CLONING ISSUES IN REPRODUCTION, SCIENCE AND MEDICINE

A Report from

The Human Genetics Advisory Commission

and

The Human Fertilisation and Embryology Authority

Human Genetics
Advisory Commission

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CONTENTS

FOREWORD

The considerable public interest aroused by the birth of Dolly the sheep in February 1997 led the Human Genetics Advisory Commission and the Human Fertilisation and Embryology Authority to hold a consultation exercise on cloning earlier this year.

We are grateful to the great number of individuals and organisations who have contributed to our request for views and advice. We were pleased to see that our exercise stimulated a number of organisations and communities to debate the implications of "Dolly" and submit collective responses to the consultation.

Our Report takes account not only of the responses to the consultation, but also more recent scientific reports in this fast moving field, and attempts to identify where developments might lead in the foreseeable future.

The Report makes a number of recommendations. We hope that it will also contribute to improved understanding of the issues around human cloning and nuclear transfer technology, and how they might best be addressed in the future. It is our wish that the wide potential benefits of this technology are maximised, while at the same time concerns are recognised and adequate safeguards are implemented.

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December 1998

SUMMARY

This Report sets out the scientific developments which led the Human Genetics Advisory Commission (HGAC) and the Human Fertilisation and Embryology Authority (HFEA) to undertake a public consultation on human cloning. It presents the findings of the consultation exercise and the current legal and administrative arrangements covering treatment using human embryos.

Concern expressed about human reproductive cloning, including safety and other ethical issues, was widespread and supported a total ban on its use for any purpose. However, many saw benefit in new techniques which might be developed to treat serious medical conditions. These applications, including developments reported since the consultation period ended, together with the current legal position and concerns expressed by some respondents are considered in the Report.

The Report concludes that the Human Fertilisation and Embryology Act 1990 has proved effective in dealing with new developments relating to human cloning. It recommends that these safeguards be recognised as wholly adequate to forbid human reproductive cloning in the UK. However, it suggests that the Government might wish to consider the possibility of introducing legislation that would explicitly ban human reproductive cloning regardless of the technique used, so that the full ban would not depend upon the decision of a statutory body (the HFEA) but would itself be enshrined in statute.

Some of the therapeutic advances now being developed were never envisaged when the 1990 Act was drafted. Therefore, the Report also recommends that the Secretary of State for Health should consider specifying in regulations two further purposes for which the HFEA might issue licences for research, so that potential benefits can clearly be explored. Firstly, the

development of methods of therapy for mitochondrial disease and secondly the development of therapeutic treatments for diseased or damaged tissues or organs.

Some responses expressed the view that there is a need for international legislation to prohibit human reproductive cloning. The Report reviews international developments relating to cloning and highlights the difficulties there can be in finding mutually acceptable and internationally agreed definitions for even quite simple concepts.

Views expressed about genetic identity indicated that concerns were less about entitlement to a unique genetic identity, but highlighted collateral issues like confidentiality and consent - issues which are not unique to human genetics.

The consultation process itself highlighted the need for greater public understanding of human genetics, and the Report mentions some initiatives arising out of the consultation which promoted wider public debate.

Finally, in recognition of the pace of scientific advances in the area of human genetics, the Report recommends that the issues are examined again in five years time in the light of developments and public attitudes towards them.

Section 1

INTRODUCTION

1.1 In February 1997 Dolly the sheep, the first vertebrate cloned from a somatic cell of an adult animal, generated considerable public interest and much media comment. A major motivation for the work was to improve methods for the genetic improvement of livestock. The technology could also be used to improve the efficiency of production of transgenic livestock, with potential benefits in, for example, increasing production of human proteins in the milk of transgenic animals (e.g. proteins used to treat blood clotting disorders such as haemophilia). Although hailed as a remarkable scientific development, concern was raised both nationally and internationally about the implications and use of this technology, particularly the possibility of cloning human beings. Reactions were worldwide and resulted in several international initiatives.

1.2 Dolly was the result of a collaborative project between the Roslin Institute and PPL Therapeutics PLC to test the suitability of different sources of cells for nuclear replacement. She was derived from cells taken from the udder of a 6 year old Finn Dorset ewe which were then cultured in the laboratory. 277 of these cells were then fused with 277 unfertilised eggs, from which the nucleus had been removed, to create "reconstructed eggs". This process resulted in 29 viable reconstructed eggs, each with a nucleus from the adult animal, which were then implanted into surrogate Blackface ewes. One gave birth to Dolly.[1]

1.3 However, Dolly was not the first sheep to be created using nuclear replacement technology. In 1996, it was reported that sheep embryos had been cloned using nuclear replacement technology and had resulted in the birth of two genetically identical sheep, Megan and Morag[2]. The difference

[1] "Viable Offspring Derived from Foetal and Adult Mammalian Cells", Nature, **385**, 881: 1997
[2] "Sheep Cloned by Nuclear Transfer from a Cultured Cell Line", Nature, **380,** 64-6: 1996

between Dolly and Megan and Morag was the nuclear donor source: Dolly was derived from an adult sheep, Megan and Morag from a sheep embryo.

1.4 At the end of the year following the birth of Dolly, the Roslin Institute and PPL Therapeutics PLC announced the birth of Polly[3]. She was a transgenic sheep produced by transfer of the nucleus of a cultured fetal fibroblast. She carried a human gene for blood clotting Factor IX, which is used for treatment of Haemophilia.

1.5 The announcement of Dolly the Sheep prompted an inquiry by the House of Commons Science and Technology Committee, who published their findings in March 1997 in a report, "The Cloning of Animals from Adult Cells"[4]. The Committee believed that concerns over the cloning of Dolly may have overshadowed potential benefits, and trusted that the Human Genetics Advisory Commission would advise on the implications of the work for human genetics. It also recommended that work which would create "experimental human beings" should not be carried out, and suggested that Parliament should reaffirm a ban on human reproductive cloning.

1.6 This last point was addressed in a reply to a Parliamentary Question given by the Minister of State for Public Health on 26 June 1997[5] who said, "We regard the deliberate cloning of human beings as ethically unacceptable. Under United Kingdom law, cloning of individual humans cannot take place whatever the origin of the material and whatever technique is used."

1.7 The Human Genetics Advisory Commission (HGAC) was established in December 1996 in response to a report by the House of Commons Science and Technology Committee, as a non-statutory advisory body. It provides independent advice to UK Health and Industry Ministers on issues arising from developments in human genetics that have social, ethical and/or economic consequences. The Commission was also asked to advise on

[3] "Transgenic Sheep Expressing Human Factor IX", Science, **278**, 2130-2133: 1997
[4] The Science and Technology Committee, Fifth Report of Session 1996-97 (HC373-I)
[5] Official Report 26 June 1997, Column 615

ways to build public understanding of the new genetics. The Commission is charged with setting its own priorities, although from time to time it may be requested to provide urgent advice to Ministers. A list of HGAC members is attached at Annex A.

1.8 The Human Fertilisation and Embryology Authority (HFEA) took up its powers in August 1991 as a result of the passage of the Human Fertilisation and Embryology Act 1990 (HFE Act). The first statutory body of its type in the world, the HFEA's creation reflected public and professional unease about the potential future of human embryo research and infertility treatments, and a widespread desire for statutory regulation of this ethically sensitive area. The HFEA's principal tasks are to license and monitor those clinics that carry out *in vitro* fertilisation, donor insemination and human embryo research. The HFEA regulates the storage of gametes and embryos and keeps a register of all licensed treatments carried out in the UK. It also keeps under review information about the development of human embryos and the provision of treatment services and activities governed by the HFE Act and advises the Secretary of State for Health if asked about those matters. A list of HFEA members is attached at Annex B.

