Minutes of Authority meeting 15 December 2016

Strategic delivery:	☐ Setting standards	☐ Increasing and informing choice	☐ Demonstrating efficiency economy and value
Details:			
Meeting	Authority		
Agenda item	2		
Paper number	HFEA (18/01/17) 819		
Meeting date	18 January 2017		
Author	Erin Barton, Governance Manager		
Output:			
For information or decision?	For decision		
Recommendation	Members are asked to confirm the minutes as a true and accurate record of the meeting		
Resource implications			
Implementation date			
Communication(s)			
Organisational risk	☐ Low	☐ Medium	☐ High
Annexes			

Minutes of the Authority meeting on 15 December 2016 held at ETC Venues, Victoria, 1 Drummond Gate, London SW1V 2QW

Members present	Sally Cheshire (Chair) Rebekah Dundas Dr Andy Greenfield Yacoub Khalaf Margaret Gilmore	Ruth Wilde Dr Anne Lampe Anthony Rutherford Kate Brian Bobbie Farsides
Apologies	Bishop Lee Rayfield Anita Bharucha	
Observers/Presenters	(Department of Health)	
Staff in attendance	Peter Thompson Juliet Tizzard Catherine Drennan Anna Rajakumar	Erin Barton

Members

There were 10 members at the meeting, 6 lay members and 4 professional members

1. Welcome, apologies and declarations of interest

1.1. The Chair opened the meeting by welcoming Authority members and members of the public. As with previous meetings, it was being audio recorded and the recording would be made available on the HFEA website to enable interested members of the public who were not able to attend the meeting to listen to the HFEA's deliberations.

1.2. Apologies were received from Bishop Lee Rayfield and Anita Bharucha.

1.3. The Chair welcomed Bobbie Farsides, Professor of Clinical and Biomedical Ethics at the Brighton and Sussex Medical School, who had just been appointed to the Board. The Chair also said farewell to Rebekah Dundas who had been a member of the Authority for a decade, as this was her last meeting.

1.4. Declarations of interest were made by:

- Ruth Wilde (Senior Fertility Counsellor at a licensed centre).
- Kate Brian (Regional organiser for London and the South East for Infertility Network UK)
- Yacoub Khalaf (Person Responsible at a licensed centre)
- Anthony Rutherford (Person Responsible at a licensed centre)

2. Minutes of Authority meeting held on 16 November 2016

2.1. Members agreed the minutes of the meeting held on 16 November, for signature by the Chair.

3. Mitochondrial donation

3.1. The Chair introduced the main topic of the meeting; to decide whether to approve the use of mitochondrial donation techniques in clinical practice in the UK. Members were reminded of the long history behind the decision including the establishment of an independent expert panel of scientists and clinicians in 2011 to consider the safety and efficacy of mitochondrial donation techniques, in particular pronuclear transfer (PNT) and maternal spindle transfer (MST).

3.2. Regulations were debated and passed by Parliament in February 2015 and a regulatory framework was put in place for when the regulations came into force in October that year. It was widely understood during the Parliamentary debates that the HFEA would need to take a decision, based on research evidence, as to when it would be ethical to move from research to clinical treatment. Early in 2016 key pieces of research had been published which led the HFEA to reconvene the expert panel for a fourth time. Their report, which was published on 30 November 2016, suggested that research had progressed to the point where we should consider offering it in clinical treatment.

Safety and efficacy

3.3. Authority member and Chair of the expert panel, Dr Andy Greenfield, introduced the report and presented an overview of the most recent research using MST and/or PNT. The expert panel reviewed this research extensively and formed a considered judgement that the blastocysts produced using these techniques were of sufficient quality to be considered for use in clinical practice. The panel concluded that it was now appropriate to offer mitochondrial donation techniques as a clinical risk reduction treatment for carefully selected patients.

