Executive Licensing Panel - minutes

Centre 0035 (Oxford Fertility) Interim Inspection Report

Research Project R0196

Friday, 23 September 2016

HFEA, 10 Spring Gardens, London SW1A 2BU

Panel members	Juliet Tizzard (Chair) Joanne Anton Anna Rajakumar	Director of Strategy & Corporate Affairs Head of Regulatory Policy Scientific Policy Manager
Members of the Executive	Dee Knoyle	Secretary
External adviser		
Observers		

Declarations of interest

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

The panel had before it:

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

1. Consideration of application

1.1. Oxford Fertility, centre 0035, holds a treatment (including embryo testing) and storage licence and three research licences. This research project, R0196, is entitled ‘Studying mitochondrial DNA quality control in human oocytes and pre-implantation embryos’. The project does not involve the derivation of human embryonic stem cell lines intended for human application.

1.2. The panel noted that this research licence was initially granted in January 2015.

1.3. The panel noted that the current research licence is due to expire on 28 January 2018.

1.4. The panel noted that all licensed material used in the project is obtained from Oxford Fertility, centre 0035.

1.5. The panel noted that an inspection was carried out on 27 July 2016. This was the first visit since the licence was granted. At the time of the inspection there were no areas of practice that required improvement.

1.6. The panel noted the inspectorate's recommendation for the continuation of the centre’s research licence.

2. Decision

2.1. The panel endorsed the inspectorate's recommendation to continue the centre’s research licence.

3. Chair’s signature

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

Signature

Name

Juliet Tizzard

Date

5 October 2016

Research Interim Inspection Report

Date of Inspection: 27 July 2016

Purpose of inspection: The purpose of this interim inspection is to assess whether research using human embryos is carried out in compliance with the Human Fertilisation and Embryology (HF&E) Act 1990 (as amended) and the Code of Practice and that progress is made towards achieving the stated aims of the project. The report summarises the findings of the inspection highlighting areas of firm compliance and good practice, as well as areas where improvement may be required to meet regulatory standards. It is primarily written for the Authority's Executive Licensing Panel (ELP) which makes the decision about the centre's licence.

Length of inspection: 3 hours

Inspectors: Sara Parlett and Douglas Gray

Inspection details:
The report covers the pre-inspection analysis, the visit and information received from the centre.

Date of Executive Licensing Panel: 23 September 2016

Centre details

Project title	Studying mitochondrial DNA quality control in human oocytes and pre-implantation embryos
Centre name and number	Oxford Fertility (0035)
Research project licence number	R0196/1/a
Centre addresses	Institute of Reproductive Sciences Oxford Business Park North Oxford, Oxfordshire OX4 2HW
Person Responsible	Dr Karen Turner
Licence Holder	Dr Ingrid Granne
Treatment centres donating to this research project	Oxford Fertility (0035)
Date licence issued	29 January 2015
Licence expiry date	28 January 2018
Additional conditions applied to this licence	None

Contents

Report to Executive Licensing Panel

Brief description of the centre and its licensing history

Oxford Fertility is a large treatment, storage and research centre which provides a full range of treatment services and has three research licences.

An interim inspection of all three research licences was conducted on the same day and the three separate reports will be considered by the same ELP. This report is specific to research project R0196: Studying mitochondrial DNA quality control in human oocytes and pre-implantation embryos.

This research licence was initially granted in January 2015. This visit represents the first inspection of this project since the licence was granted.

The project does not involve the derivation of human embryonic stem cell lines intended for human application.

Summary for licensing decision

In considering overall compliance, the inspection team considers that it has sufficient information drawn from documentation submitted by the centre prior to inspection, and from observations and interviews conducted during the inspection visit, to draw a conclusion on the continuation of the centre's licence.

The ELP is asked to note that at the time of the inspection there were no areas of practice that require improvement.

Recommendation to the Executive Licensing Panel

The inspection team recommends the continuation of the centre's licence.

Summary of project

This section presents information submitted by the PR in initial licence application and the Research Information and Data Sheet for 2015.

