HFEA Licence Committee Meeting

13 March 2014

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

Minutes – Item 3

Centre 0102 (Guy's Hospital) - Research Renewal Project R0133

Members of the Committee: Andy Greenfield (professional) (Chair) Bishop Lee Rayfield (lay) Debbie Barber (professional) Jane Dibblin (lay)	Legal Adviser: Rosalind Foster, Browne Jacobson Committee Secretary: Lauren Crawford Also in Attendance: Sam Hartley, Head of Governance and Licensing

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

The following papers were considered by the Committee:

- Update report on actions since the renewal inspection
- Inspection report
- Renewal application
- Publications x3
- Peer review
- Licence Committee minutes
- Interim 12 April 2013
- Change of PR 1 April 2011

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, 'Developing criteria for estimating quality of stem cells derived from human embryos' (R0162), was first licensed in 2002. The current licence is due to expire on 30 April 2014, having been last renewed for three years by a Research Licence Committee (RLC) in 2011.

Consideration

2. The Committee noted that at the time the renewal inspection took place, 17 December 2013 there was one 'other' area of non-compliance that had been identified by the Inspectorate that required improvement and that a recommendation had been made for this.

3. The Committee noted that the PR has made a commitment to fully implement the recommendation within the timescale detailed within the report.

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 proposed 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 'keeping embryos' 'storage of embryos' 'use of embryos' and 'creation of embryos'.

9. The Committee were satisfied that the activities to be licensed, with one exception, were necessary or desirable in line with the purposes of the project. The Committee did not see any evidence that the activity 'creation of embryos' was necessary or desirable, having noted that neither the Peer Review or the inspection report provided any reasoning or evidence to support this activity. The Committee also noted that in the last reported year (2012) no embryos had been created.

10. The Committee noted the recommendation from the Inspectorate to renew the centre's research licence for a period of three years without additional conditions.

Decision

11. The Committee were not satisfied that they had enough information to grant the recommended licence in respect of the creation of embryos. The Committee were however satisfied in respect of the other activities applied for and indicated that they agreed in principle to the renewal of the licence as recommended in respect of those other activities.

12. The Committee agreed to adjourn the item and asked the Executive to provide comments from the Peer Reviewer and the PR as to whether the activity of the creation of embryos is necessary or desirable for this project.

13. The Committee noted that the centre's licence is due to expire on the 30 April 2014, before the date of the next Licence Committee meeting and that the centre's licence will cease to have effect if they are not issued a Special Direction for the continuation of licensed activities at the centre.

14. The Committee agreed to issue a Special Direction for the continuation of the centres licence for a period of three months, from 1 May 2014 until 31 July 2014.

Signed: Date: 27/03/2014

Andy Greenfield (Chair)

Research Renewal Inspection Report

Purpose of this inspection report

The HFEA license and monitor establishments undertaking human embryo research. Licences for individual research projects can be granted for up to three years. This is a report of an inspection, carried out to assess whether this centre complies with essential requirements when carrying out research using human embryos. 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 the licence.

Date of inspection: 17 December 2013

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

Inspection details: The report covers the performance of the centre since the last inspection, findings from the inspection, and communications received from the centre.

Date of Licence Committee: 13 March 2014

Centre Details:

Project title	Developing criteria for estimating quality of stem cells derived from human embryos
Centre name	Guys Hospital
Centre number	0102
Research licence number	R0133-4-c
Centre address	Stem Cell and Embryology Research Laboratories Assisted Conception Unit 11th Floor Tower Wing Guy's Hospital London SE1 9RT
Person Responsible	Dr Dusko Ilic
Licence Holder	Mr Yacoub Khalaf
Treatment centres donating to this research project	Lister Fertility Clinic (0006) Sussex Downs Fertility Centre (0015) Herts and Essex Fertility Centre (0030) BMI Chelsfield Park ACU (0086) The Woking Nuffield Hospital (0144) Chelsea and Westminster Hospital (0158) Salisbury Fertility Centre (0197) South East Fertility Clinic (0208)
Date licence issued	1 May 2011
Licence expiry date	30 April 2014
Additional conditions applied to this licence	None

Contents

Section 1: Summary report

Brief description of the centre and its licensing history:

Centre 0102 is a treatment and research centre. The current research project, entitled "Developing criteria for estimating quality of stem cells derived from human embryos" (R0133), was first licensed in April 2002.
The current licence is due to expire on 30 April 2014. It was previously inspected on 16 January 2013. There are no additional conditions on the licence.
Due to cessation of funding, at present no embryos are being used to create human embryonic stem cell lines. The PR would like to renew the licence as requests from external sources for the production of lines with specific genetic mutations would still be considered by the researchers.

