Research Licence Inspection Report

Project Title	**In vitro Development and Implantation of Normal Human Pre-embryos and Comparison with Uni- and Poly-pronucleate Pre-embryos.**
Research Licence Number	**R0026**
Person Responsible	**Daniel Brison (Centres 0033 0067)** **Sue Kimber (0175)**
Nominal Licensee	**Brian Lieberman (Centre 0033)** **Daniel Brison (Centre 0175)** **Cheryl Fitzgerald (Centre 0067)**
Inspection type Licence expiry date Date Renewal fee paid	**Interim** **31/12/2010** **N/A**
Project Title	**Derivation of human embryonic stem cell lines from embryos, including those created from clinically unused oocytes or abnormally fertilised embryos**
Research licence Number	**R0170/R0171**
Person Responsible	**Daniel Brison (Centres 0033, 0067 & 0175)**
Nominal Licensee	**Brian Lieberman (Centres 0033)** **Cheryl Fitzgerald (Centre 0067)** **Susan Kimber (Centre 0175)**
Inspection type Licence expiry date	**Interim** **31/12/2009**
Centre Number	**0067, 0033 & 0175**

Centre Name and address	**Centre 0067 NHS - treatment and research** Department of Reproductive Medicine St Mary's Hospital, Manchester M13 OJH **Centre 0033 Private – treatment and research** Manchester Fertility Services 120 Princess Road, Manchester M15 5AT **Centre 0175 University - research only** Faculty of Life Sciences, University of Manchester, Floor 2 Core Technology Facility, 46. Grafton St Manchester M13 9NT
Treatment centres donating to these research projects	Centres 0033 & 0067
Inspection date	26 September 2007
Licence Committee Date	January 2008
Inspector(s)	Wil Lenton (HFEA, Chair) Bryan Woodward (External)

About the Inspection:
The purpose of the inspection is to ensure that research is carried out in compliance with the HF&E Act 1990, Code of Practice, licence conditions and directions and that progress is made towards achieving the stated aims of the project.

The report is used to summarise the findings of the inspection highlighting areas of firm compliance and good practice, as well as areas where improvement may be required to meet regulatory standards. It is primarily written for the Licence Committee who makes the decision about the centre's licence renewal application. The report is also available to patients and the public following the Licence Committee meeting.

This report covers the period between 01/01/2006 and 30/12/2006

Brief Description of the Projects

Project ***R0026*** entitled: "In vitro Development and Implantation of Normal Human Pre-embryos and Comparison with Uni- and Poly-pronucleate Pre-embryos", has been licensed since 1991.

The lay summary of the project is as follows:

In spite of the fact that clinical in vitro fertilisation (IVF) has been used as a treatment for infertility for more than 20 years, human embryos created by IVF continue to develop poorly in the laboratory, and the success rate of IVF is low. Only one in every 5 or 10 embryos goes on to form a baby after transfer to the womb.

The aim of this research is to investigate the way normal human embryos develop in the laboratory, and compare them to embryos which develop abnormally. This will help us to improve laboratory conditions to allow normal embryo development, which will increase success rates of IVF.

We are looking particularly at genes and proteins which control cell death in embryos, and the ability of cells in the embryo to stick to one another, and make contact to the wall of the womb, in order to implant and develop.

We are also studying master genes which control other genes, particularly those which are involved in giving cells in the embryo the ability to go on to form any cell in the adult body.

Project ***R0170/0171*** entitled: "Derivation of human embryonic stem cell lines from embryos, including those created from clinically unused oocytes or abnormally fertilised embryos", has been licensed since 1994.

The lay summary of the project is as follows:

Human embryo stem (hES) cells can be made to develop into a variety of specific cell types and as such have many potential medical uses, including the treatment of degenerative diseases by the replacement of defective cells, the safety testing of new medicines and

treatments, and the study of disease. These cells can be isolated from the inner cells of early embryos produced during in vitro fertilisation treatment before they are transferred to establish a pregnancy. A variety of hES cell lines are required to understand both their biological properties and limitations. Large numbers of hES cell lines will be required for research and for their use in medical treatments, in order to provide the correct tissue match, similar to existing organ transplantation programmes.

