

# Licence Committee - minutes

## Centre 0017 (Newcastle Fertility at Life)

### Variation of Licensed Activities to include Mitochondria Pronuclear Transfer (PNT)

Thursday, 9 March 2017

HFEA, 10 Spring Gardens, London SW1A 2BU

Committee members	Lee Rayfield (Chair) Ruth Wilde Kate Brian Anita Bharucha	
Members of the Executive	Siobhain Kelly Dee Knoyle	Interim Head of Governance Secretary
Legal Adviser	Sarah Ellson	Fieldfisher
Specialist Adviser	Bert Smeets	
Observers	None	

### Declarations of interest:

- Members of the committee declared that they had no conflicts of interest in relation to this item.

### The committee had before it:

- 8th edition of the HFEA Code of Practice
- Standard licensing and approvals pack for committee members

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## The following papers were considered by the committee:

- Inspection report, including Annex I
- Annex II, supporting information required by Directions 0008:
  - Application form
  - Copy of Hyslop et al., (2016)
  - CV and supporting reference for Dr Louise Hyslop
  - Assessment of competence for Dr Louise Hyslop in carrying out PNT
  - A list of key performance indicators
  - Procedures for follow up
  - Information provided to patients on mitochondrial donation, oocyte vitrification and frozen embryo transfer
  - Information provided to mitochondrial donors
- Licensing minutes up to the centre's last renewal inspection:
  - ELP 20 May 2016 - Interim inspection
  - Executive Licensing 30 May 2014 – Licence renewal

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## 1. Background

- 1.1. Newcastle Fertility Centre at LIFE, centre 0017 has held a treatment (including embryo testing) and storage licence with the HFEA since 1992 and provides a full range of fertility services. The centre's licence is due to expire on 31 July 2018.
- 1.2. The centre also has a research licence for project R0152, entitled 'Towards improving assisted reproductive technologies for the treatment of infertility and prevention of disease' under which its research into mitochondrial donation techniques has taken place.
- 1.3. The HFEA received an application from the centre on 16 December 2016 to vary its treatment licence to include Pronuclear Transfer (PNT) which requires the HFEA to make 'express provision' in the licence to permit mitochondrial donation treatments using Pronuclear Transfer (PNT). This includes an application to add to the centre's licence a named embryologist who is competent in PNT to fulfil the role of Mitochondrial Donation Practitioner.
- 1.4. The Person Responsible (PR) must make a separate application(s) to the HFEA for permission to allow PNT in individual patients and these applications will be considered case by case by the HFEA's Statutory Approvals Committee.
- 1.5. Once a patient has been assessed as suitable for PNT by the centre's multi-disciplinary team and following specific authorisation from HFEA's Statutory Approvals Committee, a suitable donor will undergo stimulation and egg collection. The procedure will then take place using fresh donor eggs, and thawed eggs from the patient. Embryo(s) created through PNT will be transferred to the recipient patient, or frozen for future use.

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## 2. Consideration of application

### Application

- 2.1. The committee noted that the Person Responsible (PR) wished to vary the centre's licence, treatment (including embryo testing) and storage to include mitochondrial donation (PNT).

### Suitability of premises, equipment and processes

- 2.2. The committee noted that the centre plans to cease activity in March 2017 for six weeks whilst its laboratories undergo a full refit with new equipment.
- 2.3. The committee noted that an inspection took place on 23 and 24 January 2017. At the time of the inspection there were no critical areas of non-compliance, six major areas of non-compliance, two of which relate directly to the laboratory refit and two 'other' areas of practice were identified. The committee noted the following recommendations made by the inspectorate, in particular the non-compliances relating to non CE marked reagents, the training of nurses and the Counsellor involved in mitochondrial donation and treatment and exploring opportunities to facilitate the uptake of counselling:  
Major areas of non-compliance recommendations yet to be implemented:

- Following the laboratory refit, a deep clean should take place and testing completed to show appropriate air quality, evidence should be sent to the inspectorate before any licensed activity takes place in the laboratory;
- Equipment to be used during the processing and culture of embryos for the purposes of PNT should be validated or re-validated as necessary following the laboratory refit and before recommencing any licensed treatment confirmation and, for equipment to be used in PNT, documented validations should be sent to the inspectorate;
- Final versions of the centre's documented process for ensuring the safety of non CE marked reagents should be released and forwarded to the inspectorate by 23 April 2017, and evidence that the first batch of these reagents have been assessed should be sent to the inspectorate before they are used;

