Annex A

Public consultation

1 The Working Party agreed at an early stage that steps should be taken to collect the views of interested parties on xenografts. Early in April 1995 about 130 organisations and individuals were contacted directly and a brief announcement and invitation to comment were carried in the Daily Telegraph, Guardian, Independent and The Times. Copies of the letters and information sent out are in Annex B.

2 The list of individuals and organisations contacted is in Annex C. Efforts were made to ensure that the following areas were represented: researchers and practitioners in the field; animal rights and animal welfare organisations; organisations lobbying on genetic engineering; commercial interests and religious groups. It was anticipated that professionals working in the field would alert the Working Party to current scientific developments and issues; other interest groups and members of the public would give a sense of the strength of feeling or indicate themes that might otherwise be missed. The list of submissions received is in Annex D.

3 Most submissions came from organisations or from individuals with an organisational affiliation. The largest group of responses came from universities, colleges, learned societies, research institutes and research councils. The next largest group was that representing religious organisations. Several submissions came from what can be broadly termed animal interest groups. A few submissions came from those with direct commercial interests in this field.

4 The response from members of the public was small. The Working Party received five submissions from individuals writing entirely in their private capacity as concerned citizens and a submission from a group of sixth-formers from Dalriada School, Ballymoney, Northern Ireland. In comments ranging from two or three sentences to half a paragraph, 26 pupils gave their individual reactions to the concept of a xenograft and the possibilities it offers. Almost all the issues discussed in this report were raised in some form across this set of responses. Reactions of amazement and initial doubt amongst these young people gave way, for the most part, to acceptance of something that might benefit humankind - though three responses ruled the idea of xenografts out completely. “That”, commented one member of the Working Party, “is as good an indication as any of the range of public opinion in this area.”
The submissions varied considerably. The Working Party is especially grateful for the several specially prepared submissions that were received, running to more than ten, and, in one case, almost forty pages. These represented many hours – sometimes, quite clearly, weeks – of work, and the Working Party is thankful for the public spirit that prompted such extensive effort. Several submissions took the form of a short letter making two or three points relevant to an area discussed in the report, or drawing attention to relevant research, legislation and policy development. Short as these letters were, they were often the result of considerable deliberation and consultation, and the Working Party was much helped by the way in which they gave an overview and a sense of what was at stake. The Working Party also received copies of academic work in progress: chapters from books, excerpts from dissertations, collections of published papers, and copies of articles. This response from specialists in different fields was an immeasurable help to the Working Party.

Despite the quality and usefulness of the material that emerged from the consultation, it cannot be taken as a representative indication of public opinion as a whole. The Working Party notes, for example, that the opinions have come more from researchers than from practitioners, and that health workers other than doctors have not responded at all. Interestingly, too, no practising transplant surgeons took the opportunity to express views. A patient perspective emerged very rarely: no patient group responded to the consultation. Beyond this, there are the caveats that often apply to an exercise such as this. The comments are drawn in the main from a more affluent, more educated and more privileged section of the population. Except in so far as the views of some religious leaders represent them, opinions of people from ethnic minority groups remain unexplored. Women's voices are in a small minority among the responses. The sixth-form group gave an important insight into views of young people, but again the bias is towards those from the more privileged sections of the community.

The Working Party paid careful attention to the results of the consultation and the submissions were discussed at Working Party meetings. It served as a guide to the range of views that is to be found among interested parties and members of the public. Thus, the public consultation formed an important component of the Working Party's consideration of the issues and the Working Party is grateful to all those who took the trouble to respond.
Annex B

Consultation letters and information pack

Consultation letter to professional bodies

The Nuffield Council on Bioethics is described in the enclosed leaflet. The Council has set up a working party to investigate the issues surrounding the present and proposed uses of animal cells, tissues and organs in the treatment of human disease. I enclose the working party’s terms of reference and a list of the members.

The issues raised by this new technology are numerous and include at least: the use and genetic modification of animals in principle; the effects on patients, medical practice and the health care system; and other institutional implications.

I am writing to ask if you wish to comment on any aspect of this study. If so, your comments should be addressed to:

   Xenografts
   Nuffield Council on Bioethics
   28 Bedford Square
   London WC1B 3EG

The published report of the study may well include a list of those who have commented. For whatever reason if you wish not to be included in such a list, please make this clear in your comments.

