Licence Committee - minutes

Centre 0067 (St Mary's Hospital)
Renewal Research Licence – Research Project R0026

Thursday, 8 November 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Andy Greenfield (Chair) Kate Brian Anita Bharucha Ruth Wilde New Authority member - Gudrun Moore (Observed for induction)	
Members of the Executive	Dee Knoyle Julie Katsaros (Observer)	Committee Secretary HFEA Inspector (induction)
Legal Adviser	Graham Miles	Blake Morgan LLP
Specialist Adviser		
Observers		

Declarations of interest:

- Members of the committee declared that they had no conflicts of interest in relation to this item.

The committee had before it:

- 8th edition of the HFEA Code of Practice
- Standard licensing and approvals pack for committee members

The following papers were considered by the committee:

- Renewal Inspection Report
- Renewal Application form
- Publication 1
- Publication 2
- Publication 3
- Peer review
- Previous licensing minutes:
    - 6 October 2017 - interim inspection
    - 5 November 2015 – renewal inspection

1. Background

1.1. St Mary's Hospital, centre 0067, is a treatment and storage centre and a research centre. The current research project R0026, entitled "In-vitro development and implantation of normal human pre-implantation embryos and comparison with uni- or poly-pronucleate pre-embryos", was first licensed in June 1996.

1.2. The centre's current licence was issued for three years and is due to expire on 31 December 2018.

1.3. The centre was last inspected on 11 July 2017, and at that time there were no areas of practice that required improvement.

2. Consideration of application

Application

2.1. The committee noted that an application was submitted to renew the research licence for project R0026.

2.2. The committee noted that the application to renew the research licence was made by the Person Responsible (PR) for a period of three years.

2.3. The committee noted that the centre has applied for the following activities:

- Creation of embryos
- Keeping embryos
- Use of embryos
- Storage of embryos

2.4. The committee noted that the PR also wishes storage of gametes to be included on the licence. This is not an activity that is included on the research renewal application form; however, it is necessary for the creation of embryos that the PR proposes to do over the next three years, since storage of gametes for this purpose is not covered by the Human Fertilisation and Embryology (Special Exemption) Regulations 2009.

2.5. The committee noted that the proposed activities are to be licensed for the following purposes:

- Promoting advances in the treatment of infertility
- Increasing knowledge about the causes of miscarriage
- Increasing knowledge about the development of embryos

2.6. The committee noted that the treatment centres donating to this research project include:

- St Mary's Hospital, centre 0067
- Hewitt Fertility Centre, centre 0007
- IVI Midland, centre 0008
- Manchester Fertility, centre 0033

Inspection Process

2.7. The committee noted that a desk-based assessment took place on 3 August 2018 and this report covers the performance of the centre since the last inspection, findings from the desk-based assessment, including a review of appropriate documentation and communications received from the centre. The committee noted that, at the time of the assessment, no recommendations were made for improvement.

Peer Review

2.8. The committee noted that the Peer Reviewer was supportive of the project.

Recommendation

2.9. The committee noted that the inspectorate recommends the renewal of the research licence for project R0026 for a period of three years, without additional conditions, with the above activities and purposes applied for by the PR.

3. Decision

3.1. The committee had regard to its decision tree.

Administrative Requirements

Supporting Information under General Direction 0008

Application

3.2. The committee was satisfied that the application was submitted in the form required and contained all the supporting information required by General Direction 0008. Furthermore, it was satisfied that the appropriate fees had been paid.

Ethics Approval

3.3. The committee was satisfied that the research project has been approved by South Central – Berkshire B Research Ethics Committee. Evidence was provided by the PR that this approval remains active and covers the research activity described in the licence application.

Proposed Person responsible (PR) – Professor Daniel Brison

3.4. The committee noted that the proposed PR, Professor Daniel Brison, is willing to assume the responsibility of the role of PR.

Proposed Licence Holder (LH) – Professor Sue Kimber

3.5. The committee noted that the proposed LH, Professor Sue Kimber, is willing to assume the responsibility of the role of LH and noted the change of title from Dr Sue Kimber to Professor Sue Kimber.

Research Project

3.6. The committee was satisfied that the research licence would not apply to more than one research project.

Activities

3.7. The committee was satisfied with the suitability of the activities applied for:

- Creation of embryos in vitro
- Keeping embryos
- Use of embryos
- Storage of embryos
- Storage of gametes

Permitted Research Purposes

3.8. The committee was satisfied that the activities to be licensed are necessary or desirable for the following purposes, specified in paragraphs 3A(1) and 3A(2) of Schedule 2 of the HF&E Act 1990 (as amended):

- Promoting advances in the treatment of infertility

  The project will investigate a number of relevant parameters, including the impact of growth factors in embryo culture medium, the influence of DNA damage in sperm, and the possible role of oocyte activation in fertility treatment.

