Executive Licensing Panel - minutes

Centre 0035 (Oxford Fertility) Interim Inspection Report

Research Project R0198

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, R0198, is entitled 'Artificial oocyte activation and egg/embryo movements as early indicators of embryo quality'. The project does not involve the derivation of human embryonic stem cell lines intended for human application.

1.2. The panel noted that research project R0198 was initially undertaken as part of research project R0111 at centre 0035. However, when considering the application for the renewal of research licence R0111 in 2015, the Person Responsible decided that the scope of the research work performed more accurately related to two separate projects. Therefore, a new research licence for the artificial egg activation research project was applied for and approved as project R0198.

1.3. The panel noted that the current research licence is due to expire on 23 September 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 at the time of the inspection on 27 July 2016, 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	Artificial oocyte activation and egg/embryo movements as early indicators of embryo quality
Centre name and number	Oxford Fertility (0035)
Research project licence number	R0198/1/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	24 September 2015
Licence expiry date	23 September 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 R0198: Artificial oocyte activation and egg/embryo movements as early indicators of embryo quality.

This research programme was initially undertaken as part of project R0111 at centre 0035, after the licence for that project was varied in June 2014 to allow it. When considering the application for licence renewal in 2015, the PR decided that the scope of the research work more accurately related to two separate projects. Therefore project R0111 reverted to its original scope and objectives prior to the variation in June 2014 and a new research licence for the artificial egg activation research project was applied for and approved as project R0198.

Project R0198 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 the licence renewal application and the Research Information and Data Sheet for 2015.

Lay summary of the research project:

At fertilisation, the sperm activates the egg to being development. This is called 'egg activation' and PLCzeta is a protein found in sperm which regulates these processes. If sperm do not have adequate PLCzeta protein then the egg may not be activated and fertilised. Men without adequate PLCzeta may therefore be infertile. However, we believe that we can rescue these cases of egg activation deficiency by using an artificially synthesised version of PLCzeta that we have created in our labs. We now need to make sure that this protein can restore fertility in these patients. To test that our PLCzeta protein can activate human eggs in this way we will, in a laboratory, inject it into fresh human eggs, or those which have previously failed to fertilise, and record what happens. We may also simply expose the protein to the egg by adding it to the surrounding culture media, so we can find out the best way of administering the protein to the egg. In a second part of the study, we will use high-frequency time lapse filing to observe the tiny movements that take place in an egg during the first few hours after activation. These, and other experiments on eggs and very early stage embryos, will increase our knowledge of the processes that occur around fertilisation. In the future we may be able to use our PLCzeta to help in cases where there are egg activation problems, and use the time lapse technique to predict which embryos are healthier for transfer in IVF.

Objectives of the research:

To determine the appropriate way to administer PLCzeta protein to an egg. To identify the oocyte-borne protein factor that interacts with sperm PLCzeta following fertilisation. To determine how clinical procedures (such as cryopreservation and in vitro maturation) can influence oocyte proteins involved in the PLCzeta pathway that initiates oocyte activation. To find out if cytoplasmic movements in 1-cell and 2-cell zygotes can be used to predict subsequent blastocyst and chromosomal health of embryos.

Donation and use of embryos:

In the period from 1 January 2015 to 31 December 2015, the centre reported the donation and use of 44 fresh embryos in this project.

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.
As part of the initial licensing process in 2015, a peer reviewer 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 as part of the initial licensing process in 2015 and this approval remains in place.

The research licence was granted for the following activities:

- using embryos;
- keeping embryos;
- creation of embryos.

None of these activities are prohibited by the HF&E Act 1990 (as amended). It is noted that embryos have not yet been created for this project. It is estimated that this part of the project will commence in year two of the licence.

The initial licence application in 2015 was approved to allow research for the following designated purposes:

- promoting advances in the treatment of infertility;
- 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 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 last inspection, a desk based assessment of the initial licence application in 2015.

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