To date hES lines have only been derived from embryos left over from IVF treatment programmes. These so-called "spare" embryos are in great demand for the couples' own treatment, for donation to other couples that do not have healthy eggs, and for research into infertility and improving IVF treatment. As a result, embryos donated for hES cell derivation are very scarce and this essential research is progressing very slowly. Although the first hES cell lines were reported in 1998, so far relatively few additional lines have been derived in the UK. To avoid many of the ethical and practical problems associated with the use of "spare" IVF embryos, we plan to use eggs (oocytes) that cannot be used for treatment, and are currently discarded, to create embryos specifically for hES cell derivation. Two groups of eggs will be used; those that are immature, and cannot be used safely for treatment, and those that have failed to fertilise after insemination. About 30-40% of all eggs (3-4 from each cycle of IVF treatment) fall into this category and are normally discarded. We plan to activate these eggs, or use sperm from a fertile donor, to "recover" these eggs to make embryos specifically for hES cell derivation. Although the success rate of these procedures may be lower than from normal embryos, we anticipate that many patients will be willing to give consent as the use of these eggs/embryos for research is preferable to then- being discarded. Information gained from these studies will then help to improve methods such as in vitro maturation, to be used in clinical IVF treatment.

		R0026	R0170/0171
Research activities	Research on human embryos	✓	✓
	Storage of licensed material	✓	✓
	Creation of embryos for research	✓	✓
	Derivation of human embryonic stem cells		✓
	Cell nuclear replacement		

Changes/ improvements since last inspection

Centre 0175
New purpose-built laboratories for Centre 0175 were inspected by the Executive on 9th May 2007 and found to be fit for purpose. No variation of the current licenses was necessary as the facilities were within the currently-licensed premises.

There have been some staff changes in the research teams of both projects.

Additional licence conditions and recommendations and actions taken by centre since last inspection

Licences R0026/R0170/0171 was issued without additional conditions:

Since the last inspection the centre now
- records the donation and use of both gametes and embryos to research projects, and
- formal records are kept of decisions made in research meetings.

As requested by the Licence Committee.

Summary for Licence Committee

R0170/0171
Progress has been achieved in relation to the stated aims the research projects.

- Two hES cell lines have been derived since the last inspection and submitted to the UK Stem Cell Bank.

R0026
Work has continued to make progress in relation to the stated aims of the project

- Two papers have been submitted to appropriate scientific journals for peer review (one being accepted for publication)

The inspection team support the continuance of research licences R0170/0171 and R0026.

Proposed licence variations

None

Report of Inspection findings

1. **Organisation**

Desired Outcome: The research is well-organised and managed and complies with the requirements of the HFE Act.

Summary of findings from inspection
Evidence of:

- Leadership and management
- Staffing
- Funding

Staff R0026*

Principal investigator	Daniel Brison and Sue Kimber
Scientists	3
Laboratory technicians	
Support staff (receptionists, record managers, quality and risk managers etc)	Staff at centres 0033 and 0067

Staff R0170/0171*

Principal investigator	Daniel Brison and Sue Kimber
Scientists	3
Laboratory technicians	
Support staff (receptionists, record managers, quality and risk managers etc)	Business manager at centre 0175 plus Staff from centres 0033 and 0067

*There is overlap between staff working on projects R0026 and R0170/0171.

Highlighted areas of firm compliance
The PRs of R0026 and R0170/0171 have extensive knowledge of the regulatory requirements of the HFEA, together with appropriate research and publishing experience. An induction programme for all new staff at centres 0033 and 0067 is currently in place which covers the regulatory requirements of the HFEA. Continuing professional development (CPD) is documented by staff. The centres' hold weekly minuted meetings which include regular updates on the research projects every 4-6 weeks. Additionaly there is a minuted meeting which takes place every two weeks for all research staff.
Issues for consideration
None
Executive recommendations for Licence Committee
None

Areas not covered in this inspection
None

2. Premises and equipment

Desired Outcome: The premises and equipment are safe, secure and suitable for their purpose.

