Scientific and Clinical Advances Advisory Committee (SCAAC) – Matters Arising

Wednesday 4th February 2026

Date	Action	Responsibility	Due date	Progress to date
09/06/2025	Authority to consider including tests in the definition of a treatment add-on the HFEA will provide information on. If approved, an expert literature review on microbiome testing and sperm DNA fragmentation should be commissioned.	Mina Mincheva, Policy Manager	Aiming for the June 2026 SCAAC meeting	In July 2025, the Authority approved amending the definition of a treatment add-on to include tests. Microbiome testing and sperm DNA fragmentation will be brought to a future meeting of the SCAAC for an official rating.
06/10/2025	The Executive to remind clinics of the rescue ICSI professional body guidance via Clinic Focus article.	Rebecca Taylor, Scientific Policy Manager	Aiming to have completed by the June 2026 SCAAC meeting	Input was sought from individuals involved in developing the professional body guidance in relation to how the guidance should be interpreted in certain circumstances. A Clinic Focus article will be published in Spring 2026.
06/10/2025	The Executive to amend the title of the 'Alternative methods to derive embryonic and embryonic-like stem cells' topic to 'Methods to derive embryonic and extraembryonic stem cells from human embryos' and review the search terms used to identify studies, ensuring they include all relevant terminology.	Rebecca Taylor, Scientific Policy Manager	04/02/2026	Actioned.

06/10/2025	The Executive to draft and publish treatment add-ons information on intraovarian and intrauterine platelet rich plasma (PRP) to the website.	Dharmi Degui, Scientific Policy Officer	04/02/2026	Text has been reviewed by members of the SCAAC and Patient Engagement Forum (PEF). The Chair has approved the text, and it will be published to the website in February 2026.

Prioritisation of horizon scanning topics and committee workplan 2026/27

Details about this paper

Area(s) of strategy this paper relates to:	Shaping the future
Meeting:	Scientific and Clinical Advances Advisory Committee (SCAAC)
Agenda item:	8
Paper number:	HFEA (04/02/2026) 005
Meeting date:	04 February 2026
Author:	Rebecca Taylor, Scientific Policy Manager
Annexes	Annex A: Briefings on key issues identified during this horizon scanning Annex B: Topic priority categorisation table Annex C: Committee workplan 2026-2027 Annex D: Committee purpose and function as per standing orders

Output from this paper

For information or recommendation?	For recommendation

Recommendation:	Members are asked to:
	• consider the scope and priority of topics identified through the horizon scanning process:
	  ○ review the Topic priority categorisation table (given in Annex B),
	  ○ agree the prioritisation (in sections 4-6)
	  ○ agree the watching brief topics (in section 7)
	• consider the recommended committee workplan for 2026/2027 (Annex C); and
	• consider whether advice from external expert speakers would help in achieving the work recommendations.

Resource implications:	Subject to committee recommendations
Implementation date:	As per committee workplan for 2026-2027 (Annex C)
Communication(s):	Publication of committee papers, minutes and associated Clinic Focus article; if required, public-facing information can be developed.
Organisational risk:	Low

1. Background

1.1. The Authority established a horizon scanning function in 2004 to identify and monitor emerging and ongoing priority topics that could impact upon the field of assisted reproduction or embryo research. By identifying these topics, the Authority can consider the potential legal, ethical and scientific implications as they arise. We are then prepared to take a policy position on how these areas should be regulated and have guidance in place to ensure practice is carried out in a safe and appropriate manner. We can also make sure the public has access to reliable information about the new techniques and treatments.

1.2. The horizon scanning process feeds into the Scientific and Clinical Advances Advisory Committee (SCAAC) workplan and the Authority's consideration of scientific and ethical issues and standards. As part of the horizon scanning process, the HFEA carries out the following activities:

- A literature review, performed every 3 years, of all prioritised topics to identify all relevant studies for each topic and any new topics/developments.
- Prioritisation of topics by the SCAAC on an annual basis and consideration of the SCAAC's workplan for that year, usually at the February meeting of the SCAAC. The literature review mentioned above will feed into this prioritisation every 3 years.
- A SCAAC paper with a literature review on each prioritised topic is brought to the SCAAC for discussion every 2 or 3 years, depending on their prioritisation and the committee's workplan. The frequency at which topics are discussed by the SCAAC is determined by their priority, date of last discussion, and relevance to the remit and ongoing work of the HFEA.
- Between discussions, the committee continues to actively monitor publications relevant to prioritised topics and other relevant developments, under the standing agenda item 'Relevant public health developments and research findings'.
- Convenes an annual Horizon Scanning Meeting during the European Society of Human Reproduction and Embryology (ESHRE) conference, bringing together international experts and regulatory bodies to discuss issues and breakthroughs on the horizon in fertility treatment and human embryo research. Learnings from such meetings are used to identify new topics and monitor developments.

1.3. This paper focuses on the process the Executive follows for carrying out literature reviews for the purpose of prioritisation, the process for prioritising topics, and asks the SCAAC to prioritise topics and agree a workplan for the coming year.

1.4. Topics were last prioritised in February 2025, when the committee agreed to introduce "Health outcomes for ART patients (including gestational surrogates, egg donors and the impact of treatment using donated eggs") and "Reproductive organoids" as medium priority topics. At the same meeting, the Committee also agreed to introduce a "watching brief" category of topics and moved five topics to that category.

2. Review of the HFEA's literature review process

2.1. During 2025, the Executive undertook a review of the horizon scanning process, largely focusing on the literature review process from an operational perspective. This was to ensure

that it remains fit for purpose, aligns with the approach used for add-on reviews, and can achieve its objectives of keeping the HFEA up to date on scientific and technological developments and research relevant to the Authority's remit.

2.2. This review had three objectives:

- Translate existing search strings from PubMed to Ovid Medline
- Consider whether horizon scanning should be expanded to cover journals in languages other than English, and if so under what circumstances
- Review the Horizon Scanning Standard Operating Procedure (SOP) used by the executive and address any gaps arising out of this.

2.3. Working with a medical librarian, the existing search strings were translated to OVID Medline, tested and where necessary refined/further developed.

2.4. The question of covering journals in languages other than English was investigated. SCAAC members were asked whether it would be beneficial to develop a list of non-English language journals to be targeted in our horizon scanning process. SCAAC members were firmly of the view that this was not necessary because of the workload involved and the fact that that good research would later be published in reputable English language journals. The Executive therefore decided to make only a small change to horizon scanning methods, namely, not to restrict search results to English language, meaning that occasionally a relevant article published in a language other than English may be identified if it has an English language abstract in Ovid Medline.

2.5. As well as reviewing the horizon scanning SOP, other approaches to horizon scanning (journal articles, horizon scanning methods from other organisations) were examined. This identified some gaps:

- How to address retracted articles and/or authors with papers retracted or under investigation.
- How to ensure that clinical trials in the fertility sector are covered before the final results of the trial are published.

2.6. There is increasing concern, not just in the fertility sector, of studies and authors whose publications raise questions and end up either under investigation or retracted. This matter was investigated and it was decided that all papers identified as relevant during horizon scanning literature searches will be run through a retraction tool called Crossref.

2.7. We used Crossref to look at individual authors (first, last and corresponding author) for the AI paper that is being brought to this meeting, but found this to be very time consuming for little additional benefit. We therefore decided not to proceed with running authors names through the tools and to run titles of article only. We would kindly remind SCAAC members that if they are aware of authors whose work has come to the attention of SCAAC, whose other work is under investigation or retracted, they should continue to inform the Executive. Each article included in any SCAAC paper will be run through Crossref, and:

- Any article that has been retracted will be removed from the reference list.
- Any article under investigation will be flagged on the reference list as such.

2.8. Should the SCAAC become aware of any author who has had other papers retracted or under investigation, then this will also be flagged on the reference list next to any article they authored.

2.9. The Executive consulted the medical librarian in relation to identifying clinical trials of interest to our horizon scanning that are still ongoing and do not yet have published peer-reviewed articles. We were advised that Ovid Medline is likely to cover most of those trials, but that as an additional measure we could undertake a search for registered clinical trials on a given horizon scanning topic (where clinical trials are likely) on the WHO international clinical trials registry.

3. Review of the HFEA's prioritisation process

3.1. As mentioned at 1.2, a literature review is performed on a regular basis of all prioritised topics to identify all relevant studies for each topic and any new topics/developments.

3.2. The Executive considered the frequency of literature searches for the purposes of prioritisation and proposed to the October 2025 SCAAC meeting that the literature reviews of all topics should be carried out every three years. This was agreed by SCAAC. As the last literature search of all prioritised topics took place in 2024, the next one will take place in 2028 (covering 2025-2027).

