

**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 EC2A4BX  
5th February 2014

**COMMITTEE MEMBERS PRESENT:** Sue Price (Chair) Joyce Harper (external advisor)  
Andy Greenfield Daniel Brison (external advisor)  
Alan Thornhill  
Hossam Abdalla

**COMMITTEE MEMBERS APOLOGIES:** Melanie Davies  
Debbie Barber  
Robin Lovell-Badge  
Lorraine Young

**MEMBERS OF THE EXECUTIVE:** Anna Rajakumar  
(Secretary)  
Hannah Verdin  
Jessica Watkin  
Anjeli Kara

**OBSERVERS:** Kim Hayes  
(Department of Health)

- 1. Apologies, welcome and declaration of interests**
  - 1.1. The Chair conveyed apologies received from Lorraine Young, Melanie Davies and Robin Lovell Badge.
  - 1.2. The Chair welcomed observer Kim Hayes (Department of Health).
  - 1.3. Interests were declared by Daniel Brison, Alan Thornhill and Hossam Abdulla.
  
- 2. Matters arising and previous actions**
  - 2.1. The minutes from the Committee's meeting on 30 October 2013 were agreed remotely prior to the meeting and the matters arising from the previous minutes were noted and agreed.

**3. Chair's business**

- 3.1. The Chair updated the Committee on the new external advisor appointment terms and thanked the external advisors for their hard work to date.
- 3.2. The Chair requested feedback from the Committee on areas of speciality required by the Committee in order to recruit new external advisors. Members agreed that the Committee would benefit from individuals with a patient voice or with clinic expertise in andrology and/or embryology.

**4. Embryo culture media update**  
**[SCAAC (02/14)01]**

- 4.1. Anjeli Kara (AK) presented a paper on embryo culture media composition. In December 2011 SCAAC discussed this topic and requested ongoing updates on the progress in research on culture media and their components.
- 4.2. Members were asked to consider the progress of research into the effects of culture media components, advise the Executive if they were aware of any developments in research, reflect on their views, and identify what needed to be communicated to the Medicines and Healthcare products Regulatory Agency (MHRA).
- 4.3. Committee members identified additional recent work being conducted in this area, which have been footnoted in the Committee paper following the meeting. Members highlighted that it would be useful to understand the effects of micronutrients shown to affect DNA methylation (e.g. folate and methionine). Perinatal outcomes and potential epigenetic effects were also discussed and the Committee felt it was a priority to monitor research in this area. They reiterated the need for large scale randomised controlled studies that compare culture media.
- 4.4. A Committee member highlighted the ACE Best Practice Workshop on Culture Systems where embryo metabolism and sequential media systems were discussed in relation to best practice. The workshop also explored how clinics should validate these products and discussed the pre-purchase tendering processes clinics use for culture media. Further to this the Committee discussed the impact of morphokinetic analysis on the study of culture media and suggested that research in this area should be monitored.
- 4.5. The Committee also noted that it would be useful to understand the current position of the expert panel coordinated by the MHRA and would like to be kept up to date on the joint working on culture media and CE marking

**Decision**

- 4.6. The Committee agreed that developments in culture media should continue to be monitored regularly remaining one of the Authorities high

priorities and agreed to pass this information on to MHRA, with the addition of studies referred to at 4.3.

**5. Prioritisation of issues identified through the horizon scanning process**

**[SCAAC (02/14)02]**

- 5.1. Anna Rajakumar (AR) introduced a paper on the prioritisation of issues identified through the horizon scanning process. Issues were mostly identified from journal articles, conference attendance and recommendations from experts.
- 5.2. A full list of identified issues (Annex A), which had been categorised as high, medium or low priority were presented. Members were asked to send on any further comments relating to Annex A following the meeting.
- 5.3. The Executive presented the Committee with a summary of the briefing notes on high priority issues (Annex B), which focused on freeze-all cycles, female fertility preservation and the safety of embryo biopsy as highlighted for 2014/15.

**Freeze-all cycles**

- 5.4. The Committee was asked to consider the benefits of 'freeze-all' cycles to agree on whether a thorough analysis of the current research in this area was required and whether new advice for patients and the sector would need to be formulated. The Executive also highlighted that it would be important to consider how freeze-all cycles are reported to HFEA and how success rate data is presented on Choose a Fertility Clinic (CaFC) and it was noted that the HFEA's Information for Quality Programme advisory group will review how freeze all cycles are reported and published
- 5.5. The Committee agreed that more detailed work in this area would be beneficial. A Member highlighted some further relevant studies including a meta-analysis looking at perinatal and obstetric outcomes following frozen embryo transfer. A Member also highlighted that there are some useful studies using Scandinavian cohorts that should be reviewed and a new elective freeze-all EFREEZE clinical trial for which funding is being sought. Further to this the Committee suggested that the Executive may like to consider inviting experts in this area to present at SCAAC.

