

Authority Paper

HUMAN FERTILISATION AND EMBRYOLOGY AUTHORITY

Committee:	Authority
Meeting Date:	12 May 2004
Agenda Item:	6
Paper Number:	HFEA (12/05/04) 149
Paper Title:	Review of Safety of Dewars (Additional Information)
Author:	Chris O'Toole
For Information or Decision?	Decision
Resource Implications:	
Recommendation to the Committee:	The Authority is asked to note the progress of the review of the safety of storage vessels used to store gametes / embryos in Assisted Conception Units.

Review of Safety of Dewars

The consultation on the review of dewar safety ended in 19th March 2004. However, the HFEA did not receive some replies until after this date including one which had carried out quite detailed costing for implementing monitoring systems.

The HFEA has now completed the Regulatory Impact Assessment (RIA), a copy of this is attached at Annex 1 to this paper. Therefore, the HFEA is now in a position to review its policy and decide what recommendations should be made to licensed centres regarding the safety of equipment used to store gametes / embryos.

A copy of the RIA has been sent to Members of the Regulation Committee and the recommendations of these members will be tabled at the Authority meeting.

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Complete Regulatory Impact Assessment

INTRODUCTION OF GUIDELINES ON THE SAFETY OF EQUIPMENT USED TO STORE CRYOPRESERVED GAMETES AND EMBRYOS IN ASSISTED REPRODUCTION LABORATORIES

The objective

1. The HFEA is a non-departmental government body responsible for licensing the creation of embryos outside the body, the storage of gametes and embryos and the use of embryos in research. The HFEA also has a statutory duty to issue a Code of Practice giving guidance to licensed centres on suitable practice to be carried out in the course these activities. The HFEA is proposing to issue guidelines on the safety of equipment used to store cryopreserved gametes and embryos. These guidelines are intended to protect the safety of cryopreserved gametes and embryos stored in assisted reproductive laboratories and the safety of laboratory staff working in these facilities.

2. The proposed guidelines would state that all centres storing patients' gametes and embryos (including donor gametes stored for 'sibling use') are expected to have effective alarms / monitoring system in place to ensure the safety of cryopreserved gametes and embryos and to protect the safety of staff working in laboratories using liquid nitrogen. An effective alarm / monitoring system needs to perform the following functions:
 - Local alarms i.e. on individual dewars for either temperature or liquid nitrogen level
 - Auto-dial (or similar e.g. link to fire alarm board) facility to contact staff outside normal working hours
 - Adequate staffing / funding to allow the implementation of formal emergency procedures including 'on-call'
 - Adequate spare storage vessels to transfer samples in the event of a vessel failure
 - Adequate ventilation systems to ensure rapid extraction of air in the event of nitrogen spillage
 - Oxygen monitoring alarms

Furthermore, centres storing gametes / embryos for patients, whose fertility may be impaired by medical treatment, would be expected to divide individual patients' samples into additional storage vessels.

3. The guidelines would be issued, in the first instance, by means of a Chair's letter but would subsequently be incorporated into the HFEA's Code of Practice. Compliance with these guidelines would be measured through the HFEA's inspection and licensing process.

Background

4. Many embryos may be produced during IVF treatment. Clinics usually transfer one or two embryos in a woman's womb during any one treatment cycle as replacing more increases the likelihood of multiple pregnancy. Most clinics have storage facilities so that spare embryos can be frozen for use in a later treatment cycle if required. This may avoid the need for repeated drug stimulation, egg retrieval, sperm collection and fertilisation. Furthermore, many clinics offer patients, whose fertility may be affected by medical treatment, the opportunity to store gametes for future use. The HFEA currently licences 97 centres to store gametes and / or embryos.
5. At present there are no national guidelines or guidance on best practice regarding the safety of equipment used to store cryopreserved gametes and embryos issued by the HFEA or the professional bodies e.g. the Association and Clinical Embryologists (ACE), the British Andrology Society (BAS) or the Association of Biomedical Andrologists (ABA).

Risk assessment

6. During the last three years there have been several incidents reported to the HFEA that have involved the loss of cryopreserved gametes and embryos due to inadequate levels of liquid nitrogen in the storage vessels (dewars). These have been caused by acute / gradual equipment failure, human error and / or inadequate protocols and controls for filling the level of liquid nitrogen in the dewars. These incidents have resulted in the loss of embryos for several couples and more than 200 patients have lost gametes.
7. In October 1999, a fatality involving use of liquid nitrogen occurred in the MRC Genetic Unit at the Western General Hospital, Edinburgh. An experienced laboratory worker died after suffering oxygen deprivation whilst filling flasks with liquid nitrogen, four other people were also injured during the same incident.

