EXPLANATORY MEMORANDUM TO

THE HUMAN TISSUE (QUALITY AND SAFETY FOR HUMAN APPLICATION) REGULATIONS

2007 No. 1523

1. This explanatory memorandum has been prepared by the Department of Health and is laid before Parliament by Command of Her Majesty.

This memorandum contains information for the Joint Committee on Statutory Instruments.

2. Description

2.1 These Regulations implement Directive 2004/23/EC[1], laying down standards of quality and safety for human tissues and cells intended for human application, and Commission Directives 2006/17/EC[2] and 2006/86/EC[3] laying down technical requirements in relation to Directive 2004/23/EC, so far as necessary to do so in relation to human tissue and cells (other than human gametes and embryos). The Directives do not apply to human organs or blood (including blood components).

2.2 These Regulations regulate activities concerning the use of human tissue and cells intended for human application (use in or on a human recipient). Detailed requirements on consents and authorisations to be obtained for the use of human material are contained in the Human Tissue Act 2004 (c.30) ("the 2004 Act") (which mainly extends to England and Wales and Northern Ireland only) and the Human Tissue (Scotland) Act 2006 (2006 asp 4) ("the Scottish 2006 Act"). The 2004 Act also regulates other uses of human tissue and cells, including a requirement to hold a licence.

3. Matters of special interest to the Joint Committee on Statutory Instruments

3.1 Section 46(1) (power to give effect to Community obligations) of the 2004 Act provides power for the Secretary of State to amend that Act for the purpose of implementing Community obligations "relating to material which consists of, includes or is derived from human cells". Section 55(1) (power to

[1] Directive 2003/33/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells (OJ L No. 102, 7.4.2004, p. 48).
[2] Commission Directive 2006/17/EC of 8 February 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells (OJ L 38, 9.2.2006, p.40).
[3] Commission Directive 2006/86/EC of 24 October 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells (OJ L294, 25.10.2006, p.32).

give effect to Community obligations) of the Scottish 2006 Act gives the Scottish Ministers a similar power in respect of that Act. However, a decision was made that it would be more appropriate to adopt a unified legislative and regulatory regime for the whole of the United Kingdom for the purpose of implementing the Directives. In order to achieve this it is necessary for the Regulations to be made under section 2(2) of the European Communities Act 1972. There is also limited overlap between the 2004 Act, the Scottish 2006 Act and the measures needing to be adopted to implement the Directives, which meant that there would have needed to be substantial amendments to both of these new Acts if the Directives had been implemented by way of their amendment. Amending the 2004 Act and the Scottish 2006 Act in this way would have made the legislation needed to implement the Directives much less accessible to the healthcare sector and the public than the proposed single set of Regulations.

3.2 The Regulations are being laid subject to the affirmative resolution procedure, which is the same procedure prescribed for regulations made under section 46 of the 2004 Act (see section 52(4) of that Act) and section 55(1) of the Scottish 2006 Act (see section 59(3) of that Act).

4. Legislative Background

4.1 These Regulations have been made under section 2(2) of the European Communities Act 1972. With the agreement of the Scottish Ministers, and by virtue of the power of the Secretary of State under section 2(2) of the European Communities Act remaining exercisable in relation to Scotland by virtue of section 57(1) of the Scotland Act 1998, these Regulations (except part 6, which amends the 2004 Act) extend to Scotland. Their purpose is to make such provision as is necessary to ensure full implementation of Directive 2004/23/EC and Commission Directives 2006/17/EC and 2006/86/EC, which lay down standards of quality and safety for human tissues and cells intended for human application, otherwise than in relation to human gametes and embryos (which are the subject of the Human Fertilisation and Embryology (Quality and Safety) Regulations 2007). The Regulations amend the 2004 Act, which established a licensing framework for the regulation of various activities involving human material, including research, public display, and storage for the purposes of transplantation. A regulatory body, the Human Tissue Authority ("the HTA"), was also created by the 2004 Act, with power to provide assistance to other public authorities in the United Kingdom.

4.2 The date for implementation of Directive 2004/23/EC was 7 April 2006. However, as the UK was going through the process of adopting legislation regulating the use of human tissue and cells at the time the Directive was adopted in 2004, and since the HTA has given directions under the 2004 Act to ensure licensed tissue establishments meet the same standards as laid down in the Directives, the United Kingdom has taken advantage of the right in Article 31(2) of the Directive to delay full implementation for one year, to allow establishments more time to prepare for its introduction.

4.3 These Regulations are subject to the affirmative resolution procedure.

4.4 A Transposition Note in respect of Directive 2004/23/EC and Commission Directives 2006/17/EC and 2006/86/EC is shown in the Annex to this Explanatory Memorandum.

4.5 The European Commission first published its proposal for Directive 2004/23/EC in June 2002 (COM (2002) 319 final). An accompanying Explanatory Memorandum and Initial Regulatory Impact Assessment were provided by the Department of Health on 8 July 2002. They were cleared by the House of Commons and House of Lords European Scrutiny Committees on the 16 October and 30 October 2002 respectively. The Department of Health wrote again on 19 May 2003 informing the Joint Parliamentary European Scrutiny Committees of the results of First Reading. An Explanatory Memorandum was sent on 13 June 2003 informing the Committees of the political agreement reached at the June Health Council. The House of Lords cleared scrutiny on 17 June 2003, but the House of Commons noted that in light of the significant additional costs that could arise as a result of the inclusion of mature gametes within the scope of the draft Directive, they would hold the document under scrutiny pending receipt of a further Regulatory Impact Assessment. The provisional Regulatory Impact Assessment was made available at the same time the Department consulted on a draft of these Regulations to enable establishments to assess the likely costs of implementation. The Committees were updated on 28 June 2006.

5. Extent

5.1 The Regulations extend in their entirety to England, Wales and Northern Ireland. The Regulations, except Part 6, also extend to Scotland.

5.2 Directive 2004/23/EC and Commission Directives 2006/17/EC and 2006/86/EC also apply to Gibraltar. The Gibraltar Authorities are responsible for implementing the Directives in relation to Gibraltar.

6. European Convention on Human Rights

The Minister of State for Health Services has made the following statement regarding Human Rights:

In my view the provisions of the Human Tissue (Quality and Safety for Human Application) Regulations 2007 are compatible with the Convention rights.

7. Policy background

7.1 These Regulations complete implementation of Directive 2004/23/EC, laying down standards of quality and safety for human tissues and cells intended for human application, and Commission Directives 2006/17/EC and 2006/86/EC laying down technical requirements in relation to Directive 2004/23/EC, in relation to human tissue and cells (other than gametes and embryos). The Directives not only cover some activities previously regulated

by the 2004 Act, but also extend to other activities (procurement, processing, testing, distribution, import and export) in relation to tissue and cells intended for human application. These activities were not previously directly subject to the licensing regime of the 2004 Act, but were regulated by directions given by the HTA under that Act.

7.2 Most of the requirements in the Directive are not new to establishments already licensed under the 2004 Act. The Directive and the implementing regulations do address other areas not currently covered by the 2004 Act, and directions given by the HTA under it, although, in practice, many existing licensed establishments will find that the standards represent acknowledged good practice.

7.3 Establishments seeking a licence will be required to comply with the following key provisions:

Staff and facilities

- Nominate a *Designated Individual* who will have the duty of ensuring compliance with the Regulations (as already happens for establishments currently licensed under the 2004 Act). The nomination will have to be approved by the HTA.

- Have facilities and use equipment and practices suitable to the activities carried out. Environmental standards must be sufficient to maintain the quality and efficacy of the tissue or cells. Suitability of premises and equipment will have to be demonstrated to HTA inspectors.

- Have appropriately qualified and experienced staff, in sufficient numbers, to operate a safe, effective service.

Quality management procedures

- A quality management system must be put in place, with written standard operating procedures, record and report forms. The quality manual must be made available at inspections.

- Reception, processing, storage and distribution must be carried out in appropriate facilities and to documented procedures. Documented processes should also include arrangements for discarding and segregating tissue and cells unsuitable for human application.

- All tissue and cells must be traceable from donor to recipient and back again. Traceability requirements also relate to materials and equipment coming into contact with the tissue or cells. Traceability data must be kept for 30 years.

- Tissue and cells transported between establishments must be moved in a container that will maintain their quality and efficacy. Shipments

must be labelled and accompanied by documentation specified in the directions to be given by the HTA under the Regulations.

- Arrangements with third party service providers must be fully documented, with written agreements between the two establishments. Third party service providers will also be subject to inspection by the HTA.

Reporting

- All serious adverse events and reactions, affecting donors or recipients, to the use of tissue or cells in treatment must be reported to the HTA. Reports must contain a minimum level of information specified by the HTA in directions to be given under the Regulations (similar to the reporting system currently in place for establishments licensed under the 2004 Act).

Records

- HTA will maintain a publicly accessible register of licensed establishments and the activities they are approved to carry out. HTA will also maintain a publicly available serious adverse incidents register.

- Medical records must be kept confidential and the identities of donors must not be disclosed to recipients (or the recipient's family) and vice versa.

- All tissue and cells containers will have to marked using a EU wide coding system (the code is currently under development by a European Commission working group, of which the UK is a member).

Selection of donors

- Donors must be given full information about the implication of donating. Consent/authorisation to the use of donated tissue and cells must also be obtained (as currently required by the 2004 Act and the Scottish 2006 Act.

- Donors will be subject to screening for infections including HIV 1 & 2, Hepatitis B & C, Syphilis and Chlamydia. Donors who, or whose sexual partners, come from high incident areas must also be screened for HTLV antibodies.

7.4 Another notable requirement in the Directives is the need for Member States to endeavour to introduce voluntary and unpaid donation (except for compensation for expenses and inconvenience). The UK responded to a questionnaire circulated by the Commission in 2006, outlining the measures taken in the UK to ensure voluntary unpaid donation and the legislation in place to restrict organ, tissue and cell trafficking. In summary, organ, tissue

and cell trafficking are offences under section of the 2004 Act and section 20 of the Scottish 2006 Act, but both Acts do allow for the reimbursement of out of pocket expenses. In the UK, reimbursement for tissue and cell donation is likely to be exceptional, for example meeting travelling expenses for the donation of bone marrow.

