Background to the novel process application for Anecova AneVivo Intrauterine device

Strategic delivery:	☒ Safe, ethical, effective treatment	☐ Consistent outcomes and support	☐ Improving standards through intelligence

Details:	
Meeting	Scientific and Clinical Advances Advisory Committee (SCAAC)
Agenda item	5
Paper number	SCAAC (08/06/2020) 005
Meeting date	08 June 2020
Author	Victoria Askew, Policy Manager
Output:	
For information or recommendation?	For recommendation
Recommendation	Member are asked to consider: • whether the process outlined in this application is sufficiently different from the processes currently authorised as to be considered 'novel' • whether there is evidence that this process is not effective • whether there is evidence that this process is not safe
Resource implications	N/A
Implementation date	N/A
Communication(s)	N/A
Organisational risk	☐ Low ☒ Medium ☐ High
Annexes	Annex A: Novel process application – IVF using the AneVivo device in interpartner and standard egg donation Annex B: Supporting information Annex C: Novel processes authorisation decision tree

1. Background – authorised processes and the role of SCAAC

1.1. A list of authorised processes, approved by the Authority, are available on the HFEA Clinic Portal, organised under licensable activities permitted by the HFE Act 1990 (as amended). Fertility clinics that hold a license with the HFEA are permitted to undertake the appropriate authorised processes, in accordance with their licence, as part of their clinical practice. If a centre wishes to use a 'novel process' which does not appear on the authorised list, they need to apply to the HFEA to seek permission to use it in clinical practice.

1.2. The Authority has delegated the authorisation of novel processes to the Statutory Approvals Committee (SAC), who are advised on the matter by SCAAC (Annex C). The role of the SCAAC is to review the novel process applications and provide an opinion to the SAC on the following questions:

- whether there is evidence to suggest the process is not safe; and
- there is evidence to suggest that the process is not effective.

1.3. SAC can make the following decision options:

- Refuse authorisation
- Adjourn decision in order to seek further information
- Authorised for use at all centres
- Authorised for use at named centres only
- Refer to the Authority for final decision

1.4. On approval, the process is labelled as 'recently approved' for the first two years and centres that would like to use the process have to inform the HFEA. At the end of the two years all centres using the process should submit an outcome report to the HFEA on safety and efficacy.

1.5. An application (Annex A) has been received for the extension of the use of the current authorised process intrauterine culture to allow the device to be used between different women. This would allow the eggs donated by a partner or donor to be inserted into a second partner or recipient for incubation. The process is currently only authorised for use in a single woman.

2. Executive Summary – previous information relevant to this application

2.1. In June 2015, a novel processes application for the intrauterine culture of gametes and embryos (including insertion and removal of device, followed by transfer of embryo(s) **to the same woman**) was discussed by SCAAC. SCAAC made the following comments:

- Due to the limitations of the data provided the Committee felt that they could not make an assessment of the efficacy of the process. However, the Committee noted that Anecova AneVivo intrauterine device has been used in for treatment in three European countries resulting in a number of live births, suggesting that it is sufficiently effective to give successful IVF outcomes some of the time.

- The Committee agreed that insufficient evidence was provided in the application to determine whether intrauterine culture of gametes and embryos in a device such as the Anecova AneVivo intrauterine device is safe.

2.2. This meeting was followed up by a teleconference between the applicant and SCAAC to provide further evidence on the process. SCAAC made the following conclusions:

- there is no evidence to show that the device is not unsafe; and
- that the clinical data on the device is too limited to demonstrate its efficacy, but there is no evidence to indicate that the process is not effective.

2.3. In July 2015, further data was submitted by the applicant to reassure SCAAC of retrieval rates of the embryo used during this process.

2.4. In August 2015, the SAC considered the application and noted that SCAAC's consideration was as follows:

- The use of intrauterine culture devices did constitute a novel process;
- The process applied for falls within two licensable activities: processing gametes and processing embryos;
- The evidence provided gave no indication that the process is unsafe;
- SCAAC did not see any evidence to suggest that intrauterine culture of gametes/embryos using a device such as the Anecova AneVivo would not be effective. However, it did not feel that there was sufficient clinical data to say whether the process has a greater or lesser efficacy than that of traditional IVF methods.

