set up by Royal Charter. In summary, the Council's mission is:

- To encourage and support high-quality research with the aim of maintaining and improving human health.
- To train skilled people, and to advance and disseminate knowledge and technology with the aim of meeting national needs in terms of health, quality of life and economic competitiveness.
- To promote public engagement with medical research.

MRC receives the majority of its funding from the Government, via the Office of Science and Technology, which is part of the Department of Trade and Industry. It funds research both via grants to universities and teaching hospitals and in its own (more than 40) Institutes and Units, several of which are involved in genetics research.

MRC invests over £ 60 million each year in basic and clinical genetics research and training, and a substantial amount of our work in other areas builds on genetic approaches.

MRC plays an active role in developing and publicising guidelines on the ethical conduct of biomedical research, and most recently published guidance on DNA and tissue collections. Genetics is also the highest priority issue in MRC's substantial programme of public communications and consultation work.

Current activities

MRC has received significant additional funding from the Government's Comprehensive Spending Review to boost its already large investment in genetics research, in order to promote the translation of knowledge of the human genome sequence into benefits for public health and healthcare. It has funded a new Functional Genetics Unit, focussing on research into the genetic basis of neurological disease using model organisms, and is planning an initiative to develop large collections of well characterised human DNA samples for research to identify genes involved in common multi-factorial diseases. A call for proposals to make collections of samples from case series and related controls will be issued soon. A large prospective cohort study for research on the interaction between genetic and environmental risk factors is also being planned jointly with the Wellcome Trust. A public consultation exercise is planned, co-ordinated with the Wellcome Trust,

[8] The In-Vitro Diagnostic Medical Device Directive (98/79/EC) L331, 7 December 1998.

to assess the public acceptability of the proposed research. High-throughput genotyping facilities and sophisticated methodology for analysis will be required to obtain maximum information from these collections, and MRC plans to fund an evaluation of genotyping technology, database systems, and statistical analysis methods.

MRC is convening a committee, chaired by the Lord Patel, to advise Council on developments in genetics and other areas that have implications for public health and the health service. The committee will also work to facilitate close interaction between the MRC and HGC.

Concordat Agreement

A partnership exists between UK Health Departments and the MRC as set out in the Concordat agreement. The aims of this partnership are:

- To ensure co-ordination in the missions and strategic planning of the MRC and the Health Departments, and that their research activities complement one another.

- To ensure that Health Department policies and priorities are informed by scientific advances and opportunities, and that Health Department research needs are understood and addressed by the MRC.

- To ensure that the NHS and public health perspectives are understood and taken account of by the MRC in decisions on research funding, and to ensure that the needs of MRC research for NHS support are understood and addressed by the Health Departments.

Nuffield Council on Bioethics

Background

The Nuffield Council on Bioethics, chaired by Professor Ian Kennedy, is an independent body established by the Trustees of the Nuffield Foundation in 1991 to consider the ethical issues arising from developments in medicine and biology. The Council is funded jointly by the Nuffield Foundation, the Wellcome Trust and the Medical Research Council.

Terms of reference

- To identify and define ethical questions raised by recent advances in biological and medical research in order to respond to, and to anticipate, public concern.

- To make arrangements for examining and report on such questions with a view to promoting public understanding and discussion; this may lead, where needed, to the formulation of new guidelines by the appropriate regulatory or other body.

- In the light of the outcome of its work, to publish reports, and to make representations, as the Council may judge appropriate.

Once the Council has identified a major ethical issue for inquiry, it establishes a multidisciplinary Working Party with the relevant expertise to examine and report on it. It has published five major reports on the ethical issues arising from: genetic screening, ownership of tissue, xenotransplantation, genetics and mental disorders, and genetically modified crops. The full text of these publications can be found on the website. The Council also works with organisations such as theatre groups to raise awareness of the issues considered in its reports. In identifying issues for inquiry, the Council consults its sponsors and government. It also has maintained close contact

with other major national bodies, eg HFEA and HGAC, to ensure that there is no duplication of topics to be examined.

Current work

An international workshop on 'The Ethics of Clinical Research in Developing Countries' was held in February 1999. A paper based on the discussion which took place at the workshop was published in September, and is being followed by a full Working Party inquiry. The Working Party, chaired by Sir Kenneth Calman, began work in January 2000 and will report in mid-2001. A workshop on 'Ethical Issues Associated with Genetic Conditions Other Than Serious Medical Ones' was held in November and will also be followed by a Working Party starting next year.