1.9 The HGAC and the HFEA decided to explore ways of holding a public consultation exercise into the implications of cloning developments. A joint working group, consisting of members of both bodies, was established to consider the planning, drafting, distribution and analysis of a joint consultation paper on the issues for human genetics arising from advances in cloning technology.

1.10 The Government response to the Science and Technology Committee's report was published in December 1997[6]. It reiterated the Minister of State for Public Health's statement, explained that the HGAC and the HFEA were exploring ways of holding a public consultation exercise on

[6] Government Response to the Fifth Report of the House of Commons Select Committee on Science and Technology, 1996-97 Session (Cm 3815)

cloning, and said that the Government would consider carefully, in the light of developments, whether the legislation needed to be strengthened in any more specific way, taking into account the views of Members of Parliament, the HGAC, the HFEA and the responses received to a more general consultation on the broader issues.

1.11 The HGAC/HFEA consultation paper[7] was published on 29 January 1998 and comments were invited by 30 April 1998. The paper differentiated between the different concepts which are all broadly termed as "cloning", and sought views on these different meanings, the ethical implications raised by the possibility of human cloning, including the safety of the technique if it were applied to humans, and the ethical concerns raised by cloning in specific circumstances. It also raised questions about more abstract concepts such as individuality and human dignity.

1.12 Since the consultation paper was circulated, there has been independent confirmation that Dolly was cloned from the cells of an adult sheep[8], and cloning by nuclear replacement using nuclei from adult cells has been successfully extended to mice[9] and also to cattle[10] (two cloned calves born recently in Japan, using a procedure similar to that which produced Dolly). It is therefore clear that the birth of Dolly was not a "one off" event, due to some unique concatenation of circumstances. The feasibility of nuclear replacement cloning is therefore not confined to one species. Although the efficiency of the procedure is very low in mice, as it is in sheep, it is likely to increase more rapidly with research on mice. The molecular genetics of mice is better understood and, moreover, the gestation time is shorter.

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[7] "Cloning Issues in Reproduction, Science and Medicine - A Consultation Document" January 1998
[8] "DNA Microsatellite Analysis of Dolly", Nature **394**, 329:1998
[9] "Full-term Development of Mice from Enucleated Oocytes Injected with Cumulus Cell Nuclei", Nature **394**, 369-374: 1988
[10] "....As Japanese Announce Cloned Calf Twins", Nature **394**, 114:1998

Section 2

CONSULTATION

2.1 The consultation document, "Cloning Issues in Reproduction, Science and Medicine", attracted a great deal of interest both nationally and internationally. It was launched at a press conference attended by representatives of the national and international press and was widely reported, with coverage including details of where copies of the document could be obtained. Over 1,000 copies were distributed. We believe the document also reached a larger audience through the HGAC website and by others copying and circulating the paper.

2.2 The consultation sought general comments about how the technology which led to "Dolly" might develop and the opportunities and problems that might be raised by human reproductive cloning and other applications of nuclear replacement technology. It also invited views on priorities for the future and the ethical settings in which these scientific developments are taking place. It sought comments on any other ethical issues raised by human cloning that respondents identified. It was requested that responses be structured around replies to six questions (see Annex C). Respondents were also invited to make suggestions about what advice might be offered to Ministers on ways to build public confidence and understanding of the new developments in genetic techniques.

2.3 Nearly 200 responses were received - about 40% from individuals and the rest from a wide range of constituencies - scientists, clinicians, academics, religious groups, ethicists, lawyers, industry and lay groups. The latter included groups of individuals in local communities that had come together to discuss the issues raised and to share views and concerns. Responses from a number of constituencies involving groups of individuals sometimes did not reach a consensus, but reflected a range of opinions.

2.4 Responses varied enormously, some expressing a horror at the very idea of any form of cloning without addressing the specific issues raised in the document, whilst others were very detailed in their consideration of the issues. Some respondents provided additional questions and arguments to those raised in the consultation document. This wide range of views was welcome, reflecting common reactions, misunderstandings and hopes and fears about this rapidly developing technology. A number of respondents congratulated the authors of the document for setting out the issues clearly, but others were concerned about the language used to express some issues. For example, it was suggested that the differentiation between reproductive and therapeutic cloning and the positive and negative phrasing of the questions may have had some influence on the responses received.

2.5 The widest spread of opinions occurred in responses from individuals and religious groups, but the overall balance of opinion was generally reflected throughout the various constituencies where sufficient numbers of responses from each grouping made comparisons possible. There were a small number of "don't know" answers to most questions, where respondents did not feel that they had sufficient knowledge to express a view. Annex C contains a short, quantitative analysis of the responses received. This is given to indicate the relative proportion of respondents taking the positions discussed without any implied suggestion that the issues can be settled simply by counting responses.

2.6 A copy of those responses received, where the respondents had no objection to their being made public, can be viewed by prior arrangement with the HGAC Secretariat at Albany House, 94-98 Petty France, London SW1H 9ST (Tel: 0171-271-2131).

Section 3

THE LEGISLATIVE AND ADMINISTRATIVE CONTEXT

Background

3.1 The history of the Human Fertilisation and Embryology Act 1990 is usually traced back to 1978 with the birth of Louise Brown, the world's first IVF baby. Although the 1990 Act also covers treatments such as donor insemination, the development of IVF treatment and human embryo research was the main impetus for the development of the current legislation and the HFEA. An important milestone was the publication in 1984 of the Warnock Report[11]. It was the Warnock Report which first suggested the setting up of a statutory body to oversee the practice of certain fertility treatments and human embryo research.

3.2 Without a licence from the HFEA the 1990 Act makes it a criminal offence to carry out any treatment using human embryos outside the body, or to use donated gametes; also to store any eggs, sperm or embryos and to undertake any research into human embryos. The Act also sets out the parameters within which the HFEA may issue treatment, storage and research licences. For example, the HFEA may not license any research project involving human embryos after the primitive streak has appeared or after the 14th day of development (whichever is the sooner). The relevant extracts from the Act are reproduced at Annex D.

3.3 Around 23% of respondents indicated that in their view any form of embryo research/manipulation was simply wrong because they believe that the embryo possesses the full moral status of a human being. There were 24% who thought that the 14 day limit was arbitrary, some of them considering that it could be open to the possibility of extension. Both these

[11] Report of the Committee of Inquiry into Human Fertilisation and Embryology, HMSO, July 1984 (Cm. 9314)

points of view are questioning decisions enshrined in the 1990 Act. Both the HGAC and HFEA have respect for these opinions. However, the relevant issues were fully debated, both in Parliament and by the wider public, at the time of the passing of the HFE Act. While the decisions then reached did not command universal ethical assent, they are the basis of the present policy and they necessarily form the framework within which the HGAC/HFEA must make their recommendations to Ministers. It would not be appropriate to use this limited enquiry into cloning to reopen the wider questions relating to work with human embryos.

Cloning

3.4 The 1990 Act (section 3 (3)(d)) expressly prohibits one type of cloning technique, namely the nuclear substitution of any cell whilst it forms part of an embryo. Further, the Act (section 3(l)) requires a licence from the Authority for any creation, use or storage of a human embryo outside the body. The technique used to create Dolly involves nuclear substitution into an egg and not into an embryo. Thus it is not specifically covered by section 3(3)(d). Some have argued that, as fertilisation is not involved, section 3(l) also does not apply. The Department of Health and the HFEA have taken Counsel's advice on this issue. As a result, both Ministers and the Authority reject this position and are content that the Act does allow the HFEA to regulate nuclear replacement into an unfertilised egg through its licensing system.