Lay summary of the research project:

Mitochondria are cell components, essential for life. However, one in 400 people has a maternally inherited mutation in mitochondrial DNA (mtDNA), the 'blue print' for mitochondrial components. MtDNA mutations can cause a range of illnesses, which may be extremely severe, and there are no curative treatments. There are centres developing techniques for replacing disabled mitochondria with healthy ones using a radical technique called "nuclear transfer", but this remains controversial. Alternative techniques are hampered by poor understanding of the underlying mechanisms around the inheritance of mtDNA. We know that MtDNA is inherited via the female line only and the severity of the disease depends on the proportion of abnormal mtDNAs in particular cells of the body. However, this proportion varies from one generation to the next and cannot be predicted. The variability in the number of abnormal mtDNAs inherited is caused by an event known as the 'mitochondrial bottleneck' which takes place in the female germline. We aim to study the biological processes that occur at this point (the mitochondrial bottleneck) as the effectiveness of medical interventions to reduce the load of mutant mtDNA will depend critically upon the timing and impact of it. Our work seeks to provide greater understanding of the biological process underlying the timing and impact of the mitochondrial bottleneck, with our overall aim to provide strategies for reducing mutant mtDNA load in embryos prior to implantation, which will translate into reduced risk of affected mothers having offspring with severe disease. To do our investigations we plan to use eggs and very early stage embryos donated from patients having In Vitro Fertilisation (IVF) at the Oxford Fertility Unit. They are eggs/embryos which are not suitable for clinical procedures and would otherwise be discarded.

Objectives of the research:

We wish to seek evidence for the presence of a mitochondrial DNA (mtDNA) bottleneck in human oocytes and preimplantation embryos. This could arise as a result either of clonal mtDNA proliferation, or as a result of mtDNA turnover of damaged mtDNA. (A third possibility that is beyond the scope of the current investigation is that the bottleneck arises through partitioning of subpopulations of mtDNA into specific cells that are destined to become the inner cells mass). Specifically:

- To investigate mtDNA synthesis in immature oocytes and preimplantation embryos (Identify newly synthesized mtDNA by pulse labelling);
- To investigate mitochondrial autophagy (self-degradation)(Compare levels of autophagy with the mtDNA synthesis at different stages of development);
- To investigate mtDNA damage in oocytes and pre-implantation embryos (Identify differences in mtDNA sequence data that suggest mtDNA turnover).

Donation and use of embryos:

In the period from 1 January 2015 to 31 December 2015, the centre reported the donation and use of three fresh embryos in this project. No embryos have been used to date in 2016.

This is because preliminary work in animal models is still underway and a post-doctoral research post to progress this work has yet to be filled.

Details of inspection findings

Inspection findings

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

What the centre does well.
When considering the initial licence application, two peer reviewers agreed that the use of human embryos was necessary and justified for the proposed research.

Evidence of approval by an ethics committee was also provided at the initial licence inspection and this approval remains in place.

The research licence was granted for the following activity and it is not prohibited by the HF&E Act 1990 (as amended):

- using embryos.

The initial licence was approved to allow research for the following designated purposes:

- developing methods for detecting the presence of gene, chromosome or mitochondrion abnormalities in embryos before implantation;
- increasing knowledge about the development of embryos.

On inspection, a review of the documentation relating to embryos donated and used for the project and discussions with centre staff, demonstrated that embryos have only been used in activities for which the centre is licensed.

What they could do better.
Nothing noted.

Have respect for the special status of the embryo when conducting licensed activities (Research Licence Conditions (RLC) R23, R24, R26, R27, R28, R29, CoP Guidance Note 22)

What the centre does well
On inspection, a review of the documentation relating to the small number of embryos donated and used for the project, and discussions with centre staff demonstrated that:

- proper records of the use of embryos for the research project are maintained (RLC R13, R14 and R15);
- robust procedures are in place to ensure proper records of the use of embryos are maintained from donation to the project, use in research through to disposal at the end of the research process (RLC R13);
- effective consent for the use of the embryos in the research project has been documented by the gamete providers (RLC R18);
- the researchers use documented practices which ensure that embryos do not develop beyond 14 days post-fertilisation or the appearance of the primitive streak, whichever is earlier (RLC R28);
- all embryos donated to the project are only used for the objectives authorised by the licence to meet the defined statutory purposes (RLC R5 and R23). This is facilitated by restricting access to embryos during use and supervision of research staff by the PR.

The PR has ensured that embryo donation and use in the project have been reported annually to the HFEA (General Direction 0002).

What they could do better
Nothing noted.

Ensure that all premises, equipment, processes and procedures used in the conduct of licensed activities are safe, secure and suitable for the purpose (RLC R10).

What the centre does well
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.

Changes and improvements since the last inspection

No recommendations for improvement were made at the initial inspection in December 2014.

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 area 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 area 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 requires improvement

Areas of practice that requires 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 for action	PR Response	Executive Review
None			

Additional information from the Person Responsible