Scientific and Clinical Advances Advisory Committee (SCAAC) – minutes

31st January 2022

Teleconference (Zoom meeting)

Authority members	Present	Tim Child (Chair) Gudrun Moore (Deputy Chair) Jason Kasraie	Anne Lampe
External advisors	Present	Richard Anderson Jane Blower Kate Brian Daniel Brison Andy Greenfield Yacoub Khalaf	Shankar Srinivas Raj Mathur Robin Lovell-Badge Kevin McEleny
	Apologies		
Members of the executive	Present	Victoria Askew (Meeting lead and Policy Manager) Ana Hallgarten (AH) (Meeting secretary and Scientific Policy Officer) Peter Thompson (Chief Executive) Julia Chain (Chair) Clare Ettinghausen (Director of Strategy and Corporate Affairs) Rachel Cutting (Director of Compliance and Information) Sonia Macleod (SM) (Scientific Policy Manager) Amber Haywood (AmH) (Policy Manager) Georgina Allen (GA) (Policy Manager)	
Invited speaker	Present	Dr Jane Stewart (Newcastle Fertility Centre at Life) Prof Mary Herbert (Newcastle University)	
Observers	Present	Bethan Segar (HFEA) Anna Wilkinson (HFEA) Anna Coundley (HFEA) Sophie Reid (HFEA) Robyn Jones (HFEA)	Georgia May (HFEA) Elliot Bridges (HFEA) Csenge Gal (Department of Health and Social Care) Amy Parsons (Department of Health and Social Care)

1. Welcome, apologies, declarations of interest

1.1. The Chair welcomed members to the meeting.

1.2. Declarations of interest were received from Tim Child, Daniel Brison, and Raj Mathur.

2. Matters arising

2.1. Minutes of the meeting held on 11th October 2021 were agreed remotely prior to the meeting.

2.2. The Scientific Policy Officer updated the Committee on the matters arising from the meeting:

2.2.1. The Committee was asked to highlight and circulate relevant papers about the effects of COVID-19 on reproduction and early pregnancy. This continues to be a standing agenda item.

2.2.2. The Committee agreed that there should be increased promotion of the HFEA website regarding the effects of COVID-19 on fertility, assisted conception, and early pregnancy. The Committee were informed that the HFEA patient and professional information on COVID-19 is assessed and updated on an ongoing basis by the HFEA. This includes patient and clinic FAQs which are updated frequently as and when COVID-19 guidance changes. It was noted that the British Fertility Society (BFS) are committed to issuing regular guidance.

2.2.3. Following the Committee's recommendation to consider androgen supplementation as a separate treatment add-on from immunological tests and treatments, a treatment add-on application form for androgen supplementation is to be completed prior to the June SCAAC meeting for consideration for addition the HFEA's traffic light rated list of add-ons.

2.2.4. The Committee agreed to several changes to the treatment add-ons webpage including additional information on Elective freeze all cycles and endometrial scratching, the creation of a webpage for Endometrial Receptivity Array (ERA), and splitting immunological tests and treatments into separate traffic light ratings and removing androgen treatments from this add-on. These updates to the HFEA website have taken place following review by an expert and the Chair of SCAAC.

3. Chair's business

3.1. The Chair reminded SCAAC that, as discussed at the previous SCAAC meeting, adverts for external advisors for SCAAC are currently live on the HFEA website.

3.2. The chair thanked Jane Blower, Anne Lampe, Daniel Brison, Andy Greenfield, and Shankar Srinivas for their contribution to SCAAC over the years.

3.3. The HFEA is looking to appoint four new external advisors to the SCAAC with the following areas of expertise:

- Clinical embryology with special interest in research
- Research and statistical methodology
- Artificial intelligence or future technology
- Developmental genetics

3.4. SCAAC members were asked to share this information with their network, or to known experts who would fill the job description.

3.5. The Chair thanked everyone for their responses to the annual SCAAC effectiveness survey. The feedback has been passed on.

4. Monitoring the effects of COVID-19 on fertility, assisted conception and early pregnancy

4.1. The Chair acknowledged the 14 reports, papers and guidelines that had been submitted, shared, and discussed with the Committee in previous meetings.

4.2. During the horizon scanning process, an additional 45 papers were identified on the effects of COVID-19 on fertility, assisted conception, and early pregnancy. The findings of these papers were summarised and presented to the executive.

4.3. The committee discussed the work from these papers. It was noted that there is currently insufficient guidance available regarding when assisted conception treatment can start following a COVID-19 infection.

4.4. The effects of COVID-19 and poor pregnancy outcomes was discussed, as was the effect of COVID-19 on sperm function in some men. It was noted that the use of COVID-19 vaccines has shown no effect on conception and pregnancy.

Action: The Committee will continue to monitor and share relevant literature. SCAAC to further discuss the effect of treatment cessation and delay caused by COVID-19.

Action: SCAAC members who are part of ARCS and the BFS to discuss these papers at ARCS and BFS meetings to give feedback to SCAAC.

