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

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

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.

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.

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 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 centreconsiders 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.

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

Inspection Report

Purpose of the Inspection Report

This is a report of an inspection to assess whether Newcastle Fertility Centre complies with essential requirements in providing safe and high quality care to patients seeking treatment using mitochondrial donation, and to their donors. The inspection was scheduled. The Authority's Licence Committee uses the application from the centre and this report to decide whether to vary the centre's licence and, if so, whether any additional conditions should be applied to the licence. The report covers a desk based review of documents and an on-site inspection. This report presents a full assessment of the impact of the variation on all areas of practice, taking into consideration the centre's ability to meet statutory requirements and Code of Practice guidance.

Date of inspection: 23 and 24 January 2017 (1.5 days)

Inspectors: Dr Douglas Gray (lead), Mrs Gill Walsh, Mrs Lesley Brown

Date of Licence Committee: 9 March 2017

Centre name	Newcastle Fertility Centre at LIFE
Centre number	0017
Licence number	L/0017/15/a
Centre address	International Centre for Life Bioscience Centre Times Square Newcastle upon Tyne NE1 4EP
Person Responsible	Dr Jane Stewart
Licence Holder	Professor Mary Herbert
Date licence issued	1 August 2014
Licence expiry date	31 July 2018
Additional conditions applied to this licence	None

Contents

Section 1: Summary report

Brief description of the centre and its licensing history:
Newcastle Fertility Centre has held a HFEA treatment (including embryo testing) and storage licence since 1992 and provides a full range of fertility services. The current treatment and storage licence runs until 2018.The centre also holds a licence for research project R0152 'Towards improving assisted reproductive technologies for the treatment of infertility and prevention of disease' under which their research into mitochondrial donation techniques has taken place.

On 15 December 2016, HFEA decided that the safety and efficacy of mitochondrial donation techniques had developed such that they should now be allowed in treatment in specific cases. An application was received from the centre on 16 December 2016 to vary their licence to make 'express provision' to permit mitochondrial donation treatments using Pronuclear Transfer (PNT). This variation also includes an application to add to the centre's licence a named embryologist competent in PNT. A separate application will be required if the centre wants to use the alternative permissible technique of Maternal Spindle Transfer (MST), or to add additional embryologists competent in PNT.

This report is solely concerned with the capability of the centre to offer PNT. The statutory framework governing mitochondrial donation requires the centre to make a separate application to the HFEA for permission to allow PNT in individual patients. All such applications will be considered by the HFEA's Statutory Approvals Committee (SAC).

A suitable patient will undergo up to three cycles of stimulation, egg collection and egg freezing so that sufficient eggs are available for the procedure (about 20 eggs). It is expected that egg collection will take place in Newcastle although it is possible (and permissible) that egg collection may, in time, take place at another HFEA licenced centre, or abroad, and the eggs later transferred to Newcastle where PNT would take place. Once a patient has been assessed as suitable for PNT by the clinic's multidisciplinary team, and following specific authorisation from HFEA's SAC, 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. An embryo(s) created through PNT will be transferred to the recipient patient, or frozen for future use.

The centre expects to provide 25 treatments involving PNT per year. There will however be a phased introduction; the centre expects that during 2017 the majority of work will see prospective patients undergoing stimulation and egg collection, those eggs will then be frozen. Subject to the approval of this variation, the centre expects that PNT procedures could take place from summer/autumn 2017. As noted above, the centre will need to make a separate application to the SAC for each patient before the approved mitochondrial donation technique is used. Up to January 2018, the centre expects to submit fewer than 10 applications.

Process(es) applied for:
Pronuclear transfer (PNT)[1]

Mitochondrial donation practitioner(s) applied for:
Dr Louise Hyslop

Summary for licensing decision:
Taking into account the essential 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), the inspection team considers that it has sufficient information to conclude that:

- the application has been submitted in the form required;
- the premises (including those of relevant third parties) are suitable, subject to a recommendation made within this report;
- the centre's practices are suitable;
- the application contains the supporting information required by General Direction 0008 in application to vary their licence to allow mitochondrial donation, except for evidence that equipment has been validated which is also subject to a recommendation.

The Committee should note that no fee is required.

The Committee is asked to note the centre plans to cease activity in March 2017 for six weeks whilst their laboratories undergo a full refit with new equipment (discussed in detail in section 2 below).

