Research Licence Inspection Report

Project Title Research Licence Number Person Responsible Nominal Licensee Inspection Type Licence Expiry Date Date fee paid	The effect of biomass reduction on embryo development after biopsy of either one or two blastomeres R Dr Maybeth Jamieson Dr Helen Lyall **Initial**
Centre Name	Assisted Conception Service, Glasgow Royal Infirmary
Centre Number	0037
Centre Address	ACS Suite, Glasgow Royal Infirmary 10 Alexandra Parade Glasgow G31 2ER
Treatment centres donating to this research project	Assisted Conception Service, Glasgow Royal Infirmary (Centre 0037)
Inspection date	7 July 2006
Licence Committee Date	26 July 2006
Inspector(s)	Tony Knox Sarah Hooper

About the Inspection:
The purpose of the inspection is to ensure that research is carried out in compliance with the HF&E Act 1990, sixth edition Code of Practice, licence conditions and directions and that progress is made towards achieving the stated aim 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 further improvement is required to meet regulatory standards. It is primarily written for the Licence Committee who make the decision about the centre's licence application. The report is also available to patients and the public following the Licence Committee meeting.

This report covers an initial inspection for research licence **R**

Brief Description of the Research Project(s)

The research project is entitled: The effect of biomass reduction on embryo development after biopsy of either one or two blastomeres

Lay summary

Some couples are at risk of transmitting a genetic disorder to their children. This is because one or both of them carry a gene for that specific disorder. One option for these couples is to become pregnant and then undergo a prenatal test such as amniocentesis or chorionic villus sampling at ~10-16 weeks. If the fetus is found to be affected then the couple have to decide whether they wish to continue with the pregnancy or have a termination. Other couples suffer repeated miscarriages due to the fetus having a chromosome abnormality. In vitro fertilisation followed by Pre-implantation Genetic Diagnosis (PGD) allows the diagnosis of abnormalities in embryos at an early stage, before they are replaced in the womb. This involves removing one or two cells from an embryo and performing a test on each cell. Only embryos free from the specific genetic disease are transferred to the patient.

Some tests are more reliable if more than one cell is removed and tested but there is debate about the effect this has on the embryo's development. This study aims to assess the impact of removed cell size and cell number upon subsequent development of the embryo.

Embryos which are unsuitable for treatment and, which have been donated for research, will be examined to quantify the impact of the size of the cells removed as well as the number.

Activities of the Centre			
	Research on human embryos	✓	
	Storage of licensed material		
	Creation of embryos		

	for research		
	Derivation of human embryonic stem cells		
	Cell nuclear replacement		

Purpose(s) of Research Project		
Promoting advances in the treatment of infertility *Human Fertilisation and Embryology Act 1990 Sch 2 3(2)(a)*		
Increasing knowledge about the causes of congenital disease *Human Fertilisation and Embryology Act 1990 Sch 2 3(2)(b)*		
Increasing knowledge about the causes of miscarriages *Human Fertilisation and Embryology Act 1990 Sch 2 3(2)(c)*		
Developing more effective techniques of contraception *Human Fertilisation and Embryology Act 1990 Sch 2 3(2)(d)*		
Developing methods for detecting the presence of gene or chromosomal abnormalities in embryos before implantation *Human Fertilisation and Embryology Act 1990 Sch 2 3(2)(e)*		
Increasing knowledge about the development of embryos *Human Fertilisation and Embryology (Research Purposes) Regulations 2001 s2(a)*	✓	
Increasing knowledge about serious disease *Human Fertilisation and Embryology (Research Purposes) Regulations 2001 s2(b)*		
Enabling any such knowledge to be applied in developing treatment for serious disease *Human Fertilisation and Embryology (Research Purposes) Regulations 2001 s2(c)*		

Changes/ improvements since last inspection

Not applicable

Summary for Licence Committee

The Centre has applied for a research licence in order to use embryos to compare the relative importance of loss of cell volume and cell number on embryos undergoing biopsy.

The Centre already has a treatment licence to carry out preimplantation genetic diagnosis as a clinical service.

The Centre has indicated that the research would fulfil two purposes under the HF&E Act 1990 as amended by the HF&E (Research Purposes) Regulations 2001 notably Developing methods for detecting the presence of gene or chromosomal abnormalities in embryos before implantation [Paragraph 3(2)(e) of Schedule 2 to the HF&E Act 1990] and Increasing knowledge about the development of embryos. However both peer reviewers have stated that the research would increase the knowledge about the development of embryos therefore should be licensed under section 2(a) of the HF&E (Research Purposes) Regulations 2001.

