Executive Licensing Panel Minutes

Centre 0102 (Guys Hospital)

Renewal Inspection Report – Research Project R0075

Date:	29 June 2021	
Venue:	HFEA Teleconference Meeting	
Attendees:	Richard Sydee (Chair) Yvonne Akinmodun Kathleen Sarsfield-Watson	Director of Finance and Resources Head of Human Resources Communications Manager
Executive:	Bernice Ash	Secretary
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.

The following papers were considered by the panel:

Papers enclosed:

- Research Renewal Desk-Based Assessment Report
- Application form
- Redacted peer review form
- Patient Information
- Consent form
- Publications submitted with application:
  - Cimadomo et al 2019
  - Noli et al 2019
- Previous licensing minutes:
  - 2020-04-07 Executive Licensing Panel Minutes, Interim Inspection Report
  - 2018-07-12 Licensing Committee Minutes, Renewal Inspection Report

1. Background

1.1. The panel noted that Guys Hospital is a treatment and research centre. Two research projects were licensed at this centre until recently; the licence for project R0133 was voluntarily revoked on 22 September 2020.

1.2. The panel noted that the research project entitled 'Improving methods for preimplantation genetic diagnosis of inherited genetic disease and predicting embryo quality', project R0075, was first licensed in 1994.

1.3. The panel noted that the centre's current licence was granted by the Licence Committee (LC) in 2018 and is due to expire on 31 August 2021.

1.4. The panel noted that In March 2020, the World Health Organisation declared a world-wide pandemic of Coronavirus (Covid-19). In response to UK measures to contain and mitigate the spread of the virus, new inspection methodologies were developed and implemented. These methods enable compliance to be reviewed through desk based assessment (DBA) and the use of virtual technology where available and appropriate. A risk based approach (RBA) can then be applied, balancing the risks of on-site inspection during the Covid-19 pandemic against those resulting from potential non-compliances, identified during DBA, if not adequately investigated.

1.5. The panel noted that HFEA licensed premises must be inspected on site every two years in accordance with Schedule 3B paragraph (4)(1) of the Human Fertilisation and Embryology (HF&E) Act 1990 (as amended). Whilst the current restrictions of the pandemic do not prohibit on-site inspection, the risks of doing so must be balanced against the need for the Authority to fulfil its legal duties.

1.6. The panel noted that an interim inspection was conducted, for research project R0075, in February 2020, and therefore the renewal inspection was conducted by DBA only, on 19 May 2021. The report covers the performance of the centre since the last inspection, findings from the desk-based evaluation, and communications received from the centre.

1.7. The panel noted that the research project does not involve the derivation of human embryonic stem cell lines for human application. Research licence conditions R41-89 are therefore not applicable to this research project.

2. Consideration of Application

2.1. The panel noted that the application was submitted, by the Person Responsible (PR), to renew the research licence for project R0075, for a period of three years.

2.2. The panel noted that the centre has applied for the following activities:

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

2.3. The panel noted that the PR has also indicated that the project currently, and in future, involves 'Fixing of embryos or eggs for research' and 'Genetic testing of cells removed from embryos'.

2.4. The panel noted that the activities licensed had previously been for the following 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 development of embryos

2.5. The panel noted that the PR did not include the following purpose in the renewal application form, though it is included on the current licence:

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

2.6. The panel noted the peer reviewer's statement that 'The purposes of the project are to learn more about genetic and mitochondrial defects during early human development, to assess and improve the current procedures used for collecting the biopsies required for such assays and to determine how well biopsies taken from the trophectoderm reflect the genetic constitution of the rest of the embryo. This ambition is likely to contribute to developing methods for detecting various abnormalities in preimplantation embryos, although the applicants have not included it in their list. Research into processes of human embryonic development is also underway to enhance knowledge and improve culture regimes for IVF embryos.'

2.7. The panel noted that the executive considered that 'Developing methods for detecting the presence of gene, chromosome or mitochondrion abnormalities in embryos before implantation' should remain on this research licence. This is based on the peer reviewer's comment and confirmation from the PR that he accepts this comment and agrees that this defined purpose should remain on this research licence.

2.8. The panel noted that the PR no longer wishes the following purpose to appear on the renewal licence and the peer reviewer does not suggest otherwise:

- Increasing knowledge about serious disease or other serious medical conditions

2.9. The panel noted that, at the time of the centre's virtual renewal inspection for project R0075, no areas of practice were identified for improvement.

2.10. The panel noted that the peer reviewer was supportive of project R0075.

2.11. The panel noted that the inspectorate recommends the renewal of the licence for project R0075 for a period of three years, without additional conditions.