At the time of inspection six major areas of non compliance (two of which relate directly to the laboratory refit) and two 'other' areas of practice were identified. The two 'other' non-compliances have already been fully implemented and appropriate action has been taken towards the remaining non-compliances. The centre PR has made a commitment to implement all of the inspectorate's recommendations within the agreed timeframes. The non-compliances identified at inspection resulted in the following recommendations:

Major areas of non compliance:

- Following the laboratory refit, a deep clean should take place and testing completed to show appropriate air quality.
- Equipment to be used during the processing and culture of embryos for the purposes of PNT should be validated or revalidated as necessary following the laboratory refit.
- Final versions of the centre's documented process for ensuring the safety of non-CE marked reagents should be released, and evidence that the first batch of these reagents having been assessed should be sent to the centre's inspector.
- Third party agreements should be documented between the two laboratories that will test the non-CE marked reagents for sterility and toxicity; and the Trust theatres that may be used for complex egg collections.
- The counsellor should receive training on the mitochondrial donation and treatment pathway, and opportunities explored to facilitate the uptake of counselling.
- A nurse(s) should be identified and specifically trained or assessed as competent for their role in mitochondrial donation and treatments.

[1] As defined by Regulation 7 of the Human Fertilisation and Embryology (Mitochondrial Donation) Regulations 2015.

‘Other’ areas of practice:

- 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.

Recommendation to the Licence Committee

The inspectors consider all remaining recommendations made in this report must be fully implemented before treatments involving PNT can take place. As noted above, the inspectors are however satisfied that the centre has already taken appropriate steps towards implementing these recommendations, and that they will be completed within the agreed timeframes and, without exception, before PNT takes place. In saying this, the executive has taken into consideration the centre's plans to not start PNT clinically until the summer/autumn of 2017, subject to the variation of their licence. The executive therefore considers it appropriate to recommend the variation of the centre's licence to permit mitochondrial donation. In making this recommendation, the inspectors have considered our approach taken previously to recommend the variation or grant of licences following inspections at which there were similar numbers and types of recommendations.

The executive also recommends that Dr Louise Hyslop be named on this licence as an embryologist assessed as competent in PNT, as she meets the test set out by the Authority.

The timescale of the laboratory refit and deadlines for the recommendations means any further information submitted by the centre may be received too late to be presented to the Committee's next meeting in May. However, the executive can provide a full update, and confirmation of the closure of all recommendations, to the Committee in July.

The Committee are reminded that following the variation of the centre's licence, that no treatments could take place until HFEA's SAC has granted patient specific approval. In submitting applications to SAC, the executive will take into consideration the centre's progress with implementing the recommendations made in this report.

Section 2: Inspection findings

This section details the centre's ability to meet requirements and best practice guidance for the provision of treatment using mitochondrial donation techniques. This has broken down in to four areas:

1. The protection of the patient, and children born following treatment at this centre
2. The experience of patients at this centre
3. The protection of gametes (sperm and eggs) and embryos at this centre
4. How this centre looks after important information

1. Protection of the patient and children born following treatment

▶ Witnessing and assuring patient and donor identification

Witnessing (Guidance note 18)
The centre's procedures for double checking the identification of gametes and embryos and the patient or donor (including mitochondrial donors) to whom they relate are compliant with HFEA requirements. This ensures that patients receive treatment using the correct gametes or embryos.

▶ Donor selection criteria and laboratory tests

Screening of donors prior to procuring, processing gametes and embryos
Payments for donors
Donor assisted conception

Screening of donors (Guidance notes 11 and 33)
It is important that donors are appropriately screened to minimise the risks of cross infection, and to minimise the risk of transmission of disease to any child born. The centre has procedures in place to ensure mitochondrial donors are screened in accordance with HFEA's Code of Practice, with one exception. The centre's documented procedure (a checklist) for screening donors includes all screening tests required for egg donors, some of which are not needed for mitochondrial donors (recommendation 7).

The mitochondrial DNA haplotype of donors and recipients will be determined and recorded; however, donors and recipients will not be matched on the basis of their haplotype. The centre have made this decision based on the available evidence, and they will continue to keep up-to-date with emerging research in this area (CoP 33.23).

Payments for donors (Guidance note 13; General Direction 0001)
It is important that the principle of altruistic donation be upheld but at the same time donors receive appropriate compensation for their time and any inconvenience caused. The centre will ensure mitochondrial and sperm donors are only compensated in line with General Directions 0001.