The application has been sent out to two peer reviewers. One has recommended that the application should be accepted without amendments. The second reviewer raised a number of issues which the centre has responded to. The reviewer has subsequently submitted a letter recommending that a licence be granted for the research project.

The premises are considered suitable for the purpose of the research.

The Executive recommends that the centre should be granted a research licence under section 2(a) of the HF&E (Research Purposes) Regulations 2001. A licence should be granted for one year initially as the centre has not previously held a HFEA Research Licence.

Proposed licence variations

Not applicable

Report of Inspection findings

1. **Organisation**

Desired Outcome: The centre and research is well-organised and managed and complies with the HF&E Act.

Summary of findings from inspection
Evidence of:

- Leadership and management
- Organisation of the centre
- Resource management
- Staffing
- Research governance e.g. ethics committee
- Funding

Full time equivalent staff

Principal investigator	1
Scientists	2
Collaborators	
Support staff (receptionists, record managers, quality and risk managers etc)	Nursing team at 0037 will be responsible for consenting patients for donation to research

Summary
All staff with access to donated material or identifying information are on the licence for Centre 0037. The Person Responsible will not be involved in the research project directly; however she will be responsible for revision of protocols and dissemination of information. Only two members of the embryology team will be involved in the research project. This aids the separation of research from clinical activities as these embryologists will not be involved with the treatment of patients who have consented to research. There is a suitable individual overseeing the recruitment of donor and nurses will be trained on the consenting protocol during a presentation in late July. The Centre will be shut for two weeks in July/August and the Person Responsible has planned to use this time to introduce all members of staff to the research project; its aims and the processes involved in consenting patients. If a licence is granted and research activities commence the Person Responsible plans to discuss research issues during the Multi-Disciplinary meetings which are held every Tuesday. The Person Responsible explained that she will make all staff aware of change in protocol via memo as is the current system within the unit. The project will be funded by centre 0037 and has been approved by local research ethics committee.

Issues for consideration
It is proposed that the role of Principal Investigator will be fulfilled by the Senior Embryologist currently responsible for biopsy of embryos for the PGD Programme. This member of staff is the only embryologist trained to perform biopsies. However, he has recently handed in his resignation from this post. Although an arrangement has been made so that he can work at the centre one day a week the centre should consider how this development will impact upon the progress of research work. The PR stated that this will be a temporary situation as they are currently advertising for a full time biopsy practitioner. An auditing system for assessing compliance with the consenting process has not been designed. However, the Person Responsible recognised the importance of such a system and plans to develop an appropriate auditing system.
Executive recommendations for Licence Committee
None
Areas not covered on this inspection
Resource management

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
- Servicing and maintenance of equipment

Summary
The research will be conducted primarily in the clinical laboratory at Centre 0037. Within this laboratory the embryos will be biopsied and cultured. They will be fixed within the cryopreservation store to ensure separation of fixative chemicals from embryos in culture. Following fixation the slides will be taken to the Obstetrics and Gynaecology Laboratory within the Hospital for analysis. On the inspection it was noted that the clinical laboratory is secure and can be accessed only by authorised personnel. Equipment which will be employed for the project was purchased during 2005 and will be subject to regular maintenance and servicing.
Issues for consideration
It is planned that slides containing the fixed material will be marked with patient identifying information. As these and the research files will be taken up to another laboratory for analysis it is possible that confidentiality of patients could be breached. As it is critical that donor identifying information is restricted to licensed staff the centre should review this procedure and consider the use of unique anonymous donor numbers.
Executive recommendations for Licence Committee
The centre should consider the anonymity of the fixed samples being used in the un-licensed premises.
Areas not covered on this inspection
Storage facilities: Embryos will not be stored as part of this project and therefore the storage facilities were not inspected.

3. Donation of material

Desired outcome: Donors are recruited appropriately and any research carried out on embryos derived from their gametes 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
- Prevention of coercion of prospective donors
- Ensuring patient consent is not breached
- Donor and patient records

Summary
The proposed Person Responsible stated that only patients who have indicated that they are willing to donate embryos to research, as indicated on the HFEA (00)6 and (00)7 forms, will be given specific information about this project of research. These patients will then be asked at the time of egg retrieval whether they wish to donate embryos for this research project and if yes, the patients will be asked to complete the appropriate consent forms with the clinician on duty. There is a designated coordinator who will be responsible for gaining donated embryos for research and she is independent of the research. The Fertility Nurses will be charged with providing patients with information and obtaining informed consent. Nursing staff will be kept up to date with research activities and implications for donors through discussions at the MDTs. The decision regarding which embryos are suitable for treatment and which are not suitable for treatment and therefore suitable for research will be made by embryologists who are not involved with the research project. The Person Responsible has designated two embryologists who will be involved in the research project. As the team is large, it currently comprises six embryologists, it is considered that this separation can be supported and maintained.
Issues for consideration
Although the procedure for providing research information and for obtaining consent was submitted within the licence application it was noted during the inspection that there was some confusion about when these processes will take place. Quite appropriately the Research Coordinator expressed concern that patients should not be overwhelmed by information. According to the Research Coordinator this issue has lead to difficulties in deciding when patients should receive information regarding research and when consent should be taken from them. It is recommended that a protocol is developed and that all staff involved with this system are trained appropriately. Consent for use in research will be checked, witnessed and documented before transfer to