It will be most useful if you let me have your comments in writing by 19 May 1995, but please do not hesitate to contact me if this will be difficult or if you have any questions,

For the Secretariat of the Working Party on Xenografts
Letter sent to those replying to newspaper advertisements

Thank you for your enquiry.

The issues surrounding the present and proposed uses of animal cells, tissues and organs in the treatment of human disease are numerous, and the Nuffield Council on Bioethics has set up a Working Party to investigate and report on those issues by the end of the year. Part of this process includes gathering public views and the Council would be grateful for any comments that you might like to make.

As background information I have enclosed:

- a leaflet describing the work of the Nuffield Council on Bioethics
- the terms of reference for the study
- some additional guidance from the Council to the Working Party
- a list of the members of the Working Party
- the text of an article from New Scientist, The organ factory of the future, which is a very readable overview of xenografts.¹

The published report of the study may well include a list of those who have commented. For whatever reason if you wish not to be included in such a list, please make this clear in your comments. Also it will be helpful if you would identify any special experience that you may have which is relevant to the study.

If you wish to contribute to this present study, it will be most useful if you let me have your comments in writing by 19 May 1995.

For the Secretariat of the Working Party on Xenografts

¹ We are grateful to David Concar and to New Scientist for permission to reprint the text of his article for this purpose. The article appeared in New Scientist, 18 June 1994, pp 24–9.
Additional guidance from the Nuffield Council on Bioethics

Recent and likely advances

1. The definition of xenografts is potentially wide. If the term, xenograft, is taken to mean the intentional transfer of cells, tissues or organs between species then it would include:
   1.1 the transplantation of non-human animal cells, tissues or organs into human beings (non-human animals will subsequently be referred to as animals);
   1.2 the transplantation of human cells, tissues or organs into animals; and
   1.3 the transplantation of cells, tissues or organs between different species of animals.

2. All these procedures are, or have been, undertaken. An example of the first is the routine and successful use of porcine heart valves in the surgical treatment of patients with heart disease; and, of the second, the insertion of human tissue into immune-deficient mice to explore the pathogenesis of disease.

Definition

3. The wider the definition of tissue then the greater is the scope of xenografts. For the purpose of the Working Party, it is suggested that a xenograft is taken to be the intentional transfer of cells, tissues or organs from animals to humans.

Technical aspects

4. It will be for the Working Party to report fully on the existing technology: what has been done already and what researchers have learned of the difficulties which will need to be overcome if xenografting is to become a safe procedure in the treatment of human illness. Whole organ xenotransplants have been undertaken over the last thirty years using primate donors, but the survival times of the recipients have been very poor: death has occurred usually within days and sometimes within minutes.

5. The human body's reaction to a graft can range from complete acceptance through toleration aided by immunosuppressant drugs to hyperacute rejection which is the sudden, extensive and total rejection of the graft. This human immunological response depends on several factors. In very general terms the closer the donor and recipient are genetically, the greater the likelihood of a successful graft: the best case is between identical twins. With a human recipient if the donor is only distantly related in genetic terms then the reaction is likely to be a hyperacute rejection and the graft will fail. One proposed solution to this difficulty is to engineer animals genetically: this would be the creation of transgenic animals as a source of cells, tissues or organs which were more acceptable to the human body. The insertion of human genes into animals is a technique which has already been developed and
researchers have already produced a pig which expressed human Decay Accelerating Factor which is an important step toward avoiding hyperacute rejection.

6 Even with the successful genetic modification of source animals there may be as yet unexplored technical problems with the remaining immunological incompatibilities such as the technique will never prove to be feasible or the effects on humans render it unacceptable.

The need for xenografts

7 The need for xenografts may be seen to arise from a shortfall between the supply and demand for human organs. A recent report stated “...there are not enough organs to meet demand, and the situation is getting worse.” (A Question of Give and Take, King’s Fund Institute Research Report 18, Page 15). That report considered ways in which the supply of human organs could be increased. The achievement of health targets, such as those set out in the Government White Paper, The Health of the Nation, may reduce but cannot eliminate the overall need arising from, say, heart disorders or renal failure. Meanwhile, advances in surgical techniques and the success of modern immunosuppressants mean that proportionally more patients could be treated with organ transplantation. The supply of cadaveric human organs is falling: improvements in road safety and car design have significantly reduced the number of accidental deaths. There are doubts that even when supplemented by live donors, organs available are insufficient.