- Increasing knowledge about the causes of miscarriage

  Investigating early human embryo development promises to contribute to our understanding of the regulation of cell fate commitment and differentiation into lineages (distinct tissues of the body), as well as implantation. These studies may be relevant to understanding why embryos do not develop to term, i.e. miscarry.

- Increasing knowledge about the development of embryos

  Understanding the regulation of cell fate and the potential of cells to differentiate into distinct tissues of the body, in order to support implantation and subsequent development, are important factors in growing our knowledge of human embryo development.

Prohibited Research Activities

3.9. The committee was satisfied that none of the proposed activities are prohibited by the HF&E Act 1990 (as amended).

3.10. The committee was satisfied that this is a research project and that no embryos used in the project would be implanted into a woman.

3.11. The committee was satisfied that the proposed research project does not involve the mixing of sperm with the egg of an animal.

Use of Human Embryos

3.12. The committee was satisfied that the use of human embryos is necessary for the purposes of the research.

3.13. The research project focuses on questions/objectives specifically in human embryogenesis and human reproduction. This project represents the development of, and extrapolation from, work that has already been performed in animal models.

3.14. The committee was satisfied that the proposed research project does not involve the derivation of human embryonic stem cell lines for human application or the genetic modification of embryos.

3.15. The committee was satisfied that no embryos would be used without obtaining proper consent for their use in research from patients.

Person Responsible (PR) – Professor Daniel Brison

3.16. The committee was satisfied that the proposed PR possesses the required qualifications and experience and that the character of the proposed PR is such as is required for supervision of the licensed activities. It was further satisfied that the proposed PR will discharge his duties under section 17 of the HFE Act 1990 (as amended).

Proposed Licence Holder (LH) – Professor Sue Kimber

3.17. The committee was satisfied that the proposed LH is suitable for the role.

Premises – The Department of Reproductive Medicine, Old Saint Mary's Hospital, Oxford Road, Manchester, M13 9WL

3.18. The committee was satisfied that the premises and facilities are suitable for the conduct of the licensed activity applied for.

Licence

3.19. The committee agreed to renew the research licence for project R0026, at centre 0067, entitled "In-vitro development and implantation of normal human pre-implantation embryos and comparison with uni- or poly-pronucleate pre-embryos", with no additional conditions for a period of three years with the following:

Activities:

- Creation of embryos
- Keeping embryos
- Use of embryos
- Storage of embryos
- Storage of gametes

for the following purposes:

- Promoting advances in the treatment of infertility
- Increasing knowledge about the causes of miscarriage
- Increasing knowledge about the development of embryos

3.20. The committee agreed that the centre's future renewal inspection report should be submitted to the Licence Committee for consideration.

4. Chair's signature

4.1. I confirm this is a true and accurate record of the meeting.

Signature

Name

Andy Greenfield

Date

3 December 2018

Research Renewal Report: Desk-based Assessment

Purpose of this inspection report

The HFEA licenses and monitors establishments undertaking human embryo research. This is a report of an assessment, carried out to assess whether this centre complies with essential requirements when carrying out such research. Licences for individual research projects can be granted for up to three years and this report provides information on the centre's application for a renewal of its existing licence. The Authority's Licence Committee uses the application and this report to decide whether to grant a new licence and, if so, whether any additional conditions should be applied to the licence.

Date of assessment: 3 August 2018

Purpose of assessment: Renewal of a licence to carry out research

Assessment details:
The report covers the performance of the centre since the last inspection, findings from the desk-based evaluation, and communications received from the centre. For this assessment, an inspector completed a robust desk-based evaluation of appropriate documentation. There was no site visit.