Existing HFEA Requirements

Licensing

3.5 Each centre in the UK which offers clinical treatments involving *in vitro* fertilisation or donor insemination, storage of gametes or embryos, or which carries out research involving the use of human embryos, must be licensed by the HFEA. All licenced centres are subject to an annual inspection. All licensing decisions are taken by Authority Licence Committees, which may refuse to grant a licence or to renew a licence. They also have the power to

suspend or revoke a licence, which has already been granted. Where there is the possibility that a criminal offence has been committed a Licence Committee will decide what action should be taken including whether the police should be involved or the matter referred to the Director of Public Prosecutions.

3.6 The HFEA is required by law to produce an Annual Report. This provides general information about the number of licenced clinics and the range of licensed research, and discusses the clinical, scientific and ethical issues around current and anticipated developments in reproductive technology. The Report also gives information about any investigations the HFEA has carried out in respect of alleged or apparent breaches of the Act.

3.7 The approval of a properly constituted independent ethics committee is a necessary prerequisite to the Authority considering an application for a research licence. In addition, all applications for research licences are submitted for peer review. Peer reviewers comment on a number of issues including the importance of the work's originality and justification for it. Their recommendations are submitted to a Licence Committee which has the responsibility of deciding whether a licence should be granted and on what conditions.

Policy

3.8 Before the consultation document was issued the HFEA had stated its policy of not permitting human reproductive cloning, a stance with which the HGAC was fully in agreement.

3.9 The Authority's policy on embryo splitting was developed in 1994 following reports in 1993 that a team of researchers in America had used embryo splitting in a research project. The Authority agreed that it would not permit embryo splitting to be used in treatment cycles and would only permit embryo splitting in research projects where the aim of the project did not

include increasing the number of embryos for transfer. Members have subsequently agreed a similar line for the nuclear replacement of eggs, that is, that no reproductive cloning involving the technique would be licensed, but that research with a non-reproductive aim would be considered.

3.10 Research applications involving the creation or use of human embryos created through the nuclear replacement of eggs are likely to be some way off for a variety of reasons. In line with general HFEA policy, further research using animal embryos is needed before the use of human embryos in research would be appropriate.

Section 4

HUMAN REPRODUCTIVE CLONING

4.1 Section 1 of this report quotes the Minister of State for Public Health's statement in June 1997 (see paragraph 1.6). Section 3 explains the legal position in detail. Nevertheless, the Working Group felt it essential as part of the consultation exercise to gauge public opinion on this issue and to ascertain the reasons for that opinion. In consequence, a specific question about whether the creation of a clone of a human person would be an ethically unacceptable act was included in the consultation document.

4.2 The consultation document set out a number of scenarios where cloning technology could be applied to make a "copy" of another human being, envisaging single or multiple "copies" of a living or a dead fetus, baby, child or adult. These included parents who might wish to "replace" an aborted fetus, dead baby or child killed in an accident; produce a sibling to be a compatible tissue or organ donor for a child dying from, say, leukaemia or kidney failure; or an individual attempting to "cheat death" by using cloning technology. Mention was also made of the possibility of selecting characteristics in offspring or to assist human reproduction in the case of infertile couples or lesbian couples. Views were sought on the acceptability of cloning in all, or any, of these circumstances.

4.3 The response to the consultation was conclusive. There was very little support for reproductive cloning, though there were a few who saw benefit in certain circumstances, mainly in connection with infertility treatment. 80% of the respondents thought it was an ethically unacceptable procedure, an opinion that was endorsed within each of the different groupings of those responding (see table 4 at Annex C).

4.4 Safety is itself an ethical issue. Nuclear replacement in animals is at present very inefficient. Few of the reconstructed embryos develop, some develop abnormally, some die at or soon after birth. In humans, the wastage of human eggs and the high risks of miscarriage and congenital malformation alone would exclude any realistic prospect of reproductive cloning. However, since issues of efficiency and safety may eventually be resolved, it is necessary to analyse further the reasons why human reproductive cloning is so widely judged to be ethically unacceptable.

4.5 A central ethical issue is the widely accepted moral principle that human beings may never be treated merely as means to an end, but only as an end. Many of the suggested reasons for which reproductive cloning might be employed have a strongly instrumental character to them, for they contemplate bringing human beings into existence for reasons outside the persons themselves. Examples would be the 'replacement' of a lost relative or the making available of compatible tissue for transplantation into another. It would be morally demeaning and psychologically damaging for someone to learn that the primary reason for their existence lay not in their own value, but in their utility for another purpose, as the substitute for someone else or for the benefit of someone else. Moreover, in the case of attempted 'replacement', the action would be based on the fallacious equation of a person with their genome (see Section 6).

4.6 These particular ethical arguments would not apply to the possible use of cloning as an extreme measure to relieve infertility in a case where nuclear replacement seems the only way to produce an embryo for implantation which incorporated genetic material derived from one of the intending parents. In these latter circumstances there would be good reason to suppose that the person brought into being would be highly valued for his or her own sake. However, other ethical considerations would also be relevant. The relief of the pain of infertility is, in general, a good end, but it is not an absolute end to be achieved without regard to the ethical acceptability of the

means employed for that achievement. The wish for genetic offspring is a natural human aspiration, but this has to be held in balance with other desirable aspects of human well being and it cannot be given an overriding priority above all other considerations. While the desire for children, and feelings of solidarity with kin are the source of much human good, too exclusive an emphasis on genetic connection can lead to distortions.

4.7 The use of reproductive cloning to relieve infertility would involve risks likely to be ethically unacceptable for human use in the foreseeable future (see paragraph 4.4 above). There are further ethical difficulties about the source of the genetic material which could be used in nuclear replacement to relieve infertility. If the nucleus was derived from one of the parents, this would generate an unbalanced genetic relationship of an entirely unprecedented kind within the family. A child cloned in this way would have a unique set of family relations, as he or she would inherit their *complete* genetic make up from one of their "parents" and have no genetic connection with the other. This complete genetic identity between the child and one parent would constitute a novel situation of which there is no previous experience and there must be uncertainties and doubts about the effects this would have on the family and the child. For these psychological and social reasons, there must be serious ethical doubts about the propriety of bringing about such a set of relationships. All these considerations give rise to serious ethical concerns about reproductive cloning as a means to relieve infertility. There is a difference from donor insemination where an entirely new individual is conceived as a result of the fertilisation of a gamete produced from one parent with a donor gamete, so there is a partial connection with one parent and none with the other.

4.8 In relation to using reproductive cloning as a means to relieve infertility it is also necessary to consider the wider question of public policy. Decisions about what may be done involve not only the couple themselves and their medical advisors but also society as a whole. For any type of infertility

treatment to function satisfactorily there has to be a degree of social acceptance of the measures being taken. It is quite clear that human reproductive cloning is unacceptable to a substantial majority of the population. A total ban on its use for any purpose is the obvious and straightforward way of recognising this. The results of the consultation fully support Government policy in this respect.

Section 5

THERAPEUTIC USE OF CELL NUCLEUS REPLACEMENT (CNR)

5.1 The consultation document attempted to distinguish between reproductive cloning or the production of an entire animal from a single cell by asexual reproduction, and what was termed "therapeutic cloning" - applications of nuclear replacement technology which do not involve the creation of genetically identical individuals. This definition led to some criticism. Some thought that the distinction between reproductive and therapeutic cloning was arbitrary, others just responded negatively to anything described as "cloning" and some were upset at the description of identical twins as "a natural form of cloning". It is clear that the term "cloning" carries an automatic stigma for many because of its association with imagery such as that portrayed in "Brave New World"[12]. To avoid this confusion this section of the Report has been headed "Therapeutic Use of Cell Nucleus Replacement (CNR)" and concentrates on new techniques which might be developed to treat serious medical conditions. This could include (see paragraph 5.10) a use of CNR which would not involve any form of cloning.