5. Horizon Scanning Prioritisation of issues

5.1. The Policy Manager (AmH) introduced the horizon scanning work. This was established in 2004 to identify and monitor issues that could have an impact on the field of assisted reproduction or embryo research. Issues are identified from journal articles, conferences, and contact with experts who are invited to the SCAAC horizon scanning meetings.

5.2. To help with the business planning process, it is important for the HFEA to be aware of which issues SCAAC members consider to be high priority. New issues which have been identified this year have been categorised as high, medium, or low priority using the following criteria:

a) Within the HFEA's remit

b) Timescale for likely introduction (2-3 years)

c) High patient demand/clinical use if it were to be introduced

d) Technically feasible

e) Ethical issues raised or public interest

5.3. New issues are high priority if they are within the HFEA's remit and meet at least two other criteria. New issues are medium priority if they are within the HFEA's remit and meet one other criterion, or are outside of HFEA remit but meet at least two other criteria. Low priority issues are those outside of HFEA's remit and unlikely to impact on research or treatment in the near future.

Published studies in these areas continue to be collected and considered as part of the horizon scanning process.

5.4. High priority categorisation is also given to established techniques or issues which fall within the HFEA's remit that require ongoing monitoring or provision of patient information

5.5. The HFEA considers the following topics to be high priority for 2022/23:

a) Treatment add-ons

b) Health outcomes in children conceived by ART (including the impact of culture media)

c) New technologies in embryo and gamete testing

d) In vitro derived gametes

e) Genome editing

f) Mitochondrial donation

g) Alternative methods to derive embryonic and embryonic-like stem cells

h) Synthetic embryo-like entities

i) Artificial intelligence (AI)

j) Extension to the '14-day rule'

5.6. One new topic has been included in the high priority list, the extension to the '14-day rule'.

5.7. The Policy Manager gave a summary of each of the high priority topics included within the horizon scanning as part of the literature review.

5.8. The Policy Manager then presented how the horizon scanning process feeds into the business planning of the HFEA, and specifically the SCAAC workplan. It was proposed that:

- SCAAC should discuss the evidence used to rate treatment add-ons at the June 2022 meeting; add-ons are a high priority area that should be kept under constant review. The Policy Manager also proposes considering the impact of stress (a medium priority item) at the meeting as it has not been discussed at SCAAC since February 2018.
- At the October 2022 meeting it was proposed that SCAAC should discuss the impact of the microbiome (a medium priority item) that was last discussed February 2019, and Synthetic embryo like entities, which is a high priority topic that was last discussed in June 2018. Although AI was last discussed in June 2021, there have been significant publications about regulation since so it has also been proposed for discussion again this year at the October meeting. Finally, it was proposed Synthetic embryo like entities should also be discussed at the October 2022 meeting.
- SCAAC should discuss the extension to the 14-day rule (high priority topic) in February 2023 and conduct the annual rating review for treatment add-ons.

5.9. Members were asked to:

- note the issues identified as high and medium priority through the horizon scanning process;
- consider the high and medium priority issues and work recommendations;

- consider whether advice from additional external advisors would help in achieving work recommendations; and
- discuss whether any additional considerations needs to be given to the use of immature sperm in the form

5.10. The committee agreed to make recommendations for experts for the upcoming topic items to present to SCAAC.

5.11. SCAAC decided that at present there should be no action regarding the use and development of round spermatid injection. It was agreed that at present the technology is nowhere near appropriate for clinical use.

5.12. There were several questions regarding the terminology being used in the discussion of in vitro derived gametes and synthetic embryo-like entities. It was questioned whether there should be a discussion regarding the current terminology that we currently use, its consistency, and whether the most 'neutral' terms possible should be used.

5.13. SCAAC members felt that the 14-day rule and synthetic embryo-like entities are topics that are interconnected and related. They suggested that the 14-day rule should be discussed prior to synthetic embryo-like entities.

5.14. There were several questions regarding the microbiome and its effects on assisted reproduction. However, this topic is to be discussed later in 2022, and possible outputs should be considered then.

Action: Amend the workplan according to the feedback from SCAAC members.

Action: Assess whether further outputs are required in the topic of the impact of the microbiome, and whether it needs to be considered as a treatment add on.

Action: SCAAC members make recommendations for external experts to discuss high priority topics at future meetings.

6. Alternative methods to derive embryonic and embryonic-like stem cells

6.1. Due to timings, the order of the agenda was changed during the meeting.

6.2. The Scientific Policy Officer (AH) presented a literature review on alternative methods to derive embryonic and embryonic-like stem cells. The paper summarised the advances that have taken place since the last update on the topic that took place at the October 2018 meeting.

6.3. The paper demonstrated the benefit of the use of induced pluripotent stem cells (iPS) in research, and clinical applications, and noted the large number of studies currently taking place. New protocols using different methods to deliver reprogramming factors to reduce genomic instability were highlighted, as was the recent updates to the Guidelines for the Field of Stem Cell Research and Regenerative Medicine from The International Society for Stem Cell Research (ICSSR).

6.4. It was noted that the understanding of naïve pluripotent stem cells (PS cells) is increasing. These cells have more potential than primed PS cells as they have similarities to early-stage embryonic cells.