Inspectors: Dr Vicki Lamb

Date of Licence Committee: 8 November 2018

Centre Details:

Project title	In-vitro development and implantation of normal human pre-implantation embryos and comparison with uni- or poly-pronucleate pre-embryos
Centre name	St Mary's Hospital
Centre number	0067
Research project number	R0026
Centre address	The Department of Reproductive Medicine, Old Saint Mary's Hospital, Oxford Road, Manchester, M13 9WL
Person Responsible (PR)	Professor Daniel Brison
Licence Holder (LH)	Dr Sue Kimber
Treatment centres donating to this research project	0007 Hewitt Fertility Centre 0008 IVI Midland 0033 Manchester Fertility 0067 St Mary's Hospital
Date licence issued	1 January 2016
Licence expiry date	31 December 2018
Additional conditions applied to this licence	None

Contents

Section 1: Summary report

Brief description of the centre and its licensing history:

Centre 0067 is a treatment and storage and also a research centre. The current research project, entitled “In-vitro development and implantation of normal human pre-implantation embryos and comparison with uni- or poly-pronucleate pre-embryos” (R0026), was first licensed in June 1996. The current licence is due to expire on 31 December 2018, having been renewed for three years by a Licence Committee on 5 November 2015. There are no additional conditions on the licence. The centre was last inspected on 11 July 2017, and at that time there were no areas of practice that required improvement. On 6 October 2017 an Executive Licensing Panel approved a change of postal address for this centre. This was due to building and layout changes at the hospital; the centre had not changed its physical location and the change of address was solely an administrative change.

Summary for licensing decision:

Taking into account the essential requirements set out in the Human Fertilisation and Embryology (HF&E) Act 1990 (as amended), the HF&E Act 2008 and the HFEA Code of Practice (CoP), the inspection team considers that it has sufficient information to conclude that:

Administrative requirements:

- the centre has submitted an appropriately completed application form
- the centre has submitted the supporting information required by General Direction 0008, including evidence of ethics approval. Patient information and consent forms have not changed since they were submitted with the previous renewal application for this centre
- the application has designated an individual to act as the Person Responsible (PR)
- the proposed licence applies to one project of research
- the centre has submitted fees to the HFEA in accordance with requirements

Research activities applied for:

An application has been made for the following activities for the purpose of research:

- Creation of embryos in vitro
- Keeping embryos
- Use of embryos
- Storage of embryos

The PR also wishes storage of gametes to be included on the licence. This is not an activity that is included on the research renewal application form but it is necessary for the creation of embryos work he intends to do over the next three years as this is not covered by The Human Fertilisation and Embryology (Special Exemption) Regulations 2009.

The proposed research project does not involve the derivation of human embryonic stem cell lines for human application. Research licence conditions R41-89 are therefore not applicable to this research project.

Purposes for which research activities may be licensed:

The activities specified above are required by the PR for the following purposes, as defined in Schedule 2 3A (1) and (2) of the HF&E Act 1990 (as amended):

- Promoting advances in the treatment of infertility
- Increasing knowledge about the causes of miscarriage
- Increasing knowledge about the development of embryos

The PR and peer reviewer consider that the research project will meet the purposes defined in Schedule 2 3A (1) and (2) to the HF&E Act 1990 (as amended) as follows:

- Promoting advances in the treatment of infertility

  The PR has stated: 'The aim of this project is to understand the way in which human embryos develop normally and abnormally in culture. In particular, we study the regulation of cell fate in embryos, in terms of survival, maintenance of pluripotency, and differentiation/cell lineage specification, and expression of molecules involved in embryo development, and the implantation process. We have a particular interest in how the in vitro environment and IVF manipulations impact on this, for example the way in which growth factors regulate cell fate, the influence of DNA damage in sperm on embryonic development, or the impact of cryopreservation on embryonic development, gene expression and implantation. This work has led to an assessment of the role of growth factors in embryo culture medium, the influence of DNA damage in sperm on fertility treatment, and the possible role of oocyte activation in fertility treatment.'

- Increasing knowledge about the causes of miscarriage

  The PR has stated: 'Understanding early human embryo development and the regulation of cell fate and pluripotency and implantation may be relevant to understanding why embryos do not develop to term, i.e. miscarry.'

- Increasing knowledge about the development of embryos

  The PR has stated: 'Understanding early human embryo development and the regulation of cell fate and pluripotency and implantation may be relevant to understanding why embryos do not develop.'

The peer reviewer agrees that the research is likely to contribute knowledge to these three areas and has stated: 'The proposed research aims to lead to a greater understanding of normal and abnormal development of human embryos, and of the regulation of cell fate, pluripotency and implantation, all of which will contribute to improvements in fertility treatment, through the development of procedures and techniques that address the present findings of frequent failed or arrested development of embryos following fertilisation *in vitro*, including failure to form blastocysts and implant, and the failure of transferred embryos to develop into successful ongoing pregnancies, or to miscarry once a pregnancy is established.'