3.3. The following aspects of this process remain unchanged:

- A literature review will be performed to retrieve literature published for each prioritised topic since it was last discussed (as an individual SCAAC paper or as part of the February prioritisation discussions).
- When a new topic is introduced/prioritised, a literature search for publications across the past ten years (as agreed at the February 2017 SCAAC meeting) is performed.
- The scope of each topic is based on the progression of research and its relevance to the remit and function of the HFEA. To account for developments in research, the search strings used are reviewed and if necessary refined whenever literature searches take place.
- Briefings on horizon scanning topics are written when a new topic is suggested for introduction or when the Executive wishes to highlight a significant development in a prioritised topic ahead of the next scheduled discussion.
- As well as other factors eg likelihood of further/novel research developments, the following criteria are used to categorise topics as high, medium, or low priority:
    - Within the HFEA's remit
    - Timescale for likely introduction (now or within 3 years)
    - High patient demand/clinical use if it were to be introduced
    - Technically feasible
    - Ethical issues raised or public interest
- Topics are **high priority** if they are within the HFEA's remit and meet at least two other criteria. High priority categorisation is also given to established techniques or issues that fall within the HFEA's remit and require ongoing monitoring or provision of patient information.
- Topics are **medium priority** if they are within the HFEA's remit and meet one other criterion, or are outside the HFEA's remit but meet at least two other criteria.
- Topics are **low priority** if they meet at least one criterion but are outside the HFEA's remit and unlikely to impact on research or treatment in the near future.
- In some cases, it may be appropriate to prioritise topics according to their relevance to the work of the HFEA rather than according to the criteria above e.g. stem cell-based embryo

models are not with the HFEA's remit but are relevant to our work on law reform, therefore are a high priority topic.

3.4. As agreed at the SCAAC's February 2024 meeting, the topic of 'Treatment add-ons' has been separated from the horizon scanning process and is to be performed independently every five years. The most recent review of the treatment add-ons ratings was conducted in July 2023. Between reviews, the committee continue to actively monitor publications that could change the rating of an existing add-on, or introduce a new add-on, under the standing item 'Relevant public health developments and research findings'.

3.5. The following sections of this paper lay out the recommended priority for each horizon scanning topic and an associated schedule for their discussion. A table detailing the priority categorisation is provided in Annex B, with the recommended workplan detailed in Annex C. There are no new horizon scanning topics proposed for 2026-27.

4. High priority issues

4.1. Listed in alphabetical order, the Executive considers the following topics to be high priority for 2026:

- Artificial intelligence (AI), robotics and automation in fertility treatment
- Emerging technologies in gamete and embryo testing
- Health outcomes in children born from ART (including the impact of culture media)
- Health outcomes for ART patients (including gestational surrogates and egg donors)
- In vitro derived gametes (IVGs)
- Methods to derive embryonic and extra embryonic cells from human embryos
- Mitochondrial donation
- Scientific considerations relevant to the '14-day rule'
- Stem cell-based embryo models (SCBEM)

5. Medium priority issues

5.1. Listed in alphabetical order, the Executive considers the following topics to be medium priority for 2026:

- Germline/heritable genome editing
- Impact of long-term cryopreservation of gametes and embryo
- Impact of the microbiome on fertility and fertility treatment outcomes
- Reproductive organoids
- Testicular tissue transplantation to restore fertility in males

6. Low priority issues

6.1. There are currently no low priority issues.

7. Watching Brief

7.1. In 2025, we introduced a list of 'watching brief' topics as part of our horizon scanning process. This allows us to monitor issues that, while not currently meeting the prioritisation criteria or opportunities that warrant continued detailed oversight by the committee.

7.2. Due to resources required, the Executive proposes that full literature searches are conducted for prioritised topics only, and not on the watching brief topics.

7.3. Watching brief topics will not be scheduled for discussion at SCAAC meetings with a paper, however the Executive and SCAAC members can highlight significant research developments relevant to the 'watching brief' topics (ie large studies of good quality) ad hoc under the standing item 'Relevant public health developments and research findings'.

7.4. Should developments be deemed significant, members will have the opportunity to consider watching brief topics for prioritisation. This expanded approach will enable the committee to remain informed and responsive to developments in these areas as they evolve.

7.5. Topics currently on the watching brief list are:

- Artificial wombs for early or whole gestation (ectogenesis)
- Impact of environmental toxins on fertility treatment outcomes
- Impact of stress on fertility treatment outcomes
- Understanding the genetic basis of infertility
- Use of ICSI for non-male and mild-male factor infertility

7.6. The Executive does not currently propose any changes to the watching brief list.

8. Recommendations

8.1. Members are asked to:

- consider the proposal from the Executive (point 7.2) that full literature searches are only undertaken for prioritised topics
- consider the scope and priority of topics identified through the horizon scanning process:
    - review the Topic priority categorisation table (given in Annex B),
    - agree the prioritisation (in sections 4-6)
    - agree the watching brief topics (in section 7)
- consider the recommended committee workplan for 2026/2027 (Annex C); and
- consider whether advice from external expert speakers would help in achieving the work recommendations.

9. Annex A: Briefings on key issues identified during horizon scanning

9.1. No new topics were identified as a result of horizon scanning activities conducted during 2025.

10. Annex B: Topic priority categorisation table

Topic	Within HFEA remit?	Timescale for likely clinical introduction now or within 3 years?	High patient demand/clinical use if introduced?	Technically feasible?	Ethical issues or public interest raised?	Recommended rating
AI robotics and automation in fertility treatment	Yes	Yes	Yes	Yes	Yes	High
Emerging technologies in gamete and embryo testing (includes metabolomic profiling)	Yes	Yes	Yes	Yes	Yes	High
Health outcomes for ART patients (including gestational surrogates and egg donors)	No	Yes	N/A	N/A	Yes	High
Health outcomes in children born from ART (including the impact of culture media)	No	Yes	N/A	N/A	Yes	High
In vitro derived gametes (IVGs)	Yes	No	Yes	No	Yes	High
Methods to derive embryonic & extraembryonic stem cells from human embryos	Yes	N/A	N/A	Yes	Yes	High
Mitochondrial donation	Yes	Yes	Possibly[1]	Yes	Yes	High
Scientific considerations relevant to '14-day rule'	Yes	N/A	N/A	Yes	Yes	High
Stem-cell based embryo models (SCBEM)	No	No	No	Yes	Yes	High

[1] This refers to the possible future use of mitochondrial donation to treat infertility, which is currently at an early stage of development. This does not refer to disease related mitochondrial donation which is already available in the UK, and does not generate a high level of patient demand.

Topic	Within HFEA remit?	Timescale for likely clinical introduction now or within 3 years?	High patient demand/clinical use if introduced?	Technically feasible?	Ethical issues or public interest raised?	Recommended rating
Germline/heritable genome editing	Yes	No	Possibly	Yes	Yes	Medium
Impact of long-term cryopreservation of gametes and embryos	Yes	Yes	Yes	Yes	Yes	Medium
Impact of the microbiome on fertility and fertility treatment outcomes	No	Yes	Yes	Yes	Yes	Medium
Reproductive organoids	No	N/A	N/A	Yes	Yes	Medium
Testicular tissue transplantation to restore fertility in males	Yes	Yes	No	Yes	No	Medium
Artificial wombs for early or whole gestation (ectogenesis)	No	No	No	No	Yes	Watching Brief
Impact of environmental toxins on fertility treatment outcomes	No	N/A	N/A	N/A	Possibly	Watching Brief
Impact of stress on fertility treatment outcomes	No	N/A	N/A	N/A	Possibly	Watching Brief
Understanding the genetic basis of infertility	No	No	Yes (if tests possible)	No	Possibly	Watching Brief
Use of ICSI for non-male and mild-male factor infertility	Yes	Yes (already used)	Yes	Yes	Yes	Watching Brief

[1] This refers to the possible future use of mitochondrial donation to treat infertility, which is currently at an early stage of development. This does not refer to disease related mitochondrial donation which is already available in the UK, and does not generate a high level of patient demand.

11. Annex C: Committee workplan 2026-2027

11.1. The table below presents the anticipated workplan of the SCAAC for 2026/27. Should the priorities of the Authority change, alterations to the workplan may be agreed with the SCAAC Chair.