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 have not changed since those submitted with the previous renewal application;
- 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 proposed research project involves the derivation of human embryonic stem cell lines for human application.

Purposes for which research activities may be licensed:

The activities specified above are required by the PR for the following purposes, as defined in Schedule 2 3A (1) and (2) of the HF&E Act 1990 (as amended):

The PR considers that the activities of 'Creation of embryos in vitro', 'Keeping embryos', 'Use of embryos' and 'Storage of embryos' are required for the following purposes:

- Increasing knowledge about the causes of any congenital disease or congenital medical condition that does not fall within Schedule 2 3A (2)(a)
- Promoting advances in the treatment of infertility
- Increasing knowledge about the development of embryos

The PR considers that the research project will meet the purposes defined in Schedule 2 3A (1) and (2) to the HF&E Act 1990 (as amended) as follows:

- Increasing knowledge about the causes of any congenital disease or congenital medical condition that does not fall within Schedule 2 3A (2)(a)

  The reason for this, as stated by the PR, is: Work includes understanding more about serious genetic and mitochondrial diseases, and also understanding about the biopsy processes used in PGD.
  The peer reviewer agrees and has stated: Human embryonic stem cell lines derived from patients who transmit congenital disease to the embryo have been and will continue to be derived with the aim of developing differentiated cell models that can be used in vitro to understand disease aetiology and to test potential therapeutics.

- Promoting advances in the treatment of infertility

  The reason for this, as stated by the PR, is: Some of the genetic diseases from which we will derive stem cells from PGD embryos unsuitable for transfer involve infertility as a result specifically of the genetic condition - e.g. Robertsonian translocation in males, cystic fibrosis in males, fragile X syndrome in women.
  The peer reviewer agrees and has stated: Some of the congenital diseases studied lead to infertility.

- Increasing knowledge about the development of embryos

  The reason for this, as stated by the PR, is: 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 differences between the two types of tissues, and thus establish the validity of genetic tests (PGD and PGS) made at the blastocyst stage.
  The peer reviewer agrees and has stated: Trophoblast cell lines will be derived with the aim of understanding the processes of embryo implantation and the relative importance of the inner cell mass and the trophoblast in preimplantation genetic diagnosis.

Prohibited research activities:
The activities to be licensed are not prohibited by the HF&E Act 1990 (as amended).

Use of embryos:
The use of human embryos is necessary. The peer reviewer has confirmed that: ‘human embryonic stem cells remain an important resource in understanding disease mechanisms and can be derived only from human embryos’.

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.

Recommendation:
The Licence Committee is asked to note that at the time of the inspection recommendations were made in relation to one 'other' area of practice that required improvement.

The PR has given a commitment to fully implement this recommendation within the timescale detailed in the report:

'Other' area of practice that requires improvement:

- If work recommences the PR should establish quality indicators for all activities authorised by the licence and audit those activities against compliance with regulatory requirements, SOPs and quality indicators.

The inspection team considers that, overall, there is sufficient information and evidence available to recommend the renewal of the centre's licence for a period of here years without additional conditions, subject to the recommendation made in this report being implemented within the prescribed timescale.

The inspection team 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 that does not fall within Schedule 2 3A (2)(a)
- Promoting advances in the treatment of infertility
- Increasing knowledge about the development of embryos

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:

Stem cells are unique cell populations that are able to copy themselves exactly and also specialise into new cell types. The most powerful human stem cells can be isolated from the earliest stages of human development and they are termed human embryonic stem cells (hESC). These cells have great potential in regenerative medicine because they can be guided to form various more specialised cell types which then may be of use in treating serious debilitating diseases such as diabetes, or to repair organs following stroke or heart attacks. Another valuable use of these cells is in studying disease progression as well as in the search for new drugs for treatment of serious illnesses. Although there has been a lot of hype about stem cells, their potential is not yet fully realised. Firstly, methods to generate the cells in a reliable and safe way have to be established. Secondly, the characteristics of the cells have to be precisely defined, which has not yet been achieved - scientists have not been able to fully track and understand changes happening during manipulation of the cells. In this project, the researchers wish to define norms and standardise protocols that would assure quality and reliability of these cells. They plan to accurately analyse how the cells copy themselves and what factors make this process more successful, such as the position of each cell in a population or the addition of external supplements. This understanding will enable them to improve the methods they use to grow the cells. They will also look at the number and arrangement of the genetic material in the cells at the beginning of the culture and again several months later to see if any changes have occurred. Even minor alterations are cause for concern and may limit the use of these particular cells. Although hESC can become any other mature cell in an adult organism, they are usually inclined to go one way rather than another and it is not yet understood why. In this project the researchers will allow the cells to differentiate and study which cell types they prefer to become. Knowing the difference in preferences of hESC lines will be of great benefit to all researchers when selecting which cell line to use in experiments. The cells that already prefer to make muscle, for example, can be chosen for work on heart disease, whereas others that would rather make neural tissue can be used in treatment of spinal cord injuries. Lastly they will look for changes that are related uniquely to specific diseases and try to identify ways to prevent or reduce these changes. Detailed characteristics of any lines developed and studied will be logged with the cell line in the UK Stem Cell Bank for the benefit of all researchers and people that will use them in the future.

