Licence Committee - minutes

Thursday, 5 November 2015

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

Centre 0175 (University of Manchester) and centre 0067 (St Mary's Hospital) – application for research licence renewal, R0171

Committee members	Andy Greenfield (Chair) Anita Bharucha Kate Brian Margaret Gilmore	
Members of the Executive	Sam Hartley	Head of Governance and Licensing
Legal Adviser	Graham Miles	Blake Morgan

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:

- 8th edition of the HFEA Code of Practice
- Standard licensing and approvals pack for committee members

The following papers were considered by the committee:

- Research Inspection reports x2
- Executive summary
- Application forms x2
- Peer review
- Previous licensing minutes for the last three years
  - 10 January 2014 Interim inspection report
  - 19 November 2012 Renewal inspection report

1. Consideration of application

1.1. The committee noted that research project R0171 'Derivation of human embryonic stem cell lines from embryos including those created from clinically unused oocytes or abnormally fertilised embryos' was first licenced in 2006. The current licence is due to expire on 31 December 2015. The committee also noted that although this research project was currently conducted across three centres, only two centres would be continuing the research. The renewal was therefore for centres 0175 (University of Manchester) and 0067 (St Mary's Hospital) only.

1.2. The committee noted that at the time of inspection, which took place on 7 July 2015, there were three areas of practice requiring improvement, relating to counselling, written information for patients, and record-keeping (with the latter area of practice relating only to centre 0067).

1.3. 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 fees had been paid. The committee noted that the application was made by the Person Responsible (PR) for the research project.

1.4. 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 his duties under section 17 of the Act. The committee noted that the inspectorate was satisfied that the PR had satisfactorily completed the PR entry programme.

1.5. The committee was satisfied that the premises to be licenced are suitable for the conduct of licensed activities as stated by the inspectorate.

1.6. The committee was satisfied that the renewed research licence would not apply to more than one research project and that the activities applied for, permitted under the Act, are creation of embryos; keeping embryos; use of embryos; and storage of embryos.

1.7. The committee found that the use of human embryos is necessary as they are essential for the derivation of human embryonic stem cells (hESCs).

1.8. The committee was further 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 to the Act, for the following reasons:

- increasing knowledge about serious disease or other serious medical conditions:

  The study of human embryonic stem cells (hESCs) may yield information concerning regulation of cell fate in the embryo proper, and this may lead to greater understanding of cell-cell communication and/or intracellular signalling pathways that may be disrupted in a variety of disease states, including cancer.

- developing treatments for serious disease or other serious medical conditions:

  Through understanding the mechanisms that lead to cellular disorders, it may be possible to develop treatments to either prevent them arising, or to ameliorate their effects.

- promoting advances in the treatment of infertility:

  Using hESCs it is possible to undertake studies on a scale that may not be feasible using human embryos, and their use may yield information more quickly than would be possible using the more limited, and more heterogeneous resource provided by human embryos donated to research.

- increasing knowledge about the development of embryos:

Human embryonic stem cells (hESCs) may be used as an in vitro model systems for examining the behaviour of human embryonic cells, and thus early human development.

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

1.10. The committee was satisfied that the research project had received the necessary level of research ethics approval.

1.11. The committee noted that the recommendation from the inspectorate was that the centre's research licence be renewed for a period for three years without any additional conditions.

2. Decision

2.1. The committee noted that three major non-compliances were identified at inspection, and that the PR had committed to addressing these. In relation to the provision of counselling, although noting the PR's commitment to addressing this non-compliance, the committee encouraged the PR to ensure that counselling and the taking of consent is not seen as purely a paper exercise; the amendment of patient information sheets is a positive step to addressing this non-compliance but it must be reinforced by the staff ensuring that patients donating frozen eggs are given a suitable opportunity to receive proper counselling.

2.2. Having noted this non-compliance, the committee agreed to renew the research licence for project R0171 at centre 0067 and 0175 for a period of three years with no additional conditions.

2.3. The licensed activities are:

- creation of embryos
- keeping embryos
- use of embryos
- storage of embryos

2.4. The committee noted that the licence covering this project at centre 0033 would expire on 31 December 2015 without renewal. It noted that there is no application to renew the licence at centre 0033 and that the PR had informed the inspector that no research was being conducted at this centre and there were there any samples in storage. Accordingly, the licence at centre 0033 will expire on 31 December 2015 and will not be renewed.

3. Chair's signature

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

Signature

Name

Andy Greenfield

Date

13 November 2015

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 inspection, 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 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: 7 July 2015

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.