7.5 At each stage of the development of the Directive and the two Commission Directives, stakeholders have had the opportunity to comment. Public consultation exercises were conducted by the European Commission before the text of each Directive was finalised. Each exercise was publicised by the competent authorities and stakeholders were encouraged to submit comments at this early stage.

During the development of the three Directives, the Department of Health also convened a programme of consultation meetings and events with stakeholders under the umbrella of its Policy Collaborative initiative. The group included stakeholder representatives from all areas of tissue banking and processing, both NHS and independent sector across the UK. Convened in 2003, the work of the group resulted in implementation guidance that was sent to NHS Trusts.

A draft of the Regulations, accompanied by the partial Regulatory Impact Assessment, went out to consultation on 3 July 2006. The closing date for comments was 13 October 2006. Account was taken of the comments received in the final draft of the regulations. Comments relating to implementation policy were passed to the HTA.

8. Impact

8.1 A Regulatory Impact Assessment is attached to this memorandum.

8.2 These Regulations will impact on the public sector, particularly the National Health Service, requiring them to ensure they are fully licensed and to make changes to their systems to ensure that the relevant standards of quality and safety are met. These Regulations are expected to increase enforcement costs for the HTA.

9. Contact

Triona Norman: (020) 7972 4921 or e-mail: triona.norman@dh.gsi.gov.uk can answer any queries regarding the instrument.

A proposal to implement European Directive 2004/23/EC setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.

Regulatory Impact Assessment

1. Title

This Regulatory Impact Assessment (RIA) considers the potential impact of the European Union (EU) Tissues and Cells Directive (the Directive) on UK establishments handling human tissues for human application. The Directive was adopted and published on 31 March 2004.

2. Purpose and intended effect

(i) Objective

The Directive and the two Commission Directives that form its technical annexes will be implemented by regulations made under section 2(2) of the European Communities Act 1972.

There are existing, separate legislative frameworks regulating reproductive cells (sperm, eggs and embryos) and all other human tissue. This separation will be maintained in the implementation process. The Directive will be implemented via:

- The Human Fertilisation & Embryology (Quality and Safety) Regulations 2007, which will amend the Human Fertilisation & Embryology Act 1990 to implement the Directive in respect of reproductive cells.

- Free standing regulations, The Human Tissue (Quality & Safety for Human Application) Regulations 2007, to implement the Directive for all other tissue. The primary legislation in this area is the Human Tissue Act 2004 and the Human Tissue (Scotland) Act 2006.

The duty to ensure compliance with the requirements of the Directive will fall to the nominated "Competent Authority" in each member state. Ministers have agreed that for reproductive cells this would be the Human Fertilisation & Embryology Authority (HFEA) and for conventional tissue banking it is the Human Tissue Authority (HTA).

The Scottish Ministers have also agreed that for conventional tissue banking the HTA should be the competent authority for Scotland and both the Human Tissue Act and the Human Tissue (Scotland) Act were drafted to allow for this. The HFEA already covers Scotland.

In 2004 the Government announced that it intended to replace the HFEA and HTA with a single regulatory body, the Regulatory Authority for Tissue and Embryos (RATE). This is in keeping with the objectives of streamlining, efficiency and cohesion, set out in *Reconfiguring the Department of Health's Arm's Length Bodies* (2004). It is envisaged that RATE will eventually become the single competent authority for the UK under the Directive.

The Directive required implementation by 7 April 2006. However, because it had regulatory frameworks in place when the Directive was adopted in 2004, the UK has been able to take advantage of a one year derogation, with the result that the Directive will take effect in the UK from April 2007.

(ii) Background

Purpose of the Directive

The purpose of the Directive is to establish a unified European Community framework to ensure high standards of quality and safety in the transplantation of human tissues and cells. It is intended that this framework should prevent the transmission of diseases by these tissues and cells, and should facilitate safer international exchanges of such cells and tissues. It is proposed to do this by:

- requiring a competent authority (or authorities) in each Member State to inspect and accredit establishments carrying out processing, storage, testing and distribution of human tissues and cells intended for human applications, such as transplantation. Inspections must be carried out at least every two years, to ensure that establishments meet the quality and safety standards set out in the Directive;

- requiring establishments handling such tissues and cells to conduct these activities in a physical environment that meets high safety standards, and to institute a quality management system;

- ensuring that human tissues and cells intended or used for human applications are traceable (from donor to recipient and vice versa) within the EU, through the introduction of a uniquely identifiable coding system;

- introducing a monitoring system for adverse events and reactions for donated and transplanted tissues and cells;

- introducing a system for the regulation of imports of human tissues and cells from non-EU countries, to ensure their safety and quality;

- requiring that tissues and cells be procured by trained and experienced staff.

- All units covered by the Directive will be required to establish written agreements with any third parties who perform activities that could affect the quality or safety of tissues or cells. Third parties must be selected on the basis of their ability to meet the Directive's standards.

Detailed requirements

The technical requirements of the Directive are set out in two European Commission Directives:

- Commission Directive 2006/17/EC, adopted on 8 February 2006, covering technical requirements relating to tissue donation, procurement and testing.

- Commission Directive 2006/86/EC, adopted on 24 October 2006, setting out requirements for traceability, adverse event/reaction reporting and technical requirements for coding, processing, preservation, storage and distribution.

Previous partial RIAs were developed prior to the adoption of Commission Directive 2006/86/EC, so were based on a provisional understanding of the technical requirements it contained. The obligations described below are indicative, not exhaustive. The Commission Directives should be consulted for detailed technical requirements.

Tissues covered

The Directive applies to tissues and cells intended for human applications, such as bone, corneas, heart valves, haematopoietic peripheral blood, umbilical-cord blood, reproductive cells (sperm, eggs and embryos), foetal tissues and cells, and adult, bone marrow and embryonic stem cells.

The Directive does not cover tissues and cells used in an autologus graft as part of the same surgical procedure, blood or blood components (as defined by Directive 2002/98/EC), organs and part organs if it is their function to be used for the same purpose as the entire organ in the human body and animal tissues and cells. The Directive does not cover research using human tissues and cells, unless such research involves application of such tissues and cells to the human body.

The Directive will affect all organisations involved in the donation, procurement, testing, processing, preservation, storage or distribution of human tissues and cells. It will also affect the individuals who donate and receive such cells.

Existing legislation

Reproductive cells

In the UK, unlike tissue establishments involved in conventional tissue banking, handling of gametes (eggs and sperm) and embryos for certain fertility treatments and related services have been subject to statutory controls under the Human Fertilisation and Embryology Act 1990 (HFE Act).

The HFE Act regulates the creation of embryos outside the body, e.g. in vitro fertilisation (IVF) and their use in treatment, use of donated gametes and embryos in treatment and the storage of gametes and embryos. The HFE Act established the HFEA to licence and regulate such establishments. Many of the provisions of the Directive are already required of HFEA licensed establishments.

However, a wider range of activities is covered by the Directive than by the HFE Act. These include treatments involving the use of a man's fresh sperm to inseminate his partner, sperm testing and preparation. Such activities are not currently subject to sector specific regulation or licensing. Unlicensed treatments and services have been subject to regulation by the Healthcare Commission, as part of its function of ensuring effective health care provision in both the National Health Service (NHS) and the independent sector.

Other human tissue

Prior to the Directive, tissue banks in the UK, outside the HFEA licensed sector, were not covered by statutory regulations but were encouraged to seek voluntary accreditation. In order to receive accreditation, banks were inspected on behalf of the Department of Health by the Medicines and Healthcare products Regulatory Agency (MHRA), and were required to comply with the *Code of Practice for Tissue Banks providing tissues of human origin for therapeutic purposes* (DH, 2001). This voluntary Code of Practice required tissue banks to have appropriate facilities and to undertake staff training. It also set out high standards for donor screening, process control and record keeping. Tissue establishments were subject to re-inspection and re-accreditation every two years.

The Departments of Health advised NHS Trusts that they should supply tissue and cells intended for transplantation only to, and obtain human tissue for transplantation only from, banks accredited under the voluntary scheme. By February 2006, 62 establishments had been accredited by MHRA (including the major suppliers of tissue such as the National Blood Authority) and applications for accreditation by a further 55 establishments were pending. However, the definition of a tissue establishment differed slightly between the Directive and the voluntary Code of Practice which meant more tissue establishments needed to comply with the Directive.

From April 2006, responsibility for the inspection and licensing of all establishments involved in the donation, procurement, testing, storage, processing and distribution of conventional (eg bone, tendons, skin, corneas, heart valves) tissue and cells intended for human application passed to the HTA as one of the two designated Competent Authorities under the requirements of the Tissue and Cells Directive..

NHS Blood and Transplant estimates that 10,000 bone transplants are performed each year, and 800 heart valve transplants. In 2005/6, UK Transplant authority was notified of 3,819 donated corneas, from which 2,502 corneal transplants were carried out. There were 2,379 haematopoietic stem cell (bone marrow) transplants in 2003, approximately 37,000 cycles of IVF treatment, and 7,000 cycles of donor insemination.

(iii) Rationale for Government intervention

The UK is obliged to implement the provision of the Directive and the two Commission Directives forming the technical annexes. Failure to do so puts the UK at risk of infraction procedures.

As the UK already had regulatory frameworks in the relevant areas and, in the case of the HFEA licensed sector, many of the requirements in the Directive were already legal requirements under the HFE Act, any failure to implement the Directive within the specified timescale is more likely to result in the European Commission proceeding against the UK. The risk of infraction proceedings is further heightened by the fact that the UK has been able to delay implementation a year longer than other Members States.

3. Consultation

(i) Within Government

Although implementation has rested with the Department of Health, the Scottish Assembly, National Assembly of Wales and the Department of Health & Social Services in Northern Ireland have been kept involved in the progress of the Directive. Representatives of all three devolved administrations have been members of an official level steering group overseeing negotiations on the Directives and their implementation at national level since 2003.

(ii) Public consultation

At each stage of the development of the Directive and the two Commission Directives, stakeholders have had the opportunity to comment. Public consultation exercises were conducted by the European Commission before the text of each Directive was finalised. Each exercise was publicised by the competent authorities and stakeholders were encourage to submit comments at this early stage.

