HFEA Licence Committee Meeting

8 May 2014

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

Minutes – Item 1

Centre 0017 (Newcastle Fertility Centre at Life) – Research Renewal Licence Report (R0152)

Members of the Committee: Andy Greenfield (lay) Chair Bishop Lee Rayfield (lay) Debbie Barber (professional) Jane Dibblin (lay) Committee Secretary: Lauren Crawford	Legal Adviser: Stephen Hocking, DAC Beachcroft LLP Also in attendance: Sam Hartley, Head of Governance and Licensing, HFEA

Declarations of Interest: Andy Greenfield declared an interest in that he chairs the Mitochondria Scientific Review Panel. Following legal advice, the committee agreed that this was not a conflict.

The following papers were considered by the Committee:

Papers enclosed:

- Desk-based assessment report
- Application form
- Peer review
- Recent publications
- Previous licensing minutes for the last three years:
    - 21 June 2013 Interim inspection
    - 23 May 2013 Interim inspection (adjourned)

The Committee also had before it:

- HFEA Protocol for the Conduct of Licence Committee Meetings and Hearings
- 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); and
- 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 Directions 0000 – 0012
- Guide to Licensing
- Compliance and Enforcement Policy
- Policy on Publication of Authority and Committee Papers

Background

1. The project, 'Pluripotency reprogramming and mitochondrial biology during early human development' was first licensed in 2004. The current licence is due to expire on 31 July 2014, having been last renewed for three years by a Research Licence Committee (RLC) in 2011.

Discussion

2. The Committee noted that the centre has requested to amend the title of the project to 'Towards improving assisted reproduction technologies for the treatment of infertility and prevention of disease'. There are no changes to the objectives of the project. The PR (Person Responsible) has included three new purposes for the project.

3. The Committee noted that at the time the desk-based renewal inspection took place, 12 February 2014, there were no areas of non-compliance that had been identified by the inspectorate.

4. The Committee had regard to its Decision Tree. The Committee was satisfied that the application was submitted in the form required, and contained the supporting information required by General Direction 0008. Furthermore, it was satisfied that the appropriate fee had been paid. The Committee noted that the application was made by the Person Responsible ("PR") for Research.

5. The Committee was satisfied that the PR possesses the required qualifications and experience and that the character of the PR is such as is required for supervision of the licensed activities. It was further satisfied that the PR will discharge her duties under section 17 of the Act. The Committee noted that the Inspector was satisfied the PR had satisfactorily completed the PR entry programme and is suitably qualified and experienced to undertake the role.

6. The Committee was satisfied that the premises to be licensed are suitable for the conduct of licensed activities as the Inspector confirmed that the premises were suitable and secure.

7. The Committee was satisfied that the licence application involved the authorisation of activities for the purpose of research.

8. The Committee was satisfied that the renewed licence would not apply to more than one project and that the activity of the licence, permitted under the Act, is for 'creation of embryos', 'keeping embryos', 'storage of embryos' and 'use of embryos'.

9. The Committee was satisfied that the use of human embryos is necessary because the high incidence of aneuploidy in a proportion of cells in the developing embryo is more or less specific to human embryos, so using the murine model would be inappropriate. In order to generate hESC lines or to translate the research to clinical applications the experiments must be conducted in human embryos.

10. The Committee noted the Peer Reviewer's comments on the application and was satisfied that the activity to be licensed is necessary or desirable for the following purposes, specified in Schedule 2 paragraph 3A(2) to the Act, for the following reasons:

    - *Increasing knowledge about serious disease or other serious medical conditions*: The proposed research includes investigations into the consequences of defects in mitochondrial DNA on early development and reprogramming. This will be achieved partly by assessing the early developmental potential of embryos created using nuclear material from eggs or oocytes from mothers carrying mtDNA defects and partly by deriving embryonic stem cell lines from affected embryos and comparing their differentiation spectrum with normal embryonic stem cell lines;
    - *Developing treatments for serious diseases or other serious medical conditions*: The research is leading to the development of a treatment that has the potential to significantly reduce the risk of transmission of abnormal mitochondria to the embryo and subsequent child;
    - *Developing methods for detecting the presence of gene, chromosome or mitochondrion abnormalities in embryos before implantation*: Methods will be developed to enable detection of mitochondrial DNA at a single cell level, and to map gene expression in different parts of the embryo;
    - *Increasing knowledge about the causes of miscarriage*: studies of oocyte aneuploidy are relevant to understanding the causes of miscarriage;
    - *Increasing knowledge about the development of embryos:* Prior to translating methods being developed in this project into clinical practice, it will be important to perform comparative studies with unmanipulated embryos created in vitro and show comparable outcomes. The information obtained in such comparisons will increase knowledge about the development of embryos;
    - *Increasing knowledge about the causes of any other congenital disease or congenital medical condition:* The applicants propose to study aneuploidy in oocytes and investigate its causes;

- *Promoting advances in the treatment of infertility*: Procedures of vitrification are being optimised in this research and these will assist in developing vitrification for fertility treatment.

11. The Committee was satisfied that the proposed project does not involve mixing sperm with the egg of an animal.

12. The Committee was satisfied that the inspector had previously seen the patient information and consent forms, and that these met the statutory requirements.

13. The Committee was satisfied that the research project had received the necessary approval from the National Research Ethics Service (NRES) Committee North East – Newcastle & North Tyneside 1.

14. The Committee noted the recommendation from the Inspectorate to renew the centre's research licence for a period of 3 years without additional conditions. Further, the Committee is asked to add the new purposes to the licence and to change the name of the project.

Decision

15. The Committee agreed to renew the research licence for project (R0152) for the activities of 'creation of embryos', 'keeping embryos', 'storage of embryos' and 'use of embryos' for a period of three years with no additional conditions.

16. The Committee agreed to change the project title and to add the new purposes to the licence as requested in the application.

Signed: Date: 22/05/2014

Andy Greenfield (Chair)

Research Renewal Inspection Report

Purpose of this inspection report

The HFEA licenses and monitors establishments undertaking human embryo research. This is a report of an evaluation of whether this centre complies with essential requirements when carrying out such research. Licences for individual research projects can be granted for up to three years and this report provides information on the centre's application for a renewal of its existing licence. The Authority's Licence Committee uses the application and this report to decide whether to grant a new licence and, if so, whether any additional conditions should be applied to that licence.

Date of inspection: 12 February 2014

Purpose of assessment: Renewal of a licence to carry out research

Assessment details:
The report covers the performance of the centre since the last inspection, findings from the desk based evaluation, and communications received from the centre. For this assessment, an inspector completed a robust desk-based evaluation of appropriate documentation and held discussions with key staff involved with the research project; there was no site visit.

Date of Licence Committee: 8 May 2014

Inspector: Dr Douglas Gray

Centre Details:

Project title	Towards improving assisted reproductive technologies for the treatment of infertility and prevention of disease
Centre name	Newcastle Fertility Centre at Life
Centre number	0017
Research project number	R0152
Centre address	Bioscience Centre, International Centre for Life, Times Square, Newcastle upon Tyne, NE1 4EP
Person Responsible	Professor Alison Murdoch
Licence Holder	Dr Mary Herbert
Treatment centres donating to this research project	Newcastle Fertility Centre at Life (0017), The Gateshead Fertility Unit (0170)
Date licence issued	01 August 2011
Licence expiry date	31 July 2014
Additional conditions applied to this licence	None

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Section 1: Summary report

Brief description of the centre and its licensing history:

The Newcastle Fertility Centre is based within the International Centre for Life. Research project R0152 has been licensed since August 2004.

To better reflect the research activities, the Person Responsible (PR) has requested that the name of the project is changed from that on the current licence which is 'Pluripotency reprogramming and mitochondrial biology during early human development', to 'Towards improving assisted reproductive technologies for the treatment of infertility and prevention of disease'. There have been no changes to the objectives of the research. The PR has included three new purposes for which the research will be carried out.

