



Research Licence Inspection Report

1. Project Title	Improving methods for pre-implantation genetic diagnosis of inherited genetic disease and predicting embryo quality
Research Licence Number	R0075
Person Responsible	Peter Braude
Nominal Licensee	Yacoub Khalaf
Inspection type	Progress
Licence expiry date	31 August 2009
2. Project Title	Correlation of embryo morphology with ability to generate embryonic stem cell lines and subsequent growth and differentiative characteristics
Research licence Number	R0133
Person Responsible	Peter Braude
Nominal Licensee	Yacoub Khalaf
Inspection type	Renewal
Licence expiry date	30 April 2008
Date Renewal fee paid	
Centre Number	0102
Centre Name	Guy's Hospital
Centre Address	4th Floor, Thomas Guy House Guy's Hospital St Thomas Street London SE1 9RT
Treatment centres donating to these research projects	1. 0006, 0100, 0102, 0109, 0144, 0158 2. 0006, 0015, 0086, 0102, 0144, 0153, 0208
Inspection date	6 February 2008
Licence Committee Date	2 April 2008
Inspector(s)	Mr Wil Lenton Dr Vicki Lamb

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 2 May 2006 and 5 February 2008.

Brief Description of the Projects

Project **R0075** entitled "**Improving methods for pre-implantation genetic diagnosis of inherited genetic disease and predicting embryo quality**" has been licensed since 1994.

The lay summary of the project is as follows:

Preimplantation genetic diagnosis (PGD) is an early alternative to prenatal diagnosis (PND) and is suitable for a small group of patients who are at substantial risk of conceiving a pregnancy affected by a known genetic defect. PGD has been applied in a number of centres around the world for a variety of indications, including the analysis of numerical and structural chromosomal abnormalities, identification of sex for X-linked disease and detection of specific genetic defects in monogenic disorders such as cystic fibrosis.

During PGD, a one or two cell biopsy is removed from an embryo created in vitro and a diagnostic test is carried out on the biopsied cell(s). The genetic status of the embryo is inferred on the basis of the result of the diagnostic test on the biopsy and unaffected or carrier embryos are replaced into the uterus. Therefore, for PGD to be feasible, techniques must be available which allow for the diagnosis of a particular gene defect on just one or two cells.

The thrust of this research project is to move forward existing technology to allow PGD to be applied in new disease areas and to develop new technology to improve the process of biopsy and embryo selection with the ultimate aim of enhancing the clinical success of the treatment.

Embryos which are surplus to treatment and have been donated to research with patients' consent will be used in one of two ways. Embryos will be tested for reliability and accuracy. For improvements in embryo selection procedures after PGD, embryos will be scored depending on their perceived quality and then subjected to procedures which allow an analysis of either their complete chromosome complement or the location and status of key regulatory molecules which may play an important role in early development. It is hoped that this data will improve methods of selecting embryos with high implantation potential.

The PR requests that the last sentence of the lay summary be changed to:

Embryos which are surplus to treatment and have been donated to research with patients' consent will be used in one of two ways. Embryos will be tested in order to estimate reliability and accuracy of new genetic tests. For improvements in embryo selection procedures after PGD, embryos will be scored depending on their perceived quality and then subjected to procedures which allow an analysis of either their complete chromosome complement or the location and status of key regulatory molecules which may play an important role in early development. It is hoped that this data will improve methods of selecting embryos with high implantation potential.

Project **R0133** entitled “**Correlation of embryo morphology with ability to generate embryonic stem cell lines and subsequent growth and differentiative characteristics**” has been licensed since April 2002.