Priority topic	Item	External speaker?	Last discussed	Meeting
AI, robotics and automation in fertility treatment	Literature review	No	February 2024	February 2026
Reproductive organoids	Literature review	Yes (agreed)	N/A – new topic	February 2026
Horizon scanning prioritisation and agreeing workplan for 2026/27	Workplan review	No	February 2025	February 2026
Emerging technologies in embryo and gamete testing	Literature review	No	June 2024	June 2026
Treatment add-on rating – sperm DNA fragmentation testing	Evidence review report	Yes (biostatistician)	June 2025	June 2026
Treatment add-on rating – microbiome testing	Evidence review report	Yes (biostatistician)	June 2025	June 2026
Stem cell-based embryo models (SCBEM)	Literature review	No	October 2024	October 2026
Scientific considerations relevant to the 14-day rule	Literature review	No	October 2024	October 2026
In vitro derived gametes (IVGs)	Literature review	No	October 2024	October 2026
Health outcomes in children born from ART (including impact of culture media)	Literature review	No	February 2025	February 2027
Mitochondrial donation	Literature review	TBC	October 2024	February 2027
Horizon scanning prioritisation and agreeing workplan for 2027/28	Workplan review	No	February 2026	February 2027
Impact of the microbiome on fertility treatment outcomes	Literature review	No	June 2025	June 2027
Health outcomes for ART patients (including gestational surrogates and egg donors)	Literature review	No	June 2025	June 2027
Impact of long-term cryopreservation	Literature review	No	February 2025	June 2027

Annex D: Committee purpose and function as per standing orders

11.2. To support the committee's discussion about their planned activity for 2026/27 the Executive would like to remind members of the purpose and function of the Committee, as detailed in section 5 of the HFEA standing orders.

11.3. Section 5.1 of Annex A states that the purpose of the Committee "is to advise the Authority on scientific and clinical developments (including research) in assisted conception, embryo research and related areas and to make decisions relating to authorised processes."

11.4. Section 5.3 of Annex A states the function of the Committee shall be to:

- make recommendations to the Authority on the safety and efficacy of scientific and clinical developments (including research) in assisted conception, embryo research and related areas;
- make recommendations to the Authority on patient information relating to those scientific and clinical developments;
- advise the Authority on significant implications for licensing and regulation arising out of such developments, and;
- where required, work with the Authority members to consider the social, ethical and legal implications arising out of such developments.

Reproductive organoids

Details about this paper

Area(s) of strategy this paper relates to:	Supporting scientific and medical innovation
Meeting:	Scientific and Clinical Advances Advisory Committee (SCAAC)
Agenda item:	6
Paper number:	HFEA (04/02/2026) 006
Meeting date:	04 February 2026
Author:	Molly Davies, Scientific Policy Officer (HFEA)
Expert speaker:	Margherita Yayoi Turco (Friedrich Miescher Institute for Biomedical Research)
Annexes	Annex A – Literature review on reproductive organoids

Output from this paper

For information or recommendation?	For recommendation
Recommendation:	Members are asked to: • consider the progress of research into reproductive organoids; • advise the Executive if they are aware of any other recent research developments; and • review whether any outputs from the HFEA are required.
Resource implications:	Within budget
Implementation date:	TBC
Communication(s):	Minutes of the committee discussion will be published on the SCAAC webpage and communicated to the sector via our Clinic Focus newsletter
Organisational risk:	Low

1. Background

1.1. Traditionally, modelling of the development or disease of tissues and organs (including male and female reproductive tract biology) have been attempted with various approaches, including two-dimensional primary cell cultures, immortalised or transformed cell lines, spheroids, organotypic tissue piece or organ explant cultures, and animal models.

1.2. Although such conventional approaches have contributed significantly to the understanding of the reproductive tract biology in health and disease, they present with many challenges and limitations. For example, with two-dimensional culture systems, cell lines present with karyotypic abnormalities, lack genetic diversity and polarised orientation, while primary cell cultures are difficult to isolate and establish and lack all cell types that reside in the original tissue. All these drawbacks limit the ability of these approaches to fully recapitulate the spatial complexity cellular interactions and cellular heterogeneity of the human reproductive tract.

1.3. Recently, organoid cultures have been developed that circumvent many of the disadvantages associated with cell lines. An organoid is defined as a three-dimensional structure grown from stem cells that consists of organ-specific cell types that self-organise through cell sorting and spatially restricted lineage commitment. Organoid cultures can be established from pluripotent stem cells (PSC), either embryonic stem cells (ESC) or induced pluripotent stem cells (iPSC), as well as from fetal or adult stem cells isolated from tissue fragments.

1.4. The development of three-dimensional organoid models which recapitulate some of the cell diversity, architecture and functional features of an organ system have been utilised for studying development, function, and disease in reproductive biology. Organoid systems to study the human reproductive tract include organoids of the ovaries, fallopian tubes, endometrial or uterine lining, the cervix, placenta, testis, and epididymis. Additionally, research into assembloids has gained traction in the past few years.

1.5. Assembloids are defined as self-organising three-dimensional culture systems, which are more complex than organoids and combine different organoids, or organoids with specialised cell types or primary tissue explants within one functional framework. In the reproductive tract modelling research, assembloids are specifically utilised to model cell interactions or molecular signalling pathways at the foetal-maternal interface, such as those involved in embryo implantation and placentation, endometrial growth, differentiation, and disease cell interactions.

1.6. The HFEA licences research projects that involve the creation, use, or destruction of human embryos. This includes research undertaken to derive novel populations of human embryonic and extraembryonic stem cell lines, as last discussed by the SCAAC in October 2025.

1.7. In line with the joint position on 'Regulating human embryonic stem cell lines for human application', the HFEA's remit includes the use of embryos in the derivation of stem cell lines but does not extend to the regulation of stem cell lines themselves. Similarly, research using alternative stem cell populations, such as induced pluripotent or adult stem cells, falls outside of the HFEA's statutory remit.

1.8. Much of the research into reproductive organoids, which are typically established from banked or alternative stem/progenitor cell sources, is therefore not licenced or regulated by the HFEA.

However, where a research project sets out to create and derive organoids from an unbanked embryo-derived stem cell source, ie stem cells established as part of the project, that project would require a HFEA research licence. Assembloid models that combine reproductive organoids with human embryos must also be licenced by the HFEA. Summaries of HFEA licenced embryo research projects are provided here: Embryo research project summaries | HFEA.

1.9. In addition, the HFEA has an established interest in reproductive organoids due to the potential for these models to address research questions that may advance understanding of infertility, related disorders, and their treatment. It is therefore important for the Authority to remain informed of the research progress in this area.

1.10. The topic of reproductive organoids, specifically of the female reproductive tract, was first considered by the Authority during HFEA's Annual Horizon Scanning Meeting 2024, where a panel of international experts discussed the stability, culture viability, and responsiveness of current models. Opportunities highlighted by the speaker included:

- Understanding fundamental biology of normal physiology (e.g. immune system, decidualization, endocrine environment)
- Investigating embryo-endometrial interactions (e.g. implantation, early placental development)
- Studying perturbation of homeostasis and modelling disease/conditions (e.g. infection)
- Development of personalised medicine approaches and testing drug responses (e.g. measuring hormonal responses; screening for compounds to improve response to hormones; assess endometrial function and tailor approached to improve IVF outcomes)
- Regenerative therapy

1.11. Following discussions, the topic of reproductive organoids was added to the SCAAC's horizon scanning list in February 2025 as a medium priority topic[1]. The scope of this topic covers both human and animal research looking at generating organoids to study the reproductive tract, in/fertility, and associated treatments. Despite the role organoid models have in cancer modelling and drug-screening, this literature review focuses primarily on non-malignant organoid systems. However, due to the prominence of cancer-based research in certain tissues, selected studies have been retained. Further details on the scope of this topic are given in Annex B of the relevant paper (HFEA (03/02/2025) 008).

1.12. As a newly introduced topic, the research developments summarised in this paper include those published across a ten-year period between January 2015 and 21st January 2026. This paper details the findings described in the literature and is not an assessment of study validity.

2. Summary of research developments

2.1. Over the past decade, reproductive organoid research has progressed from early proof-of-concept studies defining the requirements for model establishment, to the generation of more

[1] Prior to this time, related research developments were considered within the topics of 'Stem cell-based embryo models' (SCBEM), 'In vitro gametes' (IVGs), and 'Methods to derive embryonic and extraembryonic stem cells from human embryos'.

stable and reproducible tissue-specific models that are now able to recapitulate select structural and functional features of the reproductive tract organs.

2.2. Organoid models have been established for several components of the female reproductive tract, including the ovary, fallopian tubes, uterus/endometrium, cervix, and placental structures:

Ovarian organoids

2.3. In relation to ovarian function, organoid research has focused on modelling the ovarian surface epithelium, with studies demonstrating feasibility in establishing ovarian organoids of human origin from both primary cells. Predominantly utilised in the study of ovarian cancer, such ovarian surface epithelium organoid models have allowed for the study of tumour development and chemosensitivity.