- Third party agreements should be documented between the two laboratories that will test the non CE marked reagents for sterility and toxicity, and also the Trust theatres that may be used for complex egg collections. Copies of these agreements should be sent to the centre's inspectorate by 23 April 2017;
- The Counsellor should receive training on the mitochondrial donation and treatment pathway, and opportunities explored to facilitate the uptake of counselling and confirmation that the appropriate training package has been completed should be forwarded to the centre's inspectorate by 23 April 2017;
- Nurse(s) should be identified and specifically trained or assessed as competent for their role in mitochondrial donation and treatments and confirmation that the appropriate training package has been completed should be forwarded to the centre's inspectorate by 23 April 2017.

'Other' areas of practice – fully implemented:

- Documented procedures for screening donors should reflect screening requirements of mitochondrial donors;
- Written information provided to mitochondrial donors and patients should be reviewed against the guidance issued in the Code of Practice.

**2.4.** The committee noted that since the inspection the PR has fully implemented the two 'other' areas of non-compliance and appropriate action has been taken towards the remaining areas of non-compliance. The PR has made a commitment to implement all of the recommendations within the agreed timeframes.

### **Patient and donor information**

**2.5.** The committee noted that the centre has used the inspectorate's information audit tool to audit their information against the Code of Practice. A copy of this audit was forwarded to the inspectorate alongside revised patient information. The inspectorate is satisfied that guidance in the CoP has been fully incorporated into the centre's information.

### **Follow up**

**2.6.** The committee noted that the centre's procedures for screening patients are compliant with HFEA requirements.

**2.7.** The committee noted that the centre has procedures to ensure that they will meet the traceability requirements.

**2.8.** The committee noted that the centre has procedures to ensure adverse incidents in relation to mitochondrial donation are reported to the HFEA, including if a child born following mitochondrial donation treatment is born with a mitochondrial disease, birth defect, or genetic abnormality, or if there has been some other adverse outcome.

**2.9.** The committee noted that documented processes are in place setting out how children born from mitochondrial donation will be followed up, where consent has been given. This includes long-term medical follow-up of children born as a result. The centre has close links with mitochondrial disease centres and NHS England to facilitate follow-up.

### **Competence of the proposed embryologist**

**2.10.** The committee noted that the proposed embryologist, Dr Louise Hyslop is willing to assume the responsibility of the role of Mitochondrial Donation Practitioner.

**2.11.** The committee noted from the information provided that Dr Hyslop has suitable qualifications and experience for the role of Mitochondrial Donation Practitioner and that satisfactory information has been submitted to evidence Dr Hyslop's competency in PNT as required by General Directions 0008, including a suitable CV, supportive reference and data to show the Key Performance Indicators (KPI) set out in these Directions have been met.

- 2.12.** The committee noted that the centre has in place a five year plan, supported by their Trust and NHS England funding, that includes at least one additional embryologist to be recruited to contribute to the PNT program. The centre has started the recruitment process for an additional embryologist. It is expected that training in PNT techniques to competence will take about six months. Once this embryologist is competent, and has successfully applied to be added to the centre's licence, an additional embryologist may be recruited. It is intended that for each patient, PNT will be completed concurrently by two embryologists. This is because there is a short period of time during which PNT can take place, and also the impact of any practitioner-to-practitioner variability will be minimised.

### **Recommendations**

- 2.13.** The committee noted that the inspectorate considers all remaining recommendations made in the inspection report must be fully implemented before treatments involving PNT can take place. The inspectorate is satisfied that the centre has already taken appropriate steps towards implementing these recommendations, and that they will be completed within the agreed timeframes before PNT takes place. The inspectorate has taken into consideration the centre's plans to not start PNT clinically until the summer/autumn of 2017, subject to the variation of its licence. The committee noted that the inspectorate therefore considers it appropriate to recommend the variation of the centre's licence to permit mitochondrial donation.
- 2.14.** The committee noted that the inspectorate will provide a full update, and confirmation of the closure of all recommendations to the Licence Committee in July 2017.
- 2.15.** The committee noted the inspectorate's recommendation to vary the centre's licence to appoint Dr Louise Hyslop as Mitochondrial Donation Practitioner.

### **Specialist Adviser**

- 2.16.** The committee noted that the Specialist Adviser considered that the processes described in the application and supporting documents were suitable for PNT. In particular he confirmed that the available evidence supported the centre's current decision that donors and recipients will not be matched on the basis of their mitochondrial DNA haplogroup. He assisted the Committee with aspects of the patient information and counselling as reflected in its decision below.