Summary for licensing decision:

Taking into account the essential requirements set out in the Human Fertilisation and Embryology (HF&E) Act 1990 (as amended), the HF&E Act 2008 and the HFEA Code of Practice (CoP), the inspection team considers that it has sufficient information to conclude that:

Administrative requirements:

- the centre has submitted an appropriately completed application form
- the centre has submitted the supporting information required by General Direction 0008, including evidence of ethics approval, patient information and consent forms
- the application has designated an individual to act as the PR
- the proposed licence applies to one project of research
- the centre has submitted fees to the HFEA in accordance with requirements

Research activities applied for:

An application has been made for the following activities for the purpose of research:

- Storage of embryos
- Creation of embryos
- Keeping embryos
- Using embryos

Whilst the PR anticipates that future research may involve the derivation of human embryonic stem cell lines, they have confirmed these will not be used for human application. Research Licence Conditions R41-89 are therefore not applicable to this research project.

Purposes for which research activities may be licensed:

The PR and peer reviewer consider that the research project is necessary for the purposes defined in Schedule 2 3A (1) and (2) to the HF&E Act 1990 (as amended) as follows:

- Increasing knowledge about serious disease or other serious medical conditions

  The reason for this as stated by the PR is:

  > *'The project is increasing our knowledge about the transmission of abnormal mitochondria during pre-implantation human development.'*

  The peer reviewer agrees and has stated:

'The proposed research includes investigations into the consequences of defects in mitochondrial DNA on early development and reprogramming. This will be achieved partly by assessing early developmental potential of embryos created using nuclear material from eggs or oocytes from mothers carrying mtDNA defects and partly by deriving embryonic stem cell lines from affected embryos and comparing their differentiation spectrum with normal embryonic stem cell lines.'

- Developing treatments for serious disease or other serious medical conditions

  The reason for this as stated by the PR is:

  'The research is leading to the development of a treatment that has the potential to significantly reduce the risk of transmission of abnormal mitochondria to the embryo and subsequent child.'

  The peer reviewer agrees and has stated:

  'The group has considerable experience in nuclear transfer procedures and proposes to follow up on this to devise strategies for complementation of nuclear material from affected eggs with normal cytoplasm. This may then be developed into a therapy for production of normal offspring from females carrying defective mtDNA.'

- Developing methods for detecting the presence of gene, chromosome or mitochondrion abnormalities in embryos before implantation

  The reason for this, as stated by the PR, is:

  'The project requires the development of methods to detect mitochondria in single cells and the segregation of mitochondrial DNA within cells during the embryonic divisions. It also requires the development of methods to study gene expression and chromosome constitution in different parts of the embryo for comparative purposes as below.'

  The peer reviewer agrees and has stated:

  'Methods will be developed to enable detection of mitochondrial DNA at a single cell level, and to map gene expression to different parts of the embryo.'

- Increasing knowledge about the development of embryos

  The reason for this, as stated by the PR, is:

  'Prior to translation of the methods being developed in this project into clinical practice is it important that comparative studies with unmanipulated embryos created in vitro show similar outcomes. The information obtained in such comparisons will increase our knowledge about the development of embryos.'

  The peer reviewer agrees and has stated:

  'The development of both normal and affected embryos will be scrutinised in this project.'

In addition to the purposes listed above for which the centre's current licence was granted, the PR has requested that their research is considered necessary or desirable for the following additional purposes;

- Increasing knowledge about the causes of any other congenital disease or congenital medical condition

  The reason for this as stated by the PR is:
  'We are investigating the origin of oocyte aneuploidy.'

  The peer reviewer agrees and has stated:
  'The applicants propose to study aneuploidy in oocytes and investigate the causes.'

- Promoting advances in the treatment of infertility

  The reason for this as stated by the PR is:
  'The procedures of vitrification are being optimised in this research and this will also relate to vitrification for fertility treatment.'