Summary of findings from inspection:

- Suitability of premises
- Storage facilities
- Safety of equipment

Highlighted areas of firm compliance
New purpose-built laboratories for Centre 0175 were inspected by the Executive on 9th May 2007 and found to be fit for purpose. The creation and manipulation of viable embryos is carried out on licensed premises using appropriate equipment which is regularly serviced and maintained. Embryos are stored in designated secure areas with controlled access under the auspices of the licences of centres 0033, 0067 and 0175.
Issues for consideration
A research storage dewar at 0175 was not fitted with a low liquid nitrogen alarm.
Executive recommendations for Licence Committee
None
Areas not covered in this inspection
None

3. Donation of material

Desired outcome: Donors are recruited appropriately and any research carried out on their embryos is in accordance with their consent.

Summary of findings from inspection:

- Recruitment of donors
- Ensuring prospective donors have access to further guidance
- Ensuring prospective donors have time to consider donation properly
- Ensuring patient consent is not breached
- Donor and patient records

Summary
The information has not changed since the previous inspection. Thus; **Centre 0067 –** All prospective patients attend a 'waiting list' meeting where they are introduced to the concept of donating gametes and embryos to research. Patients are also given the information sheets and consent forms relating to the specific research projects undertaken in the licensed centres in Manchester. **Centre 0033 -** Patients are given the information sheets and consent for both research projects during their initial clinical consultation. Patients, from either centre 0033 or 0067, who express an interest in donating gametes and / or embryos to the stem cell project (R0170/0171) meet with either the postdoctoral scientist or the research nurse to discuss the implications of this project and to sign the consent forms. A medical consultant gives patients information and obtains consent from patients who wish to donate gametes and / or embryos to the embryo development project. The licence authorising this project of research does not have conditions that require a separation between obtaining consent to treatment and consent to research. Approximately 40% of patients consent to the donation of gametes and embryos for use in the R0171 licensed research project. The figure for R0026 is approximately 70%. If patients consent to the donation of gametes and / or embryos to be used in licensed research a coloured sticker (green for project R0026 and yellow for project R0170/0171) is placed on the treatment cycle embryo tracking form. The transfer of gametes and / or embryos from clinical use to research is witnessed by two appropriate people and this includes checking that appropriate consent is in place. Centrally held records reviewed in the course of the inspection contained necessary information to allow tracking of individual embryos. All the fresh embryos donated to research are those that are unsuitable for use in treatment and do not meet the centre's criteria for freezing. 45% of patients who receive licensed treatment at centre 0067 have embryos frozen and more than 50% of patients receiving licensed treatment at centre 0033 have embryos cryopreserved for potential future use.

The decision of whether embryos are unsuitable for use in treatment or cryopreservation is always made by a clinical embryologist not involved in research. Two of the embryologists at centre 0067 are involved, on a part time basis, in licensed research. However, they do not make decisions regarding the suitability of embryos for clinical use if they are going to be carrying out research on the embryos donated from these patients.
Issues for consideration
The centre's may want to risk assess that there are no conflicts of interest concerning personnel who coordinate the donation of material into research.
Executive recommendations for Licence Committee
None
Areas not covered in this inspection
None

4. Patient information and consents

Desired outcome: Patients are provided with appropriate information which allows them to give informed consent.

Summary of findings from inspection:

- Patient information
- Consent forms
- Patient information for projects deriving embryonic stem cells
- Consent forms for projects deriving embryonic stem cells

Highlighted areas of firm compliance
The centres have patient information and consent forms for both research projects. The information sheet and consent forms for the project that involves the derivation of human embryonic stem cell lines are based on the one developed by the national human embryonic stem cell co-ordinators group. Patient information and consents comply with all of the requirements outlined in standard licence conditions and the 7th Code of Practice (CoP7).
Summary of audit of patient records
Witnessing of the transfer of embryos to research was documented appropriately in all of the records reviewed. The transfer of embryos to research is witnessed, the operator and witness sign to confirm that the patients donating embryos have completed appropriate consents to research. Two sets of records from patients who donated embryos to either R0026 and / or R0170/0171 were reviewed during the inspection and no discrepancies found. Consent forms in all sets of records were present and consistent with the use of the material in research. Patients are made aware that they can withdraw their consents at any time.
Issues for consideration
None
Executive recommendations for Licence Committee
None
Areas not covered in by this inspection
None

5. Scientific practice R0026

Desired outcome: Research is carried out in accordance with licence conditions and makes progress towards achieving stated aims