8 In some instances, such as recipients with hepatitis B, the use of an animal rather than a human organ might offer greater chances of survival because the animal organ may be resistant to human specific diseases.

9 The study should also consider the comparative likelihood of the successful development of entirely artificial organs.

Ethical issues and questions

10 The report should consider the likely quality of life which recipients of xenografts might experience. In particular, there is an issue concerning the fate of early recipients, ie those involved at the experimental stage.

11 The report should consider whether there are grounds for the use of different species as potential sources of cells, tissues or organs and, in particular, should consider whether there should be any absolute prohibition on the use of certain species. This will include the ecological impact of such a use and the questions arising from the genetic engineering of those animals.
Animals are used by humans for a wide variety of purposes, but mainly as a source of food. This report will consider only the proposed novel and experimental use as a source of cells, tissues or organs for the treatment of human disease and not the use of animals in itself.

In the area of animal interests there is a wide spectrum of religious and philosophical views. The study should consider the various ethical frameworks within which a discussion of this novel use of animals can take place meaningfully. In Chapter 11 of *Lives in the Balance: The Report of a Working Party of the Institute of Medical Ethics* (OUP, 1991) the authors state “. . . there is no shared religious or philosophical world-view which might dictate an agreed answer to the question of how we can adjudicate on conflicts between obligations owed to humanity and to animals.” However that report achieved a working agreement which was recorded explicitly (it is reproduced in part as Annex A to this paper). Should the need arise, the Working Party on Xenografts will wish to adopt a comparable approach to record the measure of agreement that might be acceptable within the UK.

In addition to concerns that genetically engineered animals may suffer “a bad life”, there are issues arising from the special conditions under which transgenic donor animals are likely to be bred and kept: for example, will the life of such animals be significantly different from that of farm animals: and if so, what are the likely consequences?

Other issues arise from current concerns about the potential risks involved in this new area of research. One example is the transmission of disease (infectious and non-infectious) or of genetic susceptibility to disease across species boundaries, but there may be others: another would be the different biochemical functions of human and animal organs. Such risks should be discussed.

The future, successful use of animal cells, tissues or organs in transplant surgery may affect the need and the willingness to give consent to human organ donation.

The study should consider the possible effects on communal or social solidarity, most importantly the sharing of the financial risks of ill health, on which most modern health systems are based. Generally, consideration should also be given to the service and financial implications of the widespread adoption of this technology.

**Consultation document**

The study should aim to discover public and professional views by issuing a consultation document.

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2 Annex A contained the statement reproduced in paragraph 4.25 of this report.
Annex C

Individuals and organisations contacted

Revd Professor Robin Gill
Dr David King
Revd Dr John Polkinghorne
Professor Margaret Stacey
Association of the British Pharmaceutical Industry
Action of Churches Together in Scotland
Animal Aid
Animal Welfare Foundation
Association of Clinical Cytogeneticists
Association of Medical Research Charities
Association of Community Health Councils for England and Wales
British Medical Association Medical Ethics Committee
Baptist Union
BioIndustry Association
Biotechnology & Biological Sciences Research Council
Bowling Green State University, Ohio: Dept of Philosophy
British Laboratory Animals Veterinary Association
British Organ Donor Society (BODY)
British Paediatric Association
British Union Conference of Seventh-Day Adventists
British Union for the Abolition of Vivisection
British Veterinary Association
Buddhist Society, Centre for Study of Health (CSHSD)
CERES
Catholic Bishops’ Committee on Bioethical Issues
Catholic Bishops’ Conference of Scotland
Catholic Bishops’ Conference of Ireland
Catholic Bishops’ Conference of England & Wales
Central Oxford Research Ethics Committee
Centre for Bioethics & Public Policy
Centre for Medical Ethics, Jews’ College
Christian Consultative Council for the Welfare of Animals
Christian Medical Fellowship
Church in Wales: Diocese of Monmouth
Church in Wales Centre Board of Mission
Church of England Board for Social Responsibility
Church of Scotland Board for Social Responsibility
Church of Scotland Board of Social Responsibility
Church of Scotland: Society Religion & Technology Project
Clinical Genetics Society
College of Health
Compassion in World Farming
Conference of Medical Royal Colleges
Annex C: Individuals and organisations contacted

