



## Research Licence Interim Inspection Report

Project Title	The development of novel PGD procedures and the study of early human development
Centre Name	Human Genetics & Embryology Laboratories UCL
Centre Number	0245
Research licence Number	R0113
Centre Address	Department of Obstetrics & Gynaecology UCL, 86-96 Cheries Mews London, WC1E 6HX
Treatment centres donating to this research project	Assisted Conception Unit UCH (0044)
Inspection date	12 <sup>th</sup> September 2006
Licence Committee Date	29 <sup>th</sup> November 2006
Inspector(s)	Dr Elliot Lawrence (Lead)
	Mr Tony Knox
Fee Paid - date	N/A
Person Responsible	Joy Delhanty
Nominal Licensee	Paul Serhal
Licence expiry date	1 <sup>st</sup> October 2007

### **About the Inspection:**

The purpose of the inspection is to ensure that centres are providing a quality service for patients in compliance with the HF&E Act 1990, sixth edition Code of Practice, licence conditions and directions.

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 improve patient services and meet regulatory standards. It is primarily written for the Licence Committee who make 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 September 2005 and September 2006.

### **Brief Description of the Research Project**

The research project has been licensed since 1998. Originally the research project was associated with centre 0044. Due to the research being performed at a different location, the project was given a separate centre number in 2004 of 0245.

**The Research project is entitled:** The development of novel PGD procedures and the study of early human development

The project was originally licensed under purposes laid down in Schedule 2 of the Human Fertilisation and Embryology Act 1990;

3(2)(b) increasing knowledge about the causes of congenital disease.

3(2)(c) increasing knowledge about the causes of miscarriages.

3(2)(e) developing methods for detecting the presence of gene or chromosome abnormalities in embryos before implantation.

And the Human Fertilisation and Embryology Regulations 2001;

s2(a) Increasing knowledge about the development of embryos.

### **Lay Summary:**

Some couples are at high risk of passing on an inherited disease to their offspring. For such couples to have a healthy family the main option open to them is to conceive naturally and to have prenatal diagnosis, where the fetus is checked to see if it carries the inherited disease. If the test proves positive the parents have to decide if they wish to continue with the pregnancy or have a termination. To give these couples another option we have developed methods to test the embryo before it implants in the womb, called preimplantation genetic diagnosis or PGD. Each genetic disease requires an individual test to be developed so we are constantly doing research to perfect more tests and to tailor them to the families concerned.

Our work to develop the first tests also gave us new information about the problems that can affect early human embryos that are generated in the laboratory by in vitro fertilisation (IVF). This showed that about half of these embryos have at least some cells with abnormal chromosomes. We suspect that this is the main reason why so many IVF embryos die. Our current research aims to discover more about this widespread chromosomal abnormality and how it may affect the development of the embryo.

In some inherited disorders the condition gets worse with succeeding generations; one aspect of our research aims to find out more about this problem. As women age they are at increasing risk of producing eggs with extra or missing chromosomes, but for some women this process starts earlier, before their mid 30s. By detailed examination of the chromosomes of eggs that remain unfertilised after IVF treatment we are finding out some of the reasons why this might be happening. Our research will also help to devise tests to decide which eggs are the healthiest and most likely to lead to a normal baby.

<b>Activities of the Centre</b>	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

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

<b>C</b>	The centre must include the following amendment as part of the patient information; "Some oocytes donated for research may be fertilised and the resultant embryos used for research." This amendment must be completed before any further research is undertaken.
<b>A</b>	Complied: Yes
<b>R</b>	Patients should be given information earlier in their treatment in order to allow more time to contemplate the donation or seek independent counsel.
<b>A</b>	Complied: Yes
<b>R</b>	The male partner of donors who provide failed to fertilise and abnormally fertilised oocytes should also sign consent forms for donation to the programme as sperm may be contained within oocyte.
<b>A</b>	Complied: Yes

## Summary for Licence Committee

<p>The inspectorate were satisfied that the centre is well organised. No breaches were noted during the inspection but a number of recommendations have been made:</p> <ul style="list-style-type: none"><li>• It is recommended that the researcher signs for the donated oocytes and embryos when collecting them from centre 0044.</li></ul>
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## Proposed licence variations

None
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## Report of Inspection findings

### 1. Organisation

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

Summary of findings from inspection

Evidence of:

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

### Full time equivalent staff

Principal investigator	1
Scientific Officers	2
Administrators	
Collaborators	1
Support staff (receptionists, record managers, quality and risk managers etc)	

### Summary

The PR oversees and coordinates the research project activities. Minuted meetings are held on a monthly basis with the centre 0044. These were evidenced during the inspection and include discussion of PGD and training. The PR stated laboratory meetings occur weekly to discuss resource management and occasional include a seminar on the research. The availability of research material is managed between the two centres via email and telephone.