Summary of:

- Use of material
- Progress in achieving aims and objectives
- Peer review

Use of material
From the renewal inspection report of 29/11/2006, during the period 01/02/2006 to 31/07/2006 the centre had received 17 immature oocytes, 52 failed to fertilise oocytes, 184 fresh embryos and 29 frozen embryos from centre 0067. All these eggs and embryos have been used in the project of research. No further data was submitted by the centre as an annual progress report was not due until February 2008. The centre subsequently submitted a report on eggs and embryos used from 01/08/06-31/12/06 (22 immature oocytes, 15 failed to fertilise oocytes, 32 fresh embryos and 13 frozen embryos).
Project objectives and results
The objective of this project is to investigate both normal and abnormal human embryo development in culture, and the regulation by growth factors, using the techniques of fixing embryos for protein analysis by immunocytochemistry and apoptosis analysis using TUNEL, and lysing embryos for mRNA analysis of gene expression. The centres have continued to obtain data on expression of several genes involved in embryo and ES cell pluripotency and lineage specification. This information has increased the knowledge of cell fate regulation and early embryo development in general. **New project aim:** **Ovarian tissue cryopreservation and autografting to reverse chemotherapy and radiation induced infertility in women treated for cancer** This project is an extension of the work to create embryos from oocytes for research purposes. The Ovarian tissue project will be carried in collaboration with Professor J Radford (Christie Hospital) and Dr H Picton (University of Leeds). The clinical aim is to assess the genetic safety and developmental competence of oocytes derived from cryopreserved ovarian tissue (as a means to preserve fertility for female patients undergoing cancer therapies). The scientific aims of the work are to: 1. Xenograft cryopreserved human ovarian tissue into NOD-SCID mice in order to derive mature oocytes “in vivo”. This aim falls outside the HFEA remit, the centre’s programme to graft ovarian tissue into women for fertility treatment. 2. Activate or fertilise mature oocytes to form embryos at all developmental stages up to blastocyst. This work is to be done in Manchester only at Centres 0033 and 0067. 3. Analyse the developmental competence of oocytes and embryos at all stages, by : • Assessing gene expression, using standard protocols and target genes covered by

project R0026 (Manchester only, centres 0067 and 0175)

- Assessing gene expression using loss of imprinting arrays, work to be done in Leeds under HFEA licence R0104 at HFEA Centre 0052.
- Assessing karyotype, work to be done in Leeds under licence R0104 at HFEA Centre 0052.

This work has COREC approval.

Progress update:
After discussion with the PR the following areas of progress were highlighted.

1. Microarray analysis of human embryo*:*
   - Significant progress has been made looking at gene expression in oocytes, cleaved embryos and blastocysts.

2. Genes involved in maintenance of inner cell mass pluripotency and their regulation by growth factors.
   - now in press with the journal Reproduction*.*

3. Creation of research embryos from oocytes for studies of gene expression.
   - Expression of genes involved in cell fate such as Sox2 and Oct4 at different stages of development.
   - now in preparation for submission for publication in early 2008.

4. Ovarian tissue cryopreservation and autografting to reverse chemotherapy and radiation induced infertility in women treated for cancer.
   - home office approval to xenograft human ovarian tissue into SCID mice and consent from patients (n=6 at the moment) for this research.

Lay summary of research undertaken

We have gathered extensive information on the types of genes which are switched on in early embryos, by analysing messenger RNA and proteins produced by these genes. We have focussed in the past on molecules involved in cell adhesion, cell-cell communication, and the regulation of cell death (apoptosis). More recently we have looked at genes that regulate cell fate, particularly the decision to remain pluripotent (i.e. remain capable of forming all tissues in the body) or differentiate. We are expanding these studies to look at many more genes simultaneously, using gene chip technology, as it is likely that genes work together in particular pathways to regulate embryo development. We continue to compare normal embryos to abnormal ones, to try to understand the molecular basis for the abnormalities. As part of this we are creating embryos for research purposes, for example from oocytes which did not fertilise in an IVF cycle and would normally have been discarded. We are now applying to have our licence extended to include in this work oocytes which come from ovarian tissue frozen for women who are having sterilising treatments for cancer. This study is important to understand whether ovarian tissue freezing is safe and effective as a method of fertility preservation, and to learn more about early embryo development.