Donor assisted conception (Guidance note 20)
Patients potentially suitable for mitochondrial donation will be identified at a reproductive options clinic, at which options including preimplantation genetic diagnosis (PGD), chorionic villus sampling, and egg donation are also considered. Those cases identified as potentially suitable will then be referred to a multidisciplinary mitochondrial disease

team meeting, comprised of experts from the centre and their local mitochondrial disease centre. At this meeting, those patients for whom PGD is not appropriate will be identified in line with the Authority's decision in December 2016 to only permit mitochondrial donation treatments in those patients who are highly heteroplasmic or homoplasmic for abnormal mitochondria.

The centre has procedures in place to ensure that mitochondrial donors remain anonymous.

Suitable premises and suitable practices

Safety and suitability of premises and facilities
Laboratory accreditation
Infection control
Medicines management
Pre-operative assessment and the surgical pathway
Multiple births
Procuring gametes and embryos
Transport and distribution of gametes and embryos
Receipt of gametes and embryos
Imports and exports
Traceability
Quality management system
Third party agreements
Transports and satellite agreements
Equipment and materials
Process validation
Adverse incidents

Safety and suitability of premises and facilities (Guidance note 25)

It is important to ensure that all licensed activities are conducted in a suitable environment that is fit for purpose. PNT will take place in one of three isolator units located either in the embryology laboratory, or in an adjacent laboratory designated for PNT and the culture of embryos created following PNT.

The centre will be ceasing activity in March 2017 for six weeks whilst their laboratories undergo a full refit with new equipment. SLC T20 requires that gametes and embryos are processed in an environment of appropriate air quality. The air quality in the laboratories will therefore need testing following a 'deep clean' of those rooms (recommendation 1).

The centre has procedures in place that ensure that risks are taken into account so that patients and staff are in safe surroundings that prevent harm. Laboratories conducting tests that impact on the quality and safety of gametes and/or embryos (relevant third parties) are suitable.

Laboratory accreditation (Guidance note 25)

The centre's laboratories and/or third party laboratories which undertake the diagnosis and investigation of patients, patients' partners or donors, or their gametes, embryos or any material removed from them, are compliant with HFEA requirements to be accredited by CPA (UK) Ltd or another body accrediting to an equivalent standard. This is important to assure the quality of the services provided.

Infection control (Guidance Note 25); Medicines management (Guidance Note 25); and Pre-operative assessment and the surgical pathway (Guidance Note 25)
The implications of the variation on relevant practices were reviewed; the inspectors were satisfied that this variation has no additional implications beyond those assessed as compliant at the centre's last renewal inspection.

Multiple births (Guidance note 7; General Direction 0003)
The implications of the variation on relevant practices were reviewed; the inspectors were satisfied that this variation has no additional implications beyond those assessed as compliant at the centre's last renewal inspection. The centre intends to follow their existing eSET policy for patients receiving treatment with PNT.

Procurement of gametes and embryos (Guidance note 15)
The implications of the variation on relevant practices were reviewed; the inspectors were satisfied that this variation has no additional implications beyond those assessed as compliant at the centre's last renewal inspection.

Transport, distribution and receipt of gametes and embryos (Guidance note 15; General Direction 0009)
The implications of the variation on relevant practices was reviewed; the inspectors were satisfied that this variation has no additional implications beyond those assessed as compliant at the centre's last renewal inspection.

Although initially the intention is that procurement of eggs takes place only at the centre, eggs could be transported from other HFEA licenced centres for use at this centre in PNT treatment or for donation purposes. Inspectors were satisfied that the treatment and donation pathways would ensure the expert team at Newcastle provide proper information and seek relevant consents from all patients or mitochondrial donors (CoP 33.29).

The centre is aware that embryos created using mitochondrial donation techniques, could only be transferred into a women by a centre with a licence that explicitly permits those techniques.

Imports and exports (Guidance note 16; General Direction 0006)
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.

It is permissible that un-manipulated eggs could be imported from overseas for use in mitochondrial donation treatments (patients who have eggs in storage abroad or donors). Similar to above, the treatment and donation pathways would ensure the expert team at Newcastle retain oversight of the provision of proper information from all patients or mitochondrial donors, whether they are from the UK or overseas.

Traceability (Guidance note 19)
The centre has procedures to ensure that they have the ability to:

- identify and locate gametes and embryos during any step from procurement to use for human application, disposal or donation to research;
- identify the donor (including mitochondrial donors) and recipient of gametes or embryos;

- identify any person who has carried out any activity in relation to particular gametes or embryos; and
- identify and locate all relevant data relating to products and materials coming into contact with particular gametes or embryos and which can affect their quality or safety.