2.4. In addition, ovarian organoids derived from female germline stem cells, and supported by three-dimensional culture approaches, have been explored to model in vitro folliculogenesis and oocyte maturation. While some studies have reported follicular survival and the production of mature oocytes, research remains limited by challenges of cell flattening, incomplete modelling of cell types (including functional theca cells), and difficulties in maintaining long-term culture.

Fallopian tube organoids

2.5. Successful establishment of stable, long-term, three-dimensional fallopian tube organoids, was first described by Kessler et al. (2015). Possessing both secretory and ciliated cells, the model recapitulates features of the in vivo epithelium, responsive to hormone (oestradiol and progesterone) treatment. Subsequent studies have gone onto describe further methods of culturing and identifying fallopian tube organoids, which have included the designation of aldehyde dehydrogenase as a biomarker for their identification and generation of an organoid from reconstituted tissue cell lineages. As with ovarian organoids, fallopian tube organoid systems have been utilised in the study of gynaecological cancers.

Endometrial organoids

2.6. Endometrial organoids were first established as epithelial models able to recapitulate glandular architecture, lineage-specific differentiation, and cyclical hormone responsiveness characteristic of the human endometrium. Subsequent models have incorporated both epithelial and stromal compartments, enabling the study of decidualisation and stromal-epithelial signalling, but remain limited by the absence of vascular and immune components. Recent studies using co-culture and microfluidic approaches (including organ-on-a-chip platforms) have demonstrated the feasibility of engineering vascularised endometrial models.

2.7. Functionally, endometrial models are being applied in disease modelling to investigate disorders of endometrial function, including polycystic ovary syndrome, recurrent implantation failure, endometriosis, and Asherman's syndrome (intrauterine adhesions). These platforms have enabled investigation of disease-associated alternations in hormone responsiveness, signalling-pathways, and endometrial receptivity, and provide models for evaluating therapeutic compounds and strategies for tissue repair, including pre-clinical transplantation approaches.

2.8. In addition, endometrial organoids have recently been utilised in studies investigating in vitro implantation and early post-implantation development of human embryos and blastoids. Findings

from such research indicate that endometrial cells increase the efficiency of embryo and blastoid attachment and improve post-implantation development in vitro.

Cervical organoids

2.9. Human cervical epithelial organoids are well established, modelling both ecto- and endocervical epithelial lineages. Studies have demonstrated that models are able to recapitulate epithelial stratification, lineage specific gene expression, and limited hormone responses. Predominantly applied for disease modelling, cervical organoids have been used to study human papilloma viral infections and progression to cervical cancer, alongside sexually transmitted infections and treatment-induced toxicity.

Placental organoids

2.10. Placental organoid systems capable of recapitulating trophoblast cell lineages have been developed from both primary human placental tissue and pluripotent stem cell progenitors. Studies have reported recapitulation of early to mid-gestation placental structures, with organoids forming villous-like epithelial structures, but are limited by maternal components (including vasculature) restricting recreation of late-gestation structures. These organoid systems have been used to model trophoblast differentiation, maternal-foetal interface formation, and pregnancy-relevant conditions, including viral pathogenesis, impaired invasion, and disease-associated epigenetic memory.

2.11. Advances in reproductive organoid systems are also providing insights into male reproductive health, with testicular, epididymal, and prostate organoids enabling the study of early spermatogenesis, androgen signalling, and mechanisms underlying male infertility:

Testicular organoids

2.12. Testicular organoid systems are able to faithfully recapitulate key structural, cellular and signalling features of the testis in vitro, including modelling human spermatogenesis, maintaining functional Sertoli, Leydig and myoid cell populations, and replicating elements of in vivo tissue architecture. Recent studies utilising engineered microenvironments (including microfluidic platforms, air-liquid interface systems, and bio-instructive hydrogels) have demonstrated improved tissue organisation, enhanced cell interactions, and greater stability when compared to static three-dimensional cultures, reflecting the ongoing work to refine models. Despite progress, models remain limited by incomplete spatial architecture of seminiferous tubules, failure to sustain meiosis, lack of vascular and immune compartments, and poor long-term stability.

Epididymal organoids

2.13. More recently progress has been made in establishing three-dimensional epididymal organoids, with models derived from both rodent and human cell populations. These studies demonstrate the feasibility of generating region-specific epididymal organoids in vitro (including those modelling the caput, corpus and cauda) and provide a novel platform for studying epididymal development, epithelial function, and disease mechanisms underlying male infertility, such as CFTR-medicated defects associated with cystic fibrosis or obstructive azoospermia. They also provide a platform to explore the role of epididymal cells in sperm maturation, inflammatory insults, and drug/environmental exposures.

Prostate organoids

2.14. Prostate organoids have been developed primarily to model prostate development, cancer progression, and therapies. Studies describe protocols to generate long-term, genetically stable organoids from adult tissue, recapitulating both luminal and basal epithelial lineages, androgen receptor signalling, and key in vivo transcripts. In cancer models, organoids preserve tumour heterogeneity, mutational landscapes, and can be applied to study treatment responses. Application of such models in the context of infertility has been limited.

2.15. Collectively, the development of faithful organoid models is improving the research toolkit, offering opportunities to understand differentiation of organ specific tissues, hormone responsiveness, and cellular interactions in accessible in vitro systems. Despite advances, reproductive organoid systems remain limited by reduced cellular complexity and the absence of intact physiology, notably vascular and immune components that contribute to both organ development and function. Future perspectives for reproductive organoids are focused on developing representative functional models through the refinement of basement membrane extracellular matrices, multicellular co-culture strategies, and microfluidic/bioengineered systems.

3. Recommendations

3.1. Members are asked to:

- consider the progress of research into reproductive organoids;
- advise the Executive if they are aware of any other recent research developments; and
- review whether any outputs from the HFEA are required.

4. Annex A – Literature review on reproductive organoids

4.1. Annex A has been circulated to the committee as a separate Excel document, which provides details on the available research on reproductive organoids published between January 2015 and 21st January 2026. Where possible literature has been separated by relevant subheadings.

4.2. The topic search strategy, originally developed in PubMed, was adapted for Ovid Medline to align with the methodology developed for the treatment add-ons literature search, and to ensure comprehensive coverage across platforms.

Artificial Intelligence (AI), robotics and automation in fertility treatment

Details about this paper

Area(s) of strategy this paper relates to:	Supporting scientific and medical innovation
Meeting:	Scientific and Clinical Advances Advisory Committee (SCAAC)
Agenda item:	7
Paper number:	HFEA (04/02/2026) 007
Meeting date:	04 February 2026
Author:	Mina Mincheva, Policy Manager (HFEA)
Annexes	Annex A – Literature review on Artificial Intelligence (AI), robotics and automation in fertility treatment Annex B – Uses of AI across the patient pathway

Output from this paper

For information or recommendation?	For recommendation
Recommendation:	Members are asked to: • Consider the progress of research into AI, robotics and automation in fertility treatment and advise on any other relevant developments; • consider uses of AI across the patient pathway against the Authorised processes list and advise on any novel applications of AI; • advise on any other concerns/issues pertaining to uses of AI that may have licensing and regulatory implications; and • review whether any outputs from the HFEA are required.
Resource implications:	Within budget
Implementation date:	Ongoing
Communication(s):	Minutes of the committee discussion will be published on the SCAAC webpage and communicated to the sector via our Clinic Focus newsletter.
Organisational risk:	Low

1. Background

1.1. Across the UK fertility sector, Artificial Intelligence (AI) is increasingly being adopted to support the provision of fertility services. AI is a branch of computer science, statistics, and engineering that uses algorithms or models to perform tasks and exhibit behaviours such as learning, making decisions and making predictions. The subset of AI known as Machine Learning (ML) allows ML models to be developed by ML training algorithms through analysis of data, without models being explicitly programmed (IMDRF/AIMD, 2022). AI-based systems are typically implemented as software in medical devices or as Software as a Medical Device.

1.2. Medical devices are regulated by the Medicines and Healthcare products Regulatory Agency (MHRA) and are subject to ongoing MHRA post marketing surveillance and enforcement action.

1.3. While the HFEA's existing regulatory instruments (the Code of Practice, licence conditions, General Directions) were not designed specifically for AI systems, they provide a framework through which the responsible adoption of AI in fertility treatment can be overseen. HFEA's regulatory remit includes all methods by which authorised processes are carried out, including if AI, robotics and automation are used. AI tools can also be subject to an HFEA add-ons ratings, for example time-lapse incubation and imaging which uses AI-algorithms.

1.4. AI was last discussed by SCAAC in February 2024. The discussion included recommendations to the Authority to consider: further clarifying where AI technologies are being applied in the patient fertility journey and which of them may be considered add-ons to treatments; implications for licensing and regulation arising out of developments in AI, robotics and automation across the fertility treatment pathway, particularly related to technologies with patient-facing application; and correspondingly, to further communicate to the sector and patients as appropriate.