The lay summary of the project is as follows:

Stem cells are unique cell populations which are able to undergo both self renewal and differentiation. Although stem cells have been found in a wide variety of adult tissues, embryonic stem (ES) cells, which have been isolated from the inner cell mass (ICM) of blastocyst stage embryos, are thought to maintain a higher potential for differentiation into a multiple array of cell types. Mouse ES cells can be expanded indefinitely in culture in an undifferentiated state, whilst retaining the capacity of early embryonic cells to differentiate into derivatives of all three primary germ layers (Robertson, 1987). Extrapolation of these properties to human cells would provide a renewable source of tissue for a range of transplantation therapies (Trounson, 2002). Derivation of mouse ES cells is a relatively straightforward, although specialised, process but so far derivation and long term culture of human ES cells has proved extremely technically demanding. Only nine human ES cell lines are currently available commercially despite over 71 having been derived (Vastag, 2003). The remaining 62 have not been successfully cultured or characterised (Vastag, 2003). Many outstanding issues remain to be resolved regarding ES cell derivation and subsequent usefulness, not least regarding whether the behaviour of the isolated ICM can be used to gain information about the viability and implantation potential of the originating embryo. We propose to isolate ICM from human blastocysts surplus to therapeutic requirements after preimplantation genetic diagnosis and, following careful morphological and cytogenetic analysis of the parent embryo throughout its development, correlate embryo characteristics with the proliferative, karyotypic and differentiative behaviour of both the resulting ICM and any ES cell lines derived from them. Should ES lines of suitable morphology be derived as a result of this work, we propose to undertake further studies on the isolation and differentiation of neural and pancreatic islet progenitor cells from human ES cell cultures.

The PR requests that the lay summary be changed to:

Stem cells are unique cell populations which are able to undergo both self renewal and differentiation. Although stem cells have been found in a wide variety of adult tissues, embryonic stem (ES) cells, which have been isolated from the inner cell mass (ICM) of blastocyst stage embryos, are thought to maintain a higher potential for differentiation into a multiple array of cell types. Mouse ES cells can be expanded indefinitely in culture in an undifferentiated state, whilst retaining the capacity of early embryonic cells to differentiate into derivatives of all three primary germ layers (Robertson, 1987). Extrapolation of these properties to human cells would provide a renewable source of tissue for a range of transplantation therapies (Trounson, 2002). Derivation of mouse ES cells is a relatively straightforward, although specialised, process but so far derivation and long-term culture of human ES cells has proved extremely technically demanding. Only nine human ES cell lines are currently available commercially on the NIH list despite over 71 having been derived; the remaining 62 have not been successfully cultured or characterised (Vastag, 2003). There are now stem cell lines being deposited in the UK Stem Cell Bank in accordance with HFEA regulations but there are many outstanding issues which remain to be resolved regarding ES cell derivation and subsequent usefulness. Not least of these concern whether the behaviour of the isolated ICM can be used to gain information about the viability and implantation potential of the originating embryo. We propose to isolate ICM from human blastocysts surplus to therapeutic requirements after preimplantation genetic diagnosis and, following careful morphological and cytogenetic analysis of the parent embryo throughout its development, correlate embryo characteristics with the proliferative, karyotypic and differentiative behaviour of both the resulting ICM and any ES cell lines derived from them. Should ES lines of suitable morphology be derived as a result of this work, we propose to undertake further studies on the isolation and differentiation of neural and pancreatic islet progenitor cells from human ES cell cultures.

References:

Robertson, E. J. (1987). "Teratocarcinomas and embryonic stem cells." IRL press, Oxford.

Trounson, A. (2002). Human embryonic stem cells: mother of all cell and tissue types. *Reprod Biomed Online*. 4, 58-63.

Vastag, B. (2003). Medical news & perspectives: effort launched to study stem cell lines, train researchers how to nurture them. *JAMA*. 289, 1092.

		R0075	R0133
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

There have been no changes in premises or procedures since the last inspection, but new premises are being built and should be ready later this year.

The nominal licensee for R0075 has been changed since the last inspection following concerns that the separation of clinical and research roles may be compromised.

The person responsible for R0133 has also changed since the last inspection.

The PR would like to change both lay summaries as shown above. Although both the current lay summaries still accurately reflect the projects, the PR considers that they would benefit from minor updating.

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

Licences R0075 and R0133 were issued without additional conditions.

Summary for Licence Committee

This is a renewal report for R0133 and a progress report for R0075.

