Executive Licensing Panel - minutes

Centre 0021 (Hull IVF Unit)

Interim Inspection Report - Research Project R0067

Tuesday, 29 October 2019

HFEA, 10 Spring Gardens, London SW1A 2BU

Panel members	Clare Ettinghausen (Chair) Helen Crutcher Howard Ryan	Director of Strategy and Corporate Affairs Risk and Business Planning Manager Data Analyst
Members of the Executive	Bernice Ash	Secretary
External adviser		
Observers	Catherine Burwood	Licensing Manager

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:

- 9th edition of the HFEA Code of Practice
- Standard licensing and approvals pack for committee members.

1. Consideration of application

1.1. The panel considered the papers, which included a report and licensing minutes for the last three years.

1.2. The panel noted that Hull IVF Unit is licensed to provide treatment and storage services and is also licensed for research project R0067 ‘Biochemistry of early human embryos’. This project seeks to evaluate changes in the media of cultured embryos resulting from their metabolism and to correlate those changes with embryo viability and potential for live birth, as well as with secondary factors such as patient health. The project was first licensed in 1995.

1.3. The panel noted that an inspection was carried out on 20 August 2019.

1.4. The panel noted that, at the time of the inspection, no areas of non-compliance or poor practice were identified.

1.5. The panel noted the inspectorate's recommendation for the continuation of the centre’s research licence with no additional conditions.

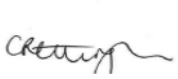
2. Decision

2.1. The panel agreed to the continuation of 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

Clare Ettinghausen

Date

4 November 2019

Research interim inspection report

Date of inspection: 20 August 2019
Purpose of inspection: Interim inspection of research licence
Inspectors: Sara Parlett and Andrew Leonard
Inspection details:
The report covers the pre-inspection analysis, the visit and information received from the centre.
Date of Executive Licensing Panel: 29 October 2019

Centre details

Project title	Biochemistry of early human embryos
Centre name	Hull IVF Unit
Centre number	0021
Research licence number	R0067
Centre address	Reproductive Medicine Research Hull York Medical School Women's and Children's Hospital Hull Royal Infirmary Anlaby Road Hull HU3 2JZ
Person Responsible	Professor Henry Leese
Licence Holder	Dr Roger Sturmey
Treatment centres donating to this research project	Hull IVF Unit
Date licence issued	1 February 2019
Licence expiry date	31 January 2022
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 (CoP) 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.

Report to Executive Licensing Panel

Brief description of the centre and its licensing history

Hull IVF Unit is licensed to provide treatment and storage services and is also licensed for research project R0067: Biochemistry of early human embryos. This project seeks to evaluate changes in the media of cultured embryos resulting from their metabolism and to correlate those changes with embryo viability and potential for live birth, as well as with secondary factors such as patient health. The project was first licensed in 1995.

The project's licence was last renewed by licence committee in November 2018, after a desk based assessment by the executive; no non compliances were reported. The project was last inspected on site in 2017; again no non compliances were reported.

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 non compliance.

Recommendation to the Executive Licensing Panel

The inspection team recommends the continuation of this centre's licence without additional conditions.

Summary of project

Lay summary of the research project

Why the project is being carried out: We know very little about the processes that form a human embryo and why some embryos turn out to be healthier than others. The purpose of our work is to carry out a detailed examination of the development of the early human embryo, particularly how it generates the energy it needs to grow. This knowledge will help optimise embryo culture and transfer procedures to enhance IVF success rates. A second area of increasing importance is how the environment in which early development occurs can influence the long-term health of the babies born. For example, a woman's body weight affects the quality of her eggs and embryos; a detailed understanding of which could increase the chances of a healthy pregnancy and a healthy baby.

What the research project aims to achieve: The first aim is to devise a simple, reliable method for embryo selection; the second is to discover whether the preconception environment, including maternal body weight can affect the health of eggs and early embryos. This information will enable couples trying for a baby naturally or through IVF to be provided with sound preconception advice.