  The peer reviewer agrees and has stated:
  'The methods for cryopreserving oocytes and embryos at various stages have been compared to establish the optimal protocol for embryo survival. In particular, the most beneficial culture and freezing regime for embryos at the blastocyst stage has already improved pregnancy rates and allowed the clinic to adopt single embryo transfer as a routine procedure.'

- Increasing knowledge about the causes of miscarriage

  The reason for this as stated by the PR is:
  'Our studies of oocyte aneuploidy are relevant to understanding the causes of miscarriage.'

  The peer reviewer agrees and has stated:
  'Miscarriage may be attributable to defects of the oocyte such as aneuploidy.'

Prohibited research activities:
The activities to be licensed are not prohibited by the HF&E Act 1990 (as amended) including those activities specifically prohibited by Sections 3, 3ZA, 4 or 4A, or by Schedule 2, paragraph 3 of the Act.

Use of embryos:
The use of human embryos is considered necessary. This is based on the application and comments by the peer reviewer:

> *'The high incidence of aneuploidy in a proportion of cells in the developing embryo is more or less specific to human embryos, so using as murine model would be inappropriate. In order to generate hESC lines or to translate the research to clinical applications the experiments must be conducted in human embryos.'*

PR considerations:
The PR is suitable and has discharged her duty under Section 17 of the HF&E Act 1990 (as amended).

Premises:
The premises are considered suitable. This is based on information submitted with this application, and the previous inspection visit.

Recommendation:
The Licence Committee is asked to note that at the time of the desk based assessment no recommendations were made.

The inspection team considers that there is sufficient information and evidence available to recommend the renewal of the centre's licence for a period of three years without additional conditions.

The inspection team recommends that the licence issued should include the following activities that the centre has applied for:

- Storage of embryos
- Creation of embryos in vitro
- Keeping embryos
- Using embryos

For the following purposes:

- Increasing knowledge about serious disease or other serious medical conditions
- Developing treatments for serious disease or other serious medical conditions
- Developing methods for detecting the presence of gene, chromosome or mitochondrion abnormalities in embryos before implantation
- Increasing knowledge about the development of embryos,

and for the following additional purposes;

- Increasing knowledge about the causes of any other congenital disease or congenital medical condition
- Promoting advances in the treatment of infertility
- Increasing knowledge about the causes of miscarriage

The inspection team further recommends that the research project title identified on the licence is amended from 'Pluripotency reprogramming and mitochondrial biology during early human development', to 'Towards improving assisted reproductive technologies for the treatment of infertility and prevention of disease'.

Section 2: Summary of the research project

This section summarises information submitted in the research licence application.

Lay summary of the research project:

The focus of our research is to extend the scope of assisted reproductive technologies (ART) to prevent transmission of mitochondrial DNA (mtDNA) disease and to improve outcomes of ART for the treatment of infertility. During the next three years, we propose to pursue the following aims.

(1) Develop new clinical treatments to minimise transmission of mtDNA mutations from a mother to her child. This part of the research programme will build on previous work in which we demonstrated that it is technically feasible to transfer nuclear genetic material, contained in pronuclei, between fertilised human eggs. We propose to further optimise and test the safety of pronuclear transfer between fertilised eggs. We will also test the efficacy of an alternative procedure known as meiosis II spindle transfer in which the nuclear genome is transferred between unfertilised eggs.

(2) Improve the outcome of infertility treatments through gaining a better understanding of the cellular and molecular events occurring during pre-implantation development in vitro, and to determine how these are affected by the routine laboratory procedures.

(3) Investigate the pathways leading to chromosomal abnormalities in eggs and embryos. We hope that these investigations will help us to better understand the mechanisms underlying chromosomal abnormalities in eggs of older women.