3. Decision

3.1. The panel had regard to its decision tree. It was satisfied that the appropriate application and fee had been submitted and that the application contained the supporting information required by General Directions 0008.

3.2. The panel noted that the premises to be licensed are suitable for the conduct of licensed activity.

3.3. The panel was satisfied that the qualifications and character of the PR are such as is required for the supervision of licensed activities and the PR will discharge his duty under section 17 of the HFE Act 1990 (as amended).

3.4. The panel was satisfied that the research project has been approved by the St Thomas's Hospital Ethics Committee. Evidence was provided by the PR that this approval remains active and covers the research activity described in the licence application.

3.5. The panel was satisfied that the research licence would not apply to more than one research project.

3.6. The panel was satisfied with the suitability of the activities applied for:

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

3.7. The panel was satisfied that the activities to be licensed are necessary or desirable for the following purposes, specified in paragraphs 3A(1) and 3A(2) of Schedule 2 of the HF&E Act 1990 (as amended):

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

Prohibited Research Activities

3.8. The panel was satisfied that none of the proposed activities are prohibited by the HF&E Act 1990 (as amended).

3.9. The panel was satisfied that this is a research project and that no embryos used in the project would be implanted into a woman.

3.10. The panel was satisfied that the proposed research project does not involve the mixing of sperm with the egg of an animal.

Use of Human Embryos

3.11. The panel was satisfied the use of human embryos is necessary for the purposes of the research.

3.12. The panel was satisfied that the proposed research project does not involve the derivation of human embryonic stem cell lines for human application or the genetic modification of embryos.

3.13. The panel was satisfied that no embryos would be used without obtaining proper consent for the use of embryos in research from patients.

3.14. The panel noted that the current research is approved by the St Thomas's Hospital Ethics Committee and remains active, covering the research activity applied for in the application.

3.15. The panel agreed to renew the research licence for project R0075 at Guys Hospital (centre 0102) entitled 'improving methods for preimplantation genetic diagnosis of inherited genetic disease and predicting embryo quality', with no additional conditions. The panel agreed that if no representations or any other information is received within 28 days, the final renewal licence should be issued.

3.16. The panel agreed to the following activities and purposes:

Activities:

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

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

4. Chair's signature

4.1. I confirm this is a true and accurate record of the meeting.

Signature

Name

Richard Sydee

Date

5 July 2021

Research renewal report: desk-based assessment

Purpose of this inspection report

The HFEA licenses and monitors establishments undertaking human embryo research. This is a report of an assessment, carried out to assess 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 Executive Licensing Panel (ELP) 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 the licence.

Date of assessment: 19 May 2021

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

Centre Details:

Project title	Improving methods for preimplantation genetic diagnosis of inherited genetic disease and predicting embryo quality
Centre name	Guys Hospital
Centre number	0102
Centre address	Stem Cell and Embryology Research Laboratories, Assisted Conception Unit, 11th Floor Tower Wing, Guy's Hospital, London, SE1 9RT, United Kingdom
Research project number	R0075
Person Responsible	Dusko Ilic
Licence Holder	Yacoub Khalaf
Treatment centres donating to this research project	Guy's Hospital (centre 0102)
Date licence issued	1 September 2018
Licence expiry date	31 August 2021
Additional conditions applied to this licence	None

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.

In March 2020, the World Health Organisation declared a world-wide pandemic of Coronavirus (Covid-19). In response to UK measures to contain and mitigate the spread of the virus, new inspection methodologies were developed and implemented.

These methods enable compliance to be reviewed through desk based assessment (DBA) and the use of virtual technology where available and appropriate. A risk based approach (RBA) can then be applied, balancing the risks of on-site inspection during the Covid-19 pandemic against those resulting from potential non compliances, identified during DBA, if not adequately investigated.

HFEA licensed premises must be inspected on site every two years in accordance with Schedule 3B paragraph (4)(1) of the Human Fertilisation and Embryology (HF&E) Act 1990 (as amended). Whilst the current restrictions of the pandemic do not prohibit on-site inspection, the risks of doing so must be balanced against the need for the Authority to fulfil its legal duties.

This centre was last inspected in February 2020 therefore this inspection was carried out by DBA only.

Inspector: Andrew Leonard

Date of Executive Licensing Panel: 29 June 2021

Contents

Section 1: Summary report

Brief description of the centre and its licensing history:

Centre 0102 is a treatment and research centre. Two research projects were licensed at this centre until recently, however the licence for project R0133 was voluntarily revoked on 22 September 2020. Research project R0075 – 'Improving methods for preimplantation genetic diagnosis of inherited genetic disease and predicting embryo quality' - was first licensed in 1994 and is the only research project now at this centre.