The Wellcome Trust

The Wellcome Trust was established in 1936 on the death of Sir Henry Wellcome, whose will decreed that the share capital of his pharmaceutical company, the Wellcome Foundation, be vested in trustees to support research of a non-commercial nature. Through the public floatation of the Wellcome Foundation in 1986 and the acquisition of the Foundation by Glaxo in 1995, the Wellcome Trust has become the world's largest charity, with a current asset base of approximately £12 billion and an annual spend in excess of £400 million.

Mission statement

- To foster and promote research with the aim of improving human and animal health.

The Trust strives to achieve this goal by providing individual researchers of the highest quality across the biomedical sciences with the resources they need to pursue their subject through research grants, infrastructure awards and training opportunities. The Trust primarily funds research in the UK, but has a growing number of international programmes, which aim to strengthen research into major diseases in developing countries. In addition, the Trust takes proactive steps towards informing public debate on the social and ethical issues surrounding biomedical research and its medical application.

On-going projects in genetics

The Trust is a major player in the human genome sequencing project through its world-leading genome campus facility at Hinxton, Cambridgeshire. It is committed to ensuring that the human genome sequence data generated is immediately and freely available to the international research community.

The Trust plans an expansion of the campus at Hinxton to foster technology transfer and commercial development around the genome campus. It is currently in discussion about planning requirements with the South Cambridgeshire District Council.

The Trust has committed £100 million to a new initiative on functional genomics, bioinformatics and biological collections. It believes that this is the logical next step in the process of ensuring that the information generated from the human genome project is translated into improvements in health.

In a unique collaboration with the pharmaceutical industry, the Trust is playing a major part in characterising the variation across the human genome that effect disease susceptibility and drug responses through the SNP Consortium. This will help to initiate the new discipline of pharmacogenetics, or tailored treatments based on an individual's genetic make-up.

The Wellcome Trust Centre for Human Genetics at Oxford was set up in 1994 as a centre of excellence for research into the genetics of complex multi-factorial diseases. In 1999, the Centre moved into a new purpose built facility on the Churchill Hospital site, Oxford. Research at the Centre focuses on three main areas: neurogenetics, genetics of inflammation and immunity, and genetics of cardiovascular disease/metabolic syndrome. In addition, the facility houses a substantial collection of family human tissue samples and has become one of the major repositories of samples for genetics research.

The Trust supports work exploring the social, ethical and public policy implications of modern biomedical science. In 1999, a call for proposals was made for projects exploring issues surrounding the collection of human biomedical samples for DNA and other analysis and for projects exploring the potential implications of pharmacogenetics.

The Trust has informed the public debate on genetics and neuroscience issues and is involved in the following work.

- Social research to support debate and inform policy development. Examples have included:
  - public consultation on genetic testing specifically to inform the HFEA's public consultation on preimplantation genetic diagnosis;
  - a one year panel study on public attitudes to gene therapy; and
  - public consultation on the proposals for biomedical collections.

- Following on from the Trust's research study "Public Perspectives on Human Cloning" in 1998, the Trust hosted a policy seminar on cloning and stem cells on November 23, 1999.

- Initiatives to support debate in schools - specifically in science, personal, social and health and citizenship lessons. In collaboration with the Office of Science and Technology, the Trust is funding a three-year programme of plays for 14–19 year-olds, which explore social and ethical issues.

- Initiatives to support healthcare professionals.

- Initiatives to support public debate through the media and science centres.

Further information, reports (many of which are free), and subscriptions to a free quarterly magazine, "Wellcome News", can be obtained from the Trust's website.

3. Broader context

Food Standards Agency

Background

The main objective of the Food Standards Agency is to protect the public health in relation to food, but also to protect the wider food standards interests of consumers such as labelling.

Main functions

- Developing policies and advising Ministers and public authorities on food safety, other interests of consumers of food, and on animal feedingstuffs.
- Providing advice and information or assistance on food safety and standards matters and animal feedingstuffs to the general public or other interests.
- Obtaining and keeping under review information about food safety and related issues (eg by commissioning advice or undertaking or commissioning research).
- Carrying out observations of the safety or quality of food at any point in the food chain (including on the farm) for the purposes of informing its general policy work.
- Setting standards for enforcement, and monitoring the performance of food law enforcement authorities (this will mainly relate to local authorities).