The SAC approved the application for the intrauterine culture of gametes and embryos (including insertion and removal of device, followed by transfer of embryo(s) to the same woman) by majority and the process was subsequently added to the authorised processes list. In agreeing to authorise the novel process, the SAC agreed with SCAAC's observation that, as it is possible that the process might offer no improvement in efficacy and might add an unnecessary cost to patients, any patient information provided by clinics should highlight this. In addition, information on the HFEA website should draw attention to the fact that the process has not yet been subject to a clinical trial, and its efficacy is therefore not known.

2.5. In line with Authority's standard operating procedure for reviewing novel processes, in February 2018, SCAAC reviewed an outcomes report provided by the applicant two years after the process's initial approval. SCAAC were asked to provide an opinion as to whether they had any concerns that intrauterine culture should be removed from the authorised process list. SCAAC raised that there was a lack of hypothesis and the data was insufficient. Members noted that the protocol used in the outcomes report is different from the protocol described in the original application, and that this raised a risk. The SCAAC requested that a representative of the applicant be invited to the next SCAAC meeting to provide further clarification.

2.6. In October 2018, Professor Nick Macklon attended the SCAAC meeting to update the Committee on activity since the novel process application was approved in 2015. Prof Macklon and the Committee made the following comments:

- Prof Macklon stressed that the treatment is not currently offered to improve pregnancy rates or to benefit the embryo, rather the claimed benefits to the woman are psychological as she can be more physically involved in the process.
- Two factors led to the introduction of the intrauterine culture technique being deprioritised. Training took place before the procedure was ready to be offered to patients. Prof Macklon at that point left the centre and the Trust then began the process of selling the clinic to a private investor.
- Data from use of the device in Spain will be presented at Fertility 2019. Prof Macklon asked the Committee to consider whether there is sufficient data to allow continued use of the device in the UK subject to further review in 2 years' time from now once there is more data. This outcome report is due to be submitted to the HFEA by the end of 2020. It is intended that this report will be presented to SCAAC for consideration at the October 2020 meeting.
- A member asked about pre-clinical experience with the device using human embryos donated to research. Prof Macklon addressed that this has not progressed due to the lack of embryos donated for research for this purpose.
- SCAAC concluded that the Executive will follow up with Prof Macklon to review the patient information relating to intrauterine culture.

2.7. In January 2019, the applicant shared slides on new data regarding the technique that had been presented at the Fertility 2019 conference, however the SCAAC suggested that this was not sufficient and additional data would still be needed for SCAAC to review whether intrauterine culture should remain on the list of approved novel processes.

2.8. In December 2019 it was reported in the press that a same sex couples undergoing partner donation during their IVF treatment had used intrauterine culture. Reported as 'shared motherhood' this allowing both partners to 'carry' the pregnancy at some point during their treatment. This did not fall under the authorised process, which only allowed intrauterine culture to take place in a single women. Due to concerns over infection risk the centre were contacted by their HFEA inspector about their misuse of this authorised process.

2.9. In January 2020, a novel processes application was received for intrauterine culture of gametes and embryos (including insertion and removal of device, followed by transfer of embryo(s) **between different women**). This would extend the use of the intrauterine device to lesbian couples undergoing partner donation and to recipients of donor eggs.

2.10. Of note, the applicant has made no claim that this treatment is intended to increase live birth rate. It is instead intended to mimic a more 'natural' environment, reduce the exposure to synthetic in vitro culture media and give some psychological benefits to patients. However, SCAAC have previously commented that the device does not mimic 'natural' development as the embryo would usually be in the fallopian tubes in the early stages of development, rather than the womb.

3. Conclusion

3.1. An application has been received for the extension of the use of the current authorised process intrauterine culture to allow the device to be used between different women. This would allow the eggs donated by a partner or donor to be inserted into a second partner or recipient for incubation. The process is currently only authorised for use in a single woman.

3.2. SCAAC has previously raised concerns about the lack of available data on the effectiveness and safety of intrauterine culture

4. Recommendations

4.1. Members are asked to consider:

- whether the process outlined in this application process is sufficiently different from the processes currently authorised as to be considered ‘novel’; and
- whether there is evidence that this process is not effective; and
- whether there is evidence that this process is not safe.