

HUMAN FERTILISATION AND EMBRYOLOGY AUTHORITY

MINUTES OF THE SCIENTIFIC AND CLINICAL ADVANCES ADVISORY COMMITTEE

Meeting held at Etc. venues Bonhill House, 1-3 Bonhill Street, London EC2A 4BX on Wednesday 22 October 2014

COMMITTEE MEMBERS	Sue Price (Chair) Andy Greenfield Alan Thornhill	Daniel Brison (external advisor) Melanie Davies (external advisor) Joyce Harper (external advisor) Robin Lovell-Badge (external advisor) Raj Mathur (external advisor)
COMMITTEE APOLOGIES	Debbie Barber	
EXECUTIVE	Anjeli Kara (Secretary) Renate Cummings-Benson	Trisram Dawahoo Hannah Verdin Matthew Watts
SPEAKERS	Siobhan Quenby	
OBSERVERS	Kim Hayes (DoH)	

1. Welcome, apologies and declarations of interest

- 1.1 The Chair welcomed Committee members to the meeting and introduced Raj Mathur as a new external advisor. Siobhan Quenby and Kim Hayes were welcomed as guest speaker and an observer on behalf of the Department of Health, respectively.
- 1.2 The Committee was informed that both Hossam Abdalla and Lorraine Young had stepped down as Committee members.
- 1.3 The Chair conveyed apologies on behalf of Debbie Barber.
- 1.4 In relation to the meeting agenda, interests were declared by Daniel Brison and Alan Thornhill.

2. Matters arising

- 2.1 Minutes of the meeting held on 6 June 2014 were agreed remotely prior to the meeting. Matters arising from the previous minutes were noted and agreed.

3. Chair's Business

- 3.1 Following previous discussions where the Committee agreed that it would benefit from individuals with a patient voice, and clinical expertise in andrology and embryology, the Chair updated the Committee on the recruitment of new external advisors.

3.2 It was highlighted that the Committee would also benefit from recruiting an epigeneticist given the recent change in membership. Suggestions of potential external advisors were welcomed by the Chair.

4. Committee workplan

4.1 The Committee discussed its forward workplan and confirmed priorities for upcoming meetings.

4.2 Based on feedback from February 2014, the Committee was reminded of the modified approach to the annual horizon scanning process that will take place at the next meeting (February 2015). Changes include extended time for the Committee to review any topics highlighted through horizon scanning and for the Executive to write a comprehensive briefing note.

4.3 It was noted that the Committee is willing to extend the length of meetings to address topics to an appropriate level of detail.

5. Reproductive immunology update

5.1 In June 2014, the Committee revisited the topic of reproductive immunology by considering paper [SCAAC (06/14) 02], which asked the Committee to:

- review recent literature in the area;
- consider the safety and efficacy issues that may arise from such techniques; and
- review HFEA website information on reproductive immunology, including any studies that should be added to the website as highlighted articles

5.2 Discussions raised further questions; particularly, whether patients should be given steroids in the first trimester as a safety concern and whether blood tests predict miscarriage or the population of uterine natural killer cells. Siobhan Quenby was invited to discuss these areas further and to update the Committee on any relevant additional information with regards to reproductive immunology.

5.3 Siobhan Quenby highlighted from the outset that reproductive immunology is a constantly evolving area of assisted reproduction and that it is key to consider both the clinical and laboratory data. As reproductive immunology explores how the immune and reproductive systems interact with one other, and is based on the theory that miscarriage may be caused by an immune response to the embryo, it was suggested that:

- rather than an embryo implanting into the endometrium, 'stromal cell selection' occurs whereby stromal cells from the endometrium encapsulate the embryo; and