R0075 is currently licensed for the following purposes:

- Human Fertilisation and Embryology Act 1990 Schedule 2 s3(2)(e) Developing methods for detecting the presence of gene or chromosome abnormalities in embryos before implantation
- Human Fertilisation and Embryology (Research Purposes) Regulations 2001: 2(2)(b) Increasing knowledge about serious disease.

R0133 is currently licensed for the following purposes:

- Human Fertilisation and Embryology (Research Purposes) Regulations 2001 s2(a) Increasing knowledge about the development of embryos

- Human Fertilisation and Embryology (Research Purposes) Regulations 2001: 2(2)(b)
Increasing knowledge about serious disease.
- Human Fertilisation and Embryology (Research Purposes) Regulations 2001 s2(c)
Enabling any such knowledge to be applied in developing treatments for serious disease.

The centre has suitably qualified and experienced staff and the premises are secure and appropriately equipped.

The issues around ensuring that effective consent for using embryos in research is in place were explored by the inspection team. A robust system appeared to be in place and no discrepancies were noted in the audit of patient records.

The inspectorate recommend that the following changes are made to the centres documentation:

- An SOP should be created for the induction of new staff as required by COP standard S.6.6.2 and S.6.2.7.

The executive recommend that R0133 is renewed for a period of three years and the lay summaries should be changed as requested by the PR.

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:

- Organisation of the centre
- Leadership and management
- Staffing
- Funding
- Resource management
- Research governance

Staff R0075*

Principal investigator	Peter Braude
Scientists	1 senior research fellow, 1 PhD student, 1 molecular biologist
Laboratory technicians	2
Support staff (receptionists, record managers, quality and risk managers etc)	Staff at centre 0102

Staff R0133*

Principal investigator	Peter Braude
Scientists	2 including 1 PhD student,
Laboratory technicians	2
Support staff (receptionists, record managers, quality and risk managers etc)	Staff from centre 0102

*There is overlap between staff working on projects R0075 and R0133.

Highlighted areas of firm compliance

The PR of both projects has extensive knowledge of the regulatory requirements of the HFEA as he was previously a member of the Human Fertility and Embryology Authority and is an accredited consultant at centre 0102. The PR has managed the project R0075 since its inception in 1994 and has over 30 years experience in human embryology and IVF. The PhD student who is working on project R0133 has relevant and valuable embryology experience.

R0075 is funded by the Medical Research Council (MRC) and other medical research charities including the Guy's and St Thomas Charity. R0133 is funded by a MRC grant to Professor Peter Braude. New funds have been obtained from the MRC to continue to derive embryonic stem cells from PGD embryos and to examine conditions that will improve derivation.

Training records for the Quality Manager, PhD student and research nurse were provided to the inspection team. These records demonstrated continuing professional development for all members of staff.

R0133 has been submitted to St Thomas' Hospital ethics committee through the National Research Ethics Service (NRES). Its role is to safeguard the participants in all research. A list of the membership of this ethics committee was provided to the team.

Meetings between the research staff are held every six weeks. Although most of these research meetings are not formally minuted the inspection team were shown records of the meetings in one of the research staff's notebook. This included who was in attendance and the discussions undertaken. Meetings with Stephen Minger's lab are held every three to six months. The inspection team were informed that Dr Alan Colman from Singapore has been appointed as overall coordinator of stem cell research at King's College and he will be arranging collaborative meetings and presentations. Presentations by the research group to the clinical staff at the treatment centre are held intermittently as part of the weekly unit academic and business meetings.

Documents connected with these projects that were supplied to the inspection team were seen to be version controlled.

The arrangements for separation of clinical and research functions were explained to the inspection team. Where staff work in both areas every effort is made to ensure they are not involved in treating patients who may donate to the research projects.

Issues for consideration

The inspection team were informed that the quality system will be extended to include monitoring of incubator temperatures.

The inspection team recommended that an SOP should be created for the induction of new staff as required by COP standard S.6.6.2 and S.6.2.7.