Prohibited research activities:

The activities to be licensed are not prohibited by the HF&E Act 1990 (as amended) including those activities specifically prohibited by Sections 3, 3ZA, 4 or 4A, or by Schedule 2, paragraph 3 of the Act.

Use of embryos:
The use of human embryos is considered necessary. This is based on the application and comments by the peer reviewer who has stated: ‘The research questions/objectives relate specifically to human embryogenesis and human reproduction, and represent the development of, and extrapolation from work that has already been carried out using animal models.’

The renewal application proposes the use of a maximum of 200 fresh eggs, 50 frozen eggs, 200 failed to fertilise embryos, 200 fresh embryos, 200 frozen embryos and 100 created embryos each year across all three sites where this project is carried out for the next three years.

The peer reviewer has stated, ‘The Person Responsible has indicated that the estimated increase in the total number of oocytes and embryos that will be used for the proposed research during the forthcoming 3 years reflects the anticipated “ramping up” of the research activity in his centre through the initiative of establishing collaborative partnerships with other fertility centres.
‘Since the proposed research aims to examine both normal-appearing and “abnormal” embryos in order to identify possible differences that may yield important information towards the research objectives, and since the “abnormal” embryos will be those deemed unsuitable for use in treatment, then the proposal will, in fact, use *both* those embryos that could have been used for human treatment (frozen embryos donated by patients who no longer wish to keep them in storage for their own use), and embryos that are considered unsuitable for use in treatment. The use of both sources of embryos is appropriate and necessary for the proposed research.’

PR considerations:
The PR is suitable and has discharged their duty under Section 17 of the HF&E Act 1990 (as amended).

Premises:
The premises are suitable. This is based on information submitted with the application and the previous inspection visit in July 2017.

Recommendation:
The Licence Committee is asked to note that there are no areas of practice that require improvement.

The inspection team considers that, overall, there is sufficient information and evidence available to recommend the renewal of the centre's licence for a period of three years without additional conditions.

The inspection team recommends that the licence issued should include the following activities:

- Creation of embryos in vitro
- Keeping embryos
- Use of embryos
- Storage of gametes
- Storage of embryos

For the following purposes:

- Promoting advances in the treatment of infertility
- Increasing knowledge about the causes of miscarriage
- Increasing knowledge about the development of embryos

The Licence Holder is Professor Sue Kimber and her title should be amended to this on the new licence.

Section 2: Summary of the research project

This section summarises information submitted in the research licence application and from the Peer Reviewer.

Lay summary of the research project:

We plan to continue our current project to understand early human embryo development by studying sperm, eggs and embryos donated by IVF patients at our participating centres. For this we use some sperm, eggs and embryos which have been frozen in IVF procedures. We analyse sperm for damage to their DNA and culture the embryos up to day 8 after fertilisation, well before the limit of 14 days post-fertilisation. We are looking at the effect of freezing on how the embryos develop using molecules which tell us about their health and normality and their ability to implant in the wall of the womb and develop. We are looking at how the different cells in the embryo differ from one another and how naturally occurring molecules added to the culture medium affect the components that the embryos make, and their ability to implant. These studies will help us to be able to identify what the normal time course of molecular changes are in early human development and what goes wrong. This work will ultimately benefit IVF treatments by increasing our understanding of human embryo development and implantation.

Objectives of the research:

1) Studies of gene expression in order to understand normal and abnormal embryonic development and in particular the regulation of cell fate and lineage allocation, including analysis of individual embryonic cells, and genes involved in implantation.
2) The impact of cryopreservation, including vitrification, on oocyte and embryo development.
3) The impact of sperm DNA damage on embryonic development, including the influence of the environment e.g. lifestyle factors and environmental exposures.
4) The impact of the environment on oocyte and embryonic development, including medium components including nutrients, oxygen, growth factors, bacteria, and the extracellular matrix molecule hyaluronate. In some studies human embryos may be created by chemical activation of failed to fertilise oocytes, these studies are important and have proved very revealing in the past as a model of abnormal human embryo development.

Summary of the research undertaken to date:

Our studies of sperm, eggs and embryos donated by IVF patients at our participating centres has provided insights into early human embryo development and implantation. We have also shown that freezing of oocytes using vitrification causes changes to the genes involved in oocyte health, with the type of culture medium used being the most important influence. Our studies of genes in embryonic development have revealed new genes and pathways which might be important in regulating embryo development and implantation into the wall of the womb. We have also measured this directly in the laboratory as the ability of the embryo to respond to molecules found naturally in the environment and to attach to cells and form an outgrowth. This work will ultimately benefit IVF treatments by increasing our understanding of human embryo development and implantation. In this work we have used approximately 200 human oocytes and 200 embryos over the last 2.5 years. We have not created any embryos specifically for research.