3.4. The panel's main concern was a phenomenon referred to as 'reversion' observed in research on embryonic stems (ES) cell lines derived from embryos generated using these techniques. In a minority of cases, mtDNA carried over with the maternal spindle or parental pronuclei could come to predominate after extended periods of culture in vitro. The Chair of the expert panel explained the difficulties in interpreting the significance of this data. ES cells were not an exact model for post-implantation development in vivo. If reversion did occur in vivo, there was the possibility that a child might be born with a mitochondrial disease following MST or PNT.

Patient selection criteria

3.5. Currently, many families with such inherited diseases had no effective treatment options for avoiding transmission of mitochondrial diseases to offspring. The Chair of the expert panel explained that the use of pre-implantation genetic diagnosis (PGD) to detect mtDNA mutations was difficult and variably successful, especially in those patients in whose germ line there were likely to be high levels of heteroplasmy or homoplasmy for the abnormal mtDNA (this meant they had either a high proportion of abnormal mtDNA or all abonormal mtDNA).

3.6. In light of recent research and the potential risk of reversion, the panel believed that it would currently be inappropriate to offer MST or PNT to patients who were likely to have an unaffected child using PGD. However, the expert panel recommended that MST and PNT should be offered as a risk reduction strategy to selected patients for whom PGD would be inappropriate.

3.7. The Chair of the expert panel provided clarification on the following points:

- Recent research did not indicate any significant difference between the two techniques, MST and PNT, with regard to safety, efficacy or the risk of reversion.
- Identification of patients suitable for MST or PNT on a case-by-case basis would be a matter of clinical judgement.
- PGD should not be necessary following MST or PNT on the basis that the embryologists performing these techniques would be highly skilled and performing a biopsy may cause further damage to the embryo. Prenatal testing was a more effective form of follow-up because reversion occurred post-implantation.
- The expert panel did not prescribe any definitive response to adverse incidents following either technique and the Authority would exercise their best judgment based on the circumstances. Members should be reassured that the embryologists permitted to use these techniques would have demonstrated that they could meet very high standards.
- The recommendation to offer treatment to a narrower cohort of patients initially was an ethical decision and was not based on any scientific evidence that it was easier to demonstrate efficacy or safety in these patients.
- It was unclear whether ES cells in culture would behave in the same way as a developing embryo. Therefore, the panel believed that further research using ES cells may not provide greater understanding of reversion. Gaining further knowledge of possible reversion in human embryos would require further research using clinical data.
- The panel recommended consideration of haplogroup matching because risks associated with a mito-nuclear mismatch were currently theoretical. They recommended that if these techniques were to be used in clinical practice, the latest evidence regarding how mitochondrial DNA haplotypes affected mito-nuclear interactions should be considered in order to inform the donor selection process.

3.8. Members stressed the importance of monitoring clinical outcomes and ensuring that a robust system was in place to collect this data. All data collected on clinical outcomes should be reviewed. Some members felt that it would also be useful to review current guidance on PGD for mitochondrial disorders, as well as the process for collecting clinical outcomes for PGD.

3.9. Given the novelty of these techniques, members felt that the provision of expert information and counselling were of paramount importance in managing patients' expectations, both during and after treatment. Members also felt that it was important to regularly review patient information and guidance for clinic staff when data on clinical outcomes became available.

3.10. Members considered that, with a small number of potential patients and donors currently waiting for this treatment, any patients who chose to identify themselves in the media would be at risk of the donor identifying any resulting children. Members acknowledged that, whilst it was not possible to prevent patients from making these decisions, the implications of such a decision should be discussed during counselling.

3.11. Members were asked to consider the safety and efficacy of the techniques and decide whether research on MST and/or PNT had now progressed to such a point where it would be appropriate to allow either technique in clinical practice.

Further to this, if the Authority agreed the above, they were asked to consider whether these techniques should initially be offered only to a narrower cohort of patients, who met specific criteria identified in the expert panel's report.