Inspectors: Vicki Lamb, Karen Conyers

Date of Licence Committee: 5 November 2015

Centre Details:

Project title	Derivation of human embryonic stem cell lines from embryos including those created from clinically unused oocytes or abnormally fertilised embryos.
Centre names and numbers	St Mary's Hospital (0067)
Research project number	R0171
Centre address	Regional IVF and DI Unit, The Department of Reproductive Medicine St Mary's Hospital Whitworth Park Manchester, M13 0JH
Person Responsible (PR)	Daniel Brison
Licence Holder (LH)	Cheryl Fitzgerald
Treatment centres donating to this research project	0007 Hewitt Fertility Centre 0008 Midland Fertility Services 0033 Manchester Fertility
Date licence issued	1 January 2013
Licence expiry date	31 December 2015
Additional conditions applied to this licence	None

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Section 1: Summary report

Brief description of the centre and its licensing history:

Centre 0067 is a treatment, storage and research centre. The current research project, entitled “Derivation of human embryonic stem cell lines from embryos including those created from clinically unused oocytes or abnormally fertilised embryos” (R0171), was first licensed in August 2006. The current licence has an error in the title, in that the words ‘including those’ have been omitted. The PR would like those words reinstated in the renewed licence.

The current licence is due to expire on 31 December 2015, having been renewed for three years by a Licence Committee on 19 November 2012. There are no additional conditions on the licence.

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 and patient information and consent forms
- 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 current licence includes the purpose ‘creation of embryos in vitro’. The PR wishes to retain this purpose on the renewed licence in order to create embryos through chemical activation. The peer reviewer supports this.

The research project previously involved the derivation of human embryonic stem cell lines for human application, but the derivation of human embryonic stem cell lines for human application has not been performed under this licence since the last renewal, and the PR has confirmed that the derivation of human embryonic stem cell lines for human application will not be occurring in future. Research licence conditions (RLC) R41-89 are therefore not applicable to this research project.

Purposes for which research activities may be licensed:

The research project is currently licensed for the following purposes:

- Increasing knowledge about serious disease or other serious medical conditions;
- Developing treatments for serious disease or other serious medical conditions;
- Promoting advances in the treatment of infertility;
- Increasing knowledge about the causes of miscarriage;
- Developing more effective techniques of contraception;
- Increasing knowledge about the development of embryos;

But, having considered the direction of the research, the PR now only wishes the project to be licensed for:

- Increasing knowledge about serious disease or other serious medical conditions;
- Developing treatments for serious disease or other serious medical conditions;
- Promoting advances in the treatment of infertility;
- Increasing knowledge about the development of embryos.

The PR and peer reviewer consider 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 serious disease or other serious medical conditions

  The PR has stated: The study of embryonic stem cell lines may generate information on the control of cell fate relevant to understanding cancer, and on cell-cell communication and/or intracellular signalling pathways which may be disrupted in disease states.

  The peer reviewer agrees and has stated: As stated by the proposers, the study of human embryonic stem cells (hESCs) may yield information concerning regulation of cell fate, and this may lead to greater understanding of cell-cell communication and/or intracellular signaling pathways that may be disrupted in disease states, including cancer.

- Developing treatments for serious disease or other serious medical conditions

  The PR has stated: The human embryonic stem cell lines derived will be used to provide differentiated target cell types which can be used in clinical cell replacement therapies of degenerative diseases.

  The peer reviewer agrees and has stated: Through understanding the mechanisms that lead to cellular disorders, it may be possible to develop treatments to either prevent them arising, or to ameliorate their effects.

- Promoting advances in the treatment of infertility

  The PR has stated: We use embryonic stem cell lines as a model system for understanding early human development, to conduct studies which would not be technically feasible with human embryos, and to target precisely the studies we do undertake on human embryos. So the use of ES cells both refines studies on human embryos, and reduces the numbers of embryos required for such studies. These studies address problems in embryo development which are directly relevant to fertility treatment.

The peer reviewer agrees and has stated: hESCs may be used as model systems for examining behaviour of human embryonic cells, and thus early human development, that may ultimately lead to a greater understanding of, and advances in treatments for infertility. Using hESCs, it is possible to undertake studies on a scale that may not be feasible using human embryos, and their use may yield information more quickly than would be possible using the more limited, and more heterogeneous resource provided by human embryos donated to research.

- Increasing knowledge about the development of embryos

  The PR has stated: We use embryonic stem cell lines as a model system for understanding early human development, to conduct studies which would not be technically feasible with human embryos, and to target precisely the studies we do undertake on human embryos. So the use of ES cells both refines studies on human embryos, and reduces the numbers of embryos required for such studies. These studies address directly problems in embryo development.

  The peer reviewer agrees and has stated: The study of human embryonic stem cells (hESCs) may yield information concerning regulation of cell fate, and this may lead to greater understanding of cell-cell communication and/or intracellular signaling pathways. hESCs may be used as model systems for examining behaviour of human embryonic cells, and thus early human development.

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 peer reviewer states that the use of human embryos is necessary for this research project because: The use of human embryos is essential for the development of human embryonic stem cell lines (hESCs).