Current work relevant to HGC

The Advisory Committee on Novel Foods and Processes and the Advisory Committee on Animal Feedingstuffs will report to the FSA. These committees have responsibility for assessing GM foods and GM animal feeds respectively. Ministers have already agreed that one of the first tasks for the FSA will be to review developments in GM foods to inform the FSA's broad policy in this matter.

The Agriculture and Environment Biotechnology Commission (AEBC)

The AEBC, along with the FSA, is the HGC's sister body. It has a remit to offer strategic advice to Government on biotechnology issues, which impact on agriculture and the environment. It will liaise closely with, but not duplicate, the work of the HGC and the FSA.

Terms of reference

- To keep under review current and possible future developments in biotechnology with actual or potential implications for agriculture and the environment.
- To advise Government on the ethical and social implications arising from these developments and their public acceptability.
- To consider and advise on any specific issues relating to relevant aspects of biotechnology as requested by Government.

As part of this the AEBC is expected to:

- identify any gaps in the regulatory and advisory framework;

- consider the wider implications of the lessons learned from individual cases requiring regulatory decision;

- advise on any changes which should be made to Government guidelines which regulatory bodies are required to follow; and

- make recommendations as to changes in the current structure of regulatory and advisory bodies.

In carrying out its work the Commission will seek to involve and consult stakeholders and the public on a regular basis on the issues which it is considering and operate in accordance with best practice for public bodies with regard to openness, transparency, accessibility, timeliness and exchange of information. In carrying out its work the Commission will take into account European and global developments.

Overview of regulation of biotechnology and human health

The regulatory roles of the Medicines Control Agency, Medical Devices Agency, UK Xenotransplantation Interim Regulatory Authority and Human Fertilisation and Embryology Authority have been explained, as have the non-statutory regulatory roles of the Gene Therapy Advisory Committee, the former Advisory Committee on Genetic Testing and the Genetics and Insurance Committee.

In addition, health-related research and production processes (e.g. fermentation to produce insulin) using genetically modified organisms in the laboratory, are regulated by the Health and Safety Executive under EU and UK legislation. If a medical biotechnology application were to involve the release of a GMO into the environment, the activity would be regulated by the Deliberate Release Regulations (see below).

Specific Legislation

The Medicines Act 1968 and the Medicines for Human Use (Marketing Authorisation etc.) Regulations 1994 gives effect in the UK to the European medicines legislation (Medicines Directive (65/65 EEC) and other medicines legislation.

The Medical Devices Directive 93/42/EEC and the Active Implantable Medical Devices Directive 90/385/EEC apply to medical devices. The In Vitro Medical Devices Directive (98/79/EC) which is currently being implemented into UK regulations will also apply to medical devices.

The Health Service Circular HSC1998/126 (Clinical Procedures involving Xenotransplantation) using powers under the NHS Act 1977 and the NHS and Community Care Act 1990, directs Health Authorities and NHS Trusts not to commission any treatments for patients involving the use of xenotransplantation procedures without the prior written approval of the Secretary of State for Health.

The Human Fertilisation and Embryology Act 1990 established the HFEA.

The Genetically Modified Organisms (Deliberate Release) Regulations 1992 apply to the deliberate release into the environment of genetically modified organisms, including those used in health applications.

The Genetically Modified Organisms (Contained Use) Regulations 1992, as amended in 1996 and 1998 apply to all use of GMOs within a contained use facility such as a laboratory or production facility – the majority of such usage is for healthcare biotechnology. The amended Directive 98/81/EC is currently being implemented into UK law.

Inter-governmental initiatives regarding the ethical implications of developments in human genetics

Council of Europe

The Council of Europe, a body set up in 1949 and now composed of 41 Member States, considers ethical issues in the field of biomedicine though a Steering Committee on Bioethics (CDBI), chaired by Dr Elaine Gadd (DH). The Convention on Human Rights and Biomedicine, which was opened for signature in 1997, contains over-arching principles in the field of genetics dealing with unjustified discrimination, predictive genetic testing and interventions on the human genome. Work to develop a Protocol on Human Genetics, which will extend and amplify the Convention principles in the field of genetics, began 18 months ago. It is probable that the Protocol will consider issues arising in the health field and in non-health fields such as employment, insurance and other settings. Dr Gadd of the Department of Health is a member of the Working Party developing the Protocol.