1.5. Following recommendations made by the Committee in 2024, the HFEA has carried out a scoping project aiming to improve our understanding of how AI and other emerging technologies are being used in fertility treatment, map the UK's regulatory landscape, and consider how the HFEA as a regulator can best support the responsible adoption of these tools across the sector within its remit. A paper (pp 55-68) outlining the outputs of this work were discussed at an Authority meeting in November 2025.

1.6. The HFEA has published information and guidance on the use of AI, robotics and automation in fertility treatment for licensed centres on the Clinic Portal. The page will be updated accordingly as regulatory guidance and policy develops over time.

1.7. The Executive notes the following risks related to AI tools in clinical treatment and laboratory processes stages of patient fertility pathway:

- Data bias – AI systems are mainly validated on non-representative retrospective datasets and are biased towards certain patient populations. This can lead to disparities of clinical outcomes for patients outside the populations in the dataset.
- Lack of validation – AI tools are increasingly being adopted in IVF labs globally. However, large multi-centre randomised controlled trials are very limited which does not provide strong evidence base-guided implementation.

- Provision of information and patient communication – The risk of the raw medical information produced by AI systems being presented directly to patients.
- Data privacy and uninformed consent – The risk of exploitation of patients' data without them being aware, particularly when patient data is being used for development of proprietary algorithms.
- Impact on workforce – While a global shortage of skilled embryologists can be addressed to some degree by AI-driven robotics and automation, - for example automation of culture dish preparation, automated cryopreservation and storage of gametes and embryos, some tasks of ICSI procedure - there is the risk that widespread adoption of such technologies may conversely result in significantly fewer embryologists being employed.
- Impact on clinical expertise – Advanced AI systems supporting decision-making may affect clinical judgement autonomy if healthcare professionals over rely on such tools. The General Medical Council has provided a resource to address questions on the use of innovative technologies in healthcare, highlighting the importance of upholding professional standards and principles of good medical practice.
- AI hallucination and provision of erroneous information – when generative AI has been implemented to produce outputs in the context of fertility treatment. For example, incorrect reporting on genetic inheritance patterns of recessive conditions or Chatbots providing information on chances of IVF success and outcomes in a patient-specific context. There is also the risk that generative AI tools using large language models (LLMs) implemented in clinics provide false or misleading information, ie hallucination pertinent to LLMs.

1.8. This topic was discussed at the HFEA's Annual Horizon Scanning Meeting (HSM) in 2024 and 2025. Discussion in 2024 included developments relevant to future uses of AI in the IVF lab; regulatory challenges arising from fast paced developments in AI use; validation, liability and standardisation considerations. The focus of 2025 HSM's discussion was on the potential of robotics and automation to revolutionise fertility treatment. Some of the highlighted benefits were standardisation of processes, improved work efficiency particularly for embryologists, and reduction in cost.

1.9. Annex A explains the scope of this topic and provides details of the available research on Artificial Intelligence (AI), robotics and automation in fertility treatment published between January 2024 and December 2025. The Executive notes that this paper provides a summary of the findings described in published literature and is not an assessment of study validity.

1.10. Different AI models have been developed across all stages of fertility treatment pathway (see Annex B for diagram visualising AI tools in patient journey). Summary of findings below are grouped based on what stage of the patient journey AI tools are being deployed or likely to be implemented.

2. Summary of research developments

Patient communication and engagement

2.1. Studies evaluated the role of digital platforms, including large language models (LLMs) in fertility information provision for patient–healthcare professional interactions and across a range

of reproductive health topics. Significant limitations were identified in accuracy of assisted reproductive technology–related content and inconsistent safety disclaimers across different LLMs. While AI-assisted consultations were associated with higher patient satisfaction and shorter consultation times, a need for implementation of standardised protocols was identified.

Consultations and clinical investigation stage

2.2. Several studies developed ML (machine learning) models to predict and improve treatment outcomes. Particular focus was on predicting expected euploid embryo yield from clinical investigation parameters; refining overall treatment process by integrating pre- and during-treatment variables (eg patient age, antral follicle count, reproductive hormone levels, and ovarian stimulation drugs); assess uterine conception environment prior to natural conception or embryo transfer using ultrasound parameters; support counselling regarding weight management and start IVF treatment using pre-gravid body mass index (BMI).

2.3. Some studies focused on ML models that can assist with treatment planning, for example developing a predictive model to assess type of ovarian response by identifying genetic polymorphisms associated with ovarian response; or employing clinical data from PGT-A cycles and interpretable ML models to investigate the impact of paternal age on embryo euploidy.

Treatment stage – clinical management and laboratory processes

2.4. Many studies reported on ML models to predict treatment outcomes in the treatment phase:

- ML models have been developed to predict clinical pregnancy, foetal heartbeat, ongoing pregnancy, live birth rate (LBR) and pregnancy loss in fresh and frozen embryo transfer (FET) cycles. Some models have used embryological parameters such as morphokinetic and morphological variables, static images or enhanced images of inner cell mass (ICM) and trophectoderm (TE). Other models have used clinical data or a combination of both embryological and patient data. A few studies have focused on improving outcomes in particular patient groups, including advanced maternal age (AMA), polycystic ovarian syndrome (PCOS), endometriosis and patients from egg donation programmes. A small number of studies used predictive models based on surgical sperm retrieval outcomes or genetic markers (e.g. Y-chromosome microdeletions). The LBR prediction performance of a centre specific model and multicentre national registry-based model produced by the Society for Assisted Reproductive Technology (SART) has also been compared.
- Several studies focused on embryo-centric prediction with the goal to optimise insemination technique or decision-making for extended embryo culture. They used patient characteristics, ovarian stimulation data and embryo parameters to predict aneuploid zygotes or blastocyst yield, to optimise number of embryos transferred or the formation of high-quality embryos.
- Some research focused on treatment strategy planning using patient characteristics and clinical parameters, for example selection of patients for IUI, defining probability of natural conception after reproductive surgery and selecting patients with high risk of fertilisation failure.
- A further group of studies used ultrasound-based radiomics from the endometrium and the peri-endometrial zone, multimodal transvaginal imaging, and clinical–radiomic integration to evaluate endometrial receptivity and predict outcomes in FET cycles.

- A study compared the effect of short and long (3 vs 16-20 hours) insemination protocols on fertilisation and clinical pregnancy rate in sibling oocytes, using Known Implantation Data (KID) scores for day 3 and day 5 calculated with Embryoscope software, concluding better embryo quality outcomes with short co-incubation for younger female patients or males with high total motile sperm count.

2.5. Research has also focused on developing ML models to predict ovulation, optimise trigger time and individualise ovarian stimulation dose:

- Studies used ML models to predict ovulation timing in natural (FET and IUI) and LH surge in GnRH antagonist stimulated cycles by integrating reproductive hormone measurements and ultrasonographic parameters. The parameters of the models incorporated preovulatory serum levels of progesterone, LH and oestradiol, and follicular diameter to improve accuracy in ovulation detection, prevent cycle cancellation and improve timing of trigger administration.
- Other ML models focus on optimal trigger day to maximise the number of mature metaphase II (MII) oocytes and useable blastocysts.
- A few studies developed ML models to optimise different aspects of the ovarian stimulation protocol, such as first FSH dose, real-time adjustments to FSH dosing and pituitary suppression protocols with the goal to obtain optimal number of MII oocytes and maximise the number of intermediate size follicles. Models have implemented combination of both static (eg age, BMI, basic hormone levels) and dynamic (eg follicle number and size, hormone levels during stimulation across stimulation days) variables.

2.6. Studies have applied ML models to assess oocyte competence for blastocyst development using imaging data:

- These include evaluation of denuded MII oocytes from static two-dimensional images using multi-class segmentation and feature extraction, with ooplasm features contributing most strongly to model performance.
- Federated ML models, (ie data were retained on regional servers to comply with data privacy laws) demonstrated that AI-derived scores from two-dimensional images correlated with zona pellucida and perivitelline space dimensions, ooplasm appearance, and subsequent blastocyst expansion grade and morphological quality.
- Additional approaches include microfluidic-based ML models incorporating biomechanical features to predict immature oocyte quality; phenotypic analysis of morphological and dynamical features from transmitted-light images or time-lapse movies; and the use of a commercially available software (Magenta) to predict blastocyst development in couples with severe male factor infertility. However, the lack of sperm-specific parameters in the latter may limit its capacity to fully capture male infertility effects despite observed negative correlations with paternal age. Magenta scores were also used to assist with egg donor allocation decisions by predicting fertilisation and blastulation competence of fresh donor oocytes.