The derivation of human embryonic stem cells is justified according to the peer reviewer because: The proposers have already derived 17 hESCs under the current HFEA research licence, and these have been made available as an international resource through banking with the UK Stem Cell bank, and been subjected to some degree of characterisation.

PR considerations:
The PR is suitable and has discharged their 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 the areas of practice that require improvement. The PR has agreed to comply with the following recommendations within the time-frames set out in this inspection report.

Major areas of non-compliance:

- The PR should ensure that patients donating fresh or frozen embryos are offered the opportunity to receive counselling about the implications of their donation.
- The PR should review the written patient information and ensure that it reflects the current aims of the research project.
- The PR should review the processes for keeping records of embryos donated to research and the research project to which they have been donated.

The inspection team recommends the renewal of the centre's licence for a period of three years without additional conditions, subject to the recommendations made in this report being implemented within the prescribed timescales.

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 serious disease or other serious medical conditions
- Developing treatments for serious disease or other serious medical conditions
- Promoting advances in the treatment of infertility
- Increasing knowledge about the development of embryos

Also the project title should be corrected to "Derivation of human embryonic stem cell lines from embryos including those created from clinically unused oocytes or abnormally fertilised 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:

We plan to continue our current project to derive embryonic stem cells from eggs and embryos donated by IVF patients at our participating centres. If eggs are used they can be cultured or chemically activated to form embryos, with or without cryopreservation. We remove cells from embryos at different stages of development from day 3 to day 8 after fertilisation. This prevents any further development of the embryo well before the limit of 14 days post-fertilisation. We take the cells from the embryos and encourage them to grown in special culture conditions usually on a layer of supportive feeder cells. If the cells do develop, they can form embryo stem cells, and eventually, an embryonic stem cell (hESC) line (defined as 3 million cells or more, some of which have been placed in frozen storage). These hESC lines are tested for their ability to form all cell types in the body, to make sure that they are genetically normal and remain so after being cultured in the laboratory, and to make sure that they are not contaminated in any way which would make them unsuitable to be used in the treatment of disease. We also study the gene expression profile of the cell lines and also some of the embryos, or cells taken from the embryos, in order to increase our basic understanding of cell fate in embryos and hESC cells. This work will ultimately benefit IVF treatments by increasing our understanding of human embryo development.

Objectives of the research:

In the continuation of this licence we will aim to:
1) derive new embryonic stem cell lines in line with the objectives of our current BBSRC/TSB and MRC funding, in order to develop more efficient methods to generate hESCs from embryos. This will be based on methods in development with our current funding and may include new culture media, substrates and feeder cells and non-invasive markers of embryonic pluripotent cells.
2) analyse expression of pluripotency-related genes in embryos. Although we also use induced pluripotent stem cells in our research, the derivation and use of human embryonic stem cells is essential as these continue to be the gold standard pluripotent stem cell for therapeutic use, and because these are the best model for study of early human embryo development.

Summary of the research undertaken to date:

We have made 17 different human embryonic stem cell lines to date from human embryos donated to research. The last 7 of these are considered clinical grade and would be suitable to make cell types for clinic transplantation to treat diseases, such as cartilage cell precursors to treat osteoarthritis or sports injuries to cartilage. All of our stem cell lines have now been fully characterised for pluripotency associated markers and the ability to generate cells from all three germ layers. The lines Man10-17 are also now characterised for HLA haplotype and for genetic abnormalities. All of the lines have also now been submitted for banking by the UK Stem Cell Bank. We now have two MRC grants to differentiate our hESC lines to chondrocyte progenitor cells at clinical grade for use in clinical trials of cartilage repair, and to develop methods to grow hESCs at scale required for clinical therapeutic use.

Donation and use of embryos:

In the period from 1 January 2014 to 31 December 2014, the project has used 129 frozen embryos. The PR estimates that a maximum of 100 frozen and 100 fresh embryos will be used in each year of the renewed licence.

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 (RLC) 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/human admixed 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 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.
- when human embryonic stem cell lines are derived, a sample of all stem cell lines is deposited in the UK Stem Cell Bank (RLC R30).

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, RLC R18, R19, R20, R21, R22. Consent for storage; CoP Guidance Note 22, RLC 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 and discussion during the inspection provided assurance that:

- 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 gametes and embryos are obtained only from centres to which a HFEA licence or third party agreement applies (RLC R31, R32, R33).

No gametes or embryos are kept in storage for longer than the statutory storage period (RLC R35, 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 gametes and embryos. A bring-forward system is maintained, ensuring gametes and embryos are stored only within the statutory storage period or the patients' consent.

What they could do better.

While patients donating fresh embryos are offered counselling, those donating frozen embryos to research are not given a suitable opportunity to receive proper counselling about the implications of their donation (RLC R18) (see recommendation 1).

