Licence Committee - minutes

Thursday, 5 November 2015

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

Centre 0021 (Hull IVF Unit) – application for research licence renewal, R0067

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 licence renewal inspection report (8 August 2015)
- Research licence renewal application form
- Anonymised peer review
- Publication submitted with the application
- Previous committee minutes:
  - RLC minutes for licence renewal, 11 September 2012
  - ELP minutes, interim inspection, 21 June 2013
- Tabled email from inspector

1. Consideration of application

1.1. The committee noted that research project R0067 'Biochemistry of Early Human Embryos' was first licenced in 1995. The current licence is due to expire on 31 January 2016.

1.2. The committee noted that at the time of inspection, which took place on 11 August 2015, there were no areas of practice requiring improvement. It further noted that the PR had clarified in an email to the inspector that the project did not require the activity of 'creation of embryos' on its licence as they had not, nor had any intention to, create embryos as part of this research. This explains why neither the inspector nor the peer reviewer had commented on this activity.

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 keeping embryos; use of embryos; and storage of embryos.

1.7. The committee found that the use of human embryos is necessary as proposed research will build on earlier findings, specifically focused on characteristics of human embryos, and animal models cannot provide entirely reliable substitutes for such studies.

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 diseases or other serious medical conditions:

  The research proposes to investigate the physiological and metabolic responses of the preimplantation human embryo to external influences, including maternal nutrition and different culture conditions, and to evaluate the findings in relation to embryonic development and the susceptibility of offspring in later life to certain serious non-communicable diseases.

- promoting advances in the treatment of infertility:

  Examination of the relationship between specific aspects of metabolic activity of individual embryos and their ability to develop into blastocysts may yield information that has clinical application in improving the selection of embryos most likely to implant and lead to pregnancy following therapeutic in vitro fertilisation.

- increasing knowledge about the development of embryos:

  Through increased understanding of the metabolism and biochemistry of early human embryos, and of the impact of exposing them to different environmental conditions, it will be possible to improve knowledge concerning the regulation of development, and where and how it may be disrupted.

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 agreed to renew the research licence for project R0067 at centre 0021 for a period of three years with no additional conditions.

2.2. The licensed activities are:

- keeping embryos
- use of embryos
- storage of embryos

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: 11 August 2015

Purpose of inspection: Renewal of a research licence

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: Andrew Leonard

Date of Licence Committee: 5 November 2015

Centre Details:

Project title	Biochemistry of Early Human Embryos
Centre name	Hull IVF Unit
Centre number	0021
Research project number	R/0067/9/a
Centre address	Women's and Children's Hospital, Hull Royal Infirmary Anlaby Road Hull HU3 2JZ
Person Responsible (PR)	Henry Leese
Licence Holder (LH)	Roger Sturmey
Treatment centres donating to this research project	Hull IVF Unit only
Date licence issued	01/02/2013
Licence expiry date	31/01/2016
Additional conditions applied to this licence	None

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Section 1: Summary report

Brief description of the centre and its licensing history:

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

The current research licence was issued on 1 February 2013 and is due to expire on 31 January 2016. The research project was last inspected on 10 May 2013 when no non-compliances were found. There are currently 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 for the research work currently being undertaken.
- The application has designated an individual to act as the PR.
- The proposed licence applies to one project of research.
- The centre has submitted fees to the HFEA in accordance with requirements.

Research activities applied for:

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

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

The proposed research project does not involve 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):

- Increasing knowledge about serious diseases 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 project will address these purposes as follows.

- Increasing knowledge about serious diseases or other serious medical conditions

The reason for this, as stated by the PR, is:
“It is increasingly clear that the origins of major serious non-communicable diseases including cardiovascular disease, diabetes and metabolic syndrome may lie in the peri-conceptual period when the preimplantation embryo is particularly sensitive to environmentally induced perturbations. The aim of our research is to understand the mechanisms by which the physiology and metabolism of the early human embryo responds to changes in maternal nutrition, and in IVF embryos in culture, which can potentially influence the susceptibility of the offspring to disease in later life.”

The peer reviewer agrees and has stated:
“The research proposes to investigate the physiological and metabolic responses of the preimplantation human embryo to external influences, including maternal nutrition and different culture conditions, and to evaluate the findings in relation to the susceptibility of offspring in later life to certain serious non-communicable diseases”

- Promoting advances in the treatment of infertility

The reason for this, as stated by the PR, is:
“In addition to discovering how the early embryo may be susceptible to sub-optimal metabolic conditions, the study the metabolic activity of early embryos has led to the identification of a number of non-invasive markers of early embryo viability. For example, we have shown that the pattern by which an early embryo on day 2 of development consumes certain key metabolic substrates and produces others can predict the likelihood of whether that embryo will form a blastocyst, the degree of DNA damage and the likelihood of implantation. By generating further data in this regard, the confidence in such assays to generate a translatable test of embryo viability will be increased. The development of such approaches should, improve success rates of ART and reduce the need for multiple embryo transfer.”