In May 1999, the Council of Europe held a conference on the ethical implications of biotechnology. One aim of that conference was to identify what actions it may be appropriate for the Council of Europe to take in this field. No decisions have yet been made concerning follow up to that conference.

The United Nations Education, Scientific and Cultural Organisation (UNESCO)

In 1997 (the year the UK rejoined) UNESCO adopted the “Universal Declaration on the Human Genome and Human Rights”. This is a document of moral, but not legal, force. The International Bioethics Committee of UNESCO, of which Professor McCall-Smith is a member, is charged with contributing to the dissemination of the principles set out in the Declaration, and further examination of the issues raised therein and by the evolution of the relevant technologies. The International Bioethics Committee met in October 1999, and considered follow up to the Declaration, but is not presently working on a follow up text. UNESCO also has an Inter-Governmental Committee, composed of Government representatives, which works in conjunction with the International Bioethics Committee. The Inter-Governmental Committee held its first meeting in October 1999.

Organisation for Economic Co-operation and Development (OECD)

OECD’s work in the field of ethics is limited, but its consideration of technical issues such as genetic testing and xenotransplantation may raise ethical issues, which may need to be addressed. In February 2000, OECD hosted a workshop on genetic testing sponsored by the UK and Austria. OECD includes representation from Europe, North America and Australasia.

World Health Organisation (WHO)

Although the World Health Assembly adopted a Resolution condemning human reproductive cloning, up until now WHO has had a very limited role in the field of biomedical ethics. In July 1999 a senior staff ethicist Professor Dan Wikler of the USA was appointed. Consideration is being given to the future role WHO should play in this field, but no firm conclusions are yet known.

European Union

The European Commission has no direct competence in biomedical ethics. The EC has an independent advisory group, the European Group on Ethics in Science and New Technologies, which produces opinions on general principles on issues in these fields. Dr Anne McLaren, who is also a member of the Human Fertilisation and Embryology Authority, represents the UK on this Group.

Devolution

Health departments

There are separate health departments for:

- England – Department of Health (DH);
- Scotland – Scottish Executive Health Department (SEHD);
- Wales – National Assembly for Wales; and
- Northern Ireland – Northern Ireland Executive Department of Health and Social Security and Public Safety (NIE). [The Northern Ireland Assembly has been suspended from 12 February 2000.]

Health care (including NHS services) is generally devolved under the devolution Acts for Scotland, Wales and Northern Ireland – ie responsibility is delegated to those territories.

Health legislation

The Department of Health is responsible for primary legislation (eg Acts) in England and Wales, secondary legislation (eg Regulations) in England, and UK-wide legislation on non-devolved matters in health. SEHD and NIE may introduce primary legislation and secondary legislation in their respective territories. The National Assembly for Wales can introduce secondary legislation for Wales.

Non-devolved ("reserved") matters

A number of issues, such as relations with the EU, which are more beneficially and effectively dealt with on a UK basis, are reserved to Westminster. Ethical and legal matters relating to human genetics, xenotransplantation, assisted conception and embryology and abortion policy, fall within the "reserved" category, as do policy on and regulation of medical devices (including genetic tests) and the control of medicines.

The Department of Health has responsibility for these matters, working in liaison with other Government Departments as appropriate and the health departments of the devolved administrations. However, the Northern Ireland Assembly will also be able to legislate on these matters with the approval of the Secretary of State, and subject to Westminster veto.