Quality management system (QMS) (Guidance note 23)
The establishment and use of a QMS is important to ensure continuous improvement in the quality of treatments and services. The centre's QMS incorporates all necessary aspects to effectively direct and monitor the mitochondrial donation treatment pathway, including standard operating procedures, audits and quality indicators.

Transport and satellite agreements (Guidance note 24; General Direction 0010)
The centre is aware that no part of PNT or MST techniques can take place under a transport or satellite arrangement.

Equipment and materials (Guidance note 26)
The centre uses equipment and materials that are broadly compliant with HFEA requirements. All of the equipment and materials used in licensed activity are designated for the purpose and are appropriately maintained in order to minimise any hazard to patients and/or staff.

- **Equipment:**

As part of the laboratory refit discussed above, all existing equipment will be removed, and much of it replaced with new equipment. A set of equipment used for all PNT procedures in Hyslop *et al*., (2016) will require revalidation after the reinstallation, and two new additional sets of equipment for PNT will require validation (recommendation 2).

- **CE marking:**

It is important that medical devices that come into contact with gametes or embryos are approved for the provision of fertility treatment, to ensure the safety of patients, their gametes and embryos.

PNT requires the use of three reagents, HVJ-E, nocodozole and latrunculin a, that fall under the scope of the Medical Devices Directive (93/42/EEC). In accordance with SLC T30, these reagents should be CE marked, wherever possible. They are marketed for research use, and not clinical application and therefore are not CE marked, nor will the manufactures apply a CE mark for the proposed use. The centre's team have sought advice from the Medicines and Healthcare Products Regulatory Agency (MHRA) responsible for the regulation of CE marked medical devices on this issue.

The reagents will be added to culture media (a CE marked medical device), and their mixing can be considered the manufacture of a new medical device. An exemption from CE marking of medical devices can therefore apply when products are manufactured 'in house' and not placed on the market, as long as certain safeguards are put in place. The inspectors reviewed measures taken by the centre and considered that the risks to patients, their gametes or embryos had been fully assessed and appropriate steps taken to mitigate such risks.

The use of these reagents has been fully validated as evidenced in Hyslop *et al.,* (2016). Assurance can be taken from this paper that the reagents do not compromise the safety or quality of gametes or embryos. The primary concern not addressed by this publication

that would normally be considered during the application of a CE mark, is batch-to-batch variation in the quality/specification of the reagents. For this, the centre has engaged with their Trust's bio manufacturing facility and their pharmacology department's 'Qualified Persons'[2]. A risk assessment has been completed, and procedures for batch testing these reagents (a 'release specification') have been put in place so that the reagents will undergo tests for sterility and toxicity before being accepted for use in PNT. The use of these reagents is also fully incorporated in the centre's QMS. The risk assessment, release specification template and accompanying SOP whilst suitable, were however still in draft format during the inspection (recommendation 3).

In summary, the inspectors are satisfied that it is not possible for the centre to use CE marked reagents, but appropriate steps have been taken to minimise any hazard in accordance with SLC T23.

Process validation (Guidance note 15)
Validation ensures that processes used are effective and do not render the gametes or embryos clinically ineffective or harmful to the recipient.

The centre's recent paper, Hyslop *et al*., (2016) has been submitted as evidence of the process of PNT having been validated. During the inspection, SOPs for the procedure were reviewed which were fully supported by the process as described in Hyslop *et al.,* (2016). With reference to this paper, only early PNT will be used clinically (as described in 'series II' experiments, without sucrose). The inspectors are therefore satisfied that the process of PNT has been validated in accordance with SLC T72.

Embryos created through PNT not required for immediate transfer will be frozen for use in future treatments cycles. No data are available for the purpose of validating the freezing and thawing of embryos created through PNT to ensure it does not render the embryos clinically ineffective. Freezing and thawing PNT embryos was not studied in Hyslop *et al*., (2016), neither was this information requested by HFEA's expert panel. The centre's team expect these embryos to show similar survival rates following freezing and thawing to embryos that have undergone biopsy procedures for PGD. The inspectors have considered what risks to patients and their embryos the absence of this information poses; the most significant being the absence of evidence that embryos created through PNT can be frozen and thawed. The inspectors consider the option to freeze surplus PNT embryos is important and are satisfied that patients will be informed of the risks. Inspectors are also satisfied the centre will monitor closely the survival rates following thawing, and validate the process based on retrospective evaluation of the clinical results (SLC T72). Overall, the inspectors are satisfied that specific validation of freezing/thawing of embryos created using PNT is not sufficiently justified.