- there may be a two-step process to embryo selection – screening for embryo abnormalities and endometrium receptivity ('decidualisation' where there is an influx of immune cells).
- 5.4 It was also presented that a correlation exists between the number of natural killer (NK) cells and the decidualisation process, and that steroids appear to reduce the production of cytokines (proteins produced by immune cells – including NK cells – that are important in cell signalling).
- 5.5 A recent study conducted by Tang et al (2013) was explored in greater detail. The study assessed the feasibility of screening women with idiopathic recurrent miscarriage for high uterine NK cell density and randomising to treatment with prednisolone or placebo when pregnant. There were no pregnancy complications or serious adverse fetal outcomes. Although this was a feasibility trial, it suggested that the number of uterine NK cells relates to patients with an increased chance of miscarriage.
- 5.6 In conclusion, Siobhan Quenby highlighted that patients should be aware of advances in basic science and meta-analysis of trials and observational studies, and that tests and treatment offered should be based on both strands of evidence. Additionally, terminology used by clinicians should be addressed – 'natural killer' cells have no killing ability and it is often perceived by patients that these cells are responsible for the failure of an embryo to implant.
- 5.7 On discussion, it was noted that there are conflicting views about the value of natural killer cell assessment and immunosuppressive therapies. In particular, the notion as to whether the endometrium selects embryos during normal reproduction, as the support for this comes from assisted reproduction in which embryos are much more likely to be abnormal.
- 5.8 The aim of the patient information provided on the HFEA website is to provide a fair, balanced and accurate picture on current progress regarding reproductive immunology to assist people who are seeking to make decisions about fertility treatment. It was voiced that this may be conveyed to greater effect if information on embryo selection (eg, the two key factors for a successful pregnancy: quality/euploid embryos and endometrial receptivity) and miscarriage was addressed prior to information on what treatments may then be offered (eg, reproductive immunology) – fundamentally, approaching patient information from a patient's perspective of 'why did my treatment cycle fail?'

Actions

5.9 The Chair invited Siobhan Quenby and the Committee to review HFEA website content regarding reproductive immunology and highlight the most important messages to convey.

6. Information for Quality – update on public consultation

6.1 The Regulatory Policy Manager updated the Committee on ‘Information for Quality’ – an ongoing programme of work that seeks to improve the effectiveness of information the Authority holds and collects.

6.2 It was explained that to achieve programme aims, continuous dialogue with stakeholders is essential. For this reason, an advisory group was established that:

- provides advice to the Authority on a range of strategic and operational issues at all stages of the programme;
- has a diverse membership that represents different interests; and
- ensures that the process takes account of views of all key stakeholders, is balanced and comprehensive.

6.3 Expert groups comprised of a variety of stakeholders have also been setup to focus on the following project strands and to feed back to the advisory group:

- **Data dictionary:** Develop and define the data required by the HFEA so that there is a clear rationale for each piece of data collected and how it is used
- **Data submission:** Improve how data is submitted to the HFEA
- **Transaction processing:** HFEA in-house group dedicated to infrastructure
- **Data outputs and reporting:** Review the reports produced by the HFEA to ensure they meet stakeholder and HFEA needs
- **Website and publishing:** Review the HFEA website so that information for patients and the general public is published in a helpful, accessible and balanced way

6.4 After engaging with stakeholders during summer 2014, the Committee was informed that the programme is now at consultation phase: expert groups have outlined their thoughts, plans and/or suggestions on the programme’s aims to which the sector can put forward their thoughts.

6.5 The Committee was supportive of the programme and its aims. In relation to its priorities, the Committee highlighted the importance of:

- **collecting sufficient data to enable long-term follow-up studies of patients and children born from assisted reproductive techniques**

The suggestion to record NHS numbers would be a welcome addition in this regard and would avoid studies that rely on probabilistic linkage and would ‘future proof’ the database by providing a consistent link.

- **recording the culture medium used in each treatment cycle**

It was noted that a member of the advisory group is in the process of writing a formal application to the Information for Quality programme board that details reasons to include this field in its dataset. The Committee was informed that this would be the process moving forward for adding or removing data fields to or from the dataset.

6.6 On reflection of the consultation document – ‘Information for Quality: We want your views’ – the Committee supported plans to accredit electronic patient record systems (used by some clinics) to meet the Authority’s standards of data submissions and thought that this would result in better quality data. The importance of centres to be able to access their data was also stressed.

6.7 The Committee also welcomed the suggestion to have the success rate per embryo transferred as the top line comparative figure for centres and voiced that inspection reports would be a useful source of qualitative information for people seeking treatment; however, they could be simplified to make easy reading.

Actions

6.8 The Committee was encouraged to respond to the consultation via an online survey or by attending a UK workshop. The Committee was informed that consultation findings will be fed back to the advisory group and thereafter the Authority at the start of 2015.