The peer reviewer agrees and has stated:
“Examination of the relationship between specific aspects of metabolic activity of individual embryos and their ability to develop into blastocysts may yield information that has clinical application in improving the selection of embryos most likely to implant and lead to pregnancy following therapeutic *in vitro* fertilisation.”

- Increasing knowledge about the development of embryos

The reason for this, as stated by the PR, is:
“Early embryos produced in vitro as part of an ART procedure are exposed to conditions that by definition are sub-optimal, compared to their natural in vivo environment. By determining the metabolic and biochemical function of early development in vitro we can improve knowledge of how such development is regulated.”

The peer reviewer agrees and has stated:
“Through increased understanding of the metabolism and biochemistry of early human embryos, and of the impact of exposing them to different environmental conditions, it will be possible to improve knowledge about the regulation of development, and where and how it may be disrupted. Greater understanding of normal regulatory mechanisms, of the variations displayed by individual human embryos, and how these do or do not relate to viability, will lead to greater insight into when, and in response to what, these mechanisms fail.”

Prohibited research activities:
The activities to be licensed are not prohibited by the HF&E Act 1990 (as amended) and do not involve 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 by the peer reviewer who has stated: "There is considerable evidence, much of it accrued by researchers in the applicant's centre, indicating that individual human embryos vary widely in their potential to continue development, and that the nutrient requirements and metabolic profile of a given embryo may reflect that embryo's potential. The proposed research will build on earlier findings, specifically focused on characteristics of human embryos, and animal models cannot provide substitutes for such studies."

The project proposes to use in each year of the licence: 50 fresh eggs, 100 failed to fertilise embryos, 200 fresh embryos and 20 frozen embryos. Regarding the use of these numbers, the peer reviewer stated: "Judging from the number of embryos that were used to generate the data presented in the paper submitted with this application (Leary et al., 2014), the estimates of the numbers that it is proposed will be used during the period of the renewed licence are fair."

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 there are no areas of practice requiring improvement.

The inspection team recommends that the licence issued should include the following activities, which are the same as those on the current licence:

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

For the following purposes, which are also the same as on the current licence:

- Increasing knowledge about serious diseases or other serious medical conditions
- Promoting advances in the treatment of infertility
- Increasing knowledge about the development of embryos

The inspector notes that the centre's address on the current licence is inaccurate since 'Reproductive Medicine Unit' has been included on the first line. The address stated at the last renewal application in 2012 was: Hull IVF Unit, Women's and Children's Hospital, Hull Royal Infirmary, Anlaby Road, Hull, HU3 2JZ. In the present licence renewal application, the address is the same albeit Women's and Children's Hospital has been abbreviated to WCH.

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:

To identify quantitative biomarkers of oocyte and embryo quality.
To discover the influence of female Body Mass Index (BMI) on embryo metabolic health and determine ways to identify the most viable embryos for embryo transfer.

Objectives of the research:

This research will provide information essential to understand the extent to which embryo metabolism can influence onward development to the blastocyst, the success of ART procedures and, crucially, the potential impact on key developmental events that may persist beyond birth. Through many years of research we have demonstrated that, in metabolic terms, a ‘quiet embryo’ is the most viable and we continue to pursue noninvasive biomarkers of embryo potential that have translational capacity. We have now contributed new knowledge on the extent to which maternal physiology [in the form of body weight] can act to change the physiology of the embryo. Building on this, we aim to elucidate links between maternal physiological characteristics and embryo viability. Specifically, we will investigate the effect of Poly Cystic Ovarian Syndrome (PCOS) on embryo metabolism, as well as other maternal metabolic factors. Moreover, since we have demonstrated that maternal body weight induces metabolic adaptation in the early embryo, we will aim to identify strategies that may be undertaken to prevent or reverse such metabolic programming. The desired output will be sound advice, based on empirical scientific findings, that can be given to patients on the impact that their physiology on the developing embryo and how changes might be made to avoid such an impact.

Summary of the research undertaken to date:

Using a range of noninvasive methods to determine embryo metabolism, we have been able to show that embryos from overweight and obese patients show significant metabolic disruption. This data has been collected using noninvasive biochemical methods to analyse the composition of the embryo culture medium after a defined period of incubation. The depletion and/or appearance of a number of compounds are determined; these include glucose, lactate, pyruvate, and amino acids. At the conclusion of incubation, the embryos are discarded in ways that allow us to maximise the information that we can obtain from each individual embryo. Thus, embryos may be permeabilised and disaggregated to allow us to measure the amount of intracellular lipid, or may be fixed and stained with fluorescent dyes so that we can determine the allocation of cells in the blastocyst. In order to understand the importance of metabolic pathways in early development, we have added a range of biochemical agents to the culture medium to inhibit or activate a pathway of interest. This includes carnitine; an activator of fatty acid metabolism; and insulin; a hormone of importance in the regulation of glucose metabolism. This approach means that we obtain the maximum amount of information from each individual precious human embryo donated for research.