Objectives of the research:

1. To continue derivation of disease-specific hESC lines per request of researchers.
2. To utilise hESC-derivation technology in validation of blastocyst quality.
3. To derive trophoblast stem cell lines from trophectoderm.

Lay summary of the research undertaken:

Derivation of hESC with clinically relevant genetic mutations continues with 24 cell lines established carrying disease-specific mutations. Since 19 Sep 2013, 15 out of these 24 lines are listed on the NIH hESC Registry, which makes them eligible for NIH funded research. Due to cessation of MRC funding for hESC derivation, since 1 April 2013 the researchers employed a new strategy of only consenting patients and deriving new hESC with clinically relevant genetic mutations when a request is made. To date, no requests have been made.
In 2011, the researchers derived eight clinical grade lines using animal product-free protocols. These were the first such hESC lines in the world. Clinical grade lines are currently undergoing further characterisation and evaluation before they can be used for the development of cell-based therapy. All hESC lines, research and clinical grade, are deposited with UK Stem Cell Bank for public use.
The researchers developed a new method that provides medium resolution HLA results from a single cell in as little as nine hours post-biopsy with no need for parental tissue samples. They have validated the strategy by analysing parents, embryos and hESC lines from three families demonstrating that this technical approach is rapid, reliable and accurate.

Donation and use of embryos:

In the period from 1 January 2012 to 31 December 2012, the centre reported the use of eight fresh embryos and 20 frozen embryos. No embryos were created for use in the project. A total of 44 cell lines have been derived since the start of this research project.

Peer review comments:

The peer reviewer considers that:

- The number of embryos is appropriate for the scope of the research objectives and methods proposed, as not all embryos lead to the successful derivation of human embryonic stem cell lines.
- The derivation of human embryonic stem cell lines is justified by the generation of disease-specific lines that can be used to understand and develop treatments for congenital diseases. Adult stem cell lines are not suitable as they are not pluripotent and so cannot give rise to all the tissues which the disease might affect; nor can they recapitulate the developmental process that may be affected by congenital diseases. It is possible to use induced pluripotent stem cells (iPSC) lines derived from adult tissue to study congenital diseases, but not congenital infertility. Moreover, it is not yet clear whether hESC or iPSC are best for generating disease model cell lines
- The derivation of disease-specific hESC lines will increase knowledge of congenital diseases and potentially advance treatment of infertility; the validation of blastocyst quality and the derivation of trophectoderm cell lines will increase our knowledge of embryo development.
- It would be appropriate to carry out the proposed research.

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:

Research Licence Conditions (RLCs) R23, R24, R26, R27, R28, R29, CoP Guidance Note 22.

What the centre does well.

Observations during the inspection 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 obtained 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 (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 reviewed regularly.
- When human embryonic stem cell lines are derived, a sample of all stem cell lines is deposited in the UK Stem Cell Bank (RLC R30a).

What they could do better.

Nothing noted on this inspection.

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 inspection provided assurance that proper information and a suitable opportunity to receive counselling are provided:

- 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).
- 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 (RLCs R32 and R33).

No embryos are kept in storage for longer than the statutory storage period (RLCs R36, R38 and R39), or the period specified in a patients' consent if less than the statutory storage period. This was assessed by reviewing the centres record of stored embryos. A bring-forward system is maintained, ensuring embryos are stored only within the statutory storage period or the patients' consent.

What they could do better.

Nothing noted on this inspection.

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; RLCs R10, R47, R48, R49, R50. Equipment and materials; RLCs R51, R52, R53, R54, R55, R56, R57, R58, R59, R60. Quality Management; RLCs R61, R62, R63, R64, R65. Patient selection and screening; RLCs R66, R67. Traceability and coding; RLCs R68, R69, R70, R71. Import, export, transport/distribution and receipt; RLCs R72, R73, R74, R75, R76, R77. Third party agreements; RLCs R78, R79, R80, R81, R82,

R83, R84.

