HFEA Executive Licensing Panel Meeting

7 March 2014

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

Minutes – Item 1

Centre 0102 (Guys Hospital), Interim Inspection Report for Research Project R0075

Members of the Panel:	**Committee Secretary:**
Mark Bennett (Chair) – Director of Finance & Facilities	Dee Knoyle
Paula Robinson – Head of Business Planning	**Observing:**
Ian Peacock – Analyst Programmer	Sam Hartley – Head of Governance and Licensing

Declarations of Interest: members of the Panel declared that they had no conflicts of interest in relation to this item.

The Panel had before it:

- HFEA Protocol for the Conduct of Meetings of Executive Licensing Panel
- 8th edition of the HFEA Code of Practice
- Human Fertilisation and Embryology Act 1990 (as amended)
- Decision trees for granting and renewing licences and considering requests to vary a licence (including the PGD decision tree)
- Guidance for members of Authority and Committees on the handling of conflicts of interest approved by the Authority on 21 January 2009.
- Guidance on periods for which new or renewed licences should be granted
- Standing Orders and Instrument of Delegation
- Indicative Sanctions Guidance
- HFEA Direction 0008 (where relevant), and any other relevant Directions issued by the Authority
- Guide to Licensing
- Compliance and Enforcement Policy
- Policy on Publication of Authority and Committee Papers

Consideration of Application

1. The Panel noted that research project R0075 is carried out at Guys Hospital.

2. The Panel noted that centre 0102 is a treatment and research centre. The current research project, entitled “Improving methods for preimplantation genetic diagnosis of inherited genetic disease and predicting embryo quality” (R0075), was first licensed in July 1994.

3. The Panel noted that the current licence is due to expire on 31 August 2015, having been renewed for three years by a Research Licence Committee (RLC) on 17 July 2012, following an inspection on 20 March 2012. There were no additional conditions on the licence.

4. The Panel noted that at the time of the inspection on 17 December 2013, there were no areas of non-compliance or poor practice identified and commended the centre.

5. The Panel noted the Inspectorate's recommendation for the continuation of the centre’s research licence with no additional conditions.

Decision

6. The Panel endorsed the Inspectorate's recommendation to continue the centre’s licence, with no additional conditions.

Signed: Date: 21 March 2014

Mark Bennett (Chair)

Research Interim Inspection Report

Date of Inspection: 17 December 2013
Purpose of inspection: Interim Inspection of Research Licence
Length of inspection: 3 hours
Inspectors: Dr Vicki Lamb

Inspection details:
The report covers the pre-inspection analysis, the visit and information received between 20 March 2012 and 21 February 2014.

Date of Executive Licensing Panel: 7 March 2014

Centre details

Project title	Improving methods for preimplantation genetic diagnosis of inherited genetic disease and predicting embryo quality
Centre name	Guys Hospital
Centre number	0102
Research licence number	R0075-11-a
Centre address	Stem Cell and Embryology Research Laboratories Assisted Conception Unit 11th Floor Tower Wing Guy's Hospital London SE1 9RT
Person Responsible	Dr Dusko Ilic
Licence Holder	Mr Yacoub Khalaf
Treatment centre donating to this research project	Lister Fertility Clinic (0006) Sussex Downs Fertility Centre (0015) Herts and Essex Fertility Centre (0030) BMI Chelsfield Park ACU (0086) The Woking Nuffield Hospital (0144) Chelsea and Westminster Hospital (0158) Salisbury Fertility Centre (0197) South East Fertility Clinic (0208)
Date licence issued	1 September 2012
Licence expiry date	31 August 2015
Additional conditions applied to this licence	None

Doc name: Interim research report 0102 R0075
TRIM reference: 2014/000493

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Purpose of the Inspection report

The purpose of the inspection is to assess whether research using human embryos is carried out in compliance with the Human Fertilisation and Embryology (HF&E) Act 1990 (as amended) and the Code of Practice and that progress is made towards achieving the stated aims of the project. The report summarises 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 Authority's Executive Licensing Panel which makes the decision about the centre's licence.

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Report to Executive Licensing Panel

Brief description of the centre and its licensing history:

Centre 0102 is a treatment and research centre. The current research project, entitled “Improving methods for preimplantation genetic diagnosis of inherited genetic disease and predicting embryo quality” (R0075), was first licensed in July 1994.