Council of Churches for Britain and Ireland
Department of Health: HEF (Medical)
Department of Health: Mr Edmund Waterhouse
Edinburgh University: Revd Professor Duncan B Forrester
Edinburgh University: Dr R A McCall Smith
Edinburgh University: Professor Neil McIntosh
Edinburgh University: Professor Timothy L S Sprigge
Essex University: Dr W Cartwright
Europe World Society for the Protection of Animals
FRAME
Farm & Food Society
Farm Animal Welfare Coordinating Executive
Genetics Forum
Institute of Health Services Management
Institute of Liver Studies
Institute of Medical Ethics
International Supreme Council of Sikhs
Islamic Cultural Centre
Jain Samaj
Joint Ethico-Medical Committee of Catholic Union of GB and Guild of Catholic Doctors
Joint UK Focus for Biomedical Engineering
King's Fund
Laboratory Animal Science Association
MAFF: Biotechnology Unit
Medical Research Council
Methodist Church Division of Social Responsibility
Monash University, Centre for Human Bioethics: Professor Peter Singer
National Alliance of Women's Organisations
National Anti-vivisection Society
National Consumer Council
National Federation of Women's Institutes
National Spiritual Assembly of the Bahá'ís of the United Kingdom
Nottingham University: B Mepham and C Moore
Office of the Chief Rabbi
Open University: Dr Donna L Dickenson
Patients Association
Presbyterian Church General Secretary
Quaker Concern for Animal Welfare
Quaker Home Service
Royal Society for the Prevention of Cruelty to Animals
Research Defence Society
Royal College of General Practitioners
Royal College of Nursing
Royal College of Obstetricians and Gynaecologists
Royal College of Pathologists
Royal College of Physicians of Edinburgh
Royal College of Physicians & Surgeons of Glasgow
Royal College of Physicians of Ireland
Animal-to-Human Transplants: the ethics of xenotransplantation
Annex D

Submissions

Animal Aid
Association of the British Pharmaceutical Industry
Banner M, King’s College, University of London (Dept of Theology and Religious Studies)
Barwell L
BioInformation (International) Ltd
Biotechnology & Biological Sciences Research Council
British Biotech
British Laboratory Animals Veterinary Association
British Union for the Abolition of Vivisection
Caddick J, Emmanuel College, University of Cambridge
Centre for Bioethics and Public Policy
Christian Medical Fellowship
Church in Wales
Church of England, Board for Social Responsibility
Church of Scotland, Board of Social Responsibility
Church of Scotland, Working Group on Genetic Engineering in Non-human Life Forms of the Society, Religion and Technology Project
Clark S, University of Liverpool (Dept of Philosophy)
Dalriada School, Ballymoney, N Ireland
Farmers’ Forum
Frey R, Bowling Green State University, Ohio (Dept of Philosophy)
Genetics Forum
Gill R, University of Kent
Imutran Ltd
Institute of Medical Ethics
Jain Academy
Joint Ethico-Medical Committee of The Catholic Union of Great Britain and Guild of Catholic Doctors
Levitt M, Centre for Professional Ethics, University of Central Lancashire
Medical Research Council
Mepham B and Moore C, Centre for Applied Bioethics, University of Nottingham
Methodist Church, Division of Social Responsibility
McIntosh N, University of Edinburgh (Dept of Child Life and Health)
McLaughlan A, Bell College of Technology, Hamilton
National Kidney Federation
National Spiritual Assembly of the Bahá’ís of the United Kingdom
Onions D, University of Glasgow (Dept of Veterinary Pathology)
Polkinghorne Revd Professor J, Queen’s College, University of Cambridge
PPL Therapeutics
Prowse H
Quaker Concern for Animal Welfare
Reform Synagogues of Great Britain, Medical Ethics Group
Reiss M, Homerton College, Cambridge
Animal-to-Human Transplants: the ethics of xenotransplantation

Roberts S
Royal College of Obstetricians and Gynaecologists
Royal College of Pathologists
Royal College of Physicians
Royal College of Veterinary Surgeons
Royal Society of Edinburgh
Royal Society for the Prevention of Cruelty to Animals
Silcock S
Skoczylas T
Stacey M, Warwick University
Strathern M, University of Cambridge (Dept of Social Anthropology)
Townswomen’s Guild
Union of Muslim Organisations of UK and Eire
Woods T, Brunel University (Centre for the Study of Health)