2.7. Many studies report on commercial and bespoke ML models to perform embryo evaluation, focusing on non-invasive ploidy testing and utilisation of time-lapse data for embryo ranking:

- AI approaches are increasingly applied to non-invasive embryo ploidy assessment. They use time-lapse imaging (TLI), static two-dimensional/three-dimensional morphological images and integrated clinical data within PGT-A or PGT-SR cycles. Commercial (e.g. KIDScore,

iDAScore, ERICA) and in-house developed ML and explainable artificial intelligence (XAI) models demonstrate associations between different morphokinetic and morphological parameters – eg trophectoderm cell number and cell size variance, and inner cell mass area – and known embryo ploidy status. Some approaches report improved embryo utilisation and higher live birth rates when ML-guided grading systems are applied. Complementary algorithmic approaches address technical barriers in non-invasive chromosome screening, such as detection of maternal DNA contamination and correction of copy number variation in spent culture media. Studies emphasise data integration to enhance predictive accuracy, while others highlight biological limitations, including overlapping morphokinetic profiles between euploid embryos and embryos with chromosomal gains.

- Several studies report on predictive models for embryo competence, including implantation potential and blastocyst formation by training algorithms on morphological and morphokinetic variables acquired with TLI systems. Some ML models focus on automatic prediction of morphokinetic stage and timings of embryo development to select embryos based on developmental stage rather than embryo age; others integrate TLI, patient and PGT-A data to predict competence by defining time cut-offs at developmental stages and associating them with ploidy. Studies also report on self-supervised learning models and interpretable AI to predict blastulation, embryo quality and implantation potential, as well as foundation models that use large scale unlabelled imaging data to improve accuracy in several embryology-related tasks. Overall, studies argue that use of subtle differences in embryo kinetics in ML models can enhance model transparency and optimise workflows.
- The only RCT study to assess the effectiveness of TLI data-based deep-learning models for embryo selection on clinical outcomes (Illingworth *et al*., 2024) was discussed at the October 2024 SCAAC meeting. Discussion highlighted the operational benefits of introducing AI technologies into the embryology lab.

2.8. Further, research on embryo ranking emphasise the use of morphological, morphokinetic and other non-invasive assessment methods for training ML models to provide standardised objective embryo evaluation:

- BlastScoringNet to select among blastocysts with similar/same morphological grades but different potential to result in live birth by quantification blastocyst's ICM and TE morphology with continuous scores.
- integrating YOLO, v8 (You Only Look Once) – a type of Convolutional Neural Network for object detection widely applied to medical imaging problems – and image processing techniques (Gradient Vector Flow and Normalized Uniformity Value) to improve accuracy in blastomere detection and cell uniformity assessment.
- developing scores and comparing embryos resulting in singleton vs multiple pregnancies, or sibling embryos with known clinical outcomes to not transferred sibling embryos.
- generative models (diffusion models and generative adversarial networks) for embryo cell stage prediction using real and synthetic data to improve classification performance.
- ML models using integrated data (manual embryo grading, TLI data, morphological parameters, clinical outcomes and ploidy analysis in PGT-A cycles) to compare ML scoring to manual grading or to explore the association between blastocyst collapse and aneuploidy.

- complementary frameworks incorporating modified ribosomal small RNAs profiling, Raman spectroscopy, or metabolic profiling of spent culture media further extend embryo quality prediction beyond morphological parameters.
- a few studies compared agreement between manual morphological grading and ML (machine learning) algorithms for embryo selection, reporting equivalent or superior performance of ML models.
- Overall, studies show that embryos labelled with high scores by ML models are associated with better clinical outcomes (implantation and LBR); the importance of increasing the size of training data in deep learning models to improve model performance for predicting clinical outcomes is also highlighted.

2.9. Several reports describe applications of deep learning for sperm detection, tracking and analysis of sperm parameters (ie sperm count, morphology, motility, and DNA fragmentation index, DFI), including YOLOv8-based object detection models, tracking algorithms and fluorescence-based approaches. Performance was compared against other deep learning models or conventional manual or computer-assisted semen analysis, and for DFI against flow-cytometry–based methods; it was highlighted that rich image acquisition conditions in the training datasets are key factor affecting model generalisability.

Post-treatment stage

2.10. Few studies developed ML models to predict LBR after positive pregnancy test. For example, POPI-Plus tool incorporating patient age at egg retrieval, first and second beta-human chorionic gonadotropin (beta-hCG) and IVF treatment type was developed for elective single embryo transfers (eSET). Another study reported a delta ultrasound radiomics model for predicting live birth following FET using maternal age and radiomic feature differences between gestational weeks 6 and 8 (Liu *et al*., 2025).

Operational uses

2.11. Studies report on using AI models, automation and robotics to optimise laboratory operations, quality management, and procedural consistency. These include AI models integrating clinical data and KPIs for prospective evaluation of treatment outcomes, prediction of workload and optimisation of procedural timings. Reports also highlight automated liquid-handling robotics for preparation of embryo culture dishes and automated software-guided cryostorage systems. The first live birth resulting from an automated, remotely operated ICSI was reported, with the system completing 49.6% of the required 115 micromanipulation steps autonomously (Mendizabal-Ruiz *et al*., 2025).

Basic and clinical research

2.12. Many studies focused on harnessing AI to advance male infertility diagnostics. Some studies developed ML models that integrate multi-omics data (eg single-cell transcriptomics, protein-protein interactions, whole-exome sequencing, single nucleotide polymorphisms) and clinical data (eg serum hormone profiles, metabolic data, medical records) to identify candidate genes for spermatogenic failure, with a focus on oligozoospermia and non-obstructive azoospermia (NOA). Other studies developed ML models to predict semen quality based on questionnaire

data about lifestyle and a deep learning model to predict testicular histology from ultrasound images to support clinical decision making for testicular sperm extraction.

2.13. Several studies describe the use of machine learning, deep learning, and computer vision to automate and enhance embryo image analysis across developmental stages, from cleavage to blastocyst. Approaches include three-dimensional reconstruction from multifocal time-lapse data, automated segmentation of blastomeres and blastocyst structures, consensus-compliant assessment of embryonic development from optical images, and generation of artificial embryoid images using fluorescent images of stem cell–based embryo models to study morphogenesis.

2.14. ML models have been employed in a variety of other areas of basic and clinical research:

- Transcriptomics-based models are used to evaluate efficiency of endometrial receptivity testing data, identify a disrupted window of implantation, and define endometrial signatures associated with recurrent pregnancy loss. Other ML approaches use patient characteristics, clinical variables, and hormonal data to predict IVF outcomes and ovarian reserve.
- ML methods to assess oocyte developmental competence and ageing using imaging data and gene expression databases.
- Deep learning frameworks aiming at improving non-invasive PGT (niPGT) accuracy. They integrated single-cell methylation sequencing data of cell-free DNA (cfDNA) from spent embryo culture medium to correct for maternal DNA contamination.
- Deep learning methods for image analysis to study folliculogenesis; for automation and quantification of sperm DNA fragmentation test results; for quantitative assessment of trophoblast invasion; and ultrasound follicle segmentation.

2.15. Beyond clinical IVF, MLs have been also applied to population-level fertility research to identify predictors of fecundability and fertility rates in low- and middle-income settings, as well as to estimate return rates after oocyte cryopreservation based on demographic and clinical factors. These studies highlight that such models can inform public health strategies and can help with targeted screening and tailored fertility counselling.

2.16. Several studies examine the role of generative AI, such as large language models (LLMs) and generative adversarial networks (GAN) across clinical support, research optimisation, and interpretability in reproductive medicine:

- LLMs such as GPT-4 and GPT-5 show potential for data processing, ML model optimisation, scientific writing, clinical decision-making support and education. However, studies highlight variability in their performance, with limited reliability in complex clinical scenarios and a low proportion of evidence-based and guideline-compliant recommendations in fertility care.
- In parallel, generative and adversarial models are applied to interpret image-based embryo quality classification decisions and to generate synthetic blastocyst images, supporting explainability and the creation of large training datasets for the development of more robust embryo-assessment AI systems.

2.17. In November 2025 the Alan Turing Institute announced receival of a grant to develop data-efficient AI methods that can make accurate, trustworthy predictions even from limited, noisy, or fragmented datasets, helping scientists accelerate discovery in fields where data are scarce.

The tools will also quantify uncertainty and will enable researchers to make informed decisions based on the information that is presented to them by an AI model. This capability is particularly important for AI tools that are informing scientific discovery and experimental design, which can be costly or safety critical.