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## **3. Decision**

### **Application**

- 3.1.** The committee had regard to its decision tree. It was satisfied that the appropriate application had been submitted and that the application contained the supporting information required by General Directions 0008, except for evidence that equipment has been validated which is a recommendation. The committee noted that no fee is required with this application.
- 3.2.** The committee had regard to the requirements set out in the Human Fertilisation and Embryology (HF&E) Act 1990 (as amended), the HF&E Act 2008, the HF&E (Mitochondrial Donation) Regulations 2015 and the HFEA Code of Practice (CoP).

### **Suitability of Premises, equipment and processes**

- 3.3.** The committee was satisfied that the premises (including those of relevant third parties, laboratories conducting tests that impact on the quality and safety of gametes and/or embryos) and equipment are suitable to carry out the licensed activities, subject to the recommendations made within the inspection report. The committee also noted that the timescale for the laboratory refit and deadlines for the recommendations to be implemented mean that any further information submitted by the centre may not be received in time to be

presented to the next scheduled Licence Committee meeting in May. However, the committee was satisfied that the executive will provide a full update and confirmation of the implementation of all recommendations to the Licence Committee meeting scheduled in July 2017 which is anticipated to be before any PNT procedures are undertaken.

- 3.4.** The committee was satisfied that the processes are suitable, subject to recommendations made in the inspection report.
- 3.5.** The committee noted that although initially the intention is that procurement of eggs takes place only at the centre, un-manipulated eggs could be transported from other HFEA licenced centres for use at this centre in PNT treatment or for donation purposes. The centre is aware that General Directions 0006 and the Human Fertilisation and Embryology (mitochondrial donation) Regulations 2015 prohibit the import or export of gametes and/or embryos to which mitochondrial donation techniques have been applied. Subject to the General Directions it is permissible for un-manipulated eggs or embryos to be imported from overseas for use in mitochondrial donation treatments (patients who have eggs in storage abroad or donors). The committee noted that the centre is aware that only centres with the appropriate 'express provision' in their licence are permitted to undertake any treatment activity with embryos or gametes which have been subject to mitochondrial donation treatment.
- 3.6.** The committee noted that the centre's procedures for obtaining consent are compliant with HFEA requirements. The committee was satisfied that the treatment and donation pathways would ensure that the expert team at Newcastle Fertility Centre at LIFE provide proper information and seek relevant consents from all patients or mitochondrial donors, whether they are from the UK or overseas. The inspectorate is satisfied that guidance in the HFEA Code of Practice has been fully incorporated into the centre's information for patients.
- 3.7.** The committee noted that the centre is also aware that embryos created following PNT (pronuclear transfer) will not be subject to further biopsy for the purposes of PGD (pre-implantation genetic diagnosis) or PGS (pre-implantation genetic screening).

#### **Patient and donor information and support services including counselling**

- 3.8.** The committee understood the patient information in the application to be the updated patient information said to better promote the availability of counselling.
- 3.9.** The committee considered that it is important to ensure that counselling support is offered to patients and donors at an appropriate time. It accepted that genetic counselling was a distinct issue and considered that patients were likely to have had the opportunity for such counselling prior to being proposed for PNT and noted that further genetic counselling might be required at a later stage in the treatment.
- 3.10.** Due to the novelty of mitochondrial donation treatment, the committee considered carefully whether the centre meets the requirements set out in the HFEA Code of Practice and whether the offer of counselling would be included in the treatment and donation pathways. The committee noted that the Counsellor is a member of the British Association for Counselling and Psychotherapy (BACP) and has attended a British Infertility Counselling Association (BICA) introductory course in infertility counselling and that steps have been taken to ensure sufficient counselling services are available to those seeking treatment or considering mitochondrial donation.
- 3.11.** The committee were not completely satisfied that the Counsellor has the skills and experience required to provide appropriate support relative to the additional implications of mitochondrial donation or treatment, including for example potential implications of media interest. In the light of this the committee requested that the PR sends evidence to the Inspectorate that the Counsellor meets the requirements of the Code of Practice. The committee noted that counselling will be complemented by in house discussions of the implications of treatment/donation with nurses at the centre. The committee considered that

an appropriate training package has been put in place for the Counsellor and confirmation that this has been completed should be forwarded to the inspectorate by 23 April 2017. The Committee suggested that the Counsellor should be assessed as competent in her knowledge and understanding of the patient pathway by being assessed by the PR (as is proposed with the nurse(s)).

