HFEA Executive Licensing Panel Meeting

10 January 2014

Finsbury Tower, 103-105 Bunhill Row, London, EC1Y 8HF

Minutes – Item 3

Centres 0033 (Manchester Fertility), 0067 (St Mary's Hospital) and 0175 (University of Manchester) - Interim Inspection Report for Research Project R0026

Members of the Panel:	**Committee Secretary:**
Juliet Tizzard – Interim Director of Strategy (Chair)	Dee Knoyle
Ian Peacock – Analyst Programmer	**Observing:**
Matthew Watts – Regulatory Policy Manager	Sam Hartley – Head of Governance and Licensing

Declarations of Interest: members of the Panel declared that they had no conflicts of interest in relation to this item.

The Panel also had before it:

- HFEA Protocol for the Conduct of Meetings of Executive Licensing Panel
- 8th edition of the HFEA Code of Practice
- Human Fertilisation and Embryology Act 1990 (as amended)
- Decision trees for granting and renewing licences and considering requests to vary a licence (including the PGD decision tree)
- Guidance for members of Authority and Committees on the handling of conflicts of interest approved by the Authority on 21 January 2009.
- Guidance on periods for which new or renewed licences should be granted
- Standing Orders and Instrument of Delegation
- Indicative Sanctions Guidance
- HFEA Direction 0008 (where relevant), and any other relevant Directions issued by the Authority
- Guide to Licensing
- Compliance and Enforcement Policy
- Policy on Publication of Authority and Committee Papers

Consideration of Application

1. The Panel noted that research project R0026 is carried out at three different centres, each centre holding a research licence for this project. Centre 0175 is a research only centre and centres 0067 and 0033 are treatment and storage with research centres. 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.

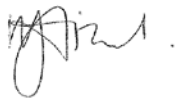
2. The Panel noted that the current licence is due to expire on 31 December 2015, having been renewed for three years by a Research Licence Committee (RLC) on 19 November 2012.

3. The Panel noted that at the time of the inspection on 8 October 2013, the Inspectorate observed one other area of non-compliance. The Panel noted the PR’s commitment to implement the recommendation to review and amend the procedure for reporting adverse incidents and submit the revised procedure to the HFEA, within the set timescales.

4. The Panel noted the Inspectorate's recommendation for the continuation of the centres' research licences with no additional conditions.

Decision

5. The Panel endorsed the Inspectorate's recommendation to continue the centres' licences, with no additional conditions, and endorsed the recommendation in the report.



Signed: Date: 24 January 2014
Juliet Tizzard (Chair)

Research Interim Inspection Report

Date of Inspection: 8 October 2013
Purpose of inspection: Interim Inspection of Research Licence
Length of inspection: 8 hours
Inspectors: Dr Vicki Lamb

Inspection details:
The report covers the pre-inspection analysis, the visit and information received between 15 September 2011 and 27 December 2013.

Date of Executive Licensing Panel: 10 January 2014

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 names and numbers	University of Manchester (0175) St Mary's Hospital (0067) Manchester Fertility (0033)
Research licence numbers	R/0026/13/a R/0026/15/a R/0026/14/a
Centre addresses	Centre 0175: Floor 2 Core Technology Facility, Faculty of Life Sciences, University of Manchester, 46 Grafton Street, Manchester, M13 9NT Centre 0067: The Department of Reproductive Medicine, Regional IVF and DI Unit, Oxford Road, Manchester, M13 9WL. Centre 0033: 3 Oakwood Square, Cheadle Royal Business Park, Cheadle, Cheshire, SK8 3SB
Person Responsible	Professor Daniel Brison (0175, 0067 and 0033)
Licence Holder	Professor Sue Kimber (0175 and 0067); Dr Brian Lieberman (0033)
Treatment centres donating to this research project	0007 0008 0033

Doc name: Interim research report R0026
TRIM reference: 2013/018425

	0067
Date licence Issued	R/0026/13/a 1 February 2013 (0175) R/0026/15/a 1 January 2013 (0067) R/0026/14/a 1 January 2013 (0033)
Licence expiry date	31 December 2015
Additional conditions applied to this licence	None

Contents

Purpose of the Inspection report

The purpose of the 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 which makes the decision about the centre's licence.

Report to Executive Licensing Panel

Brief description of the centre and its licensing history:

Research project R0026 is carried out at three different centres, each centre holding a research licence for this project. Centre 0175 is a research only centre and centres 0067 and 0033 are treatment and storage with research centres. 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 2015, having been renewed for three years by a Research Licence Committee (RLC) on 19 November 2012. The RLC considered a desk-based assessment of the research licence application. The last time the centres were visited was on 15 September 2011. There are no additional conditions on the licences.