6.5. Members were asked to:

• consider the progress of research into alternative methods to derive embryonic or embryonic-like stem cells;

• advise the Executive if they are aware of any other recent developments; and

• review whether any outputs from the HFEA are required.

6.6. Members of SCAAC discussed the progress in alternative methods to derive embryonic and embryonic-like stem cells. There was an emphasis on not describing the use of iPS cells in research as less ethically concerning than the use of embryonic stem cells.

6.7. The strong regulation of the use of embryonic cells in the UK was considered, and a member of SCAAC stated that the ICSSR guidelines consider countries which do not permit research on embryos.

6.8. It was agreed that research on embryonic derived stem cells will need to continue for the foreseeable future. Currently, the cells that are being created are an insufficient replacement for embryonic derived stem cells.

7. Mitochondrial donation (external speaker)

7.1. The Chair welcomed the guest speakers Prof Mary Herbert, Professor of Reproductive Biology and Scientific Director, Newcastle University and Dr Jane Steward, Consultant in Reproductive Medicine and Gynaecology at Newcastle's Fertility Centre.

7.2. Professor Herbert gave a briefing on the progress of the programme to date.

7.3. The research presented to SCAAC will be published in a peer reviewed journal in due course.

8. Update on evolving the treatment add-ons information

8.1. The Policy Manager (GA) presented the initial scoping work that has taken place in relation to evolving the treatment add-ons information on HFEA's website.

8.2. The Authority agreed in September that a scoping exercise should consider how the presentation of the treatment add-ons rating system could be evolved. Since then, discussions have taken place with researchers with expertise in data presentation and risk communication for insights into how the rating system could be evolved.

8.3. Based on suggestions by these experts, 10 options were developed for possible ways to change the current rating system. These options were presented to the HFEA's Licensed Centres Panel (LCP) and the Patient Organisation Stakeholder Group (POSG) to gain the views and feedback of patient organisation, and clinics. A further meeting took place with the Treatment Add-ons working group (TAG) to present the scoping work.

8.4. The Policy Manager outlined the feedback that has been received to date and spoke of the suggested next steps.

8.5. The next proposed steps for the work are as follows:

- Continue scoping work by holding detailed interviews with patients.
- Develop three options based on feedback from the initial scoping work.

- Conduct a targeted patient and clinic survey on these three options.

8.6. SCAAC was asked to:

- note the progress made in relation to scoping the evolution of the add-ons rating system,
- for their views of the options for presenting add-ons information and/or their alternative suggestions
- for their views on the proposals for engagement for evolving the rating scheme for add-ons

8.7. The Chair reminded SCAAC that the discussion today was not on possibly expanding the evidence used to determine the treatment add-ons ratings, and that this will be discussed further at a future date.

8.8. Two SCAAC members felt that although some patient groups would find different ratings for treatment add-ons with a lack of evidence or negative evidence helpful, they pointed out that often these two things cannot be separated.

8.9. SCAAC members agreed that when considering other outcomes and risks that are not to do with live birth rates, categories within treatment add-ons could be separated. One member noted that ignoring patients requesting data on different outcomes would be medical paternalism.

8.10. The Scientific Policy Manager (SM) emphasised that live-birth rate is likely to continue to be the key data informing the decisions of the treatment add-ons. However, a number of patients have noted the importance of other information as part of the treatment add-ons, as well as the refinement between different patient groups. For example, patients with recurrent pregnancy loss are interested in the effect of treatment add-ons on miscarriage rates, whereas patients with recurrent implantation failure are interested in the effect of the treatment add-on on implantation rates. Although live birth rates are the main objective of fertility treatments, different groups may require different nuance.

8.11. The current RAG system was praised by members of SCAAC for its simplicity, clarity, and its usefulness. It was suggested that the system should be modified rather than changed entirely.

8.12. There was agreement regarding the inherent connotations of ‘stop’ associated with red, and thereby the benefits of adding a new grey rating. Nonetheless, there was an emphasis on the need to clarify ‘where’ the grey rating would lie and what precisely it would mean.

8.13. There was agreement that having summaries of the RCTs used would be helpful, as would links to the scientific papers. The Scientific Policy Manager noted that many patients already seek RCTs as a primary source and that making this available easily on the HFEA website may be beneficial to the patients wanting to read this.

8.14. It was noted that an unavoidable problem with any treatment add-on rating system is encouraging patients to consider them prior to treatment. There were concerns that patients either do not look at the data and ratings on the HFEA website, or that patients look at the ratings but then ignore them once they are at their clinic.

9. Any other business

9.1. One member gave an update on Fertility 2022 which took place online from the 5th to 8th of January 2022. Over 800 delegates attended virtually to discuss a wide range of topics in the field of assisted reproduction.

9.2. The Chair gave a final thanks to Jane Blower, Anne Lampe, Daniel Brison, Andy Greenfield, and Shankar Srinivas for their roles in SCAAC.

9.3. The Chair summarised the meeting and thanked the Committee and the guest speakers.

10. Chair's signature

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

Signature

Chair: Tim Child

Date: 11.04.2022