Executive recommendations for Licence Committee

A new SOP should be created.

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
<p>The centre staff confirmed that manipulation of viable embryos is carried out only on licensed premises.</p> <p>Embryos are stored in a designated security area with controlled access under the auspices of the licence of centre 0102. This area was seen by the lead inspector and considered to be appropriate for the purpose.</p> <p>The cryostore is fitted with a low oxygen level alarm and the centre has a written protocol outlining the appropriate response to the alarm. Storage dewars are fitted with low nitrogen level alarms and these are connected to an autodialler system. A documented system for dealing with damaged storage vessels is in place.</p> <p>The research lab was seen by the scientific inspector. Personnel may only enter the lab wearing theatre clothing and hats. Shoes must also be changed. The equipment in the lab was suitable for the work undertaken. The inspector was informed that the flow hood will be updated when the centre moves to new premises later this year.</p>
Issues for consideration
None
Executive recommendations for Licence Committee
None
Areas not covered in this inspection
Servicing and maintenance of equipment

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
- Prevention of coercion of prospective donors

Highlighted areas of firm compliance

Donation to both projects has been coordinated by a designated research nurse. At present she is part of the ACU staff and devotes one day a week to this activity. Efforts are made to ensure that she is not involved in the treatment of patients who may donate their embryos to research. This is to ensure that patients do not feel obliged to consent to research.

For patients with embryos in storage, donation is broached by members of the embryology team at centre 0102 or in communications from staff at the donating centres to patients whose embryos are approaching the end of the consented storage period. Patients who express an interest in donating to research are then contacted by the research nurse who provides relevant patient information and consents. The research nurse also collects the frozen embryos from the donating centre and signs that she has taken them. A protocol for collecting embryos donated to research from other units is in place and was shared with the inspection team.

For patients who are undergoing treatment, the consent form for donation of embryos to research is given to them at their second consultation. This ensures that the patients have several weeks to consider whether to donate any embryos to research.

Researchers are advised of the date of expiry of consent to storage of frozen material. Evidence of this was provided to the inspection team and demonstrated that the system for ensuring that patient storage consents are not breached is robust.

The inspection team saw evidence that witnessing is performed when transferring material from treatment to research.

A detailed SOP for transfer of embryos to research was provided to the inspection team. This included the consent forms that must be checked, including that donor consent must be checked for embryos created from donor gametes. There was also a flow chart outlining the process.

Issues for consideration

An audit of embryos in store for both research projects was conducted on 5 December 2007. One discrepancy was found: one cane of one patient's embryos had not been included in the electronic spreadsheet. This has now been amended.

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
- Donor and patient records

Highlighted areas of firm compliance
<p>Patient information and consents were provided to the inspection team. They included information on the reasons for the research, implications for the patients and where to obtain more information. The patient information and consent forms for project R0133 have been approved by an ethics committee.</p> <p>Patient information and consents provided to the inspection team were seen to be dated and version controlled.</p>
Summary of audit of patient records
<p>Centrally held records reviewed in the course of the inspection contained necessary information to allow tracking of individual embryos and cross reference to patient records.</p> <p>Five sets of records from patients who donated embryos to research were reviewed. In all cases there was appropriate consent and the fate of the embryos was clear.</p> <p>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, with the operator and witness signing to confirm that the patients donating embryos have completed appropriate consents to research.</p>
Issues for consideration
None
Executive recommendations for Licence Committee
None
Areas not covered in this inspection
None