The current licence for the project is due to expire on 31 August 2021, having been renewed for three years by a Licence Committee in July 2018. There are no additional conditions on the licence. The centre was last inspected on 10 February 2020 when no non compliances were noted.

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, Research Licence Conditions (RLCs) 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.
- The application has designated an individual to act as the Person Responsible (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:

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

The PR has also indicated that the project currently, and in future, involves 'Fixing of embryos or eggs for research' and Genetic testing of cells removed from embryos'.

The proposed research project does not involve the derivation of human embryonic stem cell lines 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 activities specified above are required for the following purposes, as defined in Schedule 2 3A (1) and (2) of the HF&E Act 1990 (as amended):

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

This activity is currently on the research licence. The PR has stated: '*Work includes understanding more about serious genetic and mitochondrial diseases, and also understanding about the biopsy processes used in PGD.*'

- Promoting advances in the treatment of infertility

  This activity is currently on the research licence. The PR has stated: *'We will explore the differences in trophectoderm biopsy (e.g., site, size, time) and the material that is secreted by the embryos into the culture medium.'*

- Increasing knowledge about the development of embryos

  This activity is currently on the research licence. The PR has stated: *'By comparing the genetic constitution of inner cell masses isolated for stem cell research with trophectoderm from which it is separated, we can examine the constituency of findings between the two types of tissues, and thus establish the validity of genetic tests (PGD and PGS) made at the blastocyst stage.'*

The PR did not include the following purpose in the renewal application form, though it is included on the current licence:

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

The peer reviewer states however that: '*The purposes of the project are to learn more about genetic and mitochondrial defects during early human development, to assess and improve the current procedures used for collecting the biopsies required for such assays and to determine how well biopsies taken from the trophectoderm reflect the genetic constitution of the rest of the embryo. This ambition is likely to contribute to developing methods for detecting various abnormalities in preimplantation embryos, although the applicants have not included it in their list. Research into processes of human embryonic development is also underway to enhance knowledge and improve culture regimes for IVF embryos*.'

The executive therefore considers that 'Developing methods for detecting the presence of gene, chromosome or mitochondrion abnormalities in embryos before implantation' should remain on this research licence. This is based on the peer reviewer's comment and because the PR, in his response to this inspection report on page 18, confirms that he accepts the peer reviewer's comment and agrees that this defined purpose should remain on this research licence.

The PR no longer wishes the following purpose to appear on the licence and the peer reviewer does not suggest otherwise:

- Increasing knowledge about serious disease or other serious medical conditions

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 that state: 'It is essential to use human embryos for this research. Although there has recently been impressive progress in the generation of

artificial embryos ('blastoids') from pluripotent stem cell lines, it will never be possible, for ethical reasons, to demonstrate their equivalence to actual human embryos in the context of subsequent developmental potential. This research group is particularly interested in metabolic aspects of human development. The output from this group in terms of understanding regional differences in trophectoderm activity, detection of miRNAs released from embryos into the medium, and embryo development in terms of response to medium supplementation, for example, with thyroid hormone, is important for improvement to production of IVF embryos in the clinic. However, the knowledge gained from this project will feed into optimisation of blastoid production for modelling various aspects of human embryo development in vitro.'

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

Premises:
The premises are suitable. This is based on information submitted with this application and the previous inspection visit in February 2020.

Recommendation to ELP:
The ELP is asked to note that at the time of this DBA there are no areas of practice that require improvement.

The inspector considers that, overall, 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 inspector recommends that the licence issued should include the following activities that the centre has applied for:

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

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

Section 2: Summary of the research project

This section summarises information submitted in the research licence application and from the peer reviewer.

Lay summary of the research project:

Our work is aimed at both developing new approaches to diagnostic testing of preimplantation embryos, and increasing knowledge of the biology and genetics of early embryo development, with a view to understanding the basis of successful pregnancies and improving the chances of healthy offspring for couples undergoing preimplantation genetic diagnosis (PGD) and IVF procedures. We intend to work over the next three years, further developing this approach. Our aims will be: a) Improve the chances of healthy offspring by introducing and developing better strategies and protocols for embryo culture and testing, b) Explore new avenues in modelling early human development to understand biology and genetics of human embryos.

Objectives of the research:

We wish to continue to improve our PGD and IVF programmes by introducing and developing better strategies and protocols for embryo culture and testing. We also wish to understand more about the biology and genetics of early human embryos.