During the development of the three Directives, the Department of Health also convened a programme of consultation meetings and events with stakeholders under the umbrella of its Policy Collaborative initiative. The group included stakeholder representatives from all areas of tissue banking and processing, both NHS and independent sector across the UK. Convened in 2003, the work of the group resulted in implementation guidance that was sent to NHS Trusts (separate guidance was developed by the HFEA for stakeholders within the reproductive cells sector).

Both sets of draft regulations, accompanied by the partial RIA went out to consultation on 3 July 2006. The closing date for comments was 13 October 2006. Account was taken of the comments received in the final draft of the regulations. Comments relating to implementation policy were passed to the relevant competent authority.

4. Options

(i) O**ption 1 – do nothing**

This option would not achieve the objectives:

- The UK would not be part of the unified European Community framework to ensure high standards of quality and safety in the transplantation of human tissues and cells.

- For non-HFEA licensed tissue banks and units handling fresh gametes, there would be no requirement for unified coding and labelling systems, traceability, monitoring systems for adverse incidents, or regulation of imports.

- For the HFEA licensed sector there would be no requirement for a unified coding and labelling system, and traceability.

- There would be no single regulatory framework for the reproductive and non-reproductive tissue banking sectors. The Government's objective of merging the HTA and HFEA to form a new regulatory authority would be more difficult to achieve in the absence of such a unified framework.

- If the Directive is not implemented into U.K. law by 7th April 2007, the European Commission will have the right to commence infraction proceedings against the U.K under Article 226 of the European Community Treaty. If the European Court of Justice finds that a member state has failed to fulfil an obligation under the EC Treaty, the European Commission can ask the Court to impose a lump sun penalty or a daily penalty of any amount on the member state.

Risks of Option 1

As stated above, the UK would face a very real risk of infraction procedures.

While the great majority of health care in the UK is of a very high clinical standard, the complexity of modern health care carries a potential risk of serious adverse events and reactions. The Department of Health report *An Organisation with a memory* (2000) estimated that adverse events in which harm is caused to patients occur in around 10% of admissions to NHS hospitals. These adverse events and reactions cost the NHS an estimated £2 billion a year in additional hospital stays alone, without taking account of human or wider economic costs. The NHS pays around £400 million a year in settlement of clinical negligence claims, and hospital-acquired infections are estimated to cost the NHS nearly £1 billion a year. It is thought that around 15% of such infections may be avoidable.

We are still establishing figures for the number of adverse events and reactions in treatments using human tissues and cells. Such procedures are relatively complex, and may therefore carry a higher than average risk but numbers are likely to be small. The HTA has convened a working group to advise on how the notification and inspection of notified adverse events and reactions will be managed appropriately and proportionately to keep associated costs low.

Inspection and Licensing

If there is no statutory requirement for inspection and licensing of all establishments handling human tissues and cells for transplantation, it is not possible to ensure that all such units adopt appropriate standards to minimise the risks outlined above.

Quality and Safety

In addition to the general health care risks outlined above, there are a number of particular risks associated with treatments involving tissues and cells; risks of infection, contamination and graft failure.

- *Risk of infection*

  The risk of infection from tissue transplantation in the U.K. is very low. Tissues and cells for transplant are carefully screened, according to national and international guidelines.

  However, internationally, HIV, Hepatitis B, Hepatitis C and human T-lymphotropic virus (HTLV) have all been transmitted by tissue transplantation[4]. HIV has been transmitted by artificial insemination using donor sperm[5]. Classical CJD has, in up to three cases worldwide, been transmitted by corneal transplantation.[6] (It should be noted that there have been no reported cases of vCJD transmission through tissue or cell transplantation)

  A recent study estimated the incidence of HIV infection among tissue donors in the United States at 30 per 100,000. The incidence of Hepatitis B was estimated at 18 per 100,000, of Hepatitis C at 12 per 100,000, and of HTLV at 6 per 100,000.[7] The potential for transmission of such diseases underlines the need for maintenance of the highest quality and safety standards.

[4] 'Probability of Viremia with HBV, HCV, HIV and HTLV among Tissue Donors in the United States', Zou S. et al., *New England Journal of Medicine* 2004; 351: 751-759

[5] 'HIV-1 infection by artificial insemination**',** Matz B. et al., *Lancet* 1998 Mar; 351(9104):728

[6] 'Transplantation of corneal tissue from donors with disease of the central nervous system', Hogan R.N. and Cavanagh H.D., *Cornea* 1995; 14: 547-53

[7] Zou S. et al., as above.

- *Risk of contamination (including cross contamination between tissues)*

  Tissues and cells may be contaminated by bacterial or fungal agents, or potentially harmful chemicals, if stored or handled inappropriately. There have been recent cases in the USA of bacterial contamination of stored tissues, which have proved fatal to transplant recipients.[8][9] Unlike blood, which is processed in a closed system, tissue processing is undertaken in an open (albeit controlled) environment and there is, therefore, potentially a higher risk of contamination.

- *Risk of graft failure*

  Graft success depends on many factors (including operating skill and recipient diagnosis). However, inexpert removal of tissues and cells, contamination or infection, and inappropriate processing or storage, all increase the potential risk of graft failure.

While such risks can never be eliminated, they can be minimised by adherence to high standards of quality and safety.

Coding and Labelling

In the absence of a common coding and labelling system, there is no instant, automatic and universal notification of cases of infection and contamination. The current system of individual coding systems poses three main risks: delays in notification, mis-translation in moving from one coding system to another, and non-universal notification. Any of these can lead to the use of sub-optimal or unsuitable materials in transplantation with a potential consequential risk to recipients.

The importance of instant notification of infection, and traceability of tissues, is highlighted by a case in the United States, in which 58 tissues and organs were obtained from an HIV positive donor who had not yet developed antibodies.[10] In this instance, 6 of the tissues could not be accounted for by the hospitals which had received them.

[8] 'Unexplained Deaths Following Knee Surgery' *Morbidity and Mortality Weekly Report* 2001; 50(48):1080.
[9] 'Tissue Banks: The Dangers of Tainted Tissues and the Need for Federal Regulation' Statement of Jesse. L. Goodman, Director, FDA Center for Biologics Evaluation and Research, before the Committee on Governmental Affairs, U.S. Senate, May 14 2003.
[10] 'Transmission of human immunodeficiency virus type 1 from a seronegative organ and tissue donor' Simonds R.J. et al, *New England Journal of Medicine* 1992; 326: 726-732.

Monitoring of Serious Adverse Events and Reactions

Arrangements for monitoring serious adverse reactions and events in tissue banks (outside the HFEA licensed sector) currently vary between establishments.
The HTA has developed an online system for notification of serious adverse events and reactions linked to the procurement, testing, processing, preservation, storage and distribution of human tissues and cells, which is currently being user-tested. An internal HTA Steering Group and an external Working Group have been set up to support the implementation of the project. The external group consists of key stakeholders from the tissue banking field. Advice and guidance on how to report and investigate events and reactions will be provided to Designated Individuals at future training events.

Controls on Imports and Exports

The absence of regulation of imported tissue carries the risk that contaminated or infected tissue maybe sourced from abroad. That risk, in turn, acts as a disincentive to the use of imported tissue.

At the moment, relatively small numbers of tissues are sourced abroad. The Anthony Nolan Bone Marrow Trust estimates that 150 donations of bone marrow and peripheral blood stem cells are imported each year. A small number of heart valves are also sourced abroad. Such imported tissue is carefully screened before use.

As new treatments develop, particularly cell therapies, exchange of human tissues and cells between countries is likely to increase; without wider regulation the risk of receiving unsafe or poor quality tissues will also increase. Regulation of imports and exports should allow for greater confidence in the use of tissue from abroad.

Training

Since it is believed that most staff are likely to be appropriately qualified and trained, no significant risks are perceived in this area.

(ii) Option 2 – implement the directive

This option would achieve the objectives:

- It would ensure UK is part of the EU quality and safety framework.
- All tissue banks would be inspected and licensed against quality standards.
- There would be requirements for unified coding and labelling systems, traceability, monitoring systems for adverse incidents, and regulation of imports.

- There would be a single regulatory framework for the reproductive and non-reproductive tissue banking sectors. This would facilitate the merger of the HTA and HFEA to form a new regulatory authority, in line with the government's objective of streamlining arm's length bodies.

- There would be no risk of EC infraction proceedings against the UK.

Risks of Option 2

Implementation of the Directive will entail increased costs for units, and increased regulation. Some establishments that carried out small quantities of tissue banking activity (such as storage of tissue for the unit's own use) have decided to stop performing this function on clinical and cost effectiveness grounds.

5. Costs and benefits

(i) Sectors and groups affected

Approximately 150 establishments in the reproductive sector will be affected by the Directive, including HFEA licensed clinics and establishments handling fresh gamete. In the non-reproductive sector, approximately 150 tissue banks have registered with the HTA and have been deemed licensed under arrangements put in place from April 2006. These include musculoskeletal tissue banks, cardiovascular establishments, stem cell banks and ocular tissue banks procuring tissue. This section provides more detail on the types and numbers of units to which the Directive will apply.

Reproductive cells sector (91 HFEA licensed clinics, 15 satellite units and approximately 50 fresh gamete treatment, preparation and testing units

There are currently 83 units in the U.K. licensed by the HFEA for fertility and other treatments using gametes and embryos, a further 8 units which provide storage only, and 9 which conduct research only. The majority (approximately 80%) of units are private sector clinics, deriving their income from fee-paying infertility patients.

The 91 units that provide treatment or storage will be subject to the provisions of the Directive. The units which conduct only research will not be covered by the Directive. All units which are currently licensed by the HFEA, and which will be subject to the provisions of the Directive, will be required to satisfy the provisions of the Directive by April 2007.

There are 15 satellite units known as "transport" or "satellite" IVF centres, that provide treatments under the auspices of HFEA licensed units. A patient undergoing IVF, for instance, may go to a satellite unit for preparatory treatment and, in transport centres, egg collection, prior to embryo transfer at a licensed unit. These satellite units are currently required to meet HFEA standards and are covered by the licence held by the unit to which they are affiliated. Under the Directive, these units must have third party agreements in place with HFEA licensed establishments by April 2007.