Options

8. The HFEA has considered two options:
 - Allow the status quo to continue
 - Issue guidelines to all centres ensuring effective alarms / monitoring system are in place to ensure the safety of cryopreserved gametes and embryos and to protect the safety of staff working in laboratories using liquid nitrogen.

Status Quo

9. If the status quo were to continue it would be up to individual centres to decide on what safety measures should be in place to safeguard the storage of patient's gametes and embryos and to protect the health and safety of staff working with liquid nitrogen.

Introduction of guidelines

10. The introduction of guidelines would ensure that all centres have adequate monitoring systems in place to ensure the safety of cryopreserved gametes and embryos and to protect the safety of staff working in laboratories using liquid nitrogen. This option would ensure common levels of protection nationally for both patients and staff. Adequate standards, inspected against national guidelines, are considered to be key elements in minimising the risk of loss of stored gametes / embryos due to inadequate levels of liquid nitrogen in the storage vessels.

Benefits of adequate alarm systems

11. The alarm systems proposed in the guidelines would provide necessary protection to patients undergoing assisted reproduction and to patients storing gametes prior to undergoing medical treatment against loss of their stored samples due to inadequate levels of nitrogen levels in the storage vessels. Centres may also benefit from increased public confidence arising from having these monitoring systems in place. In addition, guidelines may result in savings to employers in lost productivity and sick pay.
12. The HFEA has considered whether linking alarms to an auto-dial system is completely necessary. However, without an auto-dial system (or equivalent) any incident occurring outside normal working hours would go undetected and information from BAS / ABA indicates that following a loss in nitrogen stored gametes / embryos could be rescued if the incident is responded to within 60 minutes. Therefore, the additional cost of linking alarms to an auto-dial (or similar e.g. link to fire alarm board) facility to contact staff outside normal working hours would outweigh the potential costs a centre would incur should an incident occur outside normal working hours and thus go undetected.
13. In the absence of guidelines, licensed centres without a system in place to ensure the safety of stored gametes and embryos would incur the following potential costs in the event of a failure in the storage dewars:
 - Administrative costs of contacting all affected patients (including the costs of writing to all patients, setting up a help-line, costs of additional medical staff needed for consultations with patients)
 - Costs of purchasing new storage dewars

- Cost of providing subsequent treatment to patients
- Litigation costs

Consultation on Safety of Dewars

14. As part of the HFEA review on the safety of equipment used in assisted conception laboratories the HFEA consulted all licensed centres on the introduction of guidelines on the safety of equipment used to store cryopreserved gametes and embryos.
15. 97 centres have a HFEA licence to store gametes and / or embryos. Out of these we received responses from 35 centres. Therefore 36% of centres responded to the consultation.
16. Of the 35 centres that responded 33 (94%) supported the HFEA's proposal that all centres storing patients' gametes and embryos (including donor gametes stored for 'sibling use') should have effective alarms / monitoring system in place to ensure the safety of cryopreserved gametes and embryos and to protect the safety of staff working in laboratories using liquid nitrogen.
17. The questionnaire that was sent to licensed centres asked those centres that had agreed with the proposal more detailed questions to address the following issues:
 - Local alarms i.e. on individual dewars for either temperature or liquid nitrogen level
 - Auto-dial (or similar e.g. link to fire alarm board) facility to contact staff outside normal working hours
 - Adequate spare storage vessels to transfer samples in the event of a vessel failure
 - Adequate ventilation systems to ensure rapid extraction of air in the event of nitrogen spillage
 - Oxygen monitoring alarms
 - Division of gametes / embryos between storage vessels

The responses to these questions are summarised in Appendix A to this document.

Compliance costs for licensed centres

Compliance costs for a "typical" centre

18. Compliance costs will be made up of installing appropriate alarm systems, staffing / remuneration costs required to provide appropriate out of hours 'on-call' service and the cost of additional storage vessels needed to transfer stored gametes / embryos in the event of a failure in a dewar and / or to divide individual patients' samples into additional storage vessels. The average non-recurring costs per licensed centre are estimated to be about

£12,000. This amount is based on installing alarms in a centre that has 9 dewars housed in one laboratory plus the purchasing of 3 additional dewars to facilitate the splitting of patients' gametes and embryos and to enable the centre to have an additional crystore in the event of a failure in a dewar.