What your research involves and why you need to use human embryos: The research uses highly sensitive laboratory tests, most of which are non-invasive, to study the biochemistry of individual human embryos, donated to research after treatment. The data can then be related to the ability of the embryos to develop successfully in culture. We do pilot work in the laboratory on animal embryos to confirm our approaches are feasible before conducting this essential research on spare human embryos.

How this will help you achieve your research aims: The data will (i) provide reassurance that a non-invasive test to select single embryos for transfer is safe and effective such that clinical trials could safely be undertaken (ii) demonstrate the importance of the preconception environment in ensuring the health of embryos conceived via IVF, and the short and long-term health of the babies.

Objectives of the research

We wish to illuminate understanding of the biochemistry of early human embryos. To achieve this, we will pursue the following objectives;

- Objective 1: Increasing knowledge about serious diseases or other serious medical conditions. We will do this by studying how maternal ill health can programme alterations in early embryo biochemistry. We will measure a range of biochemical endpoints including markers of metabolic activity.
- Objective 2: Promoting advances in the treatment of infertility. Concerns have been raised about the impact of the ART process on short and long-term health risks to mother and offspring. Building on existing data, we will increase the evidence base on the way in which the biochemical phenotype of an embryo can be modified by ART practices. Examples include the method of ovarian stimulation, the gamete/ embryo

culture conditions, the mode of fertilisation, and impact of cryopreservation techniques. We will also seek to understand the impact of the underlying cause of infertility on early embryos and distinguish this from the impact of ART practices by studying the biochemistry of embryos created from the gametes of fertile donors. Our overall experimental strategy will generate data of direct relevance to women undergoing ART and to those planning to conceive naturally. It is only by studying spare embryos arising from IVF that we can collect information on the physiology of the human preimplantation embryo.

- Objective 3: Increasing knowledge about the development of embryos. The methods used to measure embryo biochemistry of early embryos indicate the depletion of substrates that are parts of known metabolic pathways. We are now able to expand these data by studying directly the mitochondrial function of single preimplantation embryos. These methods have been developed in an animal model, and give information of biochemical function of early embryos in more detail than ever before. These include the proportion of energy that is 'wasted' (that is not used productively) as well as the real-time activity of the mitochondria within the embryos. This project will not use embryonic stem cells or human admixed embryos.

Donation and use of embryos

In 2018, the PR reported that 80 fresh embryos were used in the research project. There has been a recent lull in research activity and no embryos have been used so far in 2019. Further funding has been secured and work will resume before the end of the year.

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 centre was granted a renewal of its research licence by a licence committee in 2018 for the following activities: using embryos, keeping embryos and storage 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 as defined in Schedule 2 3A (1) and (2) of the HF&E Act 1990 (as amended):

- increasing knowledge about serious disease or other serious medical conditions;
- promoting advances in the treatment of infertility;
- increasing knowledge about the development of embryos.

At the last renewal, a peer reviewer agreed that the use of human embryos was necessary and justified for the proposed research project.

The research project has been approved by the East Yorkshire & North Lincolnshire Ethics Committee. Evidence was provided by the PR that this approval remains active.

What they could do better.

Nothing noted.

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.

On inspection, a review of documentation and discussions with centre staff demonstrated that:

- 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);
- 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);
- discussions with the PR provided assurance that 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 restricted access to embryos during storage and use, and supervision of research staff by the PR;
- proper records of the storage of embryos in the research project are maintained, including a storage log 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).

An audit of donor records showed that:
- effective consent for the use of the embryos in the research project had been documented by the gamete providers (RLC R18).
- embryos are not allowed to develop after 14 days or the primitive streak has appeared (if earlier) (RLC R28).

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

What they could do better.
Nothing identified.

Changes and improvements since the last inspection

Following the renewal inspection in 2018, no recommendations for improvement were made.

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 noted.			

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 noted.			

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 noted.			

Additional information from the Person Responsible
We are happy with the report and I can say that we all found the inspection a positive experience.