The majority of all submitted documents; the patient information, patient consents and protocols, have appropriate document management system footers. The remaining protocols are in the process of being version controlled in preparation for applying for Clinical Pathology Accreditation (CPA).

The project is funded by providing the PGD service and a WellBeing research grant.

### Areas for improvement

- Recommended that the cycles/PGD meeting minutes include the list of attendees.

### Executive recommendations for Licence Committee

None

### Areas not covered on this inspection

- Staffing
- Research governance

## 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

<b>Summary</b>
<p>The licensed research premises have not changed since the last inspection. The premises, located on the 3<sup>rd</sup> floor, comprises of a communal lecture area, office space and laboratory. On the ground floor is the imaging equipment located in a secure office.</p> <p>The equipment within the laboratory had up to date service contracts which were examined during the inspection.</p>
<b>Areas for improvement</b>
None
<b>Executive recommendations for Licence Committee</b>
None
<b>Areas not covered on this inspection</b>
None

### 3. Donation of material

Desired outcome: Ensure donors are recruited in a proper way and their consent is respected.

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

<b>Highlighted areas of firm compliance</b>
<p>Donors are recruited centre 0044. The research project is first mentioned at the open evening, which occurs the first Wednesday of each month for prospective patients.</p> <p>Patients are briefly told about the research project and provided with written information at their first consultation. A few days before the hCG, the nurses provide the patients with further information and the research consent forms to fill out and return on the day of egg collection. During treatment if there are any oocytes, failed to fertilise oocytes, and embryos that are unsuitable for transfer or freezing, the embryologists discuss the possibility of donating to research. This is dependent on the patient's wishes regarding research. The process was confirmed from the SOP for giving patient information and obtaining consent for research.</p> <p>Patients with stored embryos are sent an annual invoice. This billing includes information about their options; continued storage, allowing embryos to perish, donation to another couple or donation to research. Patients who indicate interest in donating embryos for research are sent further information and consent forms, if they have not already consented.</p> <p>The patient information provides contact details should a patient requires further information. This includes contact information for a counsellor should patients wish to discuss the implications of donating oocytes and embryos to research. The ability to withdraw consent to research at anytime up to when they are used is also explained.</p>
<b>Areas for improvement</b>
<ul style="list-style-type: none"><li>• It is recommended that the researcher signs for the donated oocytes and embryos when collecting them from centre 0044.</li></ul>
<b>Executive recommendations for Licence Committee</b>
None
<b>Areas not covered on this inspection</b>
None

#### 4. Patient information and consents

Desired outcome: Ensure that patients are informed in order 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

<b>Summary</b>
The patient information and consents for the research project are considered satisfactory by the Executive.  Patients are provided information about the project and contact details should they require further information. The consent forms are provided at the same time as the literature.
<b>Summary of audit of patient records</b>
Patient records are kept at centre 0044 and were not audited as part of this interim inspection
<b>Areas for improvement</b>
None
<b>Executive recommendations for Licence Committee</b>
None
<b>Areas not covered on this inspection</b>
None

## 5. Scientific practice

Desired outcome: Procedures are robust to ensure material is used appropriately

Summary of findings from inspection:

- Standard operating procedures
- Quality assurance systems
- Minimisation of material loss and wastage
- Ability to achieve set aims and objectives