In addition, a number of units that provide treatment or other related services involving the use of fresh sperm will fall within the scope of the Directive, although

they are not covered by the HFE Act. Non-donor intrauterine insemination and gamete intra-fallopian transfer (GIFT) procedures, for example, will be subject to regulation. Sperm preparation and testing will also be subject to the Directive. The HFEA has identified approximately 50 establishments that perform these procedures. These units will be required to comply with the Directive by April 2007. Some establishments have already indicated that they do not intend to continue to perform these procedures.

Non-reproductive sector (approximately 150 Tissue Banks and clinical laboratories handling human tissues and cells for human applications)

By 7 April 2006, some 120 conventional tissue establishments and around 100 small satellite units had registered with the Human Tissue Authority and had been deemed licensed within the requirements of the EU Directive. Third party organisations that supply certain services to tissue banks will also be required to comply with requirements under the Directive. Approximate figures are given below for the number of banks dealing with various types of human tissue, and the accreditation status of these establishments. It should be noted, however, that these figures are not cumulative, as a number of tissue banks handle more than one type of tissue, and will therefore be counted in more than one category.

- Musculoskeletal tissue banks – there are approximately 27 banks in England and Northern Ireland, 3 in Wales . These banks mainly collect and store bone for use in revisions of hip replacements. In 2004, the Department of Health estimated that at least 74% of these procedures were carried out in NHS Trusts that source bone only from accredited establishments. Other establishments will need to apply to be licensed if they wish to store bone for longer than 48 hours prior to use.

- Cardiovascular tissue banks – There are six banks in the UK processing cardiovascular tissue and one other storing it long term

- Haematopoietic Progenitor Cell (Stem Cell) banks – There are approximately 28 in England and Northern Ireland, 2 in Wales stem cell banks. Of these, 16 were accredited by MHRA.

- Ocular Tissue Banks – Both the Bristol and Manchester eye banks supply tissue for the great majority (c95%) of corneal and scleral transplants in the UK.

- Skin banks – Skin for allograft is stored mainly by two multi-tissue banks,. In addition, there are approximately 60 burns and plastic surgery units which store skin for autograft. These units may have little more than a fridge for storage of patients' own skin between grafting operations. Even so, they will have to comply with requirements of the Directive.

- Skin Culture – There are approximately 5 establishments storing cultured skin..

- Chondrocytes (cartilage cells) – There is one unit that stores cultured chondrocytes.

- Islets of Langerhans and Liver Cells – Two units

- Dentists – In Wales of 627 general dentist practitioners who replied to a survey in 2004/05, only six dentists said they used human material (eg ground bone as a filler for implants) in an estimated 230 procedures pa**.**

- Private Sector Establishments – There are some 7 private sector establishments. These are included in the figures given above. **Tissue banking activity in the private sector is very limited, other than in the HFEA licensed sector.**

(ii) Benefits

Benefits of Option 1

Since option 1 represents no change from the current situation, there are no benefits. None of the objectives of the Directive would be realised.

Benefits of Option 2

The purpose of this section is to identify the likely benefits of meeting the requirements of the Directive, and to estimate a value for these benefits. Identification of likely benefits and estimation of value in undertaken below.

Identification of Benefits

Inspection and Licensing

Inspection and licensing of all establishments handling human tissues and cells for human applications will ensure that all such units will be required to adopt appropriate standards.

Quality and Safety

Enhanced quality and safety requirements should reduce the general and specific risks. The controls on air quality in critical processing zones are intended to reduce the risk of contamination by infectious agents or harmful chemicals. This in turn should reduce the risk of graft failure. The introduction of quality management systems is likely to encourage the creation of a 'safety culture', which will help establishments to prevent, analyse, and learn from errors, in keeping with the recommendations of the Department of Health report, *An organisation with a memory.*

Coding and Labelling

Introduction of a universal coding and labelling system across the EU will allow instant traceability of tissue, of domestic and EU origin, and will reduce the risk that unsuitable materials are used for transplant.

Monitoring of Serious Adverse Events and Reactions

The major benefit of a national reporting system for adverse events and reactions is that it enables establishments systematically to learn from the experience of others. The collection and analysis of data on such events allows for the development of evidence-based safety initiatives, policy and guidelines.

As indicated above, units that are currently licensed by the HFEA are already required to participate in an Incident Alert System. The direct benefits of such a system have therefore already been realised for these units. It is anticipated, however, that there will be additional benefits for these establishments, arising from the introduction of reporting systems for adverse events in all EU countries. The HFEA has identified the lack of information on risk factors internationally as a key factor that prevents the fertility sector in the UK learning from other systems and identifying areas for joint action.[11] Under the Directive, there will be enhanced opportunities to learn from the experience of fertility units throughout the EU.

For fertility units that are not currently subject to HFEA regulation, and for other tissue banks, the introduction of a national reporting system will provide a new formal framework for the sharing of information, analysis of risk, and improvement of safety standards. The current lack of knowledge on the frequency of adverse events in these establishments means that it is not possible to quantify the potential benefits of such a monitoring system with any precision. The experience of the HFEA's Incident Alert System, and the National Blood Service's Serious Hazards of Transfusion (SHOT) system, may, however, provide some indication of the potential impact of such a system.

In 2005-06, 97 incidents were reported to HFEA . The HFEA analysed these incidents to identify trends and underlying risk factors. 3 alert notices were issued, identifying learning points aimed at improving safety standards.[12]

In 2003, SHOT received reports of 358 incidents where the wrong blood was transfused, and of 906 near misses. In total, these represented approximately 0.04% of blood transfusions. SHOT issued 35 specific recommendations in the light of these incidents. SHOT has been in existence for 8 years. During that time, its reports on matters such as Transfusion Related Acute Lung Injury (TRALI) and bacterial contamination of platelets have led to changes in practice by the blood services. SHOT also plays a role in the evaluation of safety measures, providing data for monitoring the impact of new initiatives. There has been a steady decline in the number of ABO incompatible transfusions reported (both in absolute terms, and as a proportion of total incidents), suggesting the development of a safety culture. It is not possible, however, to measure the contribution made by SHOT to such a development: other factors will also have played a part.

[11] HFEA Authority Paper, (18/05/05) 241
[12] As above.

Controls on Imports and Exports

Establishment of a unified framework of quality and safety standards across the EU should facilitate the exchange of tissues and cells between Member States. These measures, together with the introduction of controls on imports and exports from outside the EU, are likely to increase the confidence of the clinical community, and of patients, in the quality of tissues and cells from abroad, and facilitate growth in the number of tissues and cells exchanged between countries. These measures may be of particular benefit to patients awaiting transplant of tissues and cells which are in short supply in this country or where tissue matching is particularly difficult.

Small sized heart valves are in shorter supply than larger ones and it is usually easier to obtain larger heart valves from outside the UK – usually the EU or USA. Many additional ocular transplants would be carried out each year if more corneas were available. It is not possible to predict likely numbers of tissue and cell imports. These will depend upon demand and supply factors that will vary over time, and by tissue and cell category.

The assurance of quality and safety in imported tissue would be of greater importance if the incidence of vCJD ever reached levels which necessitated the import of tissues and cells from abroad. There have been no reported cases of vCJD transmission through tissue or cell transplant. The National CJD Surveillance Unit has, however, reported three possible cases of vCJD transmission via blood transfusion. As a result, the Departments of Health have adopted a number of precautionary measures to protect the blood supply, including the import of plasma from the United States for treating babies and young children, and for the manufacture of fractionated plasma products e.g. albumin coagulation factors and immunoglobulins. If, at any time, similar measures were considered necessary for tissues and cells, the existence of a regulatory framework for imports, which would safeguard quality and facilitate international transfer, would be of considerable benefit.

No additional benefits from this measure are envisaged in the HFEA licensed sector, as the HFEA already controls the import and export of mature gametes and embryos.

Training

No benefits are envisaged from this measure, as it is believed that existing staff are likely to be appropriately qualified and trained.

Quantification of Benefits

In order to estimate a value for benefits, a number of steps must be taken. First, it is necessary to estimate the risk of certain adverse events occurring (or favourable events failing to occur) in the current situation. Second, consider how this risk is likely to change when the Directive is implemented. Third, a monetary value should be estimated for this change.

No data are currently collected on the incidence or type of adverse events or reactions in treatments using human tissues and cells. There is, as yet, no international experience to indicate the impact of enhanced safety measures on risk factors. A number of countries, such as the United States, have recently introduced similar safety requirements to those envisaged under the Directive. However, insufficient time has elapsed to allow for evaluation of these measures.

In view of the paucity of data, it is difficult to estimate with confidence the benefits of higher quality and safety standards. Rather than relying on speculative estimates of risk reduction, this issue will be addressed by considering the converse question: what would the reduction in adverse events (or increase in successful grafts) have to be, in order for the benefits to match the costs of enhanced safety measures?

In the remainder of this section, two hypothesised benefits will be examined, and values estimated for them, drawing on economic and epidemiological studies. These are provided for illustrative purposes. As indicated above, the shortage of data, and of relevant international experience in this area, do not allow for prediction of expected benefit levels. Many potential benefits have not been examined, because no relevant economic literature has been identified.

Hypothesised Benefit 1: Corneal Transplants – reduction in graft failure

Approximately 2,500 corneal transplants are performed in the U.K. each year. Initial success rates are high, with an overall graft survival of around 90% at one year. Data from the Australian Corneal Graft Registry show that by 5 years, survival has declined to 74% with a further decline to 62% by 10 years. There has been little improvement in success rates over the last 10-15 years

The leading cause of corneal transplant failure is allograft rejection, which accounts for approximately 34% of failures. Endothelial decompensation accounts for 17% of failures, infection for 12%, and primary technical factors for 13%.[13]. Neither rejection nor endothelial decompensation are directly related to the quality of the corneal allograft. It is likely however that a higher initial endothelium cell density in the donor cornea will delay the onset of decompensation and loss of graft transparency and thus increase graft survival time.

However, the CTS Eye Banks have for the past 2-3 years been operating to the standards required by the Code of Practice for Tissue Banks. Since these standards are already high, it will be difficult to identify a specific benefit that can be directly attributed to the Directive.