5.2 There was a significant response, primarily from individuals, rejecting all research using human embryos. However, the Human Fertilisation and Embryology Act permits licensed research on human embryos up to 14 days of development (this stage of development immediately precedes the primitive streak stage at which development of individual embryos is established and cell determination for the future fetus sets in). An amendment to prohibit the creation of embryos for research was defeated by a large majority in the House of Commons and by a very large majority in the House of Lords. Thus the production of a human embryo by CNR for research purposes could be permitted, provided that the research project was

[12] "Brave New World", Aldous Huxley 1932 (Harper and Row)

licensed by the HFEA according to the strict criteria that such a licence demands.

5.3 The most likely objective of a research project involving the use of CNR would be to create a cultured cell line for the purposes of cell or tissue therapy. People who have tissues or organs damaged by injury or disease (e.g. skin, heart muscle, nervous tissue) could provide their own somatic nuclei and, by using these to replace nuclei in their own or donated eggs, individual stem cells (not embryos) could be produced in culture. These cells could then be induced (by exposure to appropriate growth factors) to form whichever type of cell or tissue was required for therapeutic purposes with no risk of tissue rejection and no need for treatment of the patient with immunosuppressive drugs.

5.4 For some processes somatic non-cloned cultured cells can be used for some kinds of tissue repair. They have a disadvantage, however, in that, depending on the age of the individual, they may have a limited life span. Other approaches to the treatment of degenerative disease and the repair of tissue damage, avoiding the risk of tissue rejection, may have been perfected before any success has been achieved with the types of embryo research outlined in paragraph 5.3 above. It may prove possible to treat tissues in such a way as to abolish their antigenicity, or custom-made "humanised" transgenic animals may provide tissues that can be successfully transplanted to any recipient, without the need for permanent treatment with immunosuppressive drugs. However, these possibilities are again speculative, and unlikely to be available for clinical testing for a decade or two. It would therefore seem unwise to rule out absolutely any lines of research not involving reproductive cloning that might prove of therapeutic value.

5.5 Some research has already been licensed by the HFEA into the possible generation *in vitro* of stem cell lines from human embryos for the purposes of analysing the factors that affect the development of embryos

fertilised and grown *in vitro* and assessing their development potential. There is a recent report from the USA of the successful derivation from human embryos (fertilised *in vitro* and donated for research) of cell lines resembling stem cells in many respects[13]. It therefore seems likely that applications for research projects involving CNR in human oocytes may be received by the HFEA within the next few years. Any such project would require a source of oocytes donated for research which at present are not widely available. However, *in vitro* techniques for maturing very immature oocytes from human ovaries are being devised, and these could possibly provide a source of enucleated oocytes adequate for research use.[14]

5.6 The eventual clinical use of such procedures would be to provide immunologically compatible tissues for the treatment of degenerative diseases of, for example, the heart, liver, kidneys and cerebral tissue, or repair damage to skin or bone. The potential value of such techniques to human medicine is enormous. However, restrictions have been placed on the Authority in Schedule 2 of the HFE Act on the circumstances in which a licence may be issued.

5.7 Schedule 2 of the 1990 Act states that the HFEA cannot authorise a research project "unless it appears to the Authority to be necessary or desirable for one the following purposes:

(a) promoting advances in the treatment of infertility;
(b) increasing knowledge about the causes of congenital disease;
(c) increasing knowledge about the causes of miscarriage;
(d) developing more effective techniques of contraception;
(e) developing methods for detecting the presence of gene or chromosome abnormalities in embryos before implantation.

or for such other purposes as may be specified in regulations."

[13] "Embryonic Stem Cell Lines derived from Human Blastocysts", Science, **282,** 1145-1147: 1998
[14] Within the confines of its remit HFEA will be looking at stem cell technology

5.8 The 1990 Act further requires that such licences can only be granted if the HFEA is satisfied that any proposed use of embryos is necessary for the purposes of the research.

5.9 Since therapeutic approaches to disease or tissue damage are not at present included in the purposes for which research can be licensed under the HFE Act (see paragraph 5.7), the making of new regulations would be required to extend the scope of the Act to include these purposes.

5.10 One potential future application of CNR would be for the avoidance of mitochondrial diseases. These life threatening and debilitating diseases are caused by defects in the mitochondria, which are small organelles located in the cytoplasm of each cell. Defective mitochondria are transmitted from the mother, in her egg cells, to all her offspring. It has been suggested that a woman suffering from such a disease could have a healthy child if the nuclear material from one of her eggs was transferred before fertilisation into a donor egg from which the nuclear material had been removed. Nuclear replacement between eggs has been successful in animals. It is not followed by the high incidence of embryonic mortality and abnormal development that characterises nuclear replacement procedures using somatic nuclei that require genetic reprogramming (as with Dolly). Nuclear replacement from one egg to another is not cloning, since after fertilisation the embryo is not identical to the mother, nor to any other embryo. Similarly, because the use of CNR for the avoidance of mitochondrial disease is not at present included in the purposes for which research can be licensed under the HFE Act (see paragraph 5.7), the making of new regulations would be required to extend the scope of the Act to include this purpose.

5.11 A significant number of respondents expressed fears and reservations about the possible commercialisation of therapeutic uses of CNR techniques. Similar anxieties arise in connection with any major advance in medical intervention. There is an understandable desire on the part of the public that

curative procedures should not simply be exploited as sources of financial gain for their developers, but that there should be respect for the public good and corresponding access to these techniques for those who would benefit from them. A balance has to be struck between affording a reasonable recompense to those who have exercised initiative (and undertaken the risk involved in major and costly development programmes) and ensuring that the needs of the sick are properly met. The system of patenting is intended to provide a degree of such safeguard, for it requires that knowledge relevant to the new invention is available in the public domain, whilst granting the discoverer a limited period of protected benefit. There does not seem to be any reason why developments in the field of nuclear replacement therapy should differ significantly from other kinds of medical advances in this respect.

5.12 It has been questioned whether the 14 day limit for human embryo research could be breached by serial nuclear transfer. The HFEA and the HGAC take the view that this is not the case. Whether the nucleus to be replaced in an enucleated oocyte is taken from an adult or from another embryo, the clock is put back to the beginning, embryonic development starts over again, and the primitive streak stage specified in the Act would still not be reached within the 14 day time limit.

Section 6

GENETIC IDENTITY

6.1 Question 3 in the consultation document addressed the issue of genetic identity. In our view, persons are more than their genes, their nature and character being substantially influenced by their nurture and life experiences. Personhood derives from a humanity that is expressed through relationships with others. This is made clear by the unquestionable individuality enjoyed by identical twins, despite their having exactly the same genome, together with the common properties that flow from that. It is clear from this example that the existence of a clone (in this case naturally occurring) is not in itself a threat to an individual's identity. Therefore, the claim that each person is entitled to a unique genetic make-up is a correspondingly questionable assertion. Of itself, it could not prove an adequate ethical objection to human reproductive cloning, though one should note that the latter could produce genetically identical persons in different generations, which is impossible naturally and which could raise novel problems of which there is no prior experience to enable evaluation.

6.2 This was acknowledged by half the respondents to Question 3 in the consultation document. Nevertheless, the responses indicated that there was uneasiness in relation to issues collaterally related to this question. These seemed to centre on three points:

(i) The right to confidentiality with respect to knowledge of one's genetic make-up. This is a part of the general medical ethical requirement of confidentiality about a patient's health information. We fully support this requirement.

(ii) The right to exercise a veto on the manipulative use that another might make of an individual's genome. Whether in relation to participation in a research programme or in relation to other use of

genetic material selected from a person, there is a clear obligation to obtain full and informed consent for any such usage.