<b>Use of material</b>
<p>The centre expects to use approximately 50 immature fresh and 20 frozen human oocytes respectively; 70 failed to fertilise eggs; 500 fresh and 10 frozen human embryos respectively next year. The oocytes and embryos for the research project are donated by patients at the Assisted Conception Unit (0044).</p> <p>In the period 1<sup>st</sup> October 2005 to 31<sup>st</sup> August 2006, 49 immature fresh oocytes; 69 failed to fertilise eggs; 447 fresh and 3 frozen human embryos respectively were received from centre 0044. All of the donated material was used in this time period.</p>
<b>Renewed project objectives</b>
<ol style="list-style-type: none"><li>1. To continue to develop PGD protocols for a range of single gene disorders, with particular emphasis on genes involved in cancer predisposition.</li><li>2. To carry out research to determine which patients would benefit from the diagnostic approach of testing the 1<sup>st</sup> PB via CGH to predict chromosome imbalance of meiotic origin in the embryo. This work arises out of previous work confirming the validity of the approach of 1<sup>st</sup> PB testing.</li><li>3. To obtain information on the mechanism and exact timing of the expansion of the triplet repeat sequence associated with myotonic dystrophy (DM1). To compare gene expression in embryos with expansion of the triplet repeat in DMPK with embryos without the expansion and also with embryos that are chromosomally chaotic.</li><li>4. To continue to add to data on abnormalities affecting specific chromosomes in a large number of unfertilised metaphase II oocytes, including immature oocytes that have been cultured to second metaphase, to provide fresh material for DNA analysis.</li><li>5. To develop methods for comprehensive chromosome analysis for diagnostic purposes in single blastomeres using array-CGH.</li><li>6. To analyse various imprinted genes to determine if the mode of imprinting is disrupted in IVF embryos.</li></ol>
<b>Lay summary of research undertaken</b>
<p>From our research carried out so far we have developed methods for testing cells from embryos before it implants in the womb for several severe genetic disorders. Most recently these include improved tests for myotonic dystrophy and cystic fibrosis and new tests for genes that predispose to cancers such as retinoblastoma familial adenomatous polyposis, neurofibromatosis type 1 and Von Hippel Lindau syndrome. Our research on the chromosome status of early human embryos is throwing light on the way that chromosome abnormalities occur, many of which are lethal to the embryo either before or after implantation. Some couples have repeated cycles of IVF treatment without achieving a pregnancy.</p>

Our recent research has shown that the reason for this repetitive failure in most cases is due to the very high frequency of embryos with grossly abnormal chromosomes. We have validated a test that could be used to find out which eggs are most likely to produce embryos with normal chromosomes; we now have to find out which couples might benefit from having this additional test before the eggs are fertilised.
Peer review comments (if applicable)
Not applicable as an interim inspection.
Issues for consideration
Executive recommendations for Licence Committee
None
Areas not covered on this inspection
None

Report compiled by:

Name: Elliot Lawrence

Designation: Inspector

Date: 05/10/06

## Appendix A: Centre Staff interviewed

The PR, Professor Joy Delhanty and 2 other members of the team.

## Appendix B: Licence history for previous 3 years

Licence	Type	Active From	Expiry Date
<a href="#">R0113/4/a</a>	Research Project	01/10/2004	30/09/2007

The Licence R0113/4/a has one additional condition and two recommendations:

**Condition:** Some of the oocytes donated for research may be fertilised and the resultant embryos used for research. This amendment must be completed before any further research is undertaken.

**Recommendation:** Patients should be given information earlier in their treatment in order to allow more time to contemplate the donation or seek independent counsel.

**Recommendation:** Advise that the consent of the male partner of donors who provide failed-to-fertilise and abnormally fertilised oocytes should also sign consent forms for donation to the programme as sperm may be contained within an oocyte.

Previously to 2004 the research licence R0113 was grant to centre 0044. Due to the laboratories being located on different premises they were issued with the centre number 0245 in 2004. The research project R0113 is allocated to centre 0245.

**Appendix C:**  
RESPONSE OF PERSON RESPONSIBLE TO INSPECTION REPORT

Centre Number: 0245

Name of PR: Professor Joy Delhanty

Date of Inspection: 12<sup>th</sup> September 2006

Date of Response: 25<sup>th</sup> October 2006.....

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

Section 1.  
Attendees will be listed at all forthcoming Cycles/PGD meetings, beginning on October 31st.

Section 3.  
We have already instituted the change that the person collecting embryos or eggs from Centre 0044 signs for them.

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

Signed.....

Name: Joy Delhanty.....

Date...25.10.06.....

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).

In Appendix C date of Inspection should be 12<sup>th</sup> September. Corrected.

In Section 2, Lecture area, office and laboratory space are situated on the 3<sup>rd</sup> floor, not the 1<sup>st</sup>. Corrected.

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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