Peer reviewers comments

N/A
Issues for consideration
None
Executive recommendations for Licence Committee
None
Areas not covered in this inspection
None

6. Scientific practice R0170/R0171

Desired outcome: Research is carried out in accordance with licence conditions and makes progress towards achieving stated aims

Summary of:

- Use of material
- Progress in achieving aims and objectives

Use of material (All material from 0067 except 1 failed to fertilise egg from 0033)
In the 6 month period from 01/07/2006 to 31/12/2006 centre 0067 received and used • 61 immature eggs, • 221 failed to fertilised eggs, • 9 fresh eggs and • 106 fresh embryos. A total of 146 embryos have also been created for use in this project. • 14 embryo's created through IVM of the 61 immature oocytes • 104 embryo's created from parthenogenetic activation of 177 failed to fertilise eggs • 24 embryo's created from 43 failed to fertilise eggs via ICSI with donor sperm • 4 embryo's created from 9 fresh eggs via ICSI with donor sperm
Project objectives and results
The overall objective of this project is to derive new human embryonic stem (hES) cell lines from fertilised embryos that may be suitable for therapeutic use in the future. In order to achieve this aim the centres use embryos that have been donated to the project as well as embryos created specially for research purposes which have been created by either the insemination of in vitro matured eggs or by parthenogenetic activation. In the past 6 months the centres have undertaken work to establish protocols for performing in vitro maturation on immature oocytes as well as optimising techniques for activating failed to fertilised oocytes using either parthenogenesis or insemination by intracytoplasmic sperm injection (ICSI).

In vitro maturation

61 immature oocytes (GV or MII) have been grown in one of three different culture media (one is commercially available while the other two are made in-house containing a variety of growth factors and hormones) for up to 48 hours.

- 22 eggs reached the MII stage i.e. a polar body was observed.
- 19 MII eggs then underwent parthenogenetic activation.
- 14 embryos have been created
- 1 developed to the blastocyst stage

No of immature eggs (GV or MI)	No of eggs cultured in IVM media	No of eggs reaching MII	No of embryos created (showing 2PN or cleavage)	No of blastocysts created
61	50	22	14	1

The majority of embryo's created arrested during early cleavage stages, with the commercially available media giving the best maturation rates over 48 hours.

Parthenogenetic activation

During the past 6 months the centres have parthenogenetically activated 177 eggs, of which 104 developed into embryos (i.e. where 1 or more pronuclei have been observed), with an activation rate of 59%.

No of eggs undergoing activation	No of embryos created (1 or more pronuclei)	No of blastocysts created
177	104	2*

*not all embryos were left in culture to develop to blastocyst, some were taken at earlier stages for gene expression analysis.

In the reporting period, 2 blastocysts have been created from parthenogenetically activated oocytes that were suitable for hES cell derivation. These were shipped to the derivation laboratory of Dr Paul DeSousa at the Roslin Institute, Edinburgh under HFEA R0136-2b. Transfer of blastocyst stage embryos to RI began in August 2006, culminating in one new hESC line to date, with other embryos developing to the outgrowth stage at present.

The remaining embryos, including those that failed to reach the blastocyst stage were analysed for various markers to investigate normalcy of these embryos, as one of the core objectives of our licence and current MRC project funding. We have shown that these embryos express Oct-4, Nanog and Sox-2, markers of pluripotency in human embryos and studies are ongoing to compare them to "normal" embryos obtained as surplusfrom IVF

Fertilisation by ICSI

The centre has created 24 embryos by injecting 43 failed to fertilise oocytes with donor sperm. One of these embryos reached the blastocyst stage and was shipped to Edinburgh for stem cell derivation. This embryo did not result in the generation of a stem cell line.

Due to the non-availability of partner sperm on the day of egg collection, a further 9 fresh mature eggs were donated to research and injected with donor sperm. 4 embryos (showing 2PN after injection) were created from these oocytes but no blastocysts were generated.

Abnormally fertilised surplus embryos *(*Abnormalities included embryos showing 1, 3 or more PN as well as those showing too fast or too slow developmental progression.)