(iii) A new kind of right is being asserted where it is also claimed, as some respondents suggested, that a person's genetic make-up should not be directly determined by the deliberate choice of another. This proposition requires careful evaluation. It would be one thing to require a person to be genetically identical to another (the reproductive cloning that we have rejected), or for someone to be given genes that made them seven feet tall because their parents wanted a basketball champion ('designer babies', an issue lying outside the scope of this Report). It would be another thing to ensure, when and where possible, that a disease gene be eliminated.

6.3 As far as the issues relevant to this Report are concerned, it does not seem that new issues arise beyond those covered already by the requirements of ethical medical practice.

Section 7

INTERNATIONAL

7.1 The consultation document gave brief details of the laws affecting cloning in several European countries. These invariably post-date the Human Fertilisation and Embryology Act 1990, which was the first to address the issues and formed the basis of much of the legislation in other countries that followed it. A list of legislation which exists in some other countries is at Annex E.

7.2 Some who responded to the consultation document saw benefit in the international harmonisation of legislation relating to cloning. There have been a number of significant international agreements to prohibit human reproductive cloning. These include:

(i) a UNESCO Declaration on the Human Genome and Human Rights, unanimously adopted on 11 November 1997[15], of which Article 11 states that "Practices which are contrary to human dignity, such as reproductive cloning of human beings, shall not be permitted";

(ii) a protocol forbidding the cloning of human beings developed under the Council of Europe Convention on Human Rights and Biomedicine[16];

(iii) a European Commission Directive on the Legal Protection of Biotechnological Inventions prohibits the issue of any patent on work leading to intentional cloning of human beings[17];

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[15] "Universal Declaration on the Human Genome and Human Rights" published by UNESCO, November 1997

[16] Council of Europe (1997). Additional Protocol to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, on the Prohibition of Cloning Human Beings. Strasbourg: Council of Europe 1997

[17] European Parliament and Council Directive on the Legal Protection of Biotechnological Inventions COM(97)446 final

(iv) at the advisory level, the European Commission's former "Group of Advisers on the Ethical Implications of Biotechnology" called for the Commission to express clear condemnation of human reproductive cloning. The Group has been expanded to form the "European Group of Ethics in Science and New Technologies" which met for the first time in February 1998. The new group is composed of 12 experts and its remit has been enlarged to cover all new technologies as well as scientific research; and

(v) at the fifty first session of the World Health Assembly, meeting in Geneva (11-16 May 1998) a resolution was adopted on the social implications of cloning on human health and circulated to member states[18]

7.3 In the United States, following the announcement of the birth of Dolly the sheep in February 1997, President Clinton asked the National Bioethics Advisory Commission for advice within 90 days on the ethical, legal and scientific issues surrounding human cloning. The publication of their report, "Cloning Human Beings"[19], contributed to the public debate in the US, but as yet no legislation has resulted. In addition, in early November 1998 President Clinton instructed the same Commission to review the implications of the potential genetic reprogramming of human nuclei transferred into enucleated cow eggs.

7.4 It will be for the Government to determine the extent to which any further specific international initiatives are supported by the United Kingdom, taking account of the strength of feeling about human reproductive cloning demonstrated by this consultation. It will be necessary to consider how carefully international initiatives have been drafted lest they should preclude

[18] WHO 51st World Health Assembly, implementation of resolution WHA50.37 - A51/6 Add.1 - 8 April 1998

[19] "Cloning Human Beings" Report and Recommendations of the National Bioethics Advisory Commission: Rockville, Maryland June 1997

the therapeutic use of cell nucleus replacement as well as human reproductive cloning. There are often difficulties over finding mutually acceptable and agreed definitions for even quite simple concepts.

Section 8

ENCOURAGING PUBLIC UNDERSTANDING

8.1 The HGAC has consistently sought to bring issues of public policy in relation to developments in human genetics before the public in a clear and accurate way to facilitate discussion. The consultation document, in a section headed, "Building Public Confidence", specifically asked for any suggestions respondents might have on what advice Ministers might be given in respect of the implications of human cloning. A small but significant number of those who responded to that particular question (13%) interpreted "building public confidence" as attempting to manipulate public opinion.

8.2 While a number of respondents specifically commented that the document had set out quite complex matters in a clear and lucid way. There was some concern that Question 2 had been phrased in a way that would elicit a positive response, that the term "therapeutic cloning" had been chosen because it implied a benefit, and that Questions 4 and 5 had used "ethically unacceptable" and "ethically acceptable" in a way that confused the issues. In fact, the intention of the consultation document was to raise the issues in a clear and accurate way that would elicit considered public response.

8.3 There is no evidence that the way in which the questions were phrased caused actual misunderstandings. Most respondents who addressed the individual questions took great care in giving detailed answers to make their views extremely clear - very few responses were limited to a "yes" or "no". The distinction between reproductive cloning and other work is valid, but at Section 5 above account has been taken of a wide range of comments about the terminology used in drawing this distinction.

8.4 Many respondents recognised that there was a need for greater public understanding of the issues. A number thought that more education was needed. Others considered that this was unlikely to produce immediate benefits and that more informed debate was required rather than scientific education, with a responsible role for the media and with leaflets and imaginative presentations as catalysts.

8.5 This view is not confined to the UK. In the USA, the National Bioethics Advisory Commission report, "Cloning Human Beings", recommended that, "Federal departments and agencies concerned with science should co-operate in seeking out and supporting opportunities to provide information and education to the public in the area of genetics, and on other developments in the biomedical sciences, especially where these affect important cultural practices, values and beliefs".

8.6 Publication of the HGAC/HFEA consultation document itself has promoted wider debate about the issues, including, for example:

(i) the Wellcome Trust commissioned research into public attitudes to cloning, based on 7 focus groups representing various interests within society[20];

ii) the Workers Education Association ran a course on modern genetics which included discussion of the consultation document by all 29 students;

iii) a parish downloaded the consultation document from the website, gathered 25 members for discussion, summarised their views and submitted them, posting them on their own website too; and

[20] "Public Perceptions on Human Cloning", Wellcome Trust December 1998

iv) Chairmen and members of the HGAC and HFEA have addressed audiences, given interviews, and written articles explaining the background to the consultation and the issues raised.

8.7 The HGAC held its first national conference, "Human Genetics - Learning for the Millennium and Beyond", at the Royal Society in London on 16 October 1998. This was aimed at those who work in education, to discuss issues that they had identified raised by human genetics, how these matters are taught and what practical steps could be taken to improve knowledge and understanding. The report of the conference will be published in the near future. The HFEA discussed cloning at its 1997 conference and is often the media's first point of contact on this issue.

8.8 Both HGAC and HFEA regularly review communications needs and consider all opportunities to explain often complex issues in simple terms to the widest possible audience.

Section 9

SUMMARY OF CONCLUSIONS AND RECOMMENDATIONS

9.1 The Human Fertilisation and Embryology Act 1990 is on the statute book, and despite the concerns of some respondents, the purpose of the consultation was not to reopen old debates about it. What needed to be considered was the effectiveness of the Act in dealing with new developments concerning cloning. The difficulty is in considering the appropriateness of controls in a rapidly changing area where it is difficult to envisage just what direction developments will take and what problems might be encountered. The safeguards provided by existing legislation are dealt with in some detail in Section 3 of this report.

9.2 The legal position is clear (Section 3). The Government has explicitly ruled out reproductive cloning and the HFEA has stated its policy that it will not license the use of nuclear replacement for this purpose. HGAC and HFEA *recommend* that these safeguards be recognised as being wholly adequate to forbid human reproductive cloning in the United Kingdom. The Government may, nevertheless, wish to consider the possibility of introducing primary or secondary legislation *explicitly* banning reproductive cloning regardless of the technique used, when there is an opportunity to do so in the legislative programme, so that the full ban would not depend upon the decision of a statutory body (the HFEA) but would itself be enshrined in statute.