**Female fertility preservation**

- 5.6. The Committee was asked to consider the viability of egg freezing techniques and resulting success rates, and reflect on whether further work needs to be conducted to inform an update of advice for patients and the sector.
- 5.7. The Committee discussed the risks associated with in vitro maturation (IVM) and suggested that it may be useful to have the view of a clinician

currently using IVM, or a researcher exploring the efficacy of this technique, to understand potential impacts e.g. on DNA methylation.

- 5.8. The Committee also discussed the research exploring the cryopreservation of ovarian tissue emphasising that whilst recent research shows promise further data is required to assess it's the viability and success. The Committee noted that developments into ovarian tissue transplantation should be monitored and when related to donation of ovarian tissue the regulatory implications will need to be considered.
- 5.9. The Committee concluded that this area should remain closely monitored and any further research and/or relevant experts should be presented to the Committee during the course of the year. The Executive noted that there is a section on the HFEA website advising on fertility preservation and amendments to this area will be reviewed by SCAAC.

#### **Safety of embryo biopsy**

- 5.10. Members were asked to consider whether there are any further studies or developments in this area and review evidence collated by the Executive in this summary on the safety of embryo biopsy in light of the recently published follow-up studies, and decide whether they wish to make any recommendations to the Authority regarding the use of embryo biopsy for tissue typing, PGD or PGS.
- 5.11. A Committee member emphasised that it would be useful to understand the proportion of embryos that fail to make blastocysts (if biopsied at the 8-cell stage) or to implant, versus un-biopsied embryos and the group recommended a speaker who the Committee may invite to speak at a later date. A Committee member also highlighted work by a group in the US, on the effects in mice, of blastomere removal by biopsy.
- 5.12. A Committee member highlighted a review by Bruce et al (2013) for addition to the literature and suggested that whilst long terms studies in this area are reassuring (e.g. Desmyttere et al (2012) cited in Annex B), the Executive should continue to monitor the research in this area.

#### **Decision**

- 5.13. The Committee therefore agreed the identified topic below should be a high priority for their 2014-15 work plan:
- Freeze-all cycles
  - Female fertility preservation
  - Safety of embryo biopsy
- 5.14. The Committee also agreed that the topics below should remain ongoing issues for 2014-2015:
- In vitro derived gamete research
  - Alternative methods for the creation of ES or ES-like cells

- Embryo culture media

- 5.15. Members highlighted further key research articles that they felt should be high priority to be added to the horizon scanning spreadsheet. They also suggested a number of experts that may be used to consult on or invited to present to the Committee.
- 5.16. The Committee highlighted that it would be useful to review and refine the horizon scanning process. The Executive agreed to draft a process pathway which would allow members to focus on reviewing and contributing to their specialist areas. The Committee also noted that the Executive should ensure that all conference abstracts are highlighted but weighted accordingly against peer reviewed published work.
- 5.17. The Committee also raised Next Generation Sequencing and developments in PGD such as karyomapping as a topic to monitor for developments. The Executive noted that a paper outlining the potential ethical and regulatory issues will be discussed by the HFEA's Ethics and Standards Committee in April 2014.

## 6. Any other business

- 6.1. The Chair introduced a number of AOB items including:

- **New technologies** - The Committee discussed the introduction of new technologies and discussed concerns passed on for SCAAC's attention relating to information on clinic websites about new technologies.
- The group discussed the extent to which clinics websites reference misleading data and advertise new technologies that may not have a sufficient evidence base to conclude efficacy. The group highlighted the need for the HFEA to be aware of this, and where appropriate reactive.
- **Definition of an embryo** - The Committee was briefed by Hannah Verdin on a topic the Executive wished to seek SCAAC's guidance on. Views were sought on the definition of an embryo which the EU commission has put forward for the purposes of patent law, allowing for the exclusion of parthenotes, thereby allowing the process used to derive stem cells from parthenotes to be patentable.
- The proposed definition was "any human ovum as soon as fertilised, as well as a non-fertilised human ovum capable of commencing the process of development of a human being just as an embryo created by fertilisation of an ovum can"
- The Committee felt that the definition by itself could not be relied on to exclude parthenotes as it depends on the interpretation of 'commencing the process of development'. Although parthenotes could never become human beings they could be said to commence the process of development to a human being as they initially undergo cell division in the same way.

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The group highlighted that while parthenotes will only have genetic material from the mother, they can be diploid.

- The group agreed that the wording needs to be carefully considered in the context of the interplay between EU and HFE Act definitions.

**Date of next meeting: 4 June 2014 at 2pm.**

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

Committee Chair Name: PA SUSAN PRICE .....

Committee Chair Signature: ..... *S Price* .....

Date: ..... 11/3/14 .....