20 abnormally fertilised embryos were donated to the research programme.
1 blastocyst was obtained from this group and transported to the Roslin Institute for stem cell derivation. No line was derived from this embryo

Normally fertilised surplus embryos (not of sufficient quality for patient treatment - fresh replacement or freezing)

106 normally fertilised embryos were donated.

No of Surplus embryos donated	No of embryos taken for gene expression analysis	No of embryos arrested at early cleavage stages	No of morulae created	No of blastocysts created
106	47*	48	3	8**

*Embryos were lysed for cDNA studies, or fixed for protein analysis
**8 blastocysts were used for derivation of embryonic stem cell lines in Centrea 00067 and 0175, with one line currently established, MAN-1, and another line currently at an early stage of development (as of February 2007)

Lysis of embryos for gene expression analysis

A total of 25 embryos of different stages were lysed and subjected to PolyA PCR amplification of cDNA. Initial analysis has shown the housekeeping gene ß-actin to be expressed in 22 of these embryos. The cDNA pools of these embryos are now being screened for a panel of markers of embryo development (Oct-4/Sox-2/Nanog/Cdx-2 etc) and compared to a panel of control cDNAs prepared from “normal” embryos which are in storage. Again, significant progress has been made but the data available are too preliminary to report at the moment.

Lay summary of research undertaken
Immature eggs and eggs which have failed to fertilise are not suitable for clinical IVF treatment and are normally discarded. In this project, these eggs have been used to establish and optimise methods for the recovery of clinically unusable oocytes by in vitro maturation and/or parthenogenic activation or fertilisation, in order to generate viable embryos for human embryonic stem cell derivation. We are also using embryos surplus to IVF treatment for this purpose, similar to most other stem cell centres in the UK. Our results have shown that maturation of immature eggs can be achieved in the laboratory using culture fluid supplemented with various factors which encourage growth. We are studying the expression of various gene patterns in eggs matured in the laboratory and comparing them to normal healthy eggs. At the moment, eggs matured in this way cannot be used for clinical treatment as not enough is known about the normalcy of these eggs but results from this project will increase this knowledge leading to the use of immature eggs for IVF treatment in the future. Parthenogenetic activation involves an egg being artificially stimulated by chemicals in order to trigger embryo development. Alternatively, eggs which have failed to fertilise may be re-inseminated using donor sperm. Eggs which have failed to fertilise after standard IVF treatment are being treated by both of these methods in the laboratory. Eggs which successfully fertilise after such treatment are cultured in the incubator for up to 7 days and carefully monitored. The normality of such embryos is established by analysing DNA prepared from the embryos for expression of genes which may act as markers of normal development. The eventual aim of the project is to derive human embryonic stem cell lines from embryos generated using these methods. Any such stem cell lines will be derived in a purpose built facility and will undergo a variety of tests to establish the normality of the cell lines before they will be submitted to the UK Stem Cell Bank.
Issues for consideration
None
Executive recommendations for Licence Committee
None
Areas not covered in this inspection
None

Report compiled by:

Name……Wil Lenton…….

Designation……Inspector…….

Date……29/11/2007……

Appendix A: Centre Staff interviewed

Daniel Brison, Person Responsible R0026 (Centres 0033 and 0067) R0170/0171 (Centres 0033, 0067 and 0175
Sue Kimber, Person Responsible R0026 (Centre 0175) and Nominal Licensee R0170/071 (Centre 0175)

Two other members of the team took part in meetings with the inspection team.

Appendix B: Licence history for previous 3 years

R0026

Status	Licence	Type	Active From	Expires
Active (0175)	R0026/11/a	Research Project	01/02/2007	31/01/2010
Active (0033)	R0026/12/a	Research Project	01/02/2007	31/01/2010
Active (0067)	R0026/13/a	Research Project	01/02/2007	31/01/2010

R0026/12/a was issued with one condition:

- The creation of embryos explicitly for use in research must not be undertaken until the following have been submitted for consideration by a Licence committee of the Authority:

  (i) local ethics committee approval,

  (ii) further discussion as to why the creation of embryos specially for research is necessary or desirable for the proposed research project,

  (iii) amended patient information and consent forms for potential egg donors

  (iv) evidence of appropriate consent for the use of donor sperm for this purpose.