The current licence is due to expire on 31 August 2015, having been renewed for three years by a Research Licence Committee (RLC) on 17 July 2012, following an inspection on 20 March 2012. There are no additional conditions on the licence.

Summary for licensing decision

In considering overall compliance, the inspection team considers that it has sufficient information drawn from documentation submitted by the centre prior to inspection and from observations and interviews conducted during the inspection visit to draw a conclusion on the continuation of the centre’s licence.

The Executive Licensing Panel is asked to note that there are no areas of non-compliance or poor practice.

Recommendation to the Executive Licensing Panel:

The inspection team recommends the continuation of this centre’s licence without additional conditions. In making this recommendation it is noted that there were no recommendations made in this inspection report.

Summary of project

Lay summary of the research project:

Preimplantation genetic diagnosis (PGD) is a reproductive option for couples at substantial risk of conceiving a pregnancy affected with a known genetic disease who wish to avoid the emotional burden associated with an affected child, termination of pregnancy or recurrent miscarriages. PGD has been offered as a service at Guy's and St Thomas' for over ten years.

For single gene diseases, one cell is removed from a 3-day old embryo and tested for the mutation. A separate PGD test has to be developed for every different mutation, requiring substantial resources not always available in state-run medicine. In addition, these tests are technically difficult and very sensitive to contamination with non-embryo DNA.

The centre intends to work over the next three years, further developing this approach for a wider range of genetic disorders. Their work is aimed at both developing new approaches to diagnostic testing of preimplantation embryos, and increasing knowledge of the biology and genetics of early embryo development, with a view to understanding the basis of successful pregnancies and improving the chances of healthy offspring for PGD and IVF couples.

Lay summary of research undertaken:

Research staff have used DNA extracted from research embryos using different commercial kits as they have become available, to see if these new kits provide better quality DNA for diagnostic tests. To date, they have not identified any kits which provide improved performance over the existing kits.

Current methodology for PGD for chromosome rearrangements uses fluorescent probes to count chromosome segments in biopsied cells. This technique has an error rate associated with the difficulty of interpreting fluorescent signals by microscopic visualisation. The researchers are developing a new approach based on testing for specific DNA sequences on the rearranged chromosomes. They have used research embryos to test and validate this new approach, by comparing the sequences in the research embryos with sequences from blood samples from consenting couples. This work is still in progress but when complete, they hope to incorporate this new approach into their existing work streams to allow more efficient and accurate diagnosis.

Using human embryonic stem cell (hES) lines derived from embryos carrying Huntington's Disease-specific mutation (licence R0133), the researchers have developed an embryo pre-selection method that provides medium resolution single nucleotide polymorphism (SNP) HLA results from a single cell (blastomere) in as little as 9 hours post sample collection, with no need for parental tissue samples. They have validated their strategy by analysing parents,

embryos, and hES cell lines from three families demonstrating that this technical approach is rapid, reliable and accurate.

With their Italian partners the researchers have developed a technique of mechanical separation of inner cell mass (ICM) from trophectoderm (TE). Using expertise in single cell analysis they have started building mRNA, transcriptomics, and methylation profile ICM and TE databases from normal embryos. Understanding fully the molecular events during implantation is necessary in order to manipulate them in a creative way, developing translational strategies to improve implantation rates and lead to higher pregnancy rates in assisted conception procedures.

Objectives of the research:

To continue to improve PGD and IVF programmes by introducing and developing better strategies and protocols for embryo culture and testing, and to understand more about the biology and genetics of early human embryos.

Donation and use of embryos:

In the period from 1 January 2012 to 31 December 2012, the centre reported the use of 33 fresh embryos and 78 frozen embryos. No embryos were created for use in the project.

Details of inspection findings

Inspection findings

Ensure that all licensed research by the centre meets ethical standards, and is done only where there is both a clear scientific justification and no viable alternative to the use of embryos
(Guidance note 29, 30, 31)

What the centre does well.