Implications for Human Genetics Commission

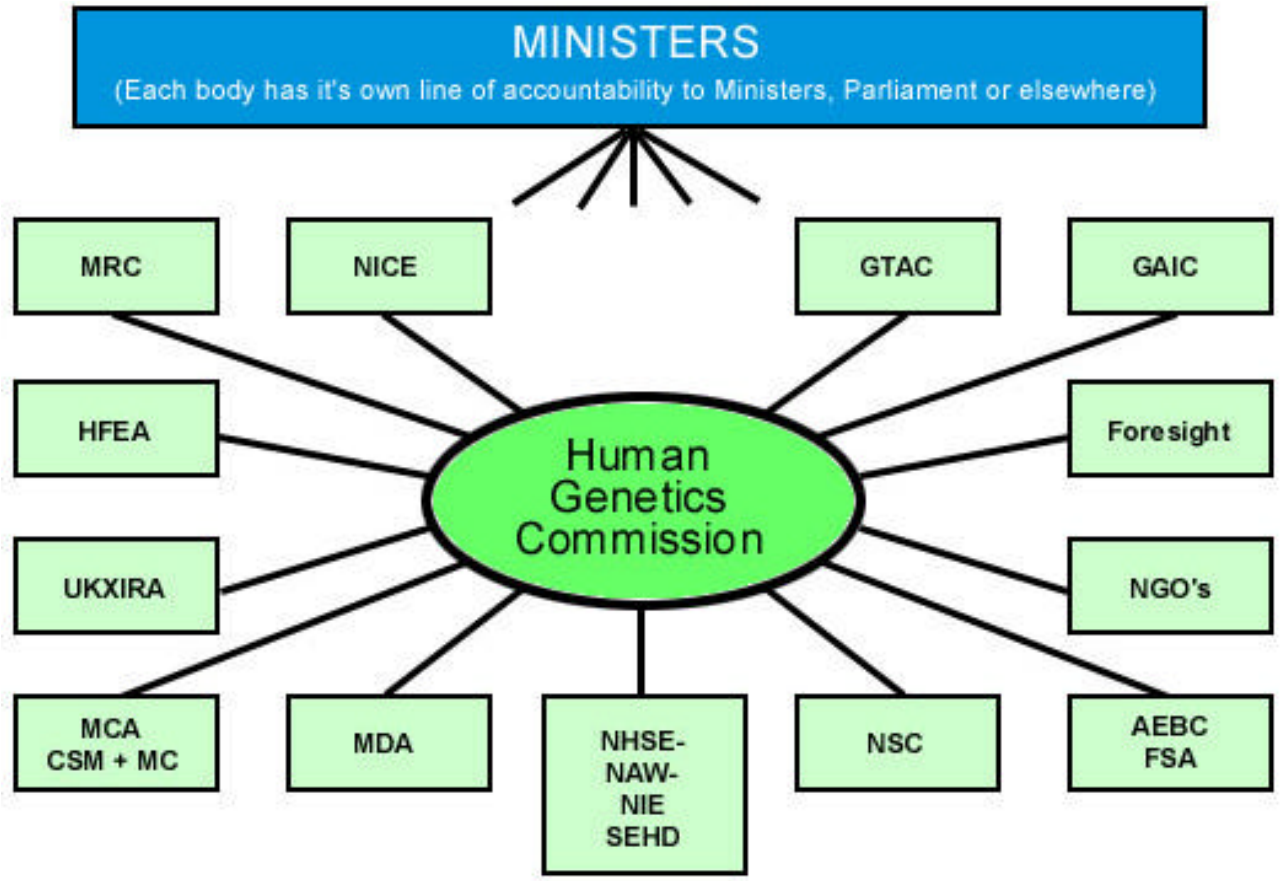
HGC is part-funded by all four health departments, and the Office of Science and Technology. If HGC makes any recommendations on reserved matters, such as (in general terms) the broad human genetics issues, the UK Government will respond from Westminster. If HGC makes any recommendations on devolved matters for Scotland, Wales or Northern Ireland, the Secretariat will

ensure that these are presented in reports so that they are clearly distinguished as matters for the relevant territories. Devolved administrations will then be able to respond to them as appropriate.

Human Genetics Commission Secretariat
March 2000

Annex A

Map of the UK Regulatory and Advisory Framework for Human Genetics



MRC - Medical Research Council

NICE - National Institute for Clinical Excellence

GTAC - Gene Therapy Advisory Committee

GAIC - Genetics And Insurance Committee

Foresight - Foresight (Health Care Panel)

NGOs - Non-Governmental Organisations (eg patient support/advocacy groups, Wellcome Trust, Nuffield Council on Bioethics)

AEBC - Agriculture and Environment Biotechnology Commission

FSA - Food Standards Agency

NSC - National Screening Committee

NHSE - NHS Executive (England)

NAW - National Assembly for Wales

SEHD - Scottish Executive Health Department

NIE - Northern Ireland Executive Department of Health and Social Security and Public Safety (The Northern Ireland Assembly has been suspended from 12 February 2000)

MDA - Medical Devices Agency

MCA - Medicines Control Agency

CSM+MC - Committee on the Safety of Medicines and Medicines Commission

UKXIRA - UK Xenotransplantation Interim Regulatory Authority

HFEA - Human Fertilisation and Embryology Authority