Reviews

2.18. Many reviews focus on overview of AI and different ML (machine learning) models in the field of reproductive medicine and their benefits and challenges associated with clinical implementation. Studies highlight AI frameworks' benefits including the potential to address inefficiencies, alleviate staff shortages, improve decision-making in the IVF laboratory, as well as to improve overall efficacy and safety of ART by optimising and personalising key steps of clinical and laboratory processes. Data quality, computational infrastructure, sustainability concerns, limited transparency in AI systems, ethical and regulatory issues are among the key barriers highlighted throughout. Future aspects for safe deployment of AI and ML models include the need to accumulate high-quality datasets from diverse clinical settings, algorithm optimisation, and advances in imaging technology.

2.19. Overall, studies describe a range of AI frameworks capable of processing the complex, multidimensional data generated during IVF procedures. These approaches are reported to support workflow efficiency, clinical decision-making, outcome prediction, and more individualised treatment planning and counselling, including the management of patient expectations. Machine-learning models are also presented as tools for greater standardisation of laboratory processes, for example by supporting embryo assessment through the integration of patient demographics with time-lapse morphological and morphokinetic data. At the same time, the literature also identifies challenges related to model validation, reliance on retrospective datasets, demographic and ethnic bias, and application of software beyond its intended scope.

3. Recommendations

3.1. Members are asked to:

- Consider the progress of research into AI, robotics and automation in fertility treatment and advise on any other relevant developments;
- consider uses of AI across the patient pathway against the Authorised processes list and advise on any novel applications of AI;
- advise on any other concerns/issues pertaining to uses of AI that may have licensing and regulatory implications; and
- review whether any outputs from the HFEA are required.

4. References

Illingworth, P.J., Venetis, C., Gardner, D.K. *et al.* Deep learning versus manual morphology-based embryo selection in IVF: a randomized, double-blind noninferiority trial. *Nat Med* **30**, 3114–3120 (2024). https://doi.org/10.1038/s41591-024-03166-5

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Mendizabal-Ruiz G, Chavez-Badiola A, Hernández-Morales E, Valencia-Murillo R, Ocegueda-Hernández V, Costa-Borges N, Mestres E, Acacio M, Matia-Algué Q, Farías AF, Carreon DSM, Barragan C, Silvestri G, Martinez-Alvarado A, Olmedo LMC, Aguilar AV, Sánchez-González DJ, Murray A, Alikani M, Cohen J. A digitally controlled, remotely operated ICSI system: case report of the first live birth. Reprod Biomed Online. 2025 May;50(5):104943. doi: 10.1016/j.rbmo.2025.104943

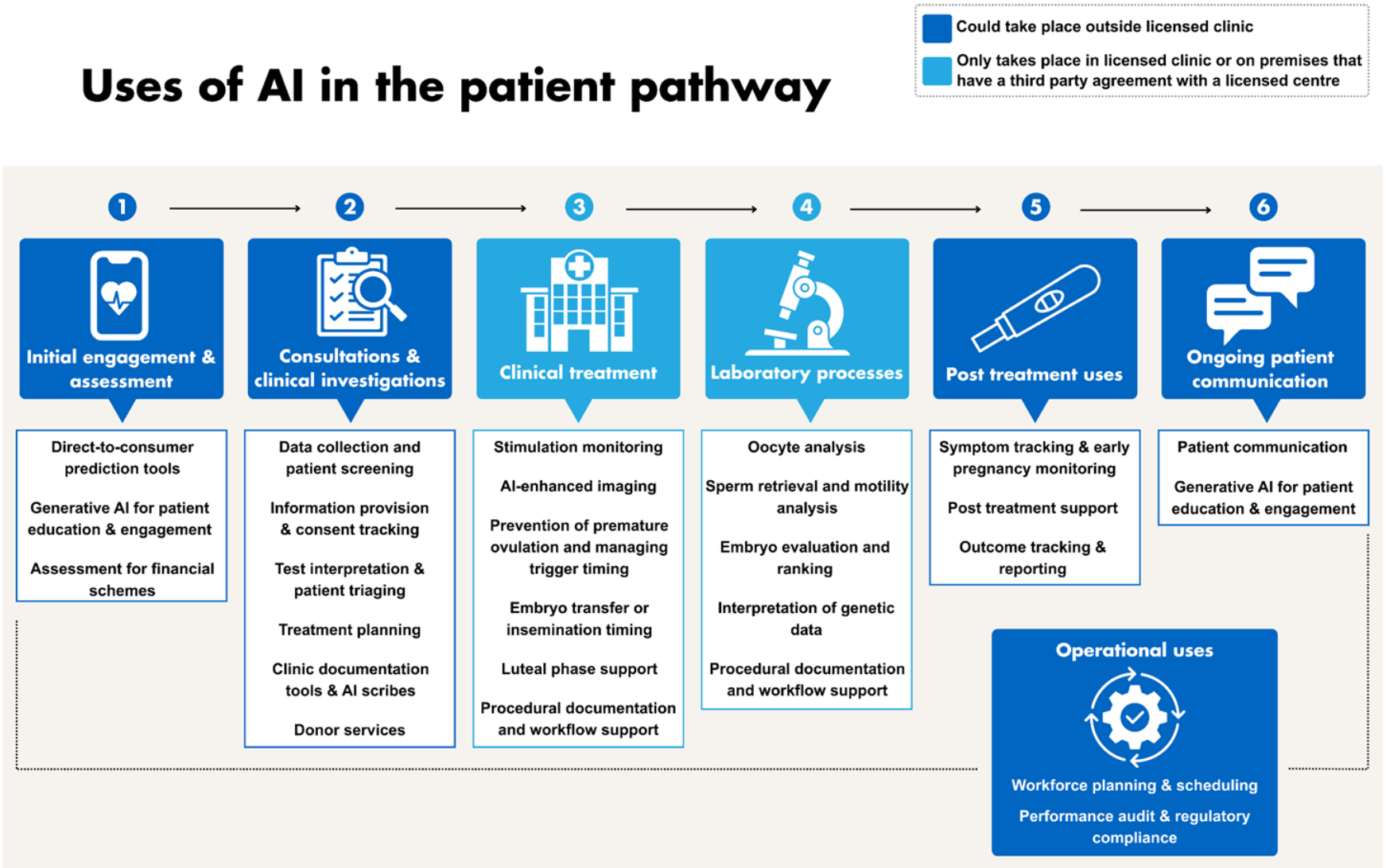
5. Annex A – Literature review on Artificial intelligence (AI), robotics and automation in fertility treatment

5.1. Annex A has been circulated to the committee as a separate Excel document, which provides details on the available research on Artificial Intelligence (AI), robotics and automation in fertility treatment published between 1st January 2024 and 31st December 2025. Where possible literature has been separated by relevant subheadings.

5.2. This topic is focused on the integration of AI, robotics or automation at any stage during the fertility journey. This includes the use of robotics for automation in the laboratory (eg automated ICSI, gamete/embryo freezing, preparation of culture dishes) or in the clinical treatment of infertility (eg endometriosis, myomectomy, fibroids, polyps), and AI tools/algorithms for basic science, embryo and gamete selection, and for prediction and improvement of outcomes before and after treatment. Time-lapse imaging is excluded from the search as it is considered under the treatment add-on 'time-lapse imaging and incubation'. Whilst patient support apps are included, AI apps to improve general health and wellbeing, which in turn impact fertility outcomes, are additionally excluded. Literature on regulation, guidelines and ethical considerations is included.

5.3. The topic search strategy, originally developed in PubMed, was adapted for Ovid Medline to align with the methodology developed for the treatment add-ons literature search, and to ensure comprehensive coverage across platforms.

6. Annex B: Uses of AI across the patient pathway



Review of authorised use of calcium ionophore

Details about this paper

Area(s) of strategy this paper relates to:	Supporting scientific and medical innovation
Meeting	Scientific and Clinical Advances Advisory Committee (SCAAC)
Agenda item	8
Paper number	HFEA (04/02/2026) 008
Meeting date	4 February 2026
Author	Rebecca Taylor, Scientific Policy Manager
Annexes	Annex 1 – Previous novel process application received for calcium ionophore for embryo development Annex 2 – Authorised process decision tree

Output from this paper

For recommendation or decision?	For decision
Recommendation:	Members are asked to: • confirm that the current inclusion of calcium ionophore on the authorised processes list does not include its use for embryo development • consider whether a novel processes application is required for the use of calcium ionophore for embryo development • consider any other steps that may be required in relation to the use of calcium ionophore for embryo development
Resource implications:	TBC
Implementation date:	N/A
Communication(s):	N/A
Organisational risk:	Medium

1. Introduction

1.1. As the UK regulator of fertility clinics, the HFEA maintains a list of authorised processes, which are arranged under each of the licensable activities permitted by the Human Fertilisation and Embryology Act 1990 (as amended). If a centre wishes to carry out a process which does not appear on the list, it must apply to the Authority for permission. The Authority delegated the authorisation of novel processes to the Scientific and Clinical Advances Advisory Committee (SCAAC) in 2024.