The renewal of research licence R0075 was granted by the RLC on 17 July 2012, the licensed activities being the creation of embryos in vitro, keeping embryos, storage of embryos and use of embryos. None of these activities are prohibited by the HF&E Act 1990 (as amended). The renewal of the licence was approved to allow research for the following designated purposes:

- Increasing knowledge about serious disease or other serious medical conditions
  HFE Act 1990 (as amended) Schedule 2 3A(2)(a)
- Increasing knowledge about the causes of any congenital disease or congenital medical condition that does not fall within paragraph (a)
  HFE Act 1990 (as amended) Schedule 2 s3A(2)(c)
- Promoting advances in the treatment of infertility
  HFE Act 1990 (as amended) Schedule 2 3A(2)(d)
- Increasing knowledge about the causes of miscarriage
  HFE Act 1990 (as amended) Schedule 2 s3A(2)(e)
- Developing methods for detecting the presence of gene, chromosome or mitochondrion abnormalities in embryos before implantation
  HFE Act 1990 (as amended) Schedule 2 3A(2)(g)
- Increasing knowledge about the development of embryos
  HFE Act 1990 (as amended) Schedule 2 3A(2)(h)

At the last renewal, the application's peer reviewer agreed that the use of human embryos was necessary and justified for the proposed research.

The research project received ethics committee approval in May 1993. More recently, a progress report was submitted to the ethics committee in August 2011, and continued approval for the research was confirmed. Evidence of this has been provided to the executive.

What they could do better.

Nothing noted on this inspection.

Have respect for the special status of the embryo when conducting licensed activities
(Guidance note 15, 18, 22, 25, 26)

What the centre does well.

An audit of records for the five sets of embryos used in the project since the last inspection demonstrated that:

- Comprehensive records of the usage of embryos in the research project are maintained from receipt at the research centre through to disposal at the end of the research process (RLC R13).
- Evidence was provided to demonstrate that effective consent had been given by the gamete providers for the use of the embryos in the research project (RLC R18).
- The researchers have a documented procedure for ensuring that embryos do not develop beyond 14 days post-fertilisation or the appearance of the primitive streak, whichever is earlier (RLC R28). The audit of records confirmed compliance with this requirement.
- All embryos donated to the project have been used for the objectives authorised by the licence to meet the defined statutory purposes (RLC R5 and R23).
- A storage log is maintained which records the storage consent expiry dates for all embryos in storage for research purposes. All frozen embryos used in the research project have been used within their consented storage period, and embryos still in store are also within their consented storage period (RLC R39).

The PR has ensured that appropriate records of embryo usage are maintained and that annual usage is reported to the HFEA (General Direction 0002 and RLC R13, R14 and R15).

What they could do better.

Nothing noted on this inspection.

Changes / improvements since last inspection on 20 March 2012:

Area for improvement	Action required	Action taken as evidenced during this inspection
None		

Areas of practice that require the attention of the Person Responsible

The section sets out matters which the Inspection Team considers may constitute areas of non compliance. These have been classified into critical, major and others. Each area of non compliance is referenced to the relevant sections of the Act, Regulations, Standard Licence Conditions, Directions or the Code of Practice, and the recommended improvement actions required are given, as well as the timescales in which these improvements should be carried out.

Critical area of non-compliance

A critical area of non compliance is an area of practice which poses a significant direct risk of causing harm to a patient, donor or to an embryo. A critical area of non compliance requires immediate action to be taken by the Person Responsible

Area of practice and reference	Action required and timescale for action	PR Response	Executive Review
None			

Major area of non-compliance

A major area of non compliance is a non critical area of non compliance:

- which poses an indirect risk to the safety of a patient, donor or to an embryo through the procurement, use, storage or distribution of gametes and embryos, which do not comply with the centre's licence;
- which indicates a major shortcoming from the statutory requirements;
- which indicates a failure of the Person Responsible to carry out his/her legal duties
- a combination of several "other" area of non compliance, none of which on their own may be major but which together may represent a major area of non compliance.

Area of practice and reference	Action required and timescale for action	PR Response	Executive Review
None			

‘Other’ areas of non-compliance or poor practice

Areas of practice that requires improvement is any area of practice, which cannot be classified as either a critical or major area of non compliance, but which indicates a departure from good practice.

Area of practice and reference	Action required and timescale for action	PR Response	Executive Review
None			

Additional information from the Person Responsible
I have reviewed the report and found it accurate. I have no objections or comments.