

## Scientific and Clinical Advances Advisory Committee Paper

<b>Paper Title</b>	<b>Simplified IVF culture system</b>
<b>Paper Number</b>	SCAAC(10/13)02
<b>Meeting Date</b>	30 October 2013
<b>Agenda Item</b>	5
<b>Author</b>	Chris O'Toole (Head of Research Regulation)
<b>For information or decision?</b>	Decision
<b>Resource Implications</b>	None
<b>Implementation</b>	None
<b>Communication</b>	None
<b>Organisational Risk</b>	Medium
<b>Recommendation to the Committee</b>	Members are asked to consider the safety and efficacy of the new low-cost method for carrying out IVF
<b>Evaluation</b>	None
<b>Annexes</b>	None

## 1. Introduction

- 1.1. Current IVF techniques involve the use of laboratories that are expensive to set up and treatments that are costly to perform. However, recently a Belgian research group (Klerkx et al 2013) has detailed a culturing system that significantly simplifies the process in a *proof of principle study*.
- 1.2. The group suggests that it has identified a simplified culturing system that does not require all the expensive equipment usually found in IVF laboratories, therefore enabling techniques to be used in developing countries. The group has developed a method which will keep embryos cultured in the acidic environment they require but using a simplified technique, without the need for CO<sub>2</sub> chambers. So far the method has given similar success rates as conventional IVF and this has sparked interest from groups wanting to offer cheaper treatment to patients here in the UK.
- 1.3. The HFEA has received an enquiry from a licensed centre in London, seeking to use the simplified culturing system in clinical practice. The Executive is still considering the correct regulatory approach, although it is clear that this does not fall under the definition of a novel process, as it does not represent a different method for creating embryos. As such, we are not seeking SCAAC's view as part of an approval of a novel process. However, we would like SCAAC's view on the safety and efficacy of this culturing system to inform our thinking.

## 2. Simplified culturing system

- 2.1. Using this new system, eggs and sperm, collected from the patients are placed and kept inside a mini-laboratory (about the size of a shoe box) in which fertilisation and the first few days of embryo development take place. Rather than using a ready-made mixture of CO<sub>2</sub> (as in a normal IVF lab), the CO<sub>2</sub> is created using a mixture of basic household chemicals.
- 2.2. The idea is it could be used in a basic clinical setting (provided it had a treatment room for egg collection and a laminar hood for sperm preparation) without the expense of setting up a full laboratory. They can carry out a simplified system of IVF at "10-15% of current costs in Western-style IVF" (approximately 200 euros per cycle).
- 2.3. The Executive understands that the simplified culture does not involve the whole process taking place in this mini laboratory. The simplified culture system appears to involve the following steps:
  - sperm is processed in an air controlled clean environment (either using a laminar flow or an IVF chamber)
  - sperm and eggs are mixed in tubes
  - the tubes are contained within the mini laboratory.

### Simplified IVF culture system

- 2.4. Therefore this 'mini laboratory' is similar will be used in a similar way to an conventional IVF incubator and that like all equipment used to carry out licensed activities it will be to validated to ensure it is suitable to culture embryos and maintain their quality prior to it be used in a HFEA licensed centre.

### 3. Safety and efficacy issues

- 3.1. The Belgian research group that has developed this technique has tested the simplified culture system on cumulus-oocyte complexes collected from superovulated mice and on fresh tripronucleate embryos and cryopreserved pronuclear and 2 cell human embryos donated for research. There pre-clinical studies demonstrated that the simplified culture system supports fertilisation and normal pre-implantation embryogenesis to the hatched blastocyst stage in both species. The research group then carried out a pilot clinical trial where they used their simplified culture system in comparison with a regular IVF culturing system, analysing embryo quality at day 3, embryo implantation rate and on-going pregnancy rate.

- 3.2. The group's work suggests the following:

- Similar rates of fertilisation and cleavage in both the simplified and .regular culture system groups
- Where n=35, 65.7% of embryos originating from the simplified culture system were considered top quality.
- Implantation rates from the WE lab group were 34.8% and 30.4% pregnancy rate.
- As of December 31<sup>st</sup> 2013 3 live births (with vaginal birth) have arisen from the simplified arm of the study.

#### *Limitations of current research*

- 3.3. The recent work is at a very early *proof of principle* stage, conducted on a small sample group, with further work yet to be published.
- 3.4. More specifically, a potential limitation of the study, cited by the group was that the research was conducted using "1000 good motile sperm cells per oocyte" (Klerkx et al 2013). It is not clear whether acceptable results would be achieved if this parameter was different.

### 4. Recommendations

- 4.1. Members are asked to consider the safety and efficacy issues that may arise from such techniques.

4.2. Members are also asked to provide a view on:

- whether the results from the pre-clinical studies and the pilot clinical trial are sufficient validation in order for the simplified culture system to be used in the UK, and
- how much evidence would be needed to support validation of this equipment

## 5. References

- E.P.F. Klerkx et al (2013) First pregnancies with a simplified IVF procedure: a crucial step to universal and accessible infertility care. *ESHRE 2013 Conference proceedings* [Accessible at: [www.eshre2013.eu/~media/Files/London/Press%20releases/Klerkx.pdf](http://www.eshre2013.eu/~media/Files/London/Press%20releases/Klerkx.pdf)]