A focus of the centre's research is to further refine the technique, particularly the carryover of abnormal mitochondria. Each clinical procedure is likely to be videoed for traceability purposes and for analysis to refine the process. Any changes to the protocol will be fully validated before being implemented. The centre will inform the executive of any such changes.

Third party agreements (Guidance note 24)
The centre's third party agreements are broadly compliant with HFEA requirements.

[2] 'Qualified Person'; a formal role under the pharmaceutical regulations whose primary responsibility is to certify batches of medicinal products prior to use in a clinical trial (human medicines products only) or prior to release for sale and placing on the market.

TPAs have been listed on the application form for Cosmobio and Calbiochem for the supply of the three reagents discussed above (see 'CE marking'). These companies have however declined to sign TPAs as the marketing and supply of those reagents is not intended for clinical application. The inspectors have considered the risks of the absence of a TPA with these companies, the most significant relating to SLC T114(e) specifying that a TPA must contain: 'any specific criteria that the service provided by the third party must meet, particularly in relation to quality and safety'. The inspectors are satisfied with steps taken by the centre to assure themselves that these suppliers have a robust QMS in place, and that the centre has implemented procedures as described above to test the quality and safety of these reagents.

TPAs were not available for the two local laboratories that will perform safety testing on the reagents, nor with the local Trust hospital operating theatres at which very occasionally egg collections may take place when additional anaesthetic support is required (recommendation 4).

Adverse incidents (Guidance note 27)
Reporting and investigation of adverse incidents is important to ensure that centres share the lessons learned from incidents and continuously improve the services it offers. 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.

Staff engaged in licensed activity

Person Responsible (PR)
Staff

Person Responsible (Guidance note 1)
The PR remains suitable. The PR is aware of requirements to vary their licence to permit treatments with MST and to add additional embryologists competent in PNT (CoP 33.4).

Staff (Guidance note 2 and 33)
The centre is broadly compliant with HFEA requirements to have suitably qualified and competent staff, in sufficient number, to carry out the licensed activities and associated services. The centre has access to a multidisciplinary team, including mitochondrial disease specialists, reproductive specialists, embryologists, clinical geneticists, genetic counsellors and molecular geneticists (CoP 33.2). A senior mitochondrial disease specialist will be involved in deciding whether a particular patient should receive mitochondrial donation treatment (CoP 33.1).

Expert consultants in mitochondrial donation have been assigned to oversee separately the patient and donor pathways. Specific training on the mitochondrial donation pathway is to be provided to all staff at the centre during February 2017. The PR has provided assurance that there are suitably experienced and qualified nursing staff in post to support patients seeking mitochondrial donation and mitochondrial donors, however the lead nurses who will specifically work alongside the clinicians have not been agreed as yet, therefore specific training and assessment of competence relative to this area of practice has not been completed (recommendation 6).

Mitochondrial donation practitioner (Guidance note 33)
The centre has applied to add one embryologist, Dr Louise Hyslop, to their licence as an authorised practitioner of PNT. 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. An assessment of the KPI data submitted is presented in Annex I (within this report) and full data submitted by the centre, and the remaining supporting information is presented in Annex II (submitted alongside this report). The Committee should note that Dr Hyslop performed all clinically relevant PNT experiments in Hyslop *et al.,* (2016), and whilst the assessment in Annex I draws upon the experiments in this paper, it also includes additional data generated since its publication.

The centre has in place a five year plan, supported by their Trust and NHS England funding, that will see at least one additional embryologist recruited to contribute to the PNT program. At the time of the inspection the centre was about to advertise 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.

Welfare of the child and safeguarding

Welfare of the child (Guidance note 8)
The implications of the variation on relevant practices were reviewed; the inspectors were satisfied that this variation has no additional implications beyond those assessed at the centre's last renewal inspection and, following a recommendation, were considered compliant.

Safeguarding (Guidance Note 25)
The implications of the variation on relevant practices were reviewed; the inspectors were satisfied that this variation has no additional implications beyond those assessed as compliant at the centre's last renewal inspection.

Embryo testing

Preimplantation genetic screening
Embryo testing and sex selection

Preimplantation genetic screening (Guidance note 9);
Embryo testing and sex selection (Guidance note 10)
Embryos created following MST or PNT will not be subject to further biopsy for the purposes of PGD or PGS (CoP 33.9).

2. The experience of patients

Treating patients fairly (Guidance note 29)
The implications of the variation on relevant practices were reviewed; the inspectors were satisfied that this variation has no additional implications beyond those assessed as compliant at the centre's last renewal inspection.