Objectives of the research:

Objective1. To develop new clinical treatments to minimise transmission of mtDNA mutations. Mutations in mtDNA can cause a range of fatal and debilitating diseases. Reports from our lab (Craven et al, 2010, Nature: 465) and others (Tachibana et al, 2013, Nature:493) indicate that inheritance of mtDNA can be uncoupled from inheritance of nuclear DNA by transplanting the nuclear genome between eggs. This can be done either before fertilisation by transplanting the meiosis II spindle (MST) and its associated chromosomes, or after fertilisation by transplanting the pronuclei (PNT) between fertilised eggs. The latter approach has been the major focus of our research to date. Our ongoing work aims to optimise PNT procedure and to test the efficacy of MST. Our primary objective is to maximise the production of good quality blastocysts and to perform a range of studies, including chromosomal analysis and gene expression studies, to compare PNT blastocysts with unmanipulated controls. We will also test the effect of PNT/MST on cell cycle and reprogramming events during the earliest stages of development. In accordance with the recommendations of the HFEA Expert Panel, we will generate ESC lines to compare those derived PNT/MST blastocysts with controls. These lines will also be used to investigate the fate of karyoplast-associated mtDNA. While our proof of concept work on PNT was conducted using abnormally fertilised eggs, these have a limited potential for onward development, and are therefore of limited value in our endeavours to
further optimise and test the safety of PNT. Thus, progress towards clinical treatments requires a supply of oocytes donated and fertilised specifically for this research project. Where possible, we will use mouse zygotes to develop and perform initial tests of experimental techniques. However, there are species differences and any meaningful tests of safety and efficacy require the use of human oocytes and zygotes.

Objective 2. To improve the outcome of infertility treatments through gaining a better understanding of the cellular and molecular events occurring during pre-implantation development in vitro, and to determine how these are affected by the routine laboratory procedures of assisted reproductive technologies. Recent advances in our understanding of how key developmental events are regulated during the pre-implantation period make it possible to perform more in depth analysis of embryo quality than was previously possible. We believe that the application of these advances to assess the effect of laboratory interventions will contribute to improved treatment outcomes. A primary focus of this part of our research is to optimise blastocyst vitrification with a view to maximising the efficiency of our blastocyst transfer programme. Our work to date indicates that the vitrification/warming procedures induce loss of cell viability in blastocysts but not in cleavage stage embryos. We therefore propose to test a number of modifications to blastocyst vitrification procedures. We also propose to further optimise the techniques of oocyte vitrification. While our results on oocyte survival are encouraging, the development of blastocysts from vitrified oocytes is variable between patients. It is not clear whether this is a consequence of biological or technical factors. We therefore propose to extend our studies on oocyte vitrification. This work will strengthen the evidence base for our own fertility preservation programme and will be valuable to the wider research and clinical community. Reliable methods for oocyte vitrification are also key to the success of the work outlined in Objective 1. The oocyte vitrification studies will require donation and fertilisation of oocytes specifically for research purposes. There is no realistic alternative to performing these experiments on human oocytes. To maximise the use of donated oocytes, we will design experiments in which oocytes included in this study can be used as controls for work outlined in Objective1.

Objective 3. Investigation of molecular and genetic events leading to formation of normal oocytes and embryos. This part of our research is focussed on understanding the mechanisms underlying meiotic chromosome segregation errors. Using mouse oocytes we have shown that female ageing is accompanied by depletion of the chromosome-associated protein complex known as cohesin (Lister et al, Current Biology, 2010). Cohesin is a conserved protein complex, which clamps sister chromatids together from the time of DNA replication until they segregate to daughter cells during cell division. Cohesin is required to maintain the unique chromosome structure required for normal segregation during the meiotic divisions. In this project, we will test the clinical significance of these findings by comparing cohesin levels between oocytes from young and older women. A greater understanding of the mechanistic basis underlying the association between female age and oocyte aneuploidy will provide insights into the possibility of developing intervention strategies to improve reproductive outcomes in older women. For these experiments we require immature oocytes (GV stage and MI oocytes) from consenting women undergoing ICSI treatment. These will be vitrified and stockpiled to facilitate the design of controlled experiments in which to perform direct comparison of levels of chromosome-associated cohesin in oocytes obtained from young and older women.

Summary of the research undertaken to date:

The activities carried out under the previous licence fell into three central aims. Progress made towards each of these is outlined below.