However, if we assume a 1% increase in the graft success rate (25 more successful grafts each year) would produce an annual benefit worth £1.3 million-£1.9 million. An increase in the success rate of 0.5% would produce a benefit valued at £660,000 - £970,000, and a 1.5% increase in the success rate would produce a benefit valued at £2 million - £3 million.

The National Institute for Health and Clinical Excellence (NICE) has adopted an Incremental Cost Effectiveness Ratio of £30,000/QALY as a benchmark in its technology appraisals. If this value is adopted in the present context, the average benefit of a successful graft is estimated at £53,000-£78,000.

Hypothesised Benefit 2: Bone Marrow Transfer (BMT): increase in imported stem cells

Almost two thousand four hundred bone marrow transplants were performed in the UK in 2003. In view of the importance of tissue matching in stem cell transplants, import and export are of more importance than in most other transplantation programmes. Each year, approximately 150 allografts are performed in the UK using stem cells imported from abroad. Approximately half of these imports are from the EU (British BMT registries export stem cells for approximately 225 allografts each year, of which approximately half are to the E.U.).[14]

It is not possible to predict whether the establishment of an EU wide framework for safety and quality, and an import/export regime for extra-EU transfers, will lead to an increase in the number of allografts using stem cells from abroad. One can, however, estimate the benefits of a given hypothesised increase.

[13] Figures from the Corneal Transplant Follow-up Study, quoted in Waldock A, Cook SD. Corneal transplantation: how successful are we? *Br J Ophthalmol* 2000;**84**:813-815
[14] Figures provided by the Anthony Nolan Trust.

The expected number of life years gained from stem cell transplants, and the quality of life, vary according to diagnosis. The majority of allograft recipients in the UK. are patients with acute myelogeneous leukaemia (AML), acute lymphoblastic leukaemia (ALL) or chronic myelogeneous leukaemia (CML). The average gain for a CML patient who receives an allograft from an unrelated donor has been estimated at 9.95 QALYs (discounted).[15] No large-scale studies of lifetime benefit for patients with AML or ALL have been identified. For all three patient groups, studies indicate that there is a substantial risk of death in the first two years after the transplant, but that patients who are disease-free two years after transplantation have an excellent prognosis.[16]

Taking the CML QALY estimate as an indicator of possible QALY gain after allogenic BMT, and valuing each QALY at £30,000 results in a valued benefit for each transplant of £298,500. Deducting from this the average cost of an allograft from an unrelated donor (£56,318)[17], a net gain of £242,182 is estimated. (It should be noted that the average cost of an allograft quoted is likely to be an underestimate of total BMT costs. No reliable data have been identified on the post-transplant costs of BMT in the U.K.)

If there were to be a one-off increase of 1% (or 15), in the annual number of imported stem cells, and this were to facilitate 15 additional bone marrow transplants, the annual benefit would be valued at £3.6 million. A 2% increase in imports, (30 additional allografts each year), would be valued at £7.2 million. An increase large enough to bring the number of stem cells imported from the E.U. up to the level of current U.K. exports to the E.U. (37 additional allografts) would be valued at £9 million. (It should be said that substantial increases in imported stem cells are not judged likely in the short-term. However, over a number of years the existence of a common E.U quality and standards framework, and a common import-export regime, may increase access to international stem cell donors).

Other Potential Benefits

Similar analysis could, in principle, be conducted for other types of tissues and cells. However, in most cases, the economic literature does not contain relevant utility estimates.

[15] Lee S.J. et al., The Costs and Cost-Effectiveness of Unrelated Donor Bone Marrow Transplantation for Chronic Phase Chronic Myelogeneous Leukemia *Blood* Vol.2 No. 11 1998: pp. 4047-4052
[16] Socié G. et al. Long-Term Survival and Late Deaths after Allogeneic Bone Marrow Transplantation *New England Journal of Medicine* 341:14-21
[17] From 2004 Reference Costs 2004, DH, uplifted to 2004-05 prices.

In the case of fertility treatments, the primary outcome considered in economic models is a live birth, rather than an improvement in health. There is, as yet, no agreement among health economists as to whether, or how, the utility of fertility treatments should be measured. One might hypothesise that the introduction of quality management systems, for instance, would have an impact on the percentage of live births, but it is not possible to assign a monetary value to any such change.

Summary of Hypothesised Benefits

The illustrative hypothesised benefits outlined above are summarised in Table 1, below.

Table 1 Estimated Values for Hypothesised Benefits of Compliance with the Directive

Hypothesised Benefit	Level of Benefit	Estimated Value of Benefit
Corneal Transplant: Increase in success rate	0.5% increase	£660,000 - £970,000
	1% increase	£1.3 million - £1.9 million
	2% increase	£2 million - £3 million
BMT: Increase in imported stem cells	1% increase	£3.6 million
	2% increase	£7.2 million
	Increase of 37	£9 million

The benefit values shown above compare with set-up costs estimated at £16.4 million - £18.18 million and annual recurring costs of £4.08 million to £11.10 million. It must be stressed, however, that these benefits are purely illustrative. They are also incomplete. For many areas of tissue banking, and for the entire reproductive sector, no estimation of benefits has been possible.

(iii) Costs

Costs will be divided into administrative and policy costs. Administrative costs are those that arise from inspection and monitoring requirements and include all information obligations such as coding and labelling and monitoring adverse events and reactions. Policy costs are those that arise from prescribed changes to achieve policy goals (e.g. measures to comply with enhanced safety requirements).

Costs of Option 1

If the Directive was not implemented, tissue establishments would not face any new administrative or policy costs as a consequence of the Directive. The UK would however face the possibility of a fine for non-compliance with the Directive possibly of some £millions.

If a European Union Member State fails to comply with an EU Directive, the European Commission has the right to commence infraction proceedings against the member state under the provisions of the European Community Treaty. If the European Court of Justice finds that a Member State has failed to comply with an obligation under this treaty, a lump sum or daily penalty of any amount may be imposed.

While tissue banks would not face any new costs under this option, they would continue to face the costs of existing inspection and licensing regimes, and of compliance with current safety and quality standards. Annex 1 sets out the cost of current inspection and licensing arrangements, as they provide a baseline for consideration of other options.

In April 2006, the HTA assumed responsibility for the regulation of tissue banks outside the embryology sector. All tissue banks in this sector will require an HTA license. HTA fees for 2006/07 are given in Annex 2.

Costs of Option 2

Administrative or Policy Costs

Until the establishment of the new regulatory authority, RATE, the HFEA will assume responsibility for the inspection and licensing under the terms of the Directive of establishments in the reproductive sector and the HTA will be responsible for non-reproductive tissue banks. Licenses have been issued from April 2006 on the basis of a self assessment completed by the tissue establishment . Two-yearly Inspection will commence after an assessment of risk.

Establishments that are currently inspected and licensed under the HFE Act, will not incur additional licensing fees to cover the initial changeover to the requirements of the regulations and the Directive. The HFEA expects that the ongoing costs of inspection and licensing will not be significantly higher than those that would have applied for inspection and licensing under the HFE Act, without implementation of the Directive.

Units in the fertility sector that handle only fresh gametes are not currently subject to the HFEA's inspection and licensing regime. These establishments will face new ongoing costs for inspection and licensing.

Once the Directive is implemented, the HTA's fees for licensing will also need to cover the costs of managing an adverse event monitoring system, and import and export controls.

Administrative Costs

Coding and Labelling

All units are expected to face some additional costs for coding and labelling systems. The European Commission has established a working group of Member States to look at options for a single European coding system that will take account of concerns on cost.

A first approximation of possible costs can be found by reference to a similar coding system operated by the National Blood Service. It is estimated that the development of software for such a system costs approximately £200,000. The National Blood Service estimates that it costs between £3,000 - £5,000 per unit for hardware such as a computer, printer and barcode reader, £1,000 for software licensing and registration, and up to £1000 per annum for labels. If all 150 tissue banks, 91 fertility clinics, 15 transport/satellite centres and 50 fresh gamete units were to adopt such a system, total set up costs would be approximately £1,220,000 - £1,836,000, and annual recurring costs would be estimated at £306,000 (for labels).

It should be noted, however, that these costs may be an overestimate, for a number of reasons:

- It may not be necessary for all units to adopt a computerised system. Any coding system is likely to be able to be read manually as well as by computer. This matter will be clarified when the Commission's work is complete (likely 2007/08)

- Many units may already own suitable hardware which can be used for coding and labelling

- All units already face costs for labels. These costs should be deducted from the annual recurring costs quoted above, in order to calculate the marginal cost of meeting the requirements of the Directive

- Costs of labelling is proportional to the number of finished product. For example more labels are needed per femur donor as each bone could be divided into up to 30 individual sachets of bone, whereas one heart yields a maximum of three parts. The hardware costs would be similar for each bank.

Monitoring of Serious Adverse Events and Reactions

For establishments currently licensed by HFEA, no additional costs are envisaged in this area, as a serious event monitoring system is already in operation for these units.

Establishments that will be licensed by the HTA, and the fresh gamete units that will be subject to HFEA regulation for the first time, will face additional costs.
The HFEA estimates the marginal annual cost of running its existing monitoring system at £100,000. This can be represented as an average cost of £990 for each of the 91 HFEA licensed units. It is likely that a substantial proportion of these costs are

fixed; that is, they will not be affected by variable factors such as the number of establishments covered or the number of incidents reported. If this is so, then one would expect that increasing the number of units covered by the HFEA scheme would lead to a less than proportionate increase in costs. In other words, the average cost per unit would be lower than the existing average of £990.

Approximately 150 tissue banks will be covered by the HTA's monitoring scheme. It is not possible to provide a precise estimate of the likely cost to these units. Some indication of the likely range may be provided by the HFEA costs cited above, and the cost of a similar scheme run by SHOT.

Funding for SHOT is provided by the National Blood Transfusion Services (NBS). SHOT estimates the annual costs of operating this system at £170,000. This can be represented as an average of £425 for the 400 hospitals (approximately) which participate in SHOT. This figure includes staff costs, publications, travel and other expenses, but does not include accommodation or support services such as IT and HR, which are provided by NBS. No estimate is available for the value of these additional factors, but it should be noted that the figure quoted is an underestimate of the true cost of the scheme.