7. HFEA website – information update

7.1 An expert group that makes up the Information for Quality programme is looking at how the Authority presents and publishes information (‘IfQ05 Websites and publishing’). The Web Editor informed the Committee of this, the importance of conveying information online across multiple platforms (eg, mobile devices, tablets) in a succinct manner, and the outcomes of recently conducted user research which saw members of the public navigate the HFEA website and highlight areas for improvement.

7.2 The Digital Communications Manager moved on to discuss:

- whether the HFEA website covers assisted reproductive techniques and technologies currently used in the sector
- how the Committee could be involved in the overall production of HFEA website pages that include scientific information

7.3 It was noted that general attention to detail and content online is shorter than in print and as such, key messages should be found at the top of website pages. As a result, the Committee suggested that where appropriate, alternative methods for

delivering information should be provided (ie, video content and diagrams) to avoid static information. Additionally, an interactive interface could be introduced so that end users could highlight to the Authority whether website content has been 'fit for purpose'.

7.4 While the Committee identified areas that could be addressed (eg, time lapse technology and embryo donation for research), the size of the upcoming project was voiced and the Committee suggested that a working group should be setup for the technical reconstruction and content of the HFEA website, alone.

7.5 The Committee suggested that when topics are discussed as part of their workplan they could include a review of related website content, whereby the most important messages to convey to people seeking, or in the process of receiving, fertility treatment are highlighted.

Actions

7.6 The Committee will help identify any assisted reproductive techniques and technologies currently used in the sector that should be mentioned on the HFEA website, by reviewing a site map provided by the Executive. When topics are discussed as part of the workplan, the Committee can highlight the most important messages to convey on the HFEA website – the topic discussed at this meeting (reproductive immunology) will be a 'trial run' to see how this could work.

8. Annual committee review

8.1 It is recognised good practice for any standing committee of a public body to review its governance arrangements and effectiveness annually. As such, the Committee was asked by the Authority to conduct a review of its effectiveness and activity.

8.2 Areas to evaluate, and the Committees initial thoughts on these areas, included:

- **Having the right delegated functions, responsibilities and goals**
Amendments to the horizon scanning process (as outlined in section 4.2) were welcomed by the Committee in streamlining their workload.
- **Having the right composition and size**
The Committee noted that although membership is fewer than needed, missing areas of expertise have been identified. These are being addressed by the Executive and take into account the recruitment of new Authority members.
- **Frequency and length of meetings to match the business**
As noted in section 4.3, the Committee is willing to convene for longer meetings to discuss topics in appropriate detail.
- **Relationships with the Executive**

While the Committee has a good relationship with the Executive, it was noted that it is not always informed about what other Authority Committees discuss.

- **Good quality administrative support (eg, accurate minutes)**
- **Ability to have candid discussions**

The Committee voiced that they are able to speak openly and learning is often 2-way; particularly when topics are discussed in detail throughout the year.

Actions

8.3 The Committee was encouraged to complete and send their annual review forms to the Committee Secretary by the agreed date.

9. Any other business

Mitochondria draft regulations

9.1 The Chair updated the Committee by noting that the Department of Health consulted on draft regulations in spring 2014 and announced that they would proceed with putting regulations before parliament. The regulations still need to be debated by both houses of parliament.

9.2 The expert panel, convened by the Authority, submitted their latest report on safety and efficacy of two mitochondrial techniques – maternal spindle transfer (MST) and pro-nuclear transfer (PNT) to government in June 2014. Since then, the panel has also produced and submitted a report on the safety and efficacy of a new technique for mitochondria replacement: polar body transfer (PBT). An overarching lay summary has been produced for public and parliament.

'Embryo testing' workshop

9.3 The Committee was invited to attend an embryo testing workshop to be held by the Authority in London on Thursday 4 December between 10.00am to 4.30pm. The workshop will address embryo testing on a wider basis by covering:

- New and upcoming techniques on the horizon
- Ethics around the disclosure of genetic information
- The interpretation of test results.

Next meeting: Wednesday 4 February 2015

I confirm this to be a true and accurate record of the Meeting.

Signature:

Susan Rice