1. Development of techniques to prevent transmission of mitochondrial DNA disease.

Mitochondria provide energy required for our cells to function properly. They contain their own DNA, which we inherit exclusively from our mothers. Mutations in mitochondrial DNA (mtDNA) can cause a range of fatal and debilitating diseases for which there are currently no curative treatments. We established that transplantation of pronuclei between fertilised eggs is technically feasible and could therefore be used to minimise transmission of mtDNA mutations from a mother to her child. Our initial experiments were performed using abnormally fertilised human eggs. However, further development and validation of the technique required a supply of normally fertilised eggs. These are obtained from altruistic donors and from women undergoing IVF treatment who opt to share their eggs in return for a reduction in the cost of treatment, or, in the case of NHS patients, an extra treatment cycle, if required. This research is ongoing. In addition to our work on the development of new techniques to prevent transmission of mtDNA mutations, we have also established a pre-implantation genetic diagnosis (PGD) programme to screen embryos for mtDNA mutations. PGD involves genetic testing of one or two cells biopsied from a 7-8 cell embryo. Only embryos with relatively low mutation loads are selected for use in treatment. Those with higher mutation loads are used to determine whether the tested cells are representative of the entire embryo.

2. Improving outcomes in infertility treatment.

The aim of this part of our research is to minimise damage to embryos during routine laboratory procedures. We have optimised cryopreservation procedures at various stages of development. Findings have already been translated to clinical treatment resulting in improved outcomes for our patients.

3. Embryonic stem cell derivation.

We performed somatic cell nuclear transfer (SCNT) using human oocytes and determined that embryos generated by SCNT contain very low levels of mtDNA from the somatic cell. This is relevant to the development of cellular therapies for people suffering from mtDNA disease. We also generated a number of embryonic stem cell (ESC) lines from fertilised embryos, including one that were produced in compliance with the current standards for clinical grade ESC lines. The research grade lines have been banked at the UKSCB and the clinical grade line is currently undergoing a due diligence process in preparation for banking with the UKSCB. Over the three year period of the licence, a total of 1065 oocytes were used, of which 619 were donated specifically for research. The remainder failed to fertilise and were therefore not suitable for used in IVF/ICSI treatment. The embryos used during the corresponding period (total 2534) were either not required or were not suitable for transfer or cryopreservation in IVF /ICSI treatment.

Donation and use of embryos:

The PR reports that 131 fresh and 101 frozen embryos were donated to the research project, and 109 embryos were created during 2013.

The peer reviewer agrees that the number of embryos already used is justified stating;

> *'The applicants have made considerable progress in their previous research, as demonstrated by the published output.'*

The PR estimates that 600 fresh embryos and 90 frozen embryos will be required, and 750 embryos will be created over the duration of the licence applied for.

The peer reviewer agrees that usage of the proposed number of embryos is justified commenting;

> *'In order for the findings to be statistically relevant sufficient numbers of embryos must be used for each experiment.'*

Section 3: Details of the assessment findings

Principle:

5. Provide prospective and current patients and donors with sufficient, accessible and up-to-date information in order to allow them to make informed decisions.

6. Ensure that patients and donors have provided all relevant consents, before any licensed activity is undertaken.

What we asessesed against:

Information, counselling and consent; CoP Guidance Note 22, RLCs R18, R19, R20, R22.

What the centre does well.

Provision of information and counselling to those consenting to donate to research

A full suite of patient information and consent forms were submitted with this licence application. An audit of these, and review of the centre's self-assessment questionnaire provides assurance that;

- prior to giving consent, those donating to research are given a suitable opportunity to receive proper counselling about the implications of their donation (RLC R18).
- necessary information is provided to patients prior to giving their consent (RLCs R19 and R20).
- a designated individual, who is not directly involved in the patient's treatment, is available to discuss with the patient the project of research and the possibility of donating material to the project (RLC R22). Contact details for this designated individual are provided in the patient information.