Counselling (Guidance note 3)
It is important to ensure that counselling support is offered to patients and donors providing relevant consent. The centre has access to one BICA accredited counsellor, and steps have been taken to ensure sufficient counselling services are available to those seeking treatment or considering mitochondrial donation. The PR is 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. The centre is yet however to provide specific training on the treatment and donation pathway to the counsellor (recommendation 5). Counselling by a BICA accredited counsellor will be complemented by in house discussions of the implications of treatment/donation with nurses at the centre.

Although counselling will be made available to all patients and donors it will not be mandatory. Being mindful that regulations do not require counselling to be received, the inspectors did consider further steps could be taken to remove potential barriers to the acceptance of counselling, such as making the offer clearer in written information and considering the possibility of counselling via telephone or video call (recommendation 5).

Egg and sperm sharing arrangements (Guidance note 12; General Direction 0001)
Whilst it is possible that mitochondrial donors are recruited through egg sharing arrangements, the variation has no additional implications. Relevant practices were reviewed at the centre's last renewal inspection and were compliant.

Surrogacy (Guidance note 14)
Whilst it is possible that those seeking mitochondrial donation may also require treatment involving surrogacy, the variation has no additional implications. Relevant practices were reviewed at the centre's last renewal inspection and were compliant.

Complaints (Guidance note 28)
The implications of the variation on relevant practices were reviewed; the inspectors were satisfied that this variation has no additional implications beyond those assessed as compliant at the centre's last renewal inspection.

Confidentiality and privacy (Guidance note 30)
The implications of the variation on relevant practices were reviewed; the inspectors were satisfied that this variation has no additional implications beyond those assessed as compliant at the centre's last renewal inspection.

Information

Information (Guidance note 4 and 33)
It is important to ensure that patients and donors are given sufficient, accessible and up-to-date information to enable them to make informed decisions. The centre's procedures for providing information to patients and donors are compliant with HFEA requirements.

Information to be provided to those seeking treatment with mitochondrial donation, and potential donors is submitted to the Committee in Annex II. An audit of the information showed that not all guidance in the Code of Practice in relation to mitochondrial donation and treatment has been incorporated. The inspectors considered it is reasonable to expect the information provided complies the Code of Practice (recommendation 8).

Consent and Disclosure of information, held on the HFEA Register, for use in research

Consent (Guidance note 5;6)
The centre's procedures for obtaining consent are compliant with HFEA requirements. This ensures that patients and donors have provided all relevant consents before carrying out any licensed activity.

Legal parenthood (Guidance note 6)
The implications of the variation on relevant practices were reviewed; the inspectors were satisfied that this variation has no additional implications beyond those assessed as compliant at the centre's last renewal inspection.

Disclosure of information, held on the HFEA Register, for use in research (General Direction 0005)
The implications of the variation on relevant practices were reviewed; the inspectors were satisfied that this variation has no additional implications beyond those assessed as compliant at the centre's last renewal inspection.

3. The protection of gametes and embryos

Respect for the special status of the embryo

The centre's ensure that the special status of the embryo is respected when licensed activities are conducted at the centre because:

- licensed activities only take place on licensed premises;
- only permitted embryos are used in the provision of treatment services;
- embryos are not selected for use in treatment for social reasons;
- embryos are not created by embryo splitting;
- embryos are only created where there is a specific reason to do so which is in connection with the provision of treatment services for a particular woman;
- embryos are only stored if those embryos were created for a woman receiving treatment services or from whom a third party agreement applies; and
- embryos will only be created by PNT when the Authority has issued a determination that there is a particular risk that an embryo may have mitochondrial abnormalities, and a significant risk that a person with those abnormalities will have or develop serious mitochondrial disease.

Screening of patients
Storage of gametes and embryos

Screening of patients (Guidance note 17)
The centre's procedures for screening patients are compliant with HFEA requirements. It is important that gamete providers are appropriately screened to minimise the risks of cross infection during treatment, processing and storage of gametes and/or embryos.

Storage of gametes and embryos (Guidance note 17)
The implications of the variation on relevant practices were reviewed; the inspectors were satisfied that this variation has no additional implications beyond those assessed as compliant at the centre's last renewal inspection.

Use of embryos for training staff and research (Guidance note 22)

Use of embryos for training staff and research (guidance note 22)
Embryos will only be used for the purpose of training staff in those activities expressly authorised by the Authority. Patient cytoplasts and donor karyoplasts remaining after treatment may be used for research purposes under the auspices of the centre's research licence for which appropriate consent will be sought.