What the centre does well.

Premises and facilities
The premises and facilities are secure, clean, well maintained and were suitable for carrying out the licensed activities (RLC R10).

Equipment and materials
All of the equipment and materials used in licensed activity are designated for the purpose and are appropriately maintained in order to minimise any hazard to patients and/or staff.

Quality management
A quality management system is in place that is broadly compliant with HFEA requirements. The quality management system is used to improve the quality and effectiveness of the service provided in accordance with the conditions of the licence.

Patient selection and screening
Procedures for screening those donating to research are compliant with HTA directions/guidance (RLCs R66 and R67).

Traceability
All information is recorded that is necessary to facilitate the traceability of stem cells derived from embryos that are intended for human application, and any information relating to the quality or safety of gametes and embryos (RLCs R68 and R69).

Data necessary to ensure traceability is kept for a minimum of 30 years in an appropriate readable storage medium, and other results are kept for at least 10 years (RLCs R70 and R71).

Import, export, transport/distribution and receipt
Procedures are in place to ensure that the movement of gametes, embryos or cells is safe and secure, the risk of contamination is mitigated and the required characteristics and biological functions of the gametes, embryos or cells are preserved (RLCs R72, R73, R74 and R75).

Third party agreements
Agreements are in place which cover the :
(a) procurement, testing or processing of gametes or embryos on behalf of the licensed centre, or
(b) supply of any goods or services (including distribution services) to the licensed centre which may affect the quality or safety of gametes or embryos (RLCs R78, R79, R80 and R81).

What they could do better.

Quality indicators are not in place for all activities authorised by this licence, and audits have not been performed for all activities (RLCs R64 and R65). See recommendation 1.

Principle:

9. Ensure that all staff engaged in licensed activity are competent and recruited in sufficient numbers to guarantee safe clinical and laboratory practice.

What we inspected against:

Research Personnel: RLCs R42, R43, R44, R45, R46.

What the centre does well.

Staff are suitably qualified and competent to carry out all of the licensed activities.

What they could do better.

Nothing noted on this inspection.

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.

A review of embryo storage and usage records indicated that proper records are maintained (RLCs R13 and R15). These records are in a form that prevents the removal of data (RLC R16).

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 and General Direction 0002).

What they could do better.

Nothing noted on this inspection.

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; RLC R40, R85, R86, R87, R88, R89.

What the centre does well.

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

All adverse incidents (including serious adverse events and reactions) are reported to the HFEA (RLCs R85, R86, R87, R88 and R89). The centre investigates all of the adverse incidents that have occurred and shares the lessons learned in order to continuously improve the services it offers.

What they could do better.

Nothing noted on this inspection.

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).

What the centre does well.

The research project has been approved by the National Research Ethics Service. 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. 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.

What they could do better.

Nothing noted on this inspection.

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

Inspection of the licensed premises indicated that all licensed research activities are performed only on the premises specified on the licence and under the supervision of the PR (RLCs R1 and R2). The PR has provided, within 28 days, all information requested in support of this inspection (RLC R3).

Discussions with the PR indicated that he understands that a research licence must be varied if changes to a research project occur which lead to the use of research activities which are not listed on the existing licence (RLC R5). The PR also understands that in the event of termination of activities he must ensure that all stored embryos and all associated information related to their traceability and quality and safety are transferred to another licensed centre or centres (RLC R9).

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 academic qualifications in the field of biological sciences and has more than two years of practical experience which is directly relevant to the activities to be authorised by the licence. The PR has successfully completed the HFEA PR Entry Programme (R1184/8).

The centre does not use any third party premises.

What they could do better.

Nothing noted on this inspection.

Section 4: Monitoring of the centre's performance

Following an interim inspection in 2013, one critical area of non-compliance was identified. This related to the use of embryos for research four days outside the consented storage period.

The PR provided information and evidence that recommendations to address this non-compliance were fully implemented within the agreed timescales.

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
None noted			

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 noted			

‘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
Quality indicators are not in place for all activities authorised by this licence, and audits have not been performed for all activities (RLCs R64 and R65).	Due to cessation of funding, at present no embryos are being used to create hESC lines. If work recommences the PR should establish quality indicators for all activities authorised by the licence and audit those activities against compliance with regulatory requirements, SOPs and quality indicators. Within three months of work recommencing.	In agreement	The Executive is satisfied with this response

Additional information from the Person Responsible