Donation and use of embryos:

The PR has reported to the HFEA that the project used 245 fresh embryos and 42 frozen embryos in 2014.

The projected use of eggs/embryos in each of the three years of the proposed licence is 50 fresh eggs, 100 failed to fertilise embryos, 200 fresh embryos and 20 frozen embryos. The PR states in the application form that this licensed material will be used as follows:

'Our experimental strategy will generate data of direct relevance to women undergoing ART and to those planning to conceive naturally. It is only by studying spare embryos arising from IVF that we can collect information on the physiology of the human preimplantation embryo. The data may also help account for the higher rates of miscarriage/cycle cancellation in this patient group. Participants: Patients will be recruited prospectively from the Hull IVF Unit. Moreover, we will seek permission to contact other clinics within the UK to consent patients retrospectively to use their frozen embryos that are stored but no longer required for treatment. We will simultaneously review data on patients available from clinical investigation of the cause of infertility and treatment. Participant BMI will be recorded at the downregulation appointment and at the commencement of treatment enabling us to estimate whether the patients can be considered weightstable as defined by the maintentance of weight over a period of three months. The groups will be matched for age and baseline differences between the groups in ovarian stimulation, gonadotrophin dosage, cause of infertility and male factor as determined by independent sample ttest.

'It is anticipated that significant differences may arise between the control and study group, since a high proportion of the OVOB patient group will be affected by Polycystic Ovary Syndrome (PCOS). A further complication is that women with a high BMI require more intense ovarian stimulation to enable successful egg recovery which may result in the collection of oocytes of poorer quality which in turn may influence the physiology of the resultant embryos. We will therefore seek to attribute any differences in outcome variables (i.e. conception, miscarriage and embryo viability) and the markers of embryo metabolism to these confounding factors using Cox proportional hazards model (an analog of multiple linear regression) to correct for these covariates.

'Noninvasive embryo assays: We will test the hypothesis that altered metabolic activity arising from increased maternal BMI may be corrected by altering the composition of the embryo culture medium. All embryos donated for research will be profiled metabolically according to our established techniques. Specifically, we will assess noninvasively: (i) Oxygen consumption, which, with lactate formation ((ii) below) is indicative of total ATP production, will be measured using a stateoftheart nanorespirometer (http://www.unisense.com/Default.aspx?ID=538). This technology is sensitive in the femtomole range and can record the oxygen consumption of donated individual embryos at all stages of development. This data will be combined with (ii) Glucose and pyruvate consumption and lactate production. These will be measured using ultramicrofluorometric assays well established in the research laboratories of Dr Roger Sturmey. With this information we are able to calculate the proportion of ATP synthesis that may be ascribed to oxidative processes and aerobic glycolysis, whether embryo metabolism differs between individual oocyte donors and how this relates to maternal body weight. In addition, it is proposed to measure: (iii) Amino acid profiles, Embryos representative of all development stages will be cultured individually in 4µl droplets of culture medium for 24h after which time they will be moved into fresh medium and their development to the blastocyst stage monitored. The spent culture droplets will be analysed for amino acids using HPLC (Houghton et al 2002). These assays are noninvasive and will therefore allow us to replace embryos in culture to study developmental endpoints. Invasive assays (iv) Endogenous triglyceride. We will assess the quantity of endogenous triglyceride (TG) in fail to fertilise oocytes, and blastocysts at the conclusion of the study period.

Endogenous energy stores play an important, neglected, role in the metabolism of the early embryos of domestic animals (Sturmey et al 2009b). Furthermore, the amount of endogenous energy stored, predominantly as TG, is fixed during oogenesis and linked to maternal diet, at least in domestic animals (Sturmey et al 2009b). We now know that embryos from women of a high BMI contain higher levels of triglyceride and we now wish to discover whether we can influence triglyceride levels by 'resetting' metabolism in the zygote. Proof of principle will be tested by using metabolic inhibitors and activators, and the amount of TG present will be determined. TG content will be measured with a highly sensitive ultramicrofluorometric method, and related to BMI and the presence of PCOS. Using LCMS we will furthermore investigate the components of lipid present in fail to fertilise oocytes and surplus embryos form overweight and obese women in an effort to discover the mechanism for the altered embryo metabolism that we have reported.