researchers. However, this witness form could not be evidenced during the inspection as it has not been developed yet. The Person Responsible should prepare the witness sheet and witnessing protocols prior to the commencement of research activities.

The Person Responsible was able to articulate the process which will be taken if a patient withdraws consent. However, the process is not currently documented. To ensure that all staff are aware of the process and its importance, a standard operation procedure should be created and circulated.

Executive recommendations for Licence Committee
All stages of the process should be formally covered in documented procedures.

Areas not covered on this inspection
Ensuring patient consent is not breached Donor and patient records

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

Summary
The centre has a patient information leaflet and consent from specific for the proposed project of research. These documents are considered satisfactory as they meet all the requirements of the HF&E Act and Code of Practice.
Summary of audit of patient records
This is an application for an initial research licence. Therefore an audit of patient records was not undertaken.
Issues for consideration
The patient information form should provide clear contact details in case patients would like to withdraw consent. The Person Responsible plans to amend the information accordingly.
Executive recommendations for Licence Committee
None
Areas not covered on this inspection
Patient information for projects deriving embryonic stem cells Consent forms for projects deriving embryonic stem cells

5. Scientific practice

Desired outcome: Research is carried out in accordance with the HF&E Act, Code of Practice, Directions and Licence Conditions and makes progress towards achieving stated aims.

Summary of findings from inspection:

- Use of material
- Progress in achieving aims and objectives
- Peer Review (if applicable)

Use of material
The Centre expects to use 100 fresh embryos per year. The embryos will be obtained from patients undergoing in vitro fertilisation treatment at the Assisted Conception Service at Glasgow Royal Infirmary.
Project objectives
The object of the proposed research is to compare the relative importance of loss of cell volume and cell number on embryos undergoing biopsy.
Summary of research undertaken
This is the report of an initial inspection therefore, no research has been undertaken.
Peer Reviewers Comments (if applicable)
The application has been sent out to two peer reviewers. One has recommended that the application should be accepted without amendments. The second reviewer raised a number of issues which the centre has responded too. The reviewer has subsequently submitted a letter recommending that a license be granted for the research project. Both reviewers have indicated that the proposed research would be necessary or desirable for increasing the knowledge about the development of embryos under section 2(a) of the HF&E (Research Purposes) Regulations 2001.
Issues for consideration
The Centre should ensure that they develop a system which records each time material is handled and how it is manipulated.
Executive recommendations for Licence Committee

The Executive recommends that the centre should be granted a research licence under section 2(a) of the HF&E (Research Purposes) Regulations 2001. A licence should be granted for one year initially has the centre has not previously held a HFEA Research Licence.
Areas not covered on this inspection
None

Report compiled by:

Name: Sarah Hopper and Tony Knox

Designation: Inspectors

Date: 07/07/06

Appendix A: Centre Staff interviewed

PR – Maybeth Jamieson
Research Coordinator

Appendix B: Licence history for previous 3 years

Not applicable

Appendix C:
RESPONSE OF PERSON RESPONSIBLE TO INSPECTION REPORT

Centre Number……037……

Name of PR……..Maybeth Jamieson…….

Date of Inspection……7/7/2006……..

Date of Response……10/7/2006……

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

Actions undertaken.

1. The patient information form has been amended to clarify how patients can withdraw consent up to the time the embryos are used (biopsied).

Actions which the PR will undertake.

1. An audit process for the consent process will be developed
2. We recognise that there is a slight chance of a breach of confidentiality if research staff process material in another laboratory. Therefore, any material and paperwork leaving licensed premises will be anonymised
3. The PR will liaise with the Research Co-ordinator (Sister Traynor) to develop appropriate timing for the consent process
4. All staff involved in the consent process will have an induction session which will be documented
5. Witnessing will be documented in laboratory records
6. An SOP for patients withdrawing consent will be developed
7. Laboratory paperwork will record when and how embryos are handled

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

Signed……

Name…….

Date……

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
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