Executive Licensing Panel - minutes

Centre 0035 (Oxford Fertility) Interim Inspection Report

Research Project R0111

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, R0111, is entitled ‘Development of a model to study implantation in the human’. The project does not involve the derivation of human embryonic stem cell lines intended for human application.

1.2. The project was first licensed in 1998. In 2014, the licence was varied to include an additional study of artificial egg activation. However, when considering the application for the renewal of the licence in 2015, the Person Responsible decided that the scope of the research work performed under R0111 more accurately related to two separate projects. Therefore, research project R0111 reverted to its 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.

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 with no additional conditions.

2. Decision

2.1. The panel endorsed the inspectorate's recommendation to continue the centre’s research licence, with no additional conditions.

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.

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	Development of a model to study implantation in the human
Centre name and number	Oxford Fertility (0035)
Research project licence number	R0111/7/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 R0111: development of a model to study implantation in the human.

The project was first licensed in 1998. In 2014, the licence was varied to include an additional study of artificial egg activation. When considering the application for the renewal of its licence in 2015, the PR decided that the scope of the research work performed under R0111 more accurately related to two separate projects. Therefore project R0111 reverted to its 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 R0111 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:

The purpose of this research is to discover more about the processes that occur during early embryo development and when an embryo implants. Donated embryos will be used in experiments to help us understand how implantation occurs successfully. We will measure the production of factors which signal the embryo's presence to the mother and are necessary for implantation. We will also use a laboratory model to investigate the interactions between the embryo and endometrium during the implantation process. In other experiments, blastocysts will be cultured with cells from the endometrium to find out more about how they attach to the endometrium and implant. We anticipate that the discoveries we make may optimise the selection of the best embryos for transfer back into the womb in IVF, and may contribute to novel therapies that will increase the chances of implantation.

Objectives of the research:

Subfertility is a common condition affecting 1 in 7 couples. It has significant consequences for couples often leading to psychological distress, depression and a reduced quality of life. Although IVF treatment has enabled many infertile couples to achieve a pregnancy, success rates are still disappointingly low even in young women, where nationally only 32% of IVF cycles result in a live birth. Many seemingly good quality embryos are transferred but fail to implant. Historically at least two embryos were replaced in an IVF cycle to increase the overall pregnancy rate, but a recent drive by the HFEA aims to decrease the morbidity and mortality associated with multiple pregnancy by increasing the proportion of cycles in which a single embryo is transferred. However even the transfer of a 'top quality' day 5 embryo will result in no more than a 50-60% implantation rate. Therefore a better understanding of the process of implantation is essential if we are to further improve pregnancy rates in IVF treatment. This process of embryo implantation involves a complex sequence of events and signal interactions between the embryo and the endometrium. In humans implantation occurs between day 20 and 24 (of a 28 day menstrual cycle), a period known as the window of implantation. During this window of implantation the embryo reaches the stage of attachment competence and whilst simultaneously the endometrium reaches a stage of receptivity. The process of embryo attachment and penetration of the underlying basement membrane is a complex and multistep event that remains poorly understood. The aim of this study is to better elucidate the processes involved. In doing so we hope to identify clinically important molecules, pathways and signalling that may ultimately be a target for developing treatments to improve IVF success rates. Our specific objectives are:

- to investigate normal human embryo development and implantation;
- dissect the molecular events in the process of embryo attachment;
- develop a 3-D model of implantation.

Donation and use of embryos:

In the period from 1 January 2015 to 31 December 2015, the centre reported the donation and use of 50 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. At the last licence renewal, 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 at the last licence renewal and this approval remains in place. The research licence was granted for the following activities, none of which are prohibited by the HF&E Act 1990 (as amended): • using embryos; • storage of embryos; • keeping embryos. The renewal of the licence was approved to allow research for the following designated purposes: • promoting advances in the treatment of infertility; • increasing knowledge about the causes of miscarriage; • 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 storage and 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 storage and use, and supervision of research staff by the PR;
- a storage log is maintained which records the storage consent expiry dates for any embryos in storage for research purposes. All frozen embryos in storage were within their consented storage period (RLC R39).

The PR has ensured that embryo donation, storage 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 licence renewal 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