The costs cited by SHOT and HFEA suggest that the estimated average annual cost to HTA regulated tissue banks would be in the range £425 - £990. However, as indicated above, the lower figure is likely to be an underestimate of the true cost. In addition, if there are substantial fixed costs, one would expect that average costs would be higher for a scheme with 150 units than for one with 400 participating units. This would suggest that the average cost might be toward the upper end of the range.

If fresh gamete units and HTA regulated tissue banks all incur annual costs between £425 and £990, the total annual cost could be in the range £102.000 - £238,000. These costs are likely to be recovered through licensing fees.

Estimated Annual Administrative Burden from April 2007/08

Activity	**Reproductive Cells**	**Conventional Tissue Banking**
Completing Application Forms or applying for variations in licenses	Assume estimate of 2 hours annually for 150 units Assume 150 units @ two hours equals 300 hours based on £60k (designated individual salary costs plus on costs) Total = £8760	HTA estimate completion will take 2 hours Assume 150 units @ two hours annually equals 300 hours based on £60k (designated individual salary costs plus on costs) Total = £8760
Preparing for Site Visit	Assume 1 day (8 hours) every 2 years – 4 hours yearly 1x DI (£60k) 1x personnel (£40k) Total = £28800	Assume 1 day (8 hours) every 2 years 4 hours yearly 1x DI (£60k) 1x personnel (£40k) Total - £28800
Site Visit	Assume 2 days every 2 years – 1day yearly 1xDI 1x personnel £57600	Assume 2 days every 2 years -1day yearly 1xDI 1x personnel £57600
Annual Reports	Assume 2 hours 1xDI Total = £8700	Assume 2 hours 1xDI £8700
Severe Adverse Event/Reaction reporting	Assume 5 hours every five years – 1hour yearly Total = £4350	Assume 5 hours every five years – 1 hour yearly Total = £4350
Total	£108,210	£108,210
Coding and Labelling	£306,000	
Total	£522,420	

Policy Costs

The policy costs of complying with the requirements of the Directive may be divided into the following broad categories:

- Licensing Costs
- Compliance with standards of quality and safety, including establishment of quality systems;
- Establishment of a system to monitor and report serious adverse events and reactions;
- Regulation of imports of human tissues and cells for human transplantation;
- Appropriate training of tissue banking and tissue procurement staff.

Quality and Safety

Most establishments are expected to face additional costs in order to meet the quality and safety requirements of the Directive. The most significant costs are likely to be incurred for the establishment and operation of quality management systems, and the up-grading of facilities to meet air quality standards where appropriate.

However, all 62 tissue establishments accredited by the MHRA under the voluntary scheme operated to an acceptable quality system and some fertility clinics will have introduced such systems. Two of the fertility clinics have provided details of the costs incurred. The establishment of such a system, and operation for the first year, cost on average £52,300, with a range of £50,000 - £54,600. Most of these costs are accounted for by staff time, and external consultancy fees. On-going annual costs, from the second year of operation, were, on average, £22,500, with a range of £10,000 - £35,000. Most of these costs are accounted for by staff time for quality co-ordination and management. The variation in on-going costs is due to differences in the amount of staff time spent on quality management after the first year. Costs to smaller/single activity establishments are not likely to be as high in relative terms.

If the remaining 89 fertility clinics, along with 15 transport centres, 50 fresh gamete units and 88 MHRA unaccredited tissue banks were to face similar costs, the total cost in the first year would be approximately £12.6 million, with a range of £12.1 million to £13.21 million. Total annual costs would be approximately £5.44 million, with a range of £2.42 million to £8.47 million. The wide range in estimated ongoing costs should be noted. With a sample of just two units, and widely divergent costs, it is not possible to provide more than a first approximation of total expected costs.

Commission Directive 2006/86/EC states that where tissues or cells are exposed to the atmosphere during processing, without a subsequent microbial inactivation process, an air quality of Grade A will be required.[18] Less stringent environment may be acceptable for procedures such as insemination where the risk of infection is significantly lower than for tissue and cell transplantation. Reference should be made to the Commission Directive to confirm requirements on air quality and other matters.

According to the Commission Directive, Grade A air quality is usually achieved by using a laminar flow cabinet though it is thought difficult to achieve Grade A without Grade B and C background air. Vertical or horizontal cabinets suitable for use by one or two people at a given time are estimated to cost £3500 – £4000. Replacement HEPA filters cost approximately £260 - £300 per cabinet each year. Servicing and disposal of used filters are estimated to cost £530 per cabinet annually. Air handling equipment is estimated at a minimum of £100,000 per room and £50,000 per additional room. Servicing of rooms costs between £2000 and £5000 pa.

[18] As defined in the current *European Guide to Good Manufacturing Practice, Annex 1 (Commission Directive 2003/94/EC)*. Grade A corresponds to a maximum of 3,500 particles of 0.5 $\mu m/m^3$ and 1 particle of 5 $\mu m/m^3$.

The number of laminar flow cabinets required will depend on the volume and type of activity. For many units, it is expected that one cabinet may be sufficient. In this case, set-up costs would be approximately £3,500 - £4,100, and annual costs approximately £790 - £825. If it is assumed that larger units dealing with high volumes of tissues and cells may require up to three laminar flow cabinets, set-up costs for these units would be approximately £10,500 - £12,300, and annual costs approximately £2,370 - £2,490.

If it is assumed that, on average, units will require two laminar flow cabinets, total set-up costs would be estimated at £1.05 - £1.23 million, and total ongoing costs at £237,000 - £249,000. However, all MHRA accredited tissue establishments undertaking critical processes will be working to Grade A against a background of Grade B and may not incur any significant additional costs

Regulation of imports and exports

It is not considered likely that establishments currently regulated by HFEA will incur additional costs in this area, as imports and exports in the fertility sector are already regulated. Fresh gamete units, which will be regulated by HFEA for the first time, are not expected to face additional costs, as international transfers of fresh gametes are considered unlikely.

HTA-regulated tissue banks will incur extra charges to cover the costs of import and export controls. The HTA has not yet provided estimates of the likely costs, or of a fee schedule to distribute these costs across units. The costs incurred by the HFEA may, however, provide a first approximation of these costs.

The HFEA estimates that the annual marginal cost of implementing import and export controls, in 2004-05, was £60,000. This can be represented as an average annual cost for the 91 HFEA licensed establishments of £659. The actual costs of the administration of such a scheme for tissue banks will depend on sector-specific issues, such as the number of cross-border tissue transfers. The average cost will also depend upon the ratio of fixed to variable costs. If a high proportion of costs are fixed, one would expect the average cost per establishment to be somewhat lower in a scheme that covers 150 establishments than in one that covers 91 establishments. If all costs were fixed, and there were no sector specific considerations, the average annual cost to tissue banks would be in the region of £400. In practice, however, there are likely to be some variable costs. The range £400 - £659 may be taken as an estimate of average cost per unit. This is equivalent to a total annual cost of £60,000 - £89,100. The average level, and the distribution of costs across units, are likely to depend, however, upon the volume and type of international tissue and cell transfers.

As indicated above, the costs of import and export controls are likely to be recovered through license fees for all establishments subject to licensing under the Directive. One-off fees may also be levied if establishments not subject to such licensing are involved in tissue or cell import and export. Such occurrences are expected to be infrequent.

Training of staff

Some additional costs could be incurred for staff training downstream. Existing staff are likely to be appropriately qualified and trained. Future staff may need to train for specific qualifications.

Total Costs of Option 2

Total estimated costs of Option 2 are shown in Table 2, below.

Table 2. Total Estimated Administrative and Policy Costs of Compliance with the Directive

	Set-up costs	**Annual Recurring Costs**
Administrative Burden	£1.528 million	£522,420
Policy		
Quality and Safety		
QMS	£13.7million - £14.96million approx	£2.74 million - £9.59 million
Air Quality	£1 – 1.5million approx	£237,000 - £249,000
Adverse Event/Reaction Monitoring		£102,000 - £238,000
Import/Export Controls		£60,000 - £89,000
Licensing		£500,000
Total	£16.22million - £17,98 million	£3.92 million - £11.18 million

6. Small Firms Impact Test

Most non-reproductive sector tissue banking is conducted within the NHS. The small firms' impact test is not relevant in these cases.

Within the reproductive sector, approximately 80% of establishments affected by the Directive are private companies. These are fertility clinics (approximately 80), which derive their income from fee-paying patients. Most of them are small businesses, according to the following definition:

- Fewer than 50 employees, and
- No more than 25% of the business owned by another enterprise (which is not a small business) and either

- Less than £4.44 million annual turnover, or

- Less than £3.18 million annual balance sheet total.

As indicated above, these units already satisfy many of the requirements under the Directive. They are not expected to face extra charges for on-going licensing and inspection, monitoring systems, or import controls.

They are likely to face set-up costs for Quality Management Systems and for the establishment of a coding and labelling scheme.

It is also expected that the introduction of enhanced quality and safety measures, and a unified coding and labelling system, allowing for instant traceability, will bring benefits to these clinics. Such measures are likely to minimise the risk of adverse events in the reproductive sector. (In the case of quality management systems, it is worth noting that some clinics have already adopted such systems voluntarily).

As indicated above, however, it is not possible to estimate a value for potential benefits in this sector, as the primary outcome considered in economic models is a live birth, and there is no agreement among health economists as to whether, or how, to measure the utility of a future life.

7. Competition assessment

The UK is obliged to implement the Directive, so the issue of competition is not a significant factor in taking forward the policy in this area. We have no evidence to suggest that the Directive would have a significant effect on competition. However, as noted above, we recognise that the requirements on the smallest operations might be such that the operation chooses not to continue to provide a service after 7 April 2007.

8. Rural Proofing

Implementation of the Directive should improve quality and safety standards for rural and urban populations.

9. Equality Impact

We have considered the race equality impact of this and have concluded that there are no race specific issues.

10. Enforcement, sanctions and monitoring

Any establishment wishing to continue operation after 7 April 2007 must hold a licence from the HFEA or HTA. Any establishment that is found to be carrying out activities covered by the Directive and implementing regulations, without a licence from the relevant competent authority, will be liable to criminal proceedings.