Donation and use of embryos:
In 2017 the researchers used 88 fresh embryos and 22 frozen embryos. They intend to obtain and use more embryos over the next three years as they have established an enhanced network of donating clinics.

Peer review comments:
The peer reviewer agreed that the number of embryos required for the project was acceptable but commented that 'it has not been made specifically clear how it is proposed that embryos in such numbers will be utilised.'

However, the peer reviewer was supportive of the continuation of this project, and noted that: 'The applicant, his colleagues and co-workers have an impressive research pedigree in the field of preimplantation embryo metabolism and associated areas, supported by extensive publication of original research in the literature.'

Section 3: Details of the inspection findings

Principle:

3. Have respect for the special status of the embryo when conducting licensed activities.

What we inspected against:

Research Licence Conditions (RLC) R23, R24, R26, R27, R28, CoP Guidance Note 22.

What the centre does well.

Observations during the last inspection in July 2017 provided assurance that the special status of the human embryo is respected:

- processes, documented in standard operating procedures (SOPs), are in place to ensure that no embryo obtained for the purposes of any research project is kept or used for any purpose other than the purposes of that research project (RLC R23). Staff training and their close supervision ensure procedures are adhered to, preventing the use of donated embryos in unlicensed activities.
- recruitment practices ensure that no money or other benefit is given to those donating embryos to research unless authorised by directions (RLC R24).
- each embryo used in the research project is uniquely labelled (RLC R26)
- documented procedures have been established, implemented and complied with to ensure that clinical and research roles are separated (RLC R27).
- procedures ensure that embryos do not develop after 14 days or the primitive streak has appeared (if earlier) (RLC R28). The culture and manipulation of each embryo is recorded in the laboratory records, which are regularly reviewed.

What they could do better.

Nothing noted.

Principle:

5. Provide prospective and current patients and donors with sufficient, accessible and up-to-date information in order to allow them to make informed decisions.

6. Ensure that patients and donors have provided all relevant consents, before any licensed activity is undertaken.

What we inspected against:

Information, counselling and consent; CoP Guidance Note 22, RLC R18, R19, R20, R21, R22. Consent for storage; CoP Guidance Note 22, RLC R31, R32, R33, R35, R36, R38, R39.

What the centre does well.

Provision of information and counselling to those consenting to donate to research

Prior to giving consent, those donating to research should be provided with relevant information, and given a suitable opportunity to receive counselling about the implications

of their donation. The PR has provided assurance that:

- prior to giving consent, those donating to research are given a suitable opportunity to receive proper counselling about the implications of their donation (RLC R18).
- necessary information is provided to patients prior to giving their consent (RLC R19 and R20).
- information is provided to patients by trained personnel in a manner and using terms that are easily understood (RLC R21). The competence of staff at the recruiting centres to provide information in this way, and to seek consent, has been assessed.
- a designated individual, who is not directly involved in the patient's treatment, is available to discuss with the patient the project of research and the possibility of donating material to the project (RLC R22). Contact details for this designated individual are provided in the patient information.

Consent for storage

Stored gametes and embryos are obtained only from centres to which a HFEA licence or third party agreement applies (RLC R31, R32, R33).

No gametes or embryos are kept in storage for longer than the statutory storage period (RLC R35, R36, R38 and R39), or the period specified in a patients' consent if less than the statutory storage period. A bring-forward system is maintained, ensuring gametes and embryos are stored only within the statutory storage period or the patients' consent.

What they could do better.

Nothing noted.

Principle:

8. Ensure that all premises, equipment, processes and procedures used in the conduct of licensed activities are safe, secure and suitable for the purpose.

What we inspected against:

Premises and facilities; RLC R10.

What the centre does well.

Premises and facilities

Based on the centre's SAQ and the last inspection visit in July 2017, the inspector is assured that the premises and facilities are secure, clean, well maintained and are suitable for carrying out the licensed activities (RLC R10).

What they could do better.

Nothing noted.

Principle:

10. Maintain proper and accurate records and information about all licensed activities

What we inspected against:

Information and record keeping; RLC R3, R14, General Direction 0002.

What the centre does well.

The PR has provided all necessary information requested during this assessment within the required timescales (RLC R3).