Decision: After an extensive and detailed debate, all members agreed with the panel's recommendation to approve the use of mitochondrial donation techniques in clinical practice in the UK as a risk reduction strategy for selected patients for whom preimplantation genetic diagnosis (PGD) would be inappropriate. The Chair confirmed that both Bishop Lee Rayfield and Anita Bharucha had also communicated their agreement with the panel's recommendation.

3.12. The Chair stressed the importance of a unanimous but cautious approach, and assured members that all of their concerns would be taken into consideration. Members agreed to continue to work with the Executive to implement any necessary changes.

Licensing framework

3.13. The Scientific Policy Manager reminded members of the previously agreed regulatory framework and explained that the decision to offer the treatment to the narrower cohort of patients would require some changes to the guidance and process for approving applications.

3.14. The Scientific Policy Manager informed members that in order to implement the expert panel's recommendation, an additional requirement would need to be introduced into the Code of Practice guidance, that mitochondrial donation could only be offered to patients for whom PGD was not appropriate. Further to this, an additional requirement was proposed in General Direction 0008 and the Code of Practice Guidance which would be reflected in the Guidance Note for use by the Statutory Approvals Committee. These additions would support the explicit narrowing of the scope to those for whom PGD was not clinically prescribed or recommended. The additional wording would provide guidance around the threshold for such patients.

Implementing the patient selection criteria

Members were asked to:

- agree the proposed approach for considering patient selection
- agree changes to the Code of Practice Guidance Note 33 on mitochondrial donation and referenced explanatory note designed to aid the Statutory Approvals Committee
- agree changes to paragraph 7 of General Direction 0008
- agree that the amendments of any relevant decision trees and patient application forms should be delegated to the appropriate Committees.

3.15. Members raised concerns about the availability of clinical geneticists with the relevant expertise in mitochondrial disease to support both the Licence Committee and the Statutory Approvals Committee at the different stages of approval. Members were reassured that a number of appropriately qualified experts had already been identified as potential peer reviewers and specialist advisors, and that committees could call upon international expertise to avoid any potential conflict of interest in such a narrow field.

Decision: All members agreed with the proposed updates subject to minor amendments to the wording, and on the basis that all of their concerns would be addressed in the relevant documentation.

Prenatal testing

3.16. The Scientific Policy Manager explained that due to the known risk of reversion, the panel had suggested that prenatal testing should be offered to all women undergoing treatment, but recognised that it was unlikely that all women would accept this offer and that they would be under no obligation to do so. The panel also felt it was important to counsel patients on the risk of miscarriage associated with these techniques.

3.17. Members were asked to agree changes to the Code of Practice Guidance Note 33 on mitochondrial donation recommending prenatal testing to all those who underwent mitochondrial donation.

Decision: All members agreed with the proposed updates.

Assessing embryologists' competency

3.18. The Authority had previously agreed that in order for a clinic to vary their licence to include mitochondrial donation techniques, the PR must demonstrate that the embryologists who would be performing these techniques were able to meet a predetermined set of performance indicators.

3.19. In light of recent research, the panel recommended the following thresholds be applied:

- **Embryo survival rates** - must exceed 70%
- **Blastocyst development rates** - 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
- **Rates of carryover of mtDNA** - should not on average exceed 2% and be no greater than 10% per embryo. (Hyslop et al - After optimisation, mtDNA carryover was reduced to <2% in the majority (79%) of PNT blastocysts so this would be achievable)

The panel noted that these parameters would need to be reviewed, as the techniques developed over time.

3.20. Some members were concerned that the wording used may prohibit a more flexible application of the thresholds where this might be appropriate, but were reassured that the performance indicators would be achievable by appropriately qualified staff.

Decision: Members agreed with the panel's recommended performance indicators, subject to further consideration of the wording.

4. Chair's signature

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

Signature 

Chair **Sally Cheshire**

Date **3/1/2017**