Summary of the research undertaken to date:

Our aims were: (i) improve our PGD and IVF programmes by introducing and developing better strategies and protocols for embryo culture and testing. (ii) understand more about the biology and genetics of early human embryos. We addressed these aims in following two projects:

1) Use of miRNA secreted into spent embryo culture medium as a biomarker for non-invasive embryo quality selection.

MicroRNAs (miRNAs) are a group of small non-coding RNAs that are involved in regulating a range of developmental and physiological processes. Dysregulation of miRNA levels is observed in multiple diseases. Early studies showed that by analysing the expression profile of miRNAs in the tissue sample of a diseased person, it was possible to classify the disease into a specific subtype. Recently, it has been found that most cells release miRNAs in the extracellular environment. Since miRNAs are highly stable in circulation, they have generated intense interest as clinical biomarkers. In a collaboration effort with a Centre for Reproductive Medicine GENERA from Italy, we profiled with high reproducibility miRNAs secreted from human blastocysts in culture media and explored this approach for non-invasive embryo selection (Cimadomo D, Rienzi L, Giancani A, Alviggi E, Dusi L, Canipari R, Noli L, Ilic D, Khalaf Y, Ubaldi FM, Capalbo A. Definition and validation of a custom protocol to detect miRNAs in the spent media after blastocyst culture: searching for biomarkers of implantation. Hum Reprod 2019;34(9):1746-1761. doi: 10.1093/humrep/dez119).

2) Mitochondria maturation and segregation in early development

We are investigating mitochondria maturation in preimplantation embryos. Oocyte and early embryonic mitochondria are typically spherical elements = 1 μM in diameter with few, truncated cristae surrounding a matrix of high-electron density. From this structurally ‘primitive’ state, mitochondria undergo stage-specific structural transformations during the preimplantation period in which they elongate and develop an extensive array of cristae that completely traverse a matrix of progressively lower electron density. In the human, it is

not until the early blastocyst stage that structural transformation takes place. It is thought that in early embryos initial ATP production and metabolism is through glycolysis and TCA. Only when mitochondria mature enough to get cristae, the metabolism switches to oxidative phosphorylation. Not only the morphology of mitochondria changes during development, their number also is differs depending on stage and cell type. Our results suggest that thyroid hormones affect mitochondrial function in human embryos: stimulate mitochondrial replication and energy production within mitochondria by switching metabolism from glycolytic pathway to more efficient oxidative phosphorylation. Our findings shed a light on metabolic switch in early embryo development and might explain why thyroid disorders in women have been associated with reduced fertility and adverse pregnancy outcome. Our data also suggest that supplementation of culture media with T3 may improve outcomes for women undergoing IVF (Noli L, Khorsandi SE, Pyle A, Giritharan G, Fogarty N, Capalbo A, Devito L, Jovanovic VM, Khurana P, Rosa H, Kolundzic N, Cvoro A, Niakan KK, Malik A, Foulk R, Heaton N, Ardawi MS, Chinnery PF, Ogilvie C, Khalaf Y, Ilic D. Effects of Thyroid Hormone on Mitochondria and Metabolism of Human Preimplantation Embryos. Stem Cells 2020;38(3)369-381).

Donation and use of embryos:

The renewal application proposes using 50 frozen embryos in each year of the three year term of the licence.

The peer reviewer agrees that the number of embryos to be used is justified, stating: “The number of embryos estimated is 50 per year. The research team has sufficient experience to calculate the numbers needed to fulfil the requirements, so it is very unlikely that there will be any wastage, yet experimental significance should be achieved.”

The embryo usage reports for 2019 and 2020 indicate that the project received 83 embryos in 2019 and 6 embryos in 2020 and used 35 embryos in 2019 and 55 embryos in 2020. The project had 334 embryos in store on 31 December 2020.

The peer reviewer agrees that the past use/creation of embryos has contributed to the research purposes, stating: “There are two major advances from this team contributing to knowledge in the field of early human development. Firstly, their metabolic studies demonstrated that supplementation of culture medium with thyroid hormone can enhance early human embryo development. This finding helps to explain why women with defective thyroids can experience pregnancy-associated problems. Secondly, they have published a couple of papers addressing the questions of whether regional differences in the embryo may affect the reliability of biopsies taken during PGD. This question will be further expanded during the next few years.”

Section 3: Details of the inspection findings

Principle:

3. Have respect for the special status of the embryo when conducting licensed activities.

What we inspected against:

RLCs R23, R24, R26, R27, R28, R29, CoP Guidance Note 22.

What the centre does well.

Observations during the last inspection in February 2020 provided assurance that the special status of the human embryo is respected.