4. Information management

Record keeping
Obligations and reporting requirements

Record keeping and document control (Guidance note 31)
The implications of the variation on relevant practices were reviewed; the inspectors were satisfied that this variation has no additional implications beyond those assessed as compliant at the centre's last renewal inspection.

Obligations and reporting requirements, including follow-up (Guidance note 32 and 33; General Direction 0005)
The team are aware of obligations for reporting information on mitochondrial donors and treatments.

Documented processes are in place setting out how children born from mitochondrial donation will be followed up, where consent has been given (COP 33.33). 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.

Areas of practice requiring action

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 Acts, Regulations, Standard Licence Conditions, General 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 risk of causing harm to a patient, donor, embryo or to a child who may be born as a result of treatment services, or a significant shortcoming from the statutory requirements. 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, embryo or to a child who may be born as a result of treatment services
- 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' areas 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
1. Premises Following the refit, laboratories will need deep cleaning, and testing completed to evidence appropriate air quality. SLC T17 and T20.	Confirmation that the deep clean has taken place, and evidence of appropriate air quality in all refurbished laboratories must be provided to the centre's inspector. As this recommendation affects all treatments, not just PNT, evidence of an appropriate air quality should be forwarded before any licensed activity takes place in the laboratory.	1. Premises: We have already scheduled cleaning and validation into our refurbishment. An independent Service provider (Vega Services) that specialise in Cleanroom validation will be validating both the isolators and the rooms for air flows, viable and non viable particle counts. This data will be forwarded to the HFEA prior to PNT.	We await confirmation of the air quality before commencing licensed activity.
2. Equipment Following the laboratory refit, validation or revalidation will be required for all equipment to be used during the processing and culture of	Documented validations, and any supporting documents such as SOPs, should be forwarded to the centre's inspector. This recommendation impacts	2. Equipment: As detailed in the departments Validation Master Plan and subsequent documentation, all critical equipment will be validated following the refurbishment as well as all new equipment. The	We request that the centre confirms the validation of necessary critical equipment before recommencing any licensed treatment. The centre should then

embryos for the purposes of PNT, including: • isolators • micromanipulator • lasers • time lapse incubators • any other equipment required during the processing and culture of embryos creating using PNT. SLC T23 and T24.	on all treatments and not just PNT. Therefore, confirmation that equipment has been validated should be provided before licensed treatments resume. However documented validations should be forwarded for all equipment to be used in PNT.	validation reports will be forwarded to the HFEA prior to performing PNT.	forward validations for those pieces of equipment specifically to be used in PNT before starting this procedure.
3. CE marking Documented procedures/templates to assure the safety of non-CE marked reagents (medical devices) are currently in draft format. SLC T23 and T30	Final versions of the centre's risk assessment, release specification template and associated SOP should be forwarded to the centre's inspector by 23 April 2017. Evidence that the first batch of the non-CE marked reagents have been assessed as suitable for release should be sent to the centre's inspector before they are used in clinical treatment.	3. We will forward the HFEA appropriate risk assessments, release specifications and SOPs for all non CE marked consumables used in PNT by the 5th of April 2017. Prior to commencing PNT we will forward our inspector the completed release specification for the first batch of non-CE marked products that will be used.	The executive is satisfied with the response provided, and we await the final risk assessment/SOP, followed by the outcome of testing of the first batches of reagents. This must be received before commencing PNT.
4. Third Party Agreements TPAs are required for: • the two laboratories that will test the non-CE marked	Copies of these TPAs should be forwarded to the centre's inspector by 23 April 2017.	4. We have attached a copy of the TPA with the Trust theatres. We will also send our inspector a copy of the TPA for the companies providing "top-	The TPA with the Trust theatres has been received and is suitable. We await receipt of the