- 3.12.** The committee noted that the option of counselling will be made available to all patients and donors and that the centre was encouraged to remove potential barriers to the acceptance of counselling and ensure that the offer of counselling is made clearer in written information and opportunities should be explored to facilitate the routine uptake of counselling incorporated into the patient pathway.. The committee understood that the patient information had been updated to better promote the availability of counselling. The committee reminded the centre of the benefits of counselling to all concerned in the process of donation and treatment and suggested that the centre considers the possibility of improving access to counselling by offering telephone or video counselling sessions.
- 3.13.** The committee was of the view that the information provided to patients about the counselling service should be further enhanced and tailored to mitochondrial donation treatment which, given its novelty and profile, raises issues additional to other treatments. Both patients and donors could benefit from exploring these additional issues in counselling and this could be made clearer on the patient and donor information. The committee considered that different information about counselling was required for patients than for donors.
- 3.14.** The committee also noted that the information provided to patients and donors needs to be updated to reflect the current details for Fertility Network UK (not Infertility Network UK).
- 3.15.** The committee also invited the centre to make clearer in the patient information the precise arrangement for storing and freezing collected eggs and to address subsequent issues of storage (and separate information about possible use in research), as well as considering how the freezing information might need to reflect the PNT procedure.

#### **Training Nurses**

- 3.16.** The committee noted that nursing staff taking on mitochondria donation and treatment will come from the existing staff. A nurse has not yet been identified or specifically trained and assessed as competent for their role in mitochondrial donation and treatments. However, an appropriate training package has been put in place and confirmation that this has been completed will be forwarded to the inspectorate by 23 April 2017.

#### **Follow Up**

- 3.17.** The committee noted that at present the proposed follow up was only at 6 months, 12 months and 4-5 years. The committee raised awareness that the follow-up of overseas patients may be more difficult to achieve than the follow-up of patients resident in the UK and the centre should have a clear plan to achieve this. The committee agreed that patients should be made aware of the benefits to future patients of follow-up post treatment and how the data collected, with their consent, will also inform research.

#### **Competence of the proposed embryologist**

- 3.18.** The committee noted that satisfactory information has been submitted to evidence Dr Hyslop's competency in PNT as required by General Directions 0008, including a suitable curriculum vitae, supportive reference, and data to show the Key Performance Indicators (KPI) set out in these Directions have been met.
- 3.19.** The committee noted that Dr Hyslop performed all clinically relevant PNT experiments in Hyslop et al., (2016), and whilst the assessment submitted draws upon the experiments in this paper, it also includes additional data generated since its publication.
- 3.20.** The committee was satisfied that Dr Louise Hyslop had demonstrated her competence to

be a Mitochondrial Donation Practitioner.

## **Licence**

- 3.21.** The committee noted that the centre has access to a multidisciplinary team, including mitochondrial disease specialists, reproductive specialists, embryologists, clinical geneticists, genetic counsellors and molecular geneticists. A senior mitochondrial disease specialist will be involved in deciding whether a particular patient should receive mitochondrial donation treatment.
- 3.22.** The committee also noted that expert consultants in mitochondrial donation have been assigned to oversee separately the patient and donor pathways.
- 3.23.** The committee decided to vary the centre's current licence for treatment (including embryo testing) and storage to include mitochondrial donation (PNT) with immediate effect. The committee agreed that 'express provision' should be made in the licence to permit mitochondrial donation treatments using Pronuclear Transfer (PNT) as required by paragraphs 9 (2) of the Regulations, to allow the centre to carry out the technique by changing the definition of 'permitted embryo' on the centre's licence. The revised definition of permitted embryo will then include embryos which have been subject to the process of PNT (paragraphs 6 of the Regulations).
- 3.24.** The committee directed that the licence should also be varied to add the mitochondrial donation standard conditions T124-T129 to the licence.
- 3.25.** The committee further directed that the centre's licence should be varied to name Dr Louise Hyslop on the front of the licence as an embryologist assessed as competent to undertake PNT.
- 3.26.** The committee agreed that the inspectorate should provide a full update and confirmation of the closure of all recommendations to the Licence Committee in July 2017.

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## **4. Chair's signature**

- 4.1.** I confirm this is a true and accurate record of the meeting.

### **Signature**



**Lee Rayfield**

**Date**

16 March 2017