9.3 When the 1990 HFE Act was passed, the beneficial therapeutic consequences that could potentially result from human embryo research were not envisaged. We therefore *recommend* that the Secretary of State should consider specifying in regulations two further purposes to be added to the list

in paragraph 3(2) of Schedule 2 (as described in paragraph 5.7 of this report) being:

- *developing methods of therapy for mitochondrial diseases*

- *developing methods of therapy for diseased or damaged tissues or organs.*

9.4 We have concluded that, as far as the issues relevant to this Report are concerned, it does not seem that new issues arise regarding the protection of genetic identity beyond those covered already by the requirements of ethical medical practice, such as confidentiality and consent. We therefore make no additional recommendations.

9.5 The international situation and initiatives undertaken in several international fora are outlined in Section 7. It will be for the Government to determine the extent to which any further specific international initiatives are supported by the United Kingdom. It is not for the HGAC or the HFEA to make specific recommendations. Nevertheless, account should be taken of the strength of feeling about human reproductive cloning demonstrated by this consultation. We attach importance to careful consideration about the difficulties we have mentioned (see paragraph 7.4) over finding mutually acceptable and agreed definitions for even quite simple concepts.

9.6 The responses received to the consultation document indicated the need for more education and informed debate about the new genetics. Section 8 refers to work already undertaken in response to this need. A report to Ministers will follow from the HGAC's October 1998 conference, "Human Genetics: Learning for the Millennium and Beyond", which will help identify further practical measures to promote open and informed discussion. Specific recommendations may be expected to arise from that.

9.7 Finally, because of the pace of scientific advances in the area of human genetics, the HGAC and the HFEA believe that the issues need to be kept under regular review to monitor scientific progress. We therefore *recommend* that the issues are re-examined again in, say, five years time, in the light of developments and public attitudes towards them in the interim.

ANNEX A

MEMBERSHIP OF THE HUMAN GENETICS ADVISORY COMMISSION

Professor Sir Colin Campbell
Chairman of HGAC
Vice Chancellor - University of Nottingham

Professor Cairns Aitken
Professor-emeritus of Rehabilitation Studies, University of Edinburgh

Dr Micheala Aldred
Director - Retinoblastoma Society

Professor Martin Bobrow
Professor of Medical Genetics - University of Cambridge

Mrs Doris Littlejohn
President - Central Office of Industrial Tribunals, Scotland

Professor Norman Nevin
Chairman - Gene Therapy Advisory Committee

Dr Onora O'Neill
Principal, Newnham College, Cambridge

Revd Dr John Polkinghorne
Chairman, Cloning Working Group
Chairman - Advisory Committee on Genetic Testing

Dr George Poste
Member, Cloning Working Group
Chief Science and Technology Officer - SmithKline Beecham Plc

Ms Moira Stuart
Reporter/presenter - British Broadcasting Corporation

ANNEX B

MEMBERSHIP OF THE HUMAN FERTILISATION AND EMBRYOLOGY AUTHORITY

Ruth Deech
Chairman of HFEA
Principal, St Anne's College, Oxford

Jane Denton
Deputy Chairman
Nursing Director, The Multiple Births Foundation

Professor Brenda Almond
Professor of Moral and Social Philosophy, University of Hull
From November 1998

Dr Gulam Bahadur
Head of Fertility Laboratories, UCLMS/UCLH Trust

Professor David Barlow
Nuffield Professor of Obstetrics and Gynaecology and Head of Department, University of Oxford, and Clinical Director, Assisted Reproduction Unit , John Radcliffe Maternity Hospital

Professor Ruth Chambers
General Practitioner and Professor of Health Commissioning, Primary Care Development Unit, School of Health, Staffordshire University
until November 1998

Moira Coath
Solicitor and Non-Executive Director of Dorset Healthcare Trust

Liz Forgan
Broadcaster, journalist, and media consultant
until November 1998

Professor Christine Gosden
Member, Cloning Working Group
Professor of Medical Genetics, University of Liverpool, Liverpool Women's Hospital

David Greggains
Director, Gorham Partners Ltd
until November 1998

Professor Andrew Grubb
Professor of Medical Law, University of Cardiff

Professor Martin Johnson
Professor of Reproductive Sciences, University of Cambridge

Richard Jones
Legal Consultant
until November 1998

Professor Henry Leese
Professor of Biology, University of York
From November 1998

Professor Stuart Lewis
Professor of Psychology Applied to Medicine, The Queen's University, Belfast

Dr Brian Lieberman
Medical Director, Regional IVF and DI Unit, St Mary's Hospital, Manchester

Dr Anne McLaren
Member, Cloning Working Group
Principal Research Associate, Wellcome CRC Institute, Cambridge

Dr Sadia Muhammed
General Medical Practitioner in York and Forensic Medical Examiner to the North Yorkshire Police
From November 1998

Ms Sara Nathan
until recently Editor Channel 4 News
From November 1998

The Right Revd Dr Michael James Nazir-Ali
Bishop of Rochester

Ms Sharmila Nebhrajani
Head of Corporate Planning at the BBC, a Chartered Accountant and former Management Consultant
From November 1998

Dr Joan Stringer
Principal and Vice Patron, Queen Margaret College, Edinburgh

Professor Allan Templeton
Professor of Obstetrics and Gynaecology, University of Aberdeen

Professor the Revd Canon Anthony Thiselton
Head of the Department of Theology, The University of Nottingham, Canon Theologian of Leicester Cathedral
until November 1998

Julia Tugendhat
Family therapist

John Williams
Dean, Faculty of Economic and Social Studies, University of Wales, Aberystwyth

ANNEX C

SUMMARY ANALYSIS OF THE RESPONSES TO THE CONSULTATION DOCUMENT

A total of 194 responses were received, 3 of which arrived some time after the deadline for responses had passed and do not therefore feature in this analysis. Respondents were asked to indicate if they wished their views to be treated in confidence. Nine said that they had no objection to their views being published, three wished them to remain in confidence. The rest expressed no view.

Just over half the responses specifically addressed the six questions in paragraph 9 of the consultation document. Not all answered all six, and some simply made their views clear on one or two of the issues. Responses have be summarised as follows:

Q1. Would research using nuclear replacement technology raise any new ethical issues in relation to what is permitted in work with embryos in the 14 day period?

Of the 122 that responded to the first question, 30% thought that using nuclear replacement technology would raise new ethical issues in relation to what is permitted in work with embryos in the 14 day period, 44% thought not. 16% thought that the 14 day limit was wrong in principle, and 4% expressed concern that the 14 day limit might be breached by serial nuclear replacement (see 5.12). 6% wanted a change in the law to make nuclear replacement technology explicitly allowable.

Q2. Are there any medical or scientific areas that might benefit from research involving human nuclear replacement?

Of the 130 who responded to second question, 55% thought that there were scientific areas that might benefit from research involving human nuclear replacement, compared with 10% who did not. A further 11% thought that other types of research could yield the same benefits. 6% felt that the

question was deliberately phrased to elicit a positive response, and around 7% felt that the question should be put in terms of what harm might arise, rather than what benefit. Nearly 10% expressed no opinion.

Q3. To what extent can a person be said to have a right to an individual genetic identity?

Of the 117 responses to question 3, 41% thought that a person could be said to have the right to an individual genetic identity, compared with 6% who thought that there was no such right. However, 50% thought that the question was not appropriate, since the consultation document had already mentioned that the experience of natural identical twins suggests that a unique genetic identity is not essential for a human being to feel, and be, individual. Most felt that individuals are more than a genetic identity and some felt that the real issue was that individuals should be able to protect their genetic identity from abuse and their genome from unauthorised use. Around 3% expressed no view.

The most clear cut responses were to questions 4 and 5.

Q4. Would the creation of a clone of a human person be an ethically unacceptable act?