19. **54% of centres agreed with the estimated capital cost to centres.** The majority of the 46% could not say what the cost would be. Some centres stated that the cost would be less for small centres. However centres also stated that the cost would be passed on to the patients.
20. Centres were also asked to state what the recurring cost of complying with the guidelines would be for their centre. The costs would include: additional staff, remuneration for 'on-call' cover, maintenance, additional liquid nitrogen cost. The responses from centres estimated these cost to be between £5,000 and 15, 000 per annum. However, one centre estimated that the cost of having a member of staff on call at night and over the weekends would be £54, 000

Total compliance costs

21. Total non-recurring compliance costs for all licensed centres are estimated to be about £840,000. This estimate is based on the assumption that 28% of all licensed centres already have effective alarms / monitoring system in place.
22. Total recurring compliance cost for all licensed centres are estimated to be £700,000 per annum.

Summary

23. It is recommended that all licensed centres should have effective alarms / monitoring system in place to ensure the safety of cryopreserved gametes and embryos and to protect the safety of staff working in laboratories using liquid nitrogen. This measure is intended to protect patients undergoing assisted reproduction and to patients storing gametes prior to undergoing medical treatment against loss of their stored samples due to inadequate levels of nitrogen levels in the storage vessels. The benefits of the introduction of these guidelines outweigh the non-recurrent financial burden on licensed centres of £12,000 and may benefit licensed centres in terms of public confidence in their services.

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Of the 33 centres that agreed with the proposal the following responses were received:

Question	No. of Centres (%)			
	Agree	Reasons & Key issues	Disagree	Reasons & Key issues
Do you agree that each storage vessel (dewar) should have individual alarms for either temperature or liquid nitrogen level ?	30 (91%)	13 centres gave reasons that included: <ul style="list-style-type: none"> • Protection against loss of gametes / embryos • Safe storage of gametes / embryos • Allow to identify a problem storage vessel • Enable any problem to be dealt with quickly 	3 (9%)	2 centres gave reasons that included: <ul style="list-style-type: none"> • Technically very difficult • No need if individual dewars are checked daily for liquid nitrogen levels.
Do you agree that these alarms should have auto-dial (or similar e.g. link to fire alarm board) facility to contact staff outside normal working hours ?	29 (88%)	14 centres gave reasons that included: <ul style="list-style-type: none"> • Allow staff to rescue samples • Allow staff to get to centre in time • Rapid notification of a problem at all times <p>Issues raised: Staffing levels – enough staff to allow adequate cover If dewar failed may need specialists e.g. fire brigade’s hazards unit to attend</p>	4 (12%)	0 centres gave reasons
Do you agree that all centres should have adequate spare storage vessels to transfer samples in the event of a vessel failure ?	30 (91%)	13 centres gave reasons that included: <ul style="list-style-type: none"> • Require alternative storage in the event of dewar failure • Ensure back up in case of dewar failure • Allows rescue of samples 	3 (9%)	3 centres gave reasons that included: <ul style="list-style-type: none"> • Space issue plus more dewars than necessary in the laboratory is less safe for staff • Incidence of catastrophic dewar failure is rare • Increased cost to centre in owning and maintaining a spare dewar

Question	No. of Centres (%)			
	Agree	Reasons & Key issues	Disagree	Reasons & Key issues
Do you agree that all laboratories that house cryostores should have adequate ventilation systems to ensure rapid extraction of air in the event of nitrogen spillage ?	30 (91%)	13 centres gave reasons that included: <ul style="list-style-type: none"> • Health and safety of staff 	3 (9%)	2 centres gave reasons that included: <ul style="list-style-type: none"> • May not need fan extraction e.g. may have door to outside that would be sufficient • Would depend on size of dewars (amount of liquid nitrogen) and the size of room / airflow
Do you agree that all laboratories that house cryostores should be equipped with an Oxygen monitoring alarm ?	31 (94%)	14 centres gave reasons that included: Issues raised: <ul style="list-style-type: none"> • Health and safety of staff 	2 (6%)	1 centres gave reasons <ul style="list-style-type: none"> • Extractors enough

Division of gametes / embryos between storage vessels

The HFEA also asked centres whether gametes / embryos stored for patients whose fertility may be impaired by medical treatment should be divided and stored in separate storage vessels. Of the 35 centres that responded to the consultation 24 (69%) agreed the individual patients' samples should be divided and stored in separate dewars. However, a number of issues were raised including:

- purchasing additional dewars would result in a problem with space within the laboratory
- the division of samples would complicate the audit of stored gametes / embryos, therefore increase the risk of errors