

# The EU Draft Technical Requirements for the Coding, Processing, Preservation, Storage and Distribution of Human Tissues and Cells

## Response of the UK Association of Clinical Embryologists

### Introduction

The UK Association of Clinical Embryologists (ACE) considers the EU Directive to make a real contribution to improving standards of laboratories involved in the procurement, processing and storage of human cells and tissues. The inclusion of reproductive cells represents both opportunities and significant challenges to all healthcare professionals working in assisted conception.

This document outlines the views of the ACE Executive, Training and Professional Development Committees. In proffering these views, the ACE has drawn on its own Standards for Assisted Conception Units drafted by ACE, the Association of Biomedical Andrologists and British Fertility Society and submitted to the Human Fertilisation and Embryology Authority (HFEA). Much of this document mirrors the Directive.

### Organisation and Management

Management systems, including organisational charts, responsibilities and accountability (defined in job descriptions) are essential elements and will be generally well established. The Directive also requires laboratories to implement a quality system (QS): though widely accepted to confer organisational benefits, there is little evidence that a QS improves patient outcomes whilst the resources needed to implement and maintain it are considerable.

In the revised ACE laboratory standards, centres are required to "operate within a quality management system ..." and it is the opinion of the ACE that this will highlight the needs for audit, quality assurance, validation and evaluation of patient satisfaction. This is considered to add momentum towards best practice and dovetails with requirements of clinical governance. However, in assisted conception units, the laboratory does not work as a unitary entity (as may be the case with other tissue establishments) and so a number of UK centres are working towards ISO9000:2001 as a QS that spans all areas including clinical, nursing and administrative functions.

It is recognised that a significant investment is needed to establish a QS, as well as ongoing costs for example in employing a Quality Manager. Most centres will avail themselves of the services of a consultant (£25,000) in the absence of staff with expertise and experience to lead the project. In addition, it is likely that remedial work and upgraded facilities and equipment will increase costs markedly: depending upon the starting standards of the unit, this might cost £25,000 - £50,000 or even more. Staff time will be another major cost, but accounting for the appointment of a Quality Manager alone might add £35,000 (including on-costs for the employing body). So, a total initial investment might be in the order of £85,000-100,000 (€119,000–140,000) with recurring costs of around £40,000 (€56,000).

### Personnel

The ACE has been successful in establishing training programmes in clinical embryology, notably its Certificate that is recognised by the UK Department of Health as an approved training scheme. This is under revision and could be modified to meet all the needs of the Directive. In addition, the NHS is

introducing a number of linked initiatives including Agenda for Change, the Knowledge and Skills Framework, National Occupational Standards and the Healthcare Science Career Framework that can be used to match training and continuing professional development with the needs of the service.

## **Equipment and Materials**

Again extensively covered by the ACE standards, the Association supports the closer monitoring, audit and control of materials used in Assisted Reproductive Technology (ART).

## **Facilities/Premises**

The ACE recognises the scope for improving standards in laboratories, but believes this must be proportionate and evidence-based. The Directive is primarily concerned with minimising the risks of contamination of human tissues/cells and their derivatives that are used therapeutically, usually in heterologous donation, in order to protect the recipient. In ART, the likely increase in risk to the recipient of gametes or embryos in an autologous donation or donation by a partner is negligible. Indeed, evidence suggests that acquired infections after ART procedures are rare and infections seen in *in vitro* culture systems are transferred from the patients themselves. There is no evidence that lower air quality causes adverse effects nor has the reverse been shown, that is that higher air quality improves outcomes. Problems associated with the mixing of patients' gametes or embryos are likely to represent a higher risk but these risks have been addressed in the UK by the adoption of double witnessing procedures (HFEA, 2002). The careful monitoring of laboratory conditions and procedures is of more relevance to ART than particulate counts, though these can be subjected to some control proportionate to the low risk.

Accepting this low risk, the option in section D.4 to allow less stringent air quality seems appropriate: D.4(c) cites insemination as an example and embryo transfer would represent an equal or lower risk; D.4(d) might allow micromanipulation including ICSI to be performed outside laminar airflow, if this is deemed to increase risks to the embryos/gametes being manipulated.

The ACE has, along with other professional bodies and learned societies, considered these risks together with the practicalities of performing ART in clean room facilities. It also believes that the impact upon patients, many of whom self-fund their treatment in the UK, should not be ignored and in striving to improve standards, there should be a sensible balance between increased costs and benefits to those patients.

The ACE considers the use of laminar air flow (preferably class II) in a grade D background is adequate to minimise risks to patients undertaking ART treatments, whilst also affording protection to the gametes and embryos being handled.

## **Traceability**

Members of the ACE contribute to the work of the Safety and New Technology Working Group of the HFEA, and the role of barcodes or radio frequency identification is being investigated. In addressing risks, the requirement of the EU Directive to show traceability with defined audit trails is welcomed. However, with most work in ART being autologous donations within a couple, clarification is needed to establish whether a unique identifier should be applied to each egg, embryo or semen sample. As with air quality, the driver within ART is to manage risks associated with mixing of samples and not to trace donated materials across the EU area. Section 5 as a whole deserves tailoring to ART, and the requirement to store serum samples for 2 years beyond tissue "expiry date" is not justified.

## **Concluding remarks**

In summary, the ACE makes the following comments:

- ⇒ there should be a clear separation of ART and tissue banking in the interpretation and implementation of the Directive that reflects the purpose for which the cells/tissues being handled are to be used (for example, it is inconceivable that embryos would not be used in treatment in the event of air quality being compromised);
- ⇒ the wide remit of the Directive renders sections of it inappropriate;
- ⇒ the introduction of a QS is welcome and reflects the ACE's standards, however the timescale now expected and the associated costs make this difficult;
- ⇒ consideration should be given to the practicalities of providing ART treatment, but more importantly recognition of low risks from environmental pathogens should allow less stringent air quality standards to be applied;
- ⇒ the ACE considers the use of laminar air flow (preferably class II) in a D background to be adequate and provide conditions that are "fit for purpose";
- ⇒ the possible deleterious effects of performing micromanipulation within laminar air flow must be considered;
- ⇒ traceability, "product recall" and the retention of serum samples for 2 years should all be tailored appropriately to ART;
- ⇒ costs of meeting standards will largely be borne by the patients themselves and should therefore produce a demonstrable improvement in outcome; for state-funded treatments, the additional costs will result in fewer cycles being performed, assuming the allocation of monies is not revised to match the increased costs per cycle, which inevitably leads either to increased waiting lists or more restricted access to treatment.

The ACE believes the Directive can make a significant contribution to improving standards, but its efforts should concentrate on risk management that is relevant to the tasks being performed. For all ART centres, implementation of the Directive will necessitate a significant investment in time, money and other resources. Inevitably, this will result in an increase in the costs of treatment. In the UK, a majority of IVF/ICSI cycles are funded by the patients, who will bear these costs. For NHS treatment, the total number of cycles carried out will have to reduce unless additional funding is provided.

**This is a huge development in the provision of assisted conception services. The ACE would like funding to be made available to support centres in implementing the Directive.**

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