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 Executive Licensing Panel is asked to note that at the time of the inspection there was one 'other' area of non-compliance or poor practice.

Since the inspection visit the Person Responsible (PR) has given a commitment to fully implement this recommendation:

'Other' area of non-compliance or poor practice:

- The PR should review and amend the procedure for reporting adverse incidents and submit the revised procedure to the HFEA.

Recommendation to the Executive Licensing Panel:

The inspection team considers that overall there is sufficient information available to recommend the continuation of this centre's licence without additional conditions. In making this recommendation it is noted that the PR has responded to the recommendation made in this inspection report.

Summary of project

Lay summary of the research project:

The researchers plan to continue the current project to understand early human embryo development by studying sperm, eggs and embryos donated by IVF patients at participating centres. If eggs are used they can be cultured or chemically activated to form embryos. For this they use some eggs and embryos which have been frozen in IVF procedures. They culture the embryos up to day 8 after fertilisation, well before the limit of 14 days post-fertilisation. They are looking at the effect of freezing on how the embryos develop using molecules which tell them about their health and normality. They are looking at how the different cells in the embryo differ from one another and how different proteins added to the culture medium affect the components that the embryos make. These studies will help them 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 understanding of human embryo development. They can also use this information to try to prevent failed development and miscarriage in the future.

Objectives of the research:

The researchers aim to continue their current research aims including:

(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. They will also include analysis of genes involved in the implantation process.
(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 to compounds such as bisphenol-A and nicotine (advanced glycosylation end products; known as AGEs) on sperm parameters and DNA integrity.
(4) The impact of the environment on oocyte and embryonic development, including growth factors and AGEs.

Donation and use of embryos:

In the period from 1 January 2012 to 31 December 2012, the centre reported the use of 23 fresh embryos and 25 frozen embryos. No embryos were created for use in the 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
(Guidance note 29, 30, 31)

What the centre does well.

The renewal of research licence R0026 was granted by the RLC on 19 November 2012, the licensed activities being the creation of embryos in vitro, keeping embryos, storage of embryos and use of embryos. None of these activities are prohibited by the HF&E Act 1990 (as amended). The renewal of the licence was approved to allow research for the following designated purposes:

- Promoting advances in the treatment of infertility
  HFE Act 1990 (as amended) Schedule 2 3A(2)(d)
- Increasing knowledge about the causes of miscarriage
  HFE Act 1990 (as amended) Schedule 2 3A(2)(e)
- Developing more effective techniques of contraception
  HFE Act 1990 (as amended) Schedule 2 3A(2)(f)
- Increasing knowledge about the development of embryos
  HFE Act 1990 (as amended) Schedule 2 3A(2)(h)

At the last renewal, the application's 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.

What they could do better.

Nothing noted on this inspection.

Have respect for the special status of the embryo when conducting licensed activities
(Guidance note 15, 18, 22, 25, 26)

What the centre does well.

An audit of records of the usage of five sets of embryos in the project demonstrated that:

- Comprehensive records of the usage of embryos in the research project are maintained from embryo donation to the project through to disposal at the end of the research process (RLC R13).
- The researchers have a documented procedure for ensuring that embryos do not develop beyond 14 days post-fertilisation or the appearance of the primitive streak, whichever is earlier (RLC R28). The audit of records confirmed compliance with this requirement.
- All embryos donated to the project have been used for the objectives authorised by the licence to meet the defined statutory purposes (RLC R5 and R23).
- A storage log is maintained which records the storage consent expiry dates for any embryos in storage for research purposes. All frozen embryos used in the research project have been used within their consented storage period, and embryos still in store are also within their consented storage period. (RLC R39).

The research identifiers for the same five sets of embryos were used to track back to five sets of patient records at centre 0067 where the treatment had taken place. Audit of these five sets of patient records indicated that effective consent for the use of the embryos in the research project had been documented by the gamete providers (RLC R18).

The PR has ensured that appropriate records of embryo usage are maintained and that annual usage is reported to the HFEA (General Direction 0002 and RLC R13, R14 and R15).

What they could do better.

The procedure for reporting adverse incidents states the incorrect timescale for reporting to the HFEA (General Direction 0011 and RLC R40).

Changes / improvements since the renewal of the licence on 19 November 2012:

Area for improvement	Action required	Action taken as evidenced during this inspection
None		

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 non-compliance or poor practice

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
The procedure for reporting adverse incidents states the incorrect timescale for reporting to the HFEA (General Direction 0011 and RLC R40).	The PR should review and amend the procedure for reporting adverse incidents and submit the revised procedure to the HFEA. By 8 January 2014.	Agreed	This is a satisfactory response.

Additional information from the Person Responsible