5. Scientific practice R0075

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
<p>Thirty four fresh embryos have been supplied for this project in the last year and thirty of these were suitable for inclusion in the project. One hundred and forty one frozen embryos have been supplied to the project in the last year and thirty seven of these have been used so far.</p> <p>In order to meet the inclusion criteria embryos must contain intact blastomeres.</p>
Project objectives
<p>The original project objectives are as follows:</p> <ol style="list-style-type: none">1. To improve accuracy of PGD and to estimate the reliability of those diagnoses by examining embryos deemed not suitable for transfer.2. To apply genetic techniques to an increasing range of genetic diseases3. To improve methods of assessing embryo quality in order to improve embryo selection procedures at embryo transfer. <p>The research team reported that progress was faster and more exciting than anticipated in most areas.</p> <p>New objectives are:</p> <ol style="list-style-type: none">1. To apply preimplantation genetic haplotyping (PGH) to an increasing range of genetic diseases and to see whether relevant trisomies can be detected at the same time as the specific genetic diagnosis.2. To examine and improve the allele dropout in whole genome amplification (WGA) and validate new WGA methods in order to improve efficiency and accuracy.3. To try and automate some of the technique so new robotic methods can be applied.4. To continue the investigation into the aneuploidy status in embryos not suitable for replacement in ART cycles by detailing the mosaicism and aneuploidy observed in embryos using WGA and PCR analysis.5. Examining further embryos at various cleavage stages to complete the work on mitochondrial DNA by real time PCR. <p>New objectives 1 and 2 will contribute to achieving original objectives 1 and 2. New objective 3 will enable original objectives 1 and 2 to be achieved more efficiently. New objectives 4 and 5 will contribute to original objective 3.</p>

Lay summary of research undertaken
<p>We have been very successful in developing the technology of preimplantation testing for a range of serious genetic disorders including Huntington's disease, sickle disease, spinal muscular atrophy, epidermolysis bullosa, and cystic fibrosis. In addition to performing nearly 600 cycles of diagnosis for patients, which makes this unit the most active and successful in the UK, we have developed a substantial new method, preimplantation genetic haplotyping - PGH. This allows application of preimplantation testing to a wider range of diseases, including sex linked disorders where we can now distinguish unaffected males in addition to unaffected or carrier females. PGH also provides a higher level of accuracy in diagnosis, as well as reducing the number of embryos in which diagnosis cannot be obtained. We have successfully applied this technique to Duchenne muscular dystrophy, cystic fibrosis for rarer haplotypes, recurrent hydatidiform mole, and intend further development for myotonic dystrophy, variants of epidermolysis bullosa, and a variety of sex-linked disorders including Alport's syndrome and haemophilia. Further research will look at effect of mosaicism on diagnosis, ability to detect frequent trisomies, and impact of mitochondrial function during early development.</p>
Issues for consideration
None
Executive recommendations for Licence Committee
None
Areas not covered in this inspection
Peer review

6. Scientific practice R0133

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
<p>One hundred and thirty nine fresh embryos have been supplied to this project and thirty five of these have been used in the project. One hundred and nine frozen embryos have been supplied and forty two have been used in the project.</p> <p>The large discrepancy in numbers donated and those used is due to a large proportion of the donated embryos not meeting the inclusion criteria for the project (particularly from translocation cases). The inclusion criteria is a developing blastocyst with a visible inner cell mass.</p> <p>A total of nine stem cell lines have been derived since the inception of the project. Six of these have been derived since the last inspection. Additionally, a further paper has been published since the last inspection.</p> <p>Section 3 (3) (a) of the Human Fertilisation and Embryology Act 1990 states that a licence cannot authorise keeping or using an embryo after the appearance of the primitive streak, where the primitive streak is to be taken to have appeared in an embryo not later than the end of the period of 14 days beginning with the day when the gametes are mixed, not counting any time during which the embryo is stored. This was discussed during the inspection and the SOP was reviewed. The SOP states that: For stem cell research, in the vast majority of cases the embryos will be in culture for 5-7 days before isolation of the inner cell mass and hence destruction of the embryo. Occasionally, whole embryos are placed in culture beyond 7 days, but the resulting cell cultures are disaggregated before 14 days regardless of culture morphology. The inspection team considered that this met the requirements of the Human Fertilisation and Embryology Act 1990.</p>
Project objectives
<p>The project objectives are as follows:</p> <ol style="list-style-type: none">1. To derive human embryonic stem cell (hESC) lines with discrete genetic mutations relevant to human disease.2. To derive hESC lines without the use of animal products.3. To derive hESC lines without the use of animal products under good manufacturing practice (GMP) laboratory conditions.
Lay summary of research undertaken
<p>There has been significant interest in the therapeutic and scientific potential of human embryonic stem (ES) cells since they were first isolated in 1998. If human ES cells could be</p>