In answer to question 4 (122 responses), 80% of respondents agreed that the creation of a clone of a human person would be an ethically unacceptable act. Just over 3% said it would be acceptable, and the same number expressed no view. 13% said it would be acceptable only in certain circumstances.

Q5. Would the likely cost in terms of failures and/or malformations inevitable in developing a programme of human reproductive cloning be ethically acceptable?

For question 5 (112 responses), 77% said that the likely cost in term of failures and/or malformations inevitable in developing a programme of human

reproductive cloning would not be ethically acceptable, 6% thought the cost would be acceptable, and 12.5% argued that the risk of harm needed to be weighed against the possible advantages. 4.5% did not know

Q6. What ethical importance might be attached to the distinction between artificial processes for which there are parallels in natural processes and those for which there are not?

Of the 114 responses to Question 6, 26% of respondents thought that the distinction was important, against less than 3% who did not. 71% thought it was wrong to attempt to differentiate in this way, many arguing that artificial processes, like surgery, produced benefits, while some natural processes were harmful.

The question of advice to Ministers attracted far fewer responses, particularly from individuals. 43% thought that more education was needed, and 34% thought that more discussion and debate on ethics should be encouraged rather than scientific education, particularly since formal education might take a generation to have much impact. Some specific ideas were mentioned, including education through the press, television and the arts, or leafleting through supermarkets. 13% interpreted "building public confidence" as indicating an attempt to manipulate public opinion

A range of other issues were raised, mainly by those who did not attempt to address the six specific questions posed. 44% of primarily individual comments were simply statements against all forms of cloning. 13% thought that the distinction made between "reproductive" and "therapeutic" cloning in the consultation document was arbitrary, and 9% saw benefit in some international legislation on cloning.

The Analysis

The responses were analysed by 9 categories - some individual responses were counted in more than one category where there were obviously dual interests. The categories were labelled as follows:

A	scientific	**B**	legal	**C**	clinical
D	ethical	**E**	individual	**F**	theological
G	lay groups	**H**	industry	**I**	academic

Each of the questions posed in the consultation document offered a range of answers. These were identified and cross-referenced with the category of respondent. The results were tabulated as follows:

Q1 - Would research using nuclear replacement technology raise any new ethical issues in relation to what is permitted in work with embryos in the 14 day period?

a yes
b no
c amend law to make nuclear replacement technology explicit
d 14 day limit is wrong in principle
e concern over extending the 14 day limit by transferring to new host embryos

TABLE 1

Answer	Total	A	B	C	D	E	F	G	H	I
a	37	5	1	3	7	10	5	3	-	3
b	54	8	-	15	3	8	7	9	3	1
c	7	1	1	1	2	2	-	-	-	-
d	20	1	1	-	1	10	5	2	-	-
e	4	-	-	1	-	1	1	1	-	-

Q2 - Are there any medical or scientific areas that might benefit from research involving human nuclear replacement?

a yes
b no
c don't know
d tackle in other ways - not by cloning
e practical aspects of technology need to be taken into account - e.g. multiple embryos
f ask what harm would arise, rather than what benefit
g immoral question - deliberately phrased to elicit positive response

TABLE 2

Answer	Total	A	B	C	D	E	F	G	H	I
a	72	10	2	17	7	12	7	13	3	1
b	13	2	-	2	-	6	2	1	-	-
c	12	-	-	3	5	1	1	1	-	1
d	14	3	-	1	1	3	5	1	-	-
e	1	-	-	-	-	-	1	-	-	-
f	5	-	-	-	-	3	1	-	-	1
g	4	1	-	-	-	-	2	1	-	-

Q3 - To what extent can a person be said to have a right to an individual genetic identity?

a there is such a right
b there is not such a right
c not an appropriate question - either because individuals are more than a genetic identity or because individuals should be able to protect their genetic identity from abuse
d don't know

TABLE 3

Answer	Total	A	B	C	D	E	F	G	H	I
a	48	5	-	9	4	15	5	9	1	-
b	7	-	2	-	1	2	2	-	-	-
c	59	8	-	12	7	9	9	8	2	4
d	3	-	-	1	-	-	2	-	-	-

Q4 - Would the creation of a clone of a human person be an ethically unacceptable act?

a yes
b no
c no, in certain circumstances
d don't know

TABLE 4

Answer	Total	A	B	C	D	E	F	G	H	I
a	98	13	1	16	8	24	16	14	3	3
b	4	1	-	-	-	2	1	-	-	-
c	16	1	1	3	4	3	1	2	-	1
d	4	1	-	1	1	-	-	1	-	-

Q5 - Would the likely cost in terms of failures and/or malformations inevitable in developing a programme of human reproductive cloning be ethically acceptable?

a yes
b no
c needs to be weighed against advantages
d don't know

TABLE 5

Answer	Total	A	B	C	D	E	F	G	H	I
a	7	1	-	2	-	1	1	1	-	1
b	86	11	3	14	10	21	13	11	1	2
c	14	1	-	1	2	4	1	3	2	-
d	5	2	-	2	-	-	1	-	-	-

Q6 - What ethical importance might be attached to the distinction between artificial processes for which there are parallels in natural processes and those for which there are not?

a important
b not important
c should not differentiate in this way

TABLE 6

Answer	Total	A	B	C	D	E	F	G	H	I
a	30	4	-	4	4	10	3	5	-	-
b	3	-	-	-	-	2	-	1	-	-
c	81	8	2	15	11	12	15	11	3	3

ADVICE TO MINISTERS

a more education needed
b "building public confidence" = manipulating public opinion
c let things happen naturally - do not push
d encourage more discussion and debate on ethics rather than scientific education
e stress the robustness of the current legislation and the way it is sensibly and sensitively implemented
f establish Royal Commission to conduct ethical review of recent innovations in biotechnology - medical, agricultural, human, animal, plant and microbiological

TABLE 7

Answer	Total	A	B	C	D	E	F	G	H	I
a	37	19	2	2	3	4	4	1	1	1
b	11	5	-	-	2	2	-	-	-	2
c	2	1	-	-	-	-	-	1	-	-
d	30	15	1	3	1	2	4	2	1	1
e	4	2	-	1	-	-	-	1	-	-
f	4	2	-	1	-	-	1	-	-	-

OTHER ISSUES RAISED

a anti-cloning
b no opinion proffered
c compare and contrast with botanical cloning
d arbitrary distinction between reproductive/therapeutic cloning
e HFEA/HGAC undemocratic and unrepresentative
f support international legislation on cloning
g is "Dolly" a one-off, unrepeatable?
h cloning experiments are still some way off
I general unspecific concern
j penalties should be introduced to discourage law-breaking
k use influence of the Arts in raising public understanding
l specific mention of the "yuk" response to cloning
m need for regular review to keep pace with change
n regulation will not work
o pro-cloning - benefits to the childless

TABLE 8

Answer	Total	A	B	C	D	E	F	G	H	I
a	58	2	1	2	2	42	5	4	-	-
b	8	-	-	2	1	2	-	1	1	1
c	1	-	-	-	-	1	-	-	-	-
d	17	1	-	3	7	2	3	1	-	-
e	9	-	-	1	2	4	1	1	-	-
f	12	1	-	1	-	8	2	-	-	-
g	1	-	-	-	1	-	-	-	-	-
h	2	1	-	1	-	-	-	-	-	-
i	3	-	-	-	-	3	-	-	-	-
j	1	-	-	-	-	1	-	-	-	-
k	3	1	1	-	1	-	-	-	-	-
l	5	-	-	-	1	1	1	1	-	1
m	3	2	-	1	-	-	-	-	-	-
n	1	-	-	-	-	1	-	-	-	-
o	1	-	-	-	-	1	-	-	-	-

ANNEX D

EXTRACTS FROM THE HUMAN FERTILISATION AND EMBRYOLOGY ACT 1990

Activities governed by the Act

3.-(1) No person shall-

(a) bring about the creation of an embryo, or

(b) keep or use an embryo,

except in pursuance of a licence.