1.2. The process for SCAAC's consideration of a novel process application is as follows:

1.2.1. SCAAC should agree that the process is sufficiently different from the processes currently authorised to be considered 'novel'. The Committee should also make a judgement on whether the evidence is sufficient to satisfy committee members that the process does not render the tissues or cells clinically ineffective or harmful to the recipient. In the event of the evidence not being fully conclusive, SCAAC members should use their judgement based on a compound level of risk and the strength of the evidence.

1.2.2. If approved, the SCAAC define the criteria for mandatory reporting including the data requirements (KPIs), timeframe and intervals for reporting. The HFEA Executive propose that SCAAC consider a standard 3-year initial period of mandatory reporting upon approval to ensure that the use of a new authorised process is reconsidered within a minimum timeframe. Depending on the perceived level of risk associated with the process or its anticipated frequency of use, the SCAAC may wish to reduce the timeframe for mandatory reporting to enable reconsidering a process at an earlier date.

1.2.3. If upon reconsideration of an authorised process, the evidence to support its ongoing use (provided as per the mandatory reporting requirements) is inconclusive, the SCAAC may:

a) Reinstate/extend the requirement for mandatory enhanced reporting,
b) Place additional conditions on the use of a process (eg restrict the process to a defined group),
c) monitor on a more regular basis through committee discussions, or
d) (in exceptional circumstances) suspend the process until a decision can be taken.

1.3. The use of calcium ionophore in fertility treatment is being brought to the attention of SCAAC due to questions from HFEA inspectors about its use outside the authorised process use of artificial oocyte activation (AOA). Upon recent investigation (outlined below), it became clear that one clinic had been told by the HFEA in 2018 that they could use calcium ionophore for embryo development and that this fell under the existing authorised use. The Committee was not consulted on this matter at the time or since. Hence the Executive is bringing this to the attention of SCAAC now.

2. Calcium ionophore – current status

2.1. The use of calcium ionophore for artificial oocyte activation (AOA) is an HFEA authorised process under "processing gametes".

2.2. Calcium ionophore for AOA was reviewed by the SCAAC in 2018: Reviewing novel processes: egg activation with calcium ionophore. The SCAAC decided that it should remain on the authorised processes list.

2.3. At the June 2023 SCAAC meeting, the Committee recommended delaying the rating of AOA using calcium ionophore until the BFS/ACRS guideline was published. The guideline was then in the final stages of being developed. For further information see SCAAC minutes June 2023.

2.4. At the October 2023 SCAAC meeting, the Committee then considered whether calcium ionophore for artificial oocyte activation (AOA) should be considered as a treatment add-on and subject to rating, in light of the newly published ACRS/BFS guideline. The Committee agreed that AOA did not meet the criteria to be considered a treatment add-on as it should not be offered to the general population.

2.5. The Committee agreed to remove AOA from the add-ons list on the HFEA website and to add information noting this removal and signposting to the relevant professional body guidance for the use of calcium ionophore for AOA. That information can be found here: Treatment add-ons with limited evidence | HFEA.

2.6. Discussions at the October 2023 SCAAC meeting confirmed that clinics using calcium ionophore for AOA should follow the relevant professional body (ACRS/BFS) guideline, which the Committee summarised as follows:

- AOA should not be used routinely with ICSI as its safety, in terms of the potential developmental consequences and birth outcomes, has yet to be established.
- ICSI with AOA may be used where two previous routine ICSI cycle(s) have resulted in <30% or no fertilisation.
- Where AOA is used, patients should be advised that safety, in terms of the potential developmental consequences and birth outcomes, has not been established.
- Patients should be provided with safety data relating to the specific AOA technique used.

2.7. A SCAAC member raised the use of calcium ionophore for poor blastocyst or embryo development. The SCAAC Deputy Chair (at that time), also an author of the ACRS/BFS guideline, said that guideline authors:

"we're aware of this research but wanted to take a cautious approach, not permitting the technique for other indications until further evidence is available."

It was also noted that there was consistent consensus among ACRS/BFS guideline authors.

2.8. For more information, please see the minutes of the October 2023 SCAAC meeting.

3. Calcium ionophore for embryo development – background

3.1. A novel process application for the use of calcium ionophore for "arrested embryo development" (also referred to as "poor embryo development") was received by the Executive in October 2018. The clinic submitting the application received a response from the Executive, which said that this use of calcium ionophore was covered by its existing authorised use. The application was not brought to SCAAC for consideration.

3.2. Upon recent examination of the correspondence relating to the embryo development novel process application, the Executive now consider that the response given at that time was problematic. The response did not specifically address the use of calcium ionophore for embryo development, but referred to its use for AOA. The precise wording was:

"*On full review, we have concluded that your proposed treatment will not be a novel process, but will fall under the use of Calcium Ionophore already approved by SCAAC. Approved with the following caveat: The HFEA's Scientific and Clinical Advances Advisory Committee considered the use of Calcium Ionophore as an egg activation technique and highlighted the theoretical risks relating to embryo viability (e.g, premature activation and triploid embryos).*

Given the theoretical risks of using Calcium Ionophore, centres using it are expected to do so only in selected patients, such as those with PLCz deficiency. Centres are expected to document their rationale for using Calcium Ionophore for individual cases. As with all treatments and processes, centres should ensure that patients are fully informed about the efficacy and potential risks and that validation is carried out.

Please do ensure that patients fully understand the potential risks and fully document the rationale for the application of the process, in the patient record, for each individual use."

3.3. It is our view that the HFEA response given to the clinic in 2018 was based only on the physical process being used, which was identical to the authorised process, and not the purpose of its use, which was embryo development rather than oocyte activation. This use was thus outside the authorised process. The professional guideline (from ARCS/BFS) subsequently published in 2023 made it clear that calcium ionophore should only be used for oocyte activation for specific patients and clinics should have followed that guideline from then on.

3.4. Based on the correspondence relating to the 2018 novel process application for the use of calcium ionophore for poor/arrested embryo development, we assume that the clinic concerned received what they considered to be a green light from the HFEA for this use. We also believe that the clinic may have considered that "specific patients" could be applied to patients with poor/arrested embryo development.

3.5. At recent clinic inspections, inspectors became aware that clinics are using calcium ionophore for embryo development, which is outside the ARCS/BFS guideline which clinics should follow. As a result, we have been looking at the following:

- Under what circumstances a clinic can decide not to follow the ACRS/BFS guideline on Artificial Oocyte Activation (wording in the Code of Practice is "should") and what steps a clinic must take if they make such a decision.
  NB: When clinics decide not to follow professional body guidance, this usually falls into three categories;

  - The guidance is out of date (it may already be in the process of being updated as a result)
  - There is new evidence available that the clinic wishes to rely on
  - The clinic has done their own validation and risk assessment and do not agree with the professional guidance, for example egg donation quarantine for frozen eggs in the latest ARCS/BFS guidance.
- What is the current status of the use of calcium ionophore for poor/arrested embryo development?

4. Recommendations

4.1.

Members are asked to:

- confirm that the current inclusion of calcium ionophore on the authorised processes list does not cover its use for poor embryo development
- consider whether a novel processes application is required for the use of calcium ionophore for poor embryo development
- consider any other steps that may be required in relation to the use of calcium ionophore for poor embryo development

5. Annex 1: 2018 SCAAC paper - Novel Process Application for Calcium Ionophore for poor embryo development

5.1. Based on the records held by the HFEA on this matter, the information that the clinic provided to the Executive was as follows:

- A document outlining the basis of their application to use calcium ionophore for arrested embryo development which covered:
    - The results of studies on using calcium ionophore to improve blastocyst development rate for patients with a history of embryo arrest
    - The clinic's standard operating procedure for the authorised process using calcium ionophore including methods and timeline for validating the results of using CI for embryo development
    - Explanation of how artificial oocyte activation (AOA) is used to improve fertilisation rates and the outcome of studies on this use
    - A detailed presentation of the proposed new process for using calcium ionophore for embryo development including timescales, responsibilities, outcome measures and validation approach methodology and reporting lines.
- A patient consent form for the use of calcium ionophore for arrested embryo development, which covered:
    - Why oocyte activation is important
    - What is artificial oocyte activation
    - Poor embryo development, how and why it occurs
    - How successful is AOA
    - How AOA is performed
    - Safety and risks for the patient
    - Fees
    - Possible alternatives to AOA
    - Consent statement for female patient to complete and sign
- A copy of the study from Ebner et al (2015): Treatment with Ca2+ ionophore improves embryo development and outcome in cases with previous developmental problems: a prospective multicenter study.

Annex 2: Authorised processes decision tree