differentiated into suitable cell types, stem cells might be used in cell replacement therapies for degenerative disease such as Type 1 diabetes and Parkinson's disease, or to repopulate the heart following myocardial damage. However there is a significant shortage of high quality human ES cell lines and few research groups have experience in the propagation and manipulation of these cells. It is thus essential for the development of human stem cell technology and for the larger goal of cellular replacement therapy for human disease that additional human cell lines are generated.

We are addressing this important issue using the combined expertise of the Stem Cell Biology Laboratory and the Assisted Conception Unit and the King's College London. With local ethical approval and under licence from the UK Human Fertilisation and Embryology Authority, we have been establishing high quality human ES cell lines from a novel source of human embryos. To date, we have derived nine human ES cell lines, including one that encodes the most common genetic mutation resulting in cystic fibrosis, two that contain the Huntington's disease mutation and one containing a clinically relevant reciprocal translocation. In addition, much of our work is focussed on the generation of human ES cell-derived therapeutically important cell populations including neural, retinal, pancreatic, cardiac, and endothelial stem cells. The tightly regulated yet permissive environment in the UK for human stem cell research, coupled with the government's commitment to the establishment of a centralised stem cell bank offers the UK the opportunity to be a leading player in the field of human regenerative medicine.

Peer reviewers comments

The application to renew the research licence for this project was subject to external peer review. The reviewer recommended that the application be accepted without any changes and commented that the application concerns commendable science with important possible future clinical applications.

Issues for consideration

None

Executive recommendations for Licence Committee

None

Areas not covered in this inspection

None

Report compiled by:

Name.....Vicki Lamb

Designation.....HFEA inspector.....

Date...20 February 2008.....

Appendix A: Centre Staff interviewed

The Person Responsible for both projects and three other members of the research team took part in meetings with the inspection team.

Appendix B: Licence history for previous 3 years

R0075

Status	Licence	Type	Active From	Expires
Active	R0075/9/a	Research Project	01/09/2006	31/08/2009
Expired	R0075/8/b	Research Project	13/06/2005	31/08/2006
Replaced by New Version	R0075/8/a	Research Project	01/09/2003	31/08/2006

There are no conditions on the current licence.

R0133

Status	Licence	Type	Active From	Expires
Active	R0133/2/c	Research Project	01/09/2006	30/04/2008
Expired	R0133/2/b	Research Project	29/06/2005	30/04/2008
Offer licence sent but not acknowledged	R0133/2/a	Research Project	01/05/2005	30/04/2008
Replaced by New Version	R0133/1/a	Research Project	15/04/2002	30/04/2005

There are no conditions on the current licence

Appendix C:

RESPONSE OF PERSON RESPONSIBLE TO INSPECTION REPORT

Centre Number...0102.....

Name of PR...Peter Braude.....

Date of Inspection...6 February 2008.....

Date of Response...11 March 2008.....

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

- An SOP will be created for the induction of new staff as required by COP standard S.6.6.2 and S.6.2.7 as part of the response to the inspection of centre 0102.

I have read the inspection report and agree to meet the requirements of the report.

Name...Peter Braude.....

Date...11 March 2008.....

2. 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).

We also welcome comments about the inspection on the inspection feedback form, a copy of which should have been handed out at the inspection. If you require a copy of the feedback form, please let us know.