reagents for sterility and toxicity; and • the Trust theatres that may be used for complex egg collections. SLC T111-114.		up" testing for our non-CE marked products. These documents will be submitted by the 05th of April 2017.	remaining two TPAs by 23 April 2017.
5. Counselling The counsellor is yet to receive training in the mitochondrial donation/treatment pathway. Inspectors considered steps could be taken to facilitate the uptake of counselling by patients and donors. SLC T12 and T58(f).	The counsellor should receive appropriate training in the mitochondrial donation pathway, and confirmation should be forwarded to the centre's inspector by 23 April 2017. When responding to this report, a brief comment should be provided on the steps taken to facilitate the uptake of counselling. Any documents, such as patient information, amended as a consequence should be forwarded to the centre's inspector by 23 April 2017.	Counsellor to attend NFCL seminar - Working Towards Clinical Mitochondrial ART. Counsellor to attend NFCL joint clinics x2 to experience the clinical work-up. Counsellor to have 1-2-1 training discussion with Dr Stewart regarding specifics of process that raises issues. Counsellor invited to attend clinics and sessions at all stages of the pathway to acquaint herself. We hope to have additional counsellor facility as the programme progresses and we will ensure that any new staff are afforded similar provision.	An appropriate training package has been put in place for the counsellor. Confirmation that this has been completed should be forwarded to the centre's inspector by 23 April 2017. Patient information has also been updated to better promote the availability of counselling and is submitted alongside this report.
6. Staff training A nurse has not yet been identified and specifically trained or assessed as competent for their role in mitochondrial donation and	Confirmation that a nurse(s) has been trained and assessed as competent should be forwarded to the centre's inspector by 23 April 2017.	Nursing staff taking on the mitochondrial donation work come from the existing staff and therefore are well aware of the development of the programme and its course. To build on that and for the newer	An appropriate training package has been put in place. Confirmation that this has been completed should be forwarded to the centre's inspector by 23 April 2017.

treatments. SLC T12 and T13.		members of the team we have a seminar in place which will be repeated as required to acquaint the whole team with the pathways invovled. (Working Towards Clinical Mitochondrial ART). Those leading the nursing elements of the patient pathway will attend the joint mitochondrial clinic (NFCL) to understand the detailed discussions undertaken at that point and will receive specific small group teaching on the consents (HFEA and In house), implications documents and procedures. Dr Stewart will sit with those giving specific information to ensure confident and competent before signing off.	

Other areas of practice that requires improvement

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 statutory requirements or good practice.

Area of practice and reference	Action required and timescale for action	PR Response	Executive Review
7. Donor screening A documented procedure (a checklist) for screening donors required updating to reflect screening requirements of mitochondrial donors, in particular those screening tests not required in comparison to egg donors. SLC T52 (a-h) and T126; Code of Practice guidance 33B.	The centre should audit their documented procedure against the mitochondrial screening requirements, amend as appropriate, and forward a copy to their inspector by 5 April 2017.	This has already been audited please see attached a copy of the Audit on Donor Screening (Clinical/Process/4).	Appropriate action has been taken to update the documented procedure. No further action required.
8. Information Written information for mitochondrial donors or patients did not explicitly cover all guidance issued in the Code of Practice. CoP Guidance Note 33.	Written information should be reviewed against the guidance issued in the Code of Practice, and amended as appropriate or consideration given to why its inclusion might not be appropriate. A summary of actions taken should be provided when responding to this report, and any amended documents	This has already been audited please see attached the Audit for "Donor Information for Mitochondrial Donors (Clinical/Patient information/10).	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 inspectors are satisfied that guidance in the CoP has been fully incorporated into the centre's information. All

	forwarded to the centre's inspector by 5 April 2017.		information leaflets are submitted to the Committee alongside this report. No further action required.

Reponses from the Person Responsible to this inspection report
Thank you - we have undertaken relevant document changes as requested. We will forward the validation programme for equipment when finalised. We have a training package currently being implemented for the Counsellor and Nursing staff to ensure that they are well equipped to deal with both patient and donor pathways.

Annex 1: Assessment of embryologist competency in PNT/MST

The following is an assessment by the inspector of the applicant's ability to meet the requirements of General Directions 0008. Full data submitted by the centre are presented in 'Annex 2: supporting information'.

Applicants name: Dr Louise Hyslop
Procedure(s) applied for: Pronuclear transfer (PNT)

General Directions 0008 KPIs	**Evidence (see Annex 2)**
ii) embryo survival rate (which must exceed 70%).	81.6% (93/114 embryos)
iii) blastocyst development rates (which must be no less than 50% of that observed in the control embryos at day 5. Where possible, controls should be age-matched to the karyoplast donor).	PNT: 32.3% (31/96) Controls: 56.7% (17/30)
iv) rate of carryover of mtDNA (should not on average exceed 2% and no greater than 10% per embryo).	Undetectable in 5/14 embryos <2% in 6/14 embryos >2 - <5% in 3/14 embryos >5% in 0/14 embryos Data confirms that the average carry over is less than 2% in 79% of embryos tested (11/14), and never greater than 10%. The mean average is 0.96%, and median is 0.14.