- Processes, documented in standard operating procedures (SOPs), are in place to ensure that no embryo for the purposes of any research project is kept or used for any purpose other than the purposes of that research project (RLC R23). Staff training and their close supervision ensure procedures are adhered to, preventing the use of donated embryos in unlicensed activities.
- Recruitment practices ensure that no money or other benefit is given to those donating embryos to research unless authorised by directions (RLC R24).
- Each embryo used in the research project is uniquely labelled (RLC R26).
- Documented procedures have been established, implemented and complied with to ensure that clinical and research roles are separated (RLC R27).
- Procedures ensure that embryos do not develop after 14 days or the primitive streak has appeared (if earlier) (RLC R28). The culture and manipulation of each embryo is recorded in the laboratory records, which are regularly reviewed.

What they could do better.

Nothing noted.

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 inspected against:

Information, counselling and consent; CoP Guidance Note 22, RLCs R18, R19, R20, R21, R22. Consent for storage; CoP Guidance Note 22, RLCs R31, R32, R33, R34, R35, R36, R37, R38, R39.

What the centre does well.

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

Prior to giving consent, those donating to research should be provided with relevant

information and given a suitable opportunity to receive counselling about the implications of their donation. Observations during the last inspection in February 2020 and information provided by the PR as part of this inspection process, provide assurance that:

- Before 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 about the research project is provided to patients before giving their consent (RLC R19 and R20).
- Information is provided to patients by trained personnel in a manner and using terms that are easily understood (RLC R21). The competence of staff at the recruiting centres to provide information in this way, and to seek consent, has been assessed.
- 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.

Consent for storage

Stored embryos are obtained only from centres to which a HFEA licence or third party agreement applies (RLC R32 and R33).

No embryos are kept in storage for longer than the statutory storage period (RLC R36, R38 and R39), or the period specified in the gamete provider's consent if less than the statutory storage period.

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 inspected against:

Premises and facilities; RLC R10.

What the centre does well.

Premises and facilities

Based on the centre's self-assessment questionnaire (SAQ) and the last inspection visit in February 2020, the inspector is assured that 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.

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

What we inspected against:
Information and record keeping; RLCs R13, R14, R15, R16, R17, General Direction 0002.

What the centre does well.
Based on the centre's SAQ and the last inspection visit in February 2020, the inspector is assured that proper records of embryo donation, storage and use are maintained (RLC R13 and R15) and that these records are in a form that prevents the removal of data (RLC R16).

Since the last inspection, the centre has submitted the annual research information and data sheet to the HFEA within the required timeframes (RLC R14 & General Direction 0002).

What they could do better.
Nothing noted.

Principle:
11. Report all adverse incidents (including serious adverse events and reactions) to the HFEA, investigate all complaints properly, and share lessons learned appropriately

What we inspected against:
Incidents; RLCs R40.

What the centre does well.
Processes are in place to detect, report to the HFEA and investigate adverse incidents (RLC R40).

What they could do better.
Nothing noted.

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 inspected 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 St Thomas's Hospital Ethics Committee.

Evidence was provided by the PR that this approval remains active and covers the research activity described in the licence application.

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. As is discussed in the 'Summary for Licensing Decision', 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, except for one statutory purpose (Developing methods for detecting the presence of gene, chromosome or mitochondrion abnormalities in embryos before implantation). This purpose was not included by the PR but the peer reviewer thought it was relevant to the project and should be included. The PR subsequently agreed that the purpose should be included on the research licence.

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.

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, R2, R3, R5, R6. The Person Responsible; HF&E Act 1990 (as amended) Section 16 & 17, RLCs R8, R9.

What the centre does well.

Licensing

Information obtained at the last inspection and a review of the SAQ confirm that all licensed research activities will be performed only at the licensed premises under the supervision of the PR (RLC R1).

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 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. The inspector considers that the PR has fulfilled his responsibilities under Section 17 of the HF&E Act 1990 (as amended).
What they could do better. Nothing noted.

Section 4: Monitoring of the centre's performance

Following an interim inspection in February 2020, no recommendations for improvement were made.

Section 5: Areas of practice that require the attention of the Person Responsible

This section sets out matters which the inspection team considers may constitute areas of non-compliance. These have been classified into critical, major and 'other'. Each area of non-compliance is referenced to the relevant sections of the Act, Regulations, Research 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
None.			

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
None.			

‘Other’ areas of practice that require 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
None.			

Additional information from the Person Responsible
I agree with the reviewer that 'Developing methods for detecting the presence of gene, chromosome, or mitochondrion abnormalities in embryos before implantation' should remain on this research licence.