Since the last inspection, the centre has submitted the annual research information and data sheet to the HFEA within the required timeframes (RLC R14 & General Direction 0002).

What they could do better.

Nothing noted.

Principle:

11. Report all adverse incidents (including serious adverse events and reactions) to the HFEA, investigate all complaints properly, and share lessons learned appropriately

What we inspected against:

Incidents; RLC R40.

What the centre does well.

Processes are in place to detect, report to the HFEA and investigate adverse incidents (RLC R40).

What they could do better.

Nothing noted.

Principle:

12. Ensure that all licensed research by the centre meets ethical standards, and is done only where there is both a clear scientific justification and no viable alternative to the use of embryos.

What we inspected against:

HF&E Act 1990 (as amended), Schedule 2 (3(5) and 3A).

What the centre does well.

The research project has been approved by the South Central – Berkshire B Research Ethics Committee. Evidence was provided by the PR that this approval remains active and covers the research activity described in the licence application.

The research project does not include any activities that have been prohibited by the HF&E Act 1990 (as amended).

A peer review was obtained for this renewal application and it is supportive of the licence renewal. Justifications that the activities to be licensed are necessary or desirable to meet the statutory purposes, have been provided by the PR and the peer reviewer, as discussed in detail in the 'Summary for Licensing Decision'. The PR and Peer Reviewer have also provided reasons why the use of human embryos is necessary.

What they could do better.
Nothing noted.

Principle:

13. Conduct all licensed activities with regard for the regulatory framework governing treatment and research involving gametes or embryos within the UK, including:

- maintaining up-to-date awareness and understanding of legal obligations;
- responding promptly to requests for information and documents;
- co-operating fully with inspections and investigations by the HFEA or other agencies responsible for law enforcement or regulation of healthcare.

What we inspected against:

Licensing; RLC R1, R3, R5, R6. The Person Responsible; HF&E Act 1990 (as amended) Section 16 & 17, RLC R8, R9.

What the centre does well.

Licensing

Information obtained at the last inspection, a review of the SAQ and discussions with the PR confirm that all licensed research activities will be performed only at the licensed premises under the supervision of the PR (RLC R1).

The Person Responsible

The PR has a key role to play in implementing the requirements of the HF&E Act 1990 (as amended) and is the person under whose supervision the licensed activities are authorised. The PR has the primary legal responsibility under Section 17 of the HF&E Act 1990 (as amended) to secure:

- that suitable practices are used in undertaking the licensed activities;
- that other persons working under the licence are suitable and;
- that the conditions of the licence are complied with.

The PR has suitable qualifications and experience for the activity authorised by the licence (HF&E Act 1990 (as amended), Section 16 (2)(ca)). The inspection team considered that the PR has fulfilled his responsibilities under Section 17 of the HF&E Act 1990 (as amended).

What they could do better.
Nothing noted.

Section 4: Monitoring of the centre's performance

Following an interim inspection in July 2017, no recommendations for improvement were made.

Section 5: Areas of practice that require the attention of the Person Responsible

The section sets out matters which the inspection team considers may constitute areas of non-compliance. These have been classified into critical, major and others. Each area of non-compliance is referenced to the relevant sections of the Act, Regulations, Standard Licence Conditions, Directions or the Code of Practice, and the recommended improvement actions required are given, as well as the timescales in which these improvements should be carried out.

Critical areas of non-compliance

A critical area of non-compliance is an area of practice which poses a significant direct risk of causing harm to a patient, donor or to an embryo. A critical area of non-compliance requires immediate action to be taken by the Person Responsible.

Area of practice and reference	Action required and timescale for action	PR Response	Executive Review
None			

Major areas of non-compliance

A major area of non-compliance is a non-critical area of non-compliance:

- which poses an indirect risk to the safety of a patient, donor or to an embryo through the procurement, use, storage or distribution of gametes and embryos, which do not comply with the centre's licence;
- which indicates a major shortcoming from the statutory requirements;
- which indicates a failure of the Person Responsible to carry out his/her legal duties
- a combination of several "other" area of non-compliance, none of which on their own may be major but which together may represent a major area of non-compliance.

Area of practice and reference	Action required and timescale for action	PR Response	Executive Review
None			

‘Other’ areas of practice that require improvement

‘Other’ areas of practice that require improvement is any area of practice, which cannot be classified as either a critical or major area of non-compliance, but which indicates a departure from good practice.

Area of practice and reference	Action required and timescale	PR Response	Executive Review
None			

Additional information from the Person Responsible