The written patient information does not reflect that while the research is still aimed at creating human embryonic stem cells these will not now be for human application (RLC R19) (see recommendation 2).

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

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; RLC R13, R14, R15, R16, R17, General Direction 0002.

What the centre does well.

Embryo storage and usage 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.
During a review of embryo donation and storage logs at centre 0067, the inspection team found three cases where embryo fate had not been recorded in the relevant log. As a result, the use of those embryos was not clear, although their fate was eventually established. Whilst the fate of the embryos was ultimately determined, the inspection team were seriously concerned that this lack of clarity demonstrated a lack of control over the logs and potentially over the correct usage, and recording of usage, of embryos by the researchers (RLC R13) (see recommendation 3).

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.

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 NRES Committee North West- Greater Manchester East 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. 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.

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; RLC R1, R2, R3, R5, R6. The Person Responsible; HF&E Act 1990 (as amended) Section 16 & 17, RLC 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 (RLC R1, R2).

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 activity to be authorised by the licence (HF&E Act 1990 (as amended), Section 16 (2) (c)). The PR has successfully completed the HFEA PR Entry Programme (PREP number R/1020/7). The inspection team considered 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 2013, a recommendation for improvement was made in relation to one major and one 'other' area of non-compliance.

The PR provided information and evidence that the recommendation was fully implemented within the agreed timescale.

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			

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
1. While patients donating fresh embryos are offered counselling, those donating frozen embryos to research are not given a suitable opportunity to receive proper counselling about the implications of their donation (RLC R18).	The PR should ensure that patients donating fresh or frozen embryos are offered the opportunity to receive counselling about the implications of their donation. The PR should inform the inspector of the actions taken to ensure counselling is offered to this patient cohort by the time this report is considered by a Licensing Committee.	We have amended our patient information sheet to include this, as advised.	This response and additional correspondence between the PR and the inspector demonstrates that patients will now be offered counselling. No further action.
2. The written patient information does not reflect that while the research is still aimed at creating human embryonic stem cells these will not now be for human application (RLC R19).	The PR should review the written patient information and ensure that it reflects the current aims of the research project. The PR should provide the inspector with a copy of the updated patient information by 7 December 2015. In the time before the written patient information is finalised,	We have amended our patient information sheet as advised and submitted this for ethical approval. We have also been verbally advising patients of the change in research direction and will continue to do this.	The PR has confirmed that the patient information has been reviewed to reflect the current aims of the research project. In separate correspondence the PR has agreed to submit a copy of the patient information by 7 December. Until the revised patient

	the PR should ensure that patients are given verbal information that reflects the current aims of the project and confirm that this is being done by the time this report is presented to a Licence Committee.		information has ethical approval, patients are being verbally advised of the current aims of the research project. Further action required.
3. During a review of embryo donation and storage logs at centre 0067, the inspection team found three cases where embryo fate had not been recorded in the relevant log. As a result, the use of those embryos was not clear, although their fate was eventually established. Whilst the fate of the embryos was ultimately determined, the inspection team were seriously concerned that this lack of clarity demonstrated a lack of control over the logs and potentially over the correct usage, and recording of usage, of embryos by the researchers (RLC R13).	The PR should review the processes for keeping records of embryos donated to research and the research project to which they have been donated. A summary report of this review, including any corrective actions to be taken and the timescale for their implementation, should be provided to the inspector by 7 October 2015. Three months after implementation of any corrective actions the PR should audit the records of embryos donated to research since the implementation of the corrective actions. A summary report of this audit should be provided to the inspector by 7 March 2016.	We have reviewed this process immediately following the inspection and advised the inspector of our findings. In short, as PR I believe that the existing longstanding system was fully in compliance with the CoP and allowed me as PR to fulfill my legal obligation to trace the fate of all embryos donated to research. However the system relied on tracking an anonymised code number for each embryo from databases held at centres 0067 or 0175 through to the researcher's individual records. As these records are legally under the control of the PR this system was sound and allowed the necessary separation between researcher and identifying patient information. However our review meeting concluded that with our	The PR provided a summary report of the review of the logs within the required timescale, and provided a brief synopsis of that review here. An audit of the system is due by 7 March 2016. Further action required.

		expansion in research activities, the system was no longer fit for purpose and was (1) cumbersome, (2) made our routine audits more cumbersome than necessary, and (3) also made external inspection more difficult. As a result we have proposed a modified system whereby all users of research embryos will, in addition to their own individual research records, maintain an integrated electronic database held at the University of Manchester on a secure shared server. This database will be updated by each researcher as they use embryos, as a condition of continued use. This database will be regularly audited against the donation database held at centres 0067 and 0175.	

‘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
We would like to thank the inspection team for a useful and positive inspection with suggestions for improvements in practice which we are very happy to take on.