Information leaflets and consent forms have been amended to reflect the proposed change in title of the research project.

What they could do better.

Nothing noted.

Principle:

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

What we assessed against:

Premises and facilities; RLC R10

What the centre does well.

Premises and facilities

The premises are suitable for carrying out the licensed activities (RLC R10). This conclusion is based on the centre's SAQ and the last research inspection visit in 2013, and the most recent treatment and storage licence renewal in February 2014 during which the premises were visited.

What they could do better.
Nothing noted.

Principle:
10. Maintain proper and accurate records and information about all licensed activities

What we inspected against:
Information and record keeping; RLC R14, General Direction 0002.

What the centre does well.
Since the last renewal inspection, the centre has submitted the annual Research Information and Data Sheet to the HFEA within the required timeframe (RLC R14 & General Direction 0002).

What they could do better.
Nothing was noted during this assessment.

Principle:
12. 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.

What we assessed against:
HF&E Act 1990 (as amended), Schedule 2 (3(5) and 3A).

What the centre does well.
The research project has been approved by the National Research Ethics Service (NRES) Committee North East - Newcastle & North Tyneside 1. Evidence was provided by the PR that this approval remains active and covers the research activity described in the licence application. The PR has provided assurance that the research ethics committee will be informed of the project title change once approval has been given by HFEA.

The research project does not include any activities that have been prohibited by the HF&E Act 1990 (as amended).

A peer review was obtained for this renewal application and it is supportive of the licence renewal. Justifications that the activities to be licensed are necessary or desirable to meet the statutory purposes, have been provided by the PR and the peer reviewer, as discussed in detail in the 'Summary for Licensing Decision'. The PR and peer reviewer have also provided reasons why the use of human embryos is necessary and the proposed number of embryos to be used is justified. Overall, the peer reviewer has agreed that it would be appropriate to carry out the proposed research.

What they could do better.
Nothing noted.

Principle:

13. Conduct all licensed activities with regard for the regulatory framework governing treatment and research involving gametes or embryos within the UK, including:

- maintaining up-to-date awareness and understanding of legal obligations;
- responding promptly to requests for information and documents;
- co-operating fully with inspections and investigations by the HFEA or other agencies responsible for law enforcement or regulation of healthcare.

What we inspected against:

Licensing; RLCs R1, R3. The Person Responsible; HF&E Act 1990 (as amended) Section 16 & 17, RLC R8.

What the centre does well.

Licensing

A review of the centre's floor plan and SAQ confirm that all licensed research activities are performed at the licensed premises under supervision of the PR (RLC R1). The PR provided all information requested in support of this inspection (RLC R3).

The Person Responsible

The PR has a key role to play in implementing the requirements of the HF&E Act 1990 (as amended) and is the person under whose supervision the licensed activities are authorised. The PR has the primary legal responsibility under Section 17 of the HF&E Act 1990 (as amended) to secure:

- that suitable practices are used in undertaking the licensed activities;
- that other persons working under the licence are suitable and;
- that the conditions of the licence are complied with.

The PR is suitable and has discharged her duty under Section 17 of the HF&E Act 1990 (as amended) and RLC 8. This conclusion is based on the centre's SAQ, evidence from the last inspection visit in February 2013, and on-going monitoring by the inspectorate that indicates that there are no outstanding non-compliances associated with the research project.

The PR has suitable qualifications and experience for the activity authorised by the licence (HF&E Act 1990 (as amended), Section 16 (2)(ca)). The PR has successfully completed the HFEA PR Entry Programme (PREP number R/1012/7).

What they could do better.

Nothing noted.

Section 4: Monitoring of the centre's performance

No recommendations for improvement were made following an interim inspection in 2013.

Section 5: 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 areas 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
No critical non-compliances were noted during this assessment.			

Major areas 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
No major non-compliances were noted during this assessment.			

‘Other’ areas of practice that requires improvement

Other areas of practice that require 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	PR Response	Executive Review
No other areas of practice that requires improvement were noted during this assessment.			

Additional information from the Person Responsible
None received.