Penalties in the Human Fertilisation & Embryology (Quality and Safety) Regulations and the Human Tissue (Quality & Safety for Human Application) Regulations allow for penalties on conviction of a term of imprisonment not exceeding two years, a fine or both.

The Directives requires inspection at least every two years. The regulations allow for more frequent inspections, including unannounced visits, as needed.

11. Implementation and delivery plan

The Human Fertilisation & Embryology (Quality and Safety) Regulations and the Human Tissue (Quality & Safety for Human Application) Regulations will implement Directive 2004/23/EC and supporting Commission Directives 2006/17/EC and 2006/86/EC. The two Competent Authorities – HTA and HFEA – will issue Directions and guidance to assist with implementation.

12. Post-implementation review

Compliance will be monitored by the HTA and HFEA. The Directive requires the Competent Authority to report to the European Commission by 7 April 2009 and every three years thereafter, a report on activities undertaken including an account of the measures taken in relation to inspection and control.

13. Summary and recommendation

As noted above, the UK is obliged to implement the Directive in full. There are no provisions for offsetting the provisions for small or public sector establishments, although Commission Directive 2006/86/EC does recognise that not all tissue handling must be carried our to Grade A, sterile conditions, which would have considerable cost savings for smaller, low risk establishments. Therefore, the recommendation is to implement the Directive in full, Option 2.

14. Summary costs and benefits table

Option	Total benefit per annum: economic, environmental, social	Total cost per annum: - economic, environmental, social - policy and administrative
1	0	0
2	£9million (see note 1)	£16.22million - £17,98 million (setup) £3.92 million - £11.18 million (annual costs)

Notes
(1) This figure represents hypothesised benefits of compliance for two tissue types corneal transplants and bone marrow transfers only. Complete figures could not be established because for many areas of tissue banking, including the entire reproductive cells sector, no estimation of benefits has been possible.

Declaration and publication

I have read the regulatory impact assessment and I am satisfied that the benefits justify the costs

Signed Rosie Winterton

Date 19.04.07

Rosie Winterton
Minister of State for Health Services,
Department of Health

Signed Caroline Flint

Date 19.04.07

Caroline Flint
Minister of State for Public Health,
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Annex A
Costs of existing inspection and licensing regimes

Treatment and gamete/embryo storage centres licensed by the HFEA are currently inspected annually. Units incurred average annual costs for inspection and licensing of £45,000 in 2004-05. Costs per unit ranged from £1,000 to more than £150,000. The costs to units depend on the number and type of procedures carried out. The fees cover inspection, licensing, and a range of other services provided by HFEA, including adverse incident monitoring, import and export processes, legal services and patient communication.

Units handling fresh gametes, which are not covered by the HFE Act, do not currently incur inspection and licensing costs.

Tissue banks which have been accredited under the U.K's voluntary code of practice incurred average annual inspection and accreditation fees of £1550 in 2004-05. Costs per establishment ranged from £1501 to £2930. The MHRA's fee schedule for these establishments is shown in Table 1, below. These fees are set on a cost-recovery basis. The HTA will assume responsibility for the inspection and licensing of these tissue banks, and of those which have not yet been accredited by MHRA, in 2006.

Table 1.
MHRA Fees for the Accreditation and Inspection of Tissue Banks, 2004-05

	Sterile Processing Site	**Storage & Distribution Only**
Application	£2444	£1402
Periodic (per annum)	£304	£187
Variations	£400 – standard £200 – administrative	£378 – standard £200 – administrative
Routine Inspections	£5557 – standard site £2698 – minor site	£1095
Non Routine Inspections[4]	Up to 1 day £1518 2 – 3 days £4048 3 days + £7590	Up to 1 day £759 2 – 3 days £2024 3 days + £3795

Annex 2.

Fees

The Human Tissue Act 2004 (HT Act) requires the HTA to charge reasonable fees for licence applications and to recover costs incurred in ensuring compliance, for example the costs of inspections. The fee structure that the HTA has agreed upon reflects a variety of factors, including its duty to be proportionate in its approach, based on an

assessment of risk, whilst covering the work involved in superintending compliance with the terms of licences.

The interim fee structure per licence to store human tissues or cells for therapeutic use, for the 2006/07 financial year is:

Criteria	**£ Fee**
Establishments without current accreditation by MHRA	4,500
Establishments accredited by MHRA and inspected more than one year ago	2,250
Establishments accredited by MHRA and inspected in the current financial year	750
Establishments which act as satellite sites	250

A satellite site is defined as an establishment which stores material on behalf of a parent organisation, under the supervision of the same Designated Individual, and which uses the same standard operating procedures (e.g. part of National Blood Service network).

Proposed fee structure for establishments storing tissue for human application 2007/08

During February 2007,The HTA consulted on a proposed fee structure for establishments storing tissue for human application take into account the need to fully Implementthe Regulations that transpose the EU Tissue and Cells Directive into UK law. The Regulations, which are likely to come fully into affect in September 2007 will, for the first time, bring into the regulatory framework the procurement, testing, processing, distribution and the import and export of tissue and cells for human application. The additional work that this involves includes:

- Licensing and inspection requirements that may be needed for establishments that do not currently fall within the licensing framework.
- Developing systems for receiving and responding to adverse events and annual reporting.
- Providing additional advice and guidance

Proposed fee level per annum

Hub: £7600
Satellite: £1000

TRANSPOSITION NOTE FOR THE HUMAN FERTILISATION AND EMBRYOLOGY (QUALITY AND SAFETY) REGULATIONS 2007

Directives
Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells (OJ L102, 7.4.2004, p.48). Commission Directive 2006/17/EC of 8 February 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells (OJ L 38, 9.2.2006, p.40). Commission Directive 2006/86/EC of 24 October 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells (OJ L294, 25.10.2006, p.32).
The Human Fertilisation and Embryology (Quality and Safety) Regulations 2007 ("the Regulations") amend the Human Fertilisation and Embryology Act 1990 (c.17)("the 1990 Act"), so far as necessary to do so, to fully implement Directive 2004/23/EC, Commission Directive 2006/17/EC and Commission Directive 2006/86/EC in relation to human reproductive cells ("gametes" i.e. sperm and eggs) and embryos.

Directive 2004/23/EC			
Article	**Objectives**	**Implementation**	**Responsibility**
1	Objective: The Directive lays down standards of quality and safety for human tissue and cells, including human gametes and embryos intended for application to humans.	No implementation measures required	The Secretary of State for Health.
2	Scope: The Directive does not apply: to certain procedures in relation to manufactured products, where	The Directive is implemented, in relation to gametes and embryos by the 1990 Act, as amended by the Regulations. The 1990 Act and the Regulations extend to the whole of the United Kingdom.	The Secretary of State for Health has policy responsibility for the Directives in relation to human fertilisation and embryology. The

	these are covered by other directives; autologous grafts within the same surgical procedure; blood; or, human organs.		Human Fertilisation and Embryology Authority (HFEA) is responsible for enforcement of the 1990 Act. The Regulations are made on behalf of the Secretary of State for Health.
3	Definitions	Sections 1 to 2A of the 1990 Act, as amended by regulations 4 to 7 of the Regulations.	The Secretary of State for Health.
4	Implementation: Requirement to appoint a competent authority. Preserves possibility of Member States introducing more stringent protective measures.	Regulation 2 of the Regulations designates the HFEA as the competent authority in relation to gametes & embryos.	The Secretary of State for Health.
5	Supervision of human tissue and cell procurement: To be by persons with appropriate training and experience.	Section 12(1) of the 1990 Act requires a person to be designated as the "person responsible", in relation to a licence, under whose supervision the licensed activities are to be carried on.	Secretary of State for Health.
6	Accreditation, designation, authorisation or licensing of tissue establishments and tissue & cell preparation processes	UK has decided to establish a licensing system. Sections 3(1) & 4(1) of the 1990, Act as amended by regulations 6 and 7 require a licences before establishments can handle gametes/embryos. Section 18 of the 1990 Act requires prior approval by HFEA to any changes in activities. Sections 18 (amended by regulation 21 of the Regulations) and 19 of the 1990 Act provide for suspension and revocation of licences.	The Secretary of State for Health. The HFEA is responsible for licensing of tissue establishments.

		Article 6(5), which provides for direct distribution for immediate transplantation, is not relevant in relation to gametes and embryos, which do not require immediate transplantation to be effective.	
7	Inspections and control measures: Requirements for competent authorities to carry out inspections, etc.	Section 9 (licence committees and other committees) of the 1990 Act, as amended by regulation 11 of the Regulations. Section 9(8) of the 1990 Act is amended by regulation 9(5) of the Regulations to increase the minimum inspection period from one to two years.	The Secretary of State for Health. The HFEA is responsible for enforcement of the 1990 Act.
8	Traceability: All tissue and cells to be traceable between donors and recipients and vice versa	Sections 12(2) (as amended by regulation 13(4)) and 24(4A) (as amended by regulation 22(6) and paragraph 1A of Schedule 3A of the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
9	Import/export of human tissues & cells: Requirements for regulation of these activities	Section 24(4) of the 1990 Act, as amended by regulation 22(6) of the Regulations.	The Secretary of State for Health. The HFEA is responsible for licensing of tissue establishments.
10	Register of tissue establishments and reporting obligations	Sections 31, 31A and 31B of the Act, as amended by regulations 23 and 24 of the Regulations.	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions, for enforcement of the 1990 Act, and for maintaining a register of tissue establishments.
11	Notification of serious adverse events and reactions: Requirements for reporting, investigation, etc. of such events and reactions	Sections 8A, 15A, 17(g) and 24(13) of the 1990 Act, as amended by regulations 10, 18, 20 and 22(7) of the Regulations.	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.