(2) No person shall place in a woman -

(a) a live embryo other than a human embryo, or

(b) any live gametes other than human gametes.

(3) A licence cannot authorise -

(a) keeping or using an embryo after the appearance of the primitive streak,

(b) placing an embryo in any animal,

(c) keeping or using an embryo in any circumstances in which regulations prohibit its keeping or use, or

(d) replacing a nucleus of a cell of an embryo with a nucleus taken from a cell of any person, embryo or subsequent development of an embryo.

(4) For the purposes of subsection (3)(a) above, the primitive streak is to be taken to have appeared in an embryo not later than the end of the period of 14 days beginning with the day when the gametes are mixed, not counting any time during which the embryo is stored.

4.-(1) No person shall-

(a) store any gametes, or

(b) in the course of providing treatment services for any woman, use the sperm of any man unless the services are being provided for the woman and the man together or use the eggs of any other woman, or

(c) mix gametes with the live gametes of any animal,

except in pursuance of a licence.

(2) A licence cannot authorise storing or using gametes in any circumstances in which regulations prohibit their storage or use.

(3) No person shall place sperm and eggs in a woman in any circumstances specified in regulations except in pursuance of a licence.

(4) Regulations made by virtue of subsection (3) above may provide that, in relation to licences only to place sperm and eggs in a woman in such circumstances, sections 12 to 22 of this Act shall have effect with such modifications as may be specified in the regulations.

(5) Activities regulated by this section or section 3 of this Act are referred to in this Act as "activities governed by this Act".

ANNEX E

BRIEF DETAILS OF THE LAWS IN SOME OTHER COUNTRIES

Australia — Legislation banning cloning exists in three states: the **Infertility Treatment Act 1995** in Victoria; the **Reproductive Technology Act 1988** in South Australia; and the **Human Reproductive Technology Act 1991** in Western Australia. The Western Australia legislation is currently under five-year compulsory review.

Belgium — Legislation covering medical ethics including cloning is currently being considered by Parliament.

Denmark — **Act No. 503 on a Scientific Ethical Committee System and the Handling of Biomedical Research Projects (1992)** Research on cloning (production of genetically identical individuals) is forbidden as is nuclear substitution.

Act No. 460 on Medically Assisted Procreation in Connection with Medical Treatment, and Research (1997) This confirms the Danish Parliament's position, of 25 January 1995, that treatment cannot be initiated in areas where a research ban already exists under the 1992 Act.

France — Human cloning is implicitly prohibited by the French bio-ethics legislation passed in 1994 (laws 94-653 and 94-654 of 29 July 1994). The French National Bioethics Committee recommended that the ban should be made more explicit when the bioethics legislation is revised in 1999.

Germany — **Federal Embryo Protection Act 1990** The creation of an embryo genetically identical to another embryo, fetus or any living or dead person is an offence.

Japan — A Committee of the Council for Science and Technology is discussing ways of regulating human cloning, and is due to report by the end of March 1999.

Norway	**Law No 56 on the medical use of biotechnology 1994** Implicitly prohibits embryo cloning.
Slovakia	**1994 Health Care Law** Implicitly prohibits embryo cloning.
Spain	**Law No 35/1988 on Assisted Reproduction Procedures** Explicitly prohibits embryo and oocyte cloning with criminal sanctions.
Sweden	**Law No 115 14 March 1991** Implicitly prohibits embryo and oocyte cloning with criminal sanctions.
Switzerland	**Federal Constitution** Legally binding, implicitly prohibits embryo cloning.

These details were correct to the best of our knowledge at the time of publication.

ANNEX F

GLOSSARY

Antigenicity: the capability, under appropriate conditions, of inducing a specific immune response.

Bioethics: the branch of ethics, philosophy and social commentary that discusses the life sciences and their potential impact on our society.

Cellular cloning: the process by which cells derived from the body ("soma") and are grown in tissue culture in a laboratory. The genetic makeup of the resulting cloned cells (the "cell line") is identical to that of the original cell.

Chromosomes: nucleic acid-protein structure in the nucleus of a cell. Chromosomes are composed chiefly of DNA, the carrier of hereditary information. Chromosomes contain genes, working lengths of DNA that carry the genetic code for specific proteins, interspersed with large amounts of DNA of unknown function. A normal human somatic cell contains 46 chromosomes; a normal human gamete cell contains 23 chromosomes.

Cloning: producing a cell or organism with the same nuclear genome as another cell or organism.

CNR: medical and scientific applications of cloning technology which do not result in the production of genetically identical fetuses or babies. These techniques may be undertaken to advance fundamental research and therefore not all such applications will lead to immediate therapeutic utility.

Diploid: a cell such as a somatic cell having two chromosome sets, as opposed to the haploid situation of eggs and sperm which have only one chromosome set.

DNA: Deoxyribonucleic acid, found primarily in the nucleus of cells (some DNA is also found in the mitochondrion). DNA carries the instructions for making all the structures and materials that the body needs to function.

Egg: the mature female germ cell: also called the "ovum" or "oocyte".

Embryo: the developing organism from the single-celled stage until significant cellular differentiation has occurred, when the organism becomes known as a "fetus".

Enucleated egg: an egg from which the nucleus has been removed.

Fertilisation: the process whereby male and female gametes unite, beginning when a sperm contacts the outside of the egg and ending with the formation of a zygote.

Fetus: the term used for the developing organism once significant cellular differentiation has occurred.

Fibroblast: a resident cell of connective tissue.

Gene: a working length of a chromosome composed of DNA. Each of the body's 100,000 genes carries the instructions that allow the cell to make one specific product such as a protein.

Genome: the complete genetic make-up of a cell or organism.

Genotype: the genetic make-up of an individual.

Germ cell: a cell all of whose surviving descendants will form sperm or eggs. All other body cells are known as "somatic" cells.

Haploid: the single chromosome set carried by the sperm and egg cells which are recombined after fertilisation to create the diploid chromosome set present in every cell of the body except sperm and eggs.

Human reproductive cloning: the creation of human beings genetically identical to one another or to any other human being.

Immunologically compatible: recognised as non-invasive by the body's immune system.

Immunosuppressive drug: medication that reduces the effect of the body's immune system to a foreign object - whether infection or tissue or organ transplant.

In Vitro Fertilisation (IVF): eggs and sperm are collected and put together to achieve fertilisation outside the body.

Mitochondria: cellular organelles that provide energy to the cell. The mitochondrion contains some of its own genes.

Mitochondrial diseases: diseases due to mutations in mitochondrial DNA rather than nuclear DNA. Since mitochondria are inherited exclusively from mothers, mitochondrial diseases show matrolineal inheritance. They include Kearn's-Sayre Syndrome and Leber's Heriditary Optic Neuropathy.

Nuclear replacement: a technique which involves inserting the nucleus from a diploid cell or another egg, into an egg from which the nucleus has been removed.

Nucleus: the cell structure that houses the chromosomes, and thus the genes.

Oocyte: the mature female germ cell: the egg.

Primitive streak: this develops in an embryo by day 14 when the cells which form the fetus separate from those which form the placenta and umbilical cord.

Reproductive cloning: where an entire animal is produced from a single cell by asexual reproduction.

Somatic cells: any cell of an embryo, fetus, child or adult not destined to become a sperm or egg cell.

Stem cell: an undifferentiated cell which is a precursor to a number of differentiated cell types.

Transgenic: containing a gene or genes not natural to the individual.

Zygote: the single-celled fertilised egg.