Please return this section of the report to:

Dr Chris O'Toole
Head of Research Regulation, HFEA
21 Bloomsbury Street
London
WC1B 3HF

Research Licence Committee Meeting

2 April 2008

21 Bloomsbury Street London WC1B 3HF

MINUTES Item 3

Research Project R0133: Correlation of embryo morphology with ability to generate embryonic stem cell lines and subsequent growth and differentiative characteristics

Licence renewal

Guy's Hospital (0102)

Research Project R0075: Improving methods for preimplantation genetic diagnosis of inherited genetic disease and predicting embryo quality

Progress report

Guy's Hospital (0102)

Members:

Emily Jackson – Chair, Lay Member
Richard Harries, Lay Member
Clare Brown, Lay Member
Maybeth Jamieson, Consultant Embryologist, Glasgow Royal Infirmary
Neva Haites, Professor of Medical Genetics, University of Aberdeen

In Attendance:

Chris O'Toole, Head of Research Regulation
Claudia Lally, Committee Secretary
Joanne McAlpine, Inspections, Logistics and Reporting Officer
(present via conference telephone:)
Vicki Lamb, HFEA Inspector

Providing Legal Advice:

Mary Timms, Field Fisher Waterhouse

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 (82 pages)
- no papers were tabled.

1. The papers for this item were presented by Vicki Lamb, HFEA Inspector. Dr Lamb informed the Committee that the issue of consents had been a key focus of this inspection, following the finding of the previous inspection that an embryo had been used in research for which no consent for this use could be found. This inspection found that a robust system has been put in place for ensuring that effective consent is in place for all material used in the project. Dr Lamb affirmed

that no discrepancies were found in the audit of patient records during the inspection.

2. Dr Lamb informed the Committee that the centre would like to make small changes to the lay summaries for both projects. These changes are supported by the Executive. She drew the Committee's attention to the fact that the inspection team has recommended that new standard operating procedures be developed for the induction of new members of staff. Dr Lamb also informed the Committee that the two projects appear to be progressing well and that the peer review contained in the committee papers at pages 75-79 is very positive about the renewal of project R0133.

3. Dr Lamb informed the Committee that the Person Responsible has satisfactorily completed the Person Responsible Entry Programme assessment.

The Committee's Decision in relation to the application to renewal the licence for research project R0133

4. The Committee endorsed the recommendation in relation to the creation of an SOP for the induction of new staff and asked that this be completed, and submitted to the Executive, by Monday 12 May. The Committee also approved the centre's request to slightly alter the lay summary of the project.

5. The Committee identified the activities to be authorised by a licence as the use of embryos in research, the storage of embryos and the derivation of human embryonic stem cell lines. The Committee agreed that they were satisfied that these activities are not prohibited under the Human Fertilisation and Embryology Act 1990.

6. The Committee decided that these activities are necessary and desirable for the following purposes:

- Increasing Knowledge about the development of embryos
Human Fertilisation and Embryology (Research Purposes) Regulations 2001 s2(2)(a)
- Increasing Knowledge about serious disease
Human Fertilisation and Embryology (Research Purposes) Regulations 2001 s2(2)(b)
- Enabling any such knowledge to be applied in developing treatments for serious disease
Human Fertilisation and Embryology (Research Purposes) Regulations 2001 s2(2)(c)

7. The Committee decided that it was satisfied that the proposed use of embryos is necessary for the purpose of research, since the use of embryos is fundamental to this project, with its focus on the generation of embryonic stem cell lines.

8. The Committee noted that no issues for consideration were raised in the inspection report in relation to patient information or consent forms. However, the Committee recognised that these will need to be changed to reflect the changes in the lay summary.

9. The Committee noted that the Person Responsible has completed the Person Responsible Entry Programme assessment and took into account the evidence in the inspection report as to the suitability of the premises. The Committee decided that the requirements for granting (and therefore renewing) a licence under section 16(2) of the Human Fertilisation and Embryology Act 1990 are satisfied.

10. The Committee noted that the centre had not yet paid its licence fee. The Committee agreed to renew the licence for a period of three years subject to the payment of this fee.

The Committee's Decision in relation to the progress report for research project R0075

11. The Committee endorsed the recommendation in relation to the creation of an SOP for the induction of new staff and asked that this be completed, and submitted to the Executive by Monday 12 May. The Committee also approved the centre's request to slightly alter the lay summary of the project.

12. The Committee agreed that they were content for this licence to continue with no additional conditions.

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