Finally, a proportion of embryos will be collected at the end of assay period to study expression profiles of key metabolic and developmental genes, to discover the extent to which metabolic reprogramming that occurs in overweight and obese patient's embryo can influence key genetic characteristics of the developing conceptus. The best embryos will obviously be transferred as part of patient treatment but we will incorporate cycle outcome of sibling embryos (which will not have been assayed) into our analysis. The odds ratio of clinical pregnancy rates and miscarriage rates (defined as early pregnancy loss prior to fetal heat <6weeks and late pregnancy loss 620 weeks) will be compared for the two groups. The information from the metabolic profiling of spare embryos – oxygen, glucose and lactate to give total ATP formation – and amino acid profiles will be correlated to the study endpoints: fertilisation; development to blastocysts; ICM:TE ratios, measured by differential staining; and also pregnancy outcomes of sibling embryos. ANOVA will be used to assess intra and inter subject variability in combination with linear regression analysis to assess the predictive accuracy of amino acid profile on blastocyst development rate. There will be no specific interventions, however throughout the course of the study we may observe a number of overweight/obese patients who fail to become pregnant in a first cycle but who, as a consequence of counselling and follow up prior to embarking on a subsequent cycle begin to normalise their body mass. Even a modest reduction of BMI could have consequences on the metabolism of the spare embryos and we will therefore test whether maternal weight loss yields embryos with a reduced metabolic profile; one conducive to more successful development.'

Peer review comments:
The peer reviewer considered that the research project should be licensed.

The peer reviewer considers that the use of human embryos will address the defined purposes as follows:

> 'Human embryos will be used in research that aims to build on the work already carried out at this centre, furthering investigation of possible links between maternal physiology and characteristics of the embryo that may be associated with embryo viability, as manifested by its ability to form a blastocyst. Earlier work on the relationship between maternal body weight and embryo development will be extended towards investigation of oocytes and embryos derived from women with PCOS. Using appropriate measures to take into consideration confounding variables, it is proposed to examine outcome measures with respect to embryo quality in terms of the patients' body weight; embryo metabolism will be assessed using techniques that are long-established in this centre, and the findings related to the characteristics of the patients from whom the originated. The publications generated by this group in this area are too many to mention, but many have been cited in the paper submitted in support of the application (Leary et al, 2014).'

The peer reviewer considers that the objectives of the project will address the defined purposes as follows:

> ‘By assessing more closely the relationship between female body weight (and PCOS) and specific alterations in metabolic (both energy and amino acid) processes in the embryos, this work will help to increase understanding of the mechanisms behind the reported differences between embryos that develop from overweight and obese women compared with those from women of normal body weight. Through greater understanding of embryo metabolism, of the differences between embryos, and how those differences may be related to embryo viability, it will be possible to develop ways of distinguishing embryos that are more likely to continue developing and to lead to a viable pregnancy from those that are less likely to, thereby increasing the precision by which embryos may be selected from a cohort for use in patients’ fertility treatment. Increasingly, it is becoming clear that certain major diseases that affect individuals in adulthood may originate during preimplantation embryogenesis or even oogenesis, so elucidation of the nature of any association between female body weight and embryo viability, and how this may be mediated, will be of great importance.’

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 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.

What they could do better.

No recommendations for improvement were made relating to this principle.

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:

- 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 (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.
- A review of research records found that the embryos reviewed had all been used within the terms of the research consent provided by the gamete providers.

Consent for storage

- Stored gametes and embryos are obtained only from centre 0021.
- The centre has effective processes for monitoring stored embryos and ensuring they remain within their consented storage period. All frozen embryos used in the research project have been used within their consented storage period (RLC R39).

What they could do better.

No recommendations for improvement were made relating to this principle.

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).

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.

What they could do better.

No recommendations for improvement were made relating to this principle.

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.

A review of records of embryo use indicated that proper records are maintained (RLC R13 and R15). 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.

No recommendations for improvement were made relating to this principle.

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.

No recommendations for improvement were made relating to this principle.

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 centre's local research ethics committee. Evidence was provided by the PR that this approval remains active.

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.

No recommendations for improvement were made relating to this principle.

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 license 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 (R/1036/7). 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.

No recommendations for improvement were made relating to this principle.

Section 4: Monitoring of the centre’s performance

Interim inspection of the research project was performed in May 2013. No non-compliance was detected so no recommendations for improvement were made.

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 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 noted		None	

Additional information from the Person Responsible
We remain grateful to our patients who donate willingly their surplus embryos to help us further our knowledge of human embryo development in vitro. This is underpinned by our HFEA licence, which we are proud to hold and we offer gratitude to our inspection team for honest, robust and clear assessment of our processes. We would furthermore like to place on record our thanks to the anonymous peer reviewer. We are pleased that we have been able to demonstrate compliance with our licence conditions, but continue to pursue best practice for research with human embryos and look forward to our continuing research, and relationship with the HFEA.