  (v) evidence of the availability of appropriate counselling for donors

R0026/11/a was issued with one condition:

- If the inner cell mass or any cells derived from it are removed from the intact embryo, they must be fixed or lysed immediately

R0170/0171

Status	Licence	Type	Active From	Expires
Active	R0170/1/b R0171/1/b	Research Project	01/06/2006	31/12/2009
Replaced by new version	R0170/1/a R0171/1/a	Research Project	01/01/2006	31/12/2009
Expired	R0156/2/a	Research Project	27/10/2004	31/10/2005

R0156 was replaced by R0170/0171 for administrative purposes.

R0170/0171 were issued without any additional conditions.

R0156/2/a was issued with one additional condition:

- Once 200 embryos have been created as part of the project, the Person Responsible must contact the Authority to communicate that fact, to update the Authority about the results of the research and to demonstrate whether the creation of more embryos is necessary. In addition the Authority would like to be told how many blastocysts have been derived from the embryos used.

Appendix C:

RESPONSE OF PERSON RESPONSIBLE TO INSPECTION REPORT

Centre Numbers:

Name of PRs: Daniel Brison

Date of Inspection: 26 09 07

Date of Response: 20 12 07

Please state any actions you have taken or are planning to take following the inspection with time scales

No action required as far as we are aware

Name: Daniel Brison

Date: 20/12/07

Correction of factual inaccuracies

Please let us know of any factual corrections that you believe need to be made (NB we will make any alterations to the report where there are factual inaccuracies. Any other comments about the inspection report will be appended to the report).

I attach a report on embryo usage for R0026 for the second half of 2006 and have also inserted this in the report above for your convenience.

Research Licence Committee Meeting

9 January 2008
21 Bloomsbury Street London WC1B 3HF

MINUTES Item 6

In vitro Development and Implantation of Normal Human Pre-embryos and Comparison with Uni- and Poly-pronucleate Pre-embryos (R0026)
Derivation of human embryonic stem cell lines from embryos, including those created from clinically unused oocytes or abnormally fertilised embryos (R0170/R0171)
Based at the Department of Reproductive Medicine St Mary's Hospital & Manchester Fertility Services & Faculty of Life Sciences University of Manchester (0067), (0033), (0175)
Interim Inspection

Members:
Emily Jackson, Lay Member – Chair
Clare Brown, Lay Member
Maybeth Jameson, Consultant Embryologist, Glasgow Royal Infirmary
William Ledger, Professor of Obstetrics and Gynaecology, University of Sheffield

Providing Scientific Advice:
Neva Haites, Professor of Medical Genetics, University of Aberdeen

In Attendance:
Graham Miles, Legal Adviser
Chris O'Toole, Head of Research Regulation
Trish Davis, Deputy Chief Executive/Director of Regulation
Joanne McAlpine, Minute Taker
Barbara Lewis, Minute Taker

Observing:
Elaine Suthers, Inspector

Conflicts 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:

- papers for Licence Committee (50 pages)

1. The papers for this item were presented by Dr Chris O'Toole, Head of Research Regulation. Dr O'Toole began by explaining that there are two research projects to consider based at three centres, and that there had been good progress on both projects. The inspection team had no major concerns on the inspection visit.

2. Dr O'Toole explained to the Committee that all the centres have regular minuted meetings to discuss the projects every 4-6 weeks. In addition, they have a further minuted meeting which takes place every two weeks for all research staff. Dr O'Toole went on to say that the patient information and consent sheets are given to patients at the appropriate time in the first initial clinical consultation. The Committee noted the progress that has been achieved across all three of the projects.

3. Dr O'Toole explained that, for the project R0026 and between the period of 01 February 2006 – 31 July 2006, the centre had received 17 immature oocytes, 52 failed to fertilise oocytes, 184 fresh embryos and 29 frozen embryos from centre 0067. All the embryos have been used in the project of research. For the purpose of projects R0170/R0171, in the six month period from 1 July 2006 – 31 December 2006, centre 0067 received and used 61 immature eggs, 221 failed to fertilise eggs, 9 fresh eggs and 106 fresh embryos. A total of 146 embryos have also been created for use in this project.

4. The Committee agreed that the centre's licence should continue with no additional conditions.

Signed..... Date 29.1.08
Emily Jackson (Chair)