12	Principles governing tissue and cell donation	Section 12(e) of the Human Fertilisation & Embryology 1990 gives HFEA direction making powers on compensation for donation of gametes or embryos. Donors cannot be paid, they can only receive reimbursement for loss of earnings, up to a specified limit, and verifiable expenses. The UK considers this level of remuneration is still appropriate and will not be making regulations to amend this section.	The Secretary of State for Health. The HFEA is responsible for enforcement of the 1990 Act.
13	Consent: Requirement for all national mandatory requirements to be met	Schedule 3 of the 1990 Act imposes certain requirements for written consent. Section 13A(4) of the 1990 Act, as inserted by regulation 15 of the Regulations.	The Secretary of State for Health. The HFEA is responsible for enforcement of the Regulations.
14	Data protection and confidentiality	Section 33 of the 1990 Act, as amended by regulation 25.	The Secretary of State for Health. The HFEA is responsible for enforcement of the 1990 Act.
15	Selection, evaluation and procurement	These provisions, as well as the technical requirements set down in Commission Directive 2006/17/EC, are implemented by paragraphs 5 to 9 of the new Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
16	Quality management: Requirements for quality systems based on principles of good practice	The technical requirements are set down in Commission Directive 2006/86/EC and implemented by paragraphs 9 to 11 of the new Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for enforcement of the 1990 Act.
17	Responsible Person: Requirement to appoint a suitably qualified responsible person and such	Section 17 of the 1990 Act, as amended by regulation 20 of the Regulations.	The Secretary of State for Health. The HFEA is responsible for enforcement of the 1990 Act.

	person's responsibilities		
18	Personnel: Requirements as to qualifications and training	The technical requirements are set down in Commission Directive 2006/86/EC and implemented by paragraph 10 of the new Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
19	Tissue and cell reception: Testing of donations and requirements for selection and acceptance	The technical requirements are set down in Commission Directive 2006/17/EC and implemented by paragraph 9 of the new Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
20	Tissue and cell processing:	The technical requirements are set down in Commission Directive 2006/86/EC and implemented by paragraph 11 of the new Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
21	Tissue and cell storage conditions	The technical requirements are set down in Commission Directive 2006/86/EC and implemented by paragraphs 4 and 11 of the new Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
22	Labelling, documentation and packaging	The technical requirements are set down in Commission Directives 2006/17/EC and 2006/86/EC and implemented by paragraphs 9 and 11 of the new Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
23	Distribution: Requirements to ensure quality and safety of tissue and cells during distribution	The technical requirements are set down in Commission Directive 2006/86/EC and implemented by paragraph 11 of the new Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.

24	Relations between tissue establishments and third parties	Various provisions in the 1990 Act, as amended, make provision in relation to relations between tissue establishments and third parties. See: sections 2A (as inserted by regulation 7), 3(1A) (as inserted by regulation 8), 4(1A) (as inserted by regulation 9(3)), 17(f) (as inserted by regulation 20) and paragraph 4 of Schedule 3 to the 1990 Act (as inserted by regulation 30 of the Regulations). .	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
25	Coding information: Member States to establish a system for identification of tissue and cells	The European Commission is still developing the EU wide coding requirements. When adopted, the HFEA has powers under section 14A, paragraph 1 of Schedule 3A to the 1990 Act to impose licence conditions to require implementation of the coding system in the UK.	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
26	Reports: Member States to send reports to Commission every three years	No implementation measures required. Section 7 of the 1990 Act requires the HFEA to prepare and send to the Secretary of State an annual report about its activities under the 1990 Act.	The Secretary of State for Health.
27	Penalties: Member States to lay down rules on penalties for breaches of national rules implementing the Directives	Section 41 of the 1990 Act, as amended by regulation 27 of the Regulations.	The Secretary of State for Health. The HFEA is responsible for enforcement of the 1990 Act and for the issuing of licences.
28	Technical requirements and their adaptation to scientific and technical progress: Procedure for adopting further technical requirements	No implementation measures required for this particular Article	The Secretary of State for Health. The HFEA is responsible for enforcement of the 1990 Act.
29	Committee:	No implementation measures	The Secretary of

	To be established to assist the Commission	required	State for Health.
30	Consultation of one or more scientific committees	No implementation measures required	The Secretary of State for Health.
31	Transposition	The Directive is implemented, in relation to gametes and embryos, by the 1990 Act, as amended by the Regulations. As UK had a regulatory framework in place for gametes and embryos when the Directive was adopted in April 2004, the UK has taken advantage of the one year derogation in Article 31(2). Regulation 1(2) brings the Regulations into force on [7 June] 2007. Regulation 1(3) will bring the regulations into force for the processing of licence applications by the HFEA from the day after the day on which the Regulations are made.	The Regulations are made on behalf of the Secretary of State for Health and extend to the whole of the United Kingdom.
32	Entry into force	No implementation measures required	The Secretary of State for Health.
33	Addressees	No implementation measures required	The Secretary of State for Health.
Annex	Information to be provided on the donation of cells and/or tissues	Section 13A(4) (as inserted by regulation 15 of the Regulations) and paragraph 3 of Schedule 3 to the 1990 Act.	The Secretary of State for Health. The HFEA is responsible for enforcement of the 1990 Act.

Directive 2006/17/EC			
Article	**Objectives**	**Implementation**	**Responsibility**
1	Definitions	Sections 1 to 2A of the 1990 Act, as amended by regulations 4 to 7 of the Regulations.	The Secretary of State for Health.
2	Requirements for the procurement of human tissues and cells	Paragraph 5 of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence

			conditions and for enforcement of the 1990 Act.
3	Selection criteria for donors of tissues and cells	Paragraphs 6 and 7 of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
4	Laboratory tests for donors	Paragraph 8 of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
5	Tissue and/or cell donation and procurement procedures and reception at the tissue establishment	Paragraph 9 of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
6	Requirements for direct distribution to the recipient of specific tissues and cells	Article 6, which provides for direct distribution for immediate transplantation, is not relevant in relation to gametes and embryos, which do not require immediate transplantation to be effective.	The Secretary of State for Health. The HFEA is responsible for giving directions and for enforcement of the 1990 Act.
7	Transposition	Regulation 1(2) brings the Regulations into force on [7 June] 2007. Regulation 1(3) will bring the regulations into force for the processing of licence applications by the HFEA on the day after the day on which the Regulations are made.	The Secretary of State for Health.
8	Entry into force	No implementation measures required	The Secretary of State for Health.
9	Addressees	No implementation measures required	The Secretary of State for Health.
Annex I	Selection criteria for donors of tissues and/or	To be implemented by the Human Tissue (Quality and Safety for Human Application)	The Secretary of State for Health. The HFEA is

	cells (except donors of reproductive cells) as referred to in Article 3(a)	Regulations 2007.	responsible for imposing licence conditions and for enforcement of the 1990 Act.
Annex II	Laboratory tests required for donors (except donors of reproductive cells) as referred to in Article 4(1)	To be implemented by the Human Tissue (Quality and Safety for Human Application) Regulations 2007.	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
Annex III	Selection criteria and laboratory tests required for donors of reproductive cells as referred to in Article 3(b) and Article 4(2)	Paragraphs 6 to 8 of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
Annex IV	Cell and/or tissue donation and procurement procedures and reception at the tissue establishment as referred to in Article 5	Paragraph 9 of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.

Directive 2006/86/EC			
Article	**Objectives**	**Implementation**	**Responsibility**
1	Scope: Technical requirements for coding, processing, preservation, storage and distribution of tissue and cells	The Directive is implemented by the 1990 Act, as amended by the Regulations, in relation to gametes and embryos.	The Secretary of State for Health.
2	Definitions	Sections 1 to 2A of the 1990 Act, as amended by regulations 4 to 7 of the Regulations.	The Secretary of State for Health.
3	Requirements for the accreditation, designation, authorisation or	Paragraph 10 of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for

	licensing of tissue establishments		imposing licence conditions and for enforcement of the 1990 Act.
4	Requirements for the accreditation, designation, authorisation, licensing of tissue and cell preparation processes	Paragraph 11 of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
5	Notification of serious adverse reactions	Paragraph 3 of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
6	Notification of serious adverse events	Paragraph 3 of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
7	Annual reports: Member States to submit to the Commission annual reports on the notification of serious adverse events and reactions	No implementation measures required. (Section 7 of the 1990 Act requires the HFEA to prepare and send to the Secretary of State an annual report about its activities under the 1990 Act.)	The Secretary of State for Health.
8	Communication of information between competent authorities and to the Commission	Section 8A of the 1990 Act, as inserted by regulation 10 of the Regulations.	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
9	Traceability: Requirements to have effective and accurate systems to identify and	Sections 12(2) (as inserted by regulation 13(4)), 24(4A) (as inserted by regulation 22(6)) and paragraph 1(a) of Schedule 3A to the 1990 Act (as inserted by	The Secretary of State for Health. The HFEA is responsible for imposing licence

	label tissue and cells, and to retain data.	regulation 30 of the Regulations).	conditions and for enforcement of the 1990 Act.
10	European Coding System: A single European identifying code to be allocated to all donated material	Section 24(12) (as inserted by regulation 22(7)) and paragraphs 1(b) and 2 of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
11	Transposition	Regulation 1(2) brings the Regulations into force on [7 June] 2007. Regulation 1(3) will bring the Regulations into force for the processing of licence applications by the HFEA from the day after the day on which the Regulations are made.	The Secretary of State for Health.
12	Entry into force	No implementation measures required	The Secretary of State for Health.
13	Addressees	No implementation measures required	The Secretary of State for Health.
Annex I	Requirements for accreditation, designation, authorisation or licensing tissue establishments as referred to in Article 3	Paragraph 10 of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
Annex II	Requirements for the authorisation of tissue and cell preparation processes at the tissue establishments as referred to in Article 4	Paragraph 9 of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
Annex III	Notification of serious adverse reactions: Form of notification and information to be provided	Paragraph 3 of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
Annex IV	Notification of serious adverse	Paragraph 3 of Schedule 3A to the 1990 Act (as inserted by	The Secretary of State for Health.

	events: Form of notification and information to be provided	regulation 30 of the Regulations).	The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
Annex V	Annual notification format	No implementation measures required	The Secretary of State for Health.
Annex VI	Information on the minimum donor/recipient data to be kept as required by Article 9	Paragraph 1(a) of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.
Annex VII	Information contained in the European Coding System	Paragraph 1(b) of Schedule 3A to the 1990 Act (as inserted by regulation 30 of the Regulations).	The Secretary of State for Health. The HFEA is responsible for imposing licence conditions and for enforcement of the 1990 Act.