

## Scientific and Clinical Advances Group

### Summary of October horizon scanning questionnaire from the HHSEP

<b>Committee:</b>	Scientific and Clinical Advances Group
<b>Meeting Date:</b>	15 December 2004
<b>Agenda Item:</b>	8
<b>Paper Number:</b>	SCAG (12/04) 04
<b>Paper Title:</b>	Horizon scanning questionnaire response summaries
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<b>For Information or Decision?</b>	Decision
<b>Recommendation to the Committee:</b>	Members are asked to (i) comment on the responses from members of the HFEA horizon scanning expert panel; (ii) suggest further questions that might be put to the Panel.

#### Background

1. As part of the developing horizon scanning function of the HFEA, a group of experts were brought together to form a panel, the HFEA horizon scanning expert panel (HHSEP). The function of the panel is to advise the HFEA of new developments in any field that may have an impact on assisted reproductive technologies. In order to stimulate contributions from members of the panel, a questionnaire was sent to the group. The questionnaire was presented to members of SCAG at the last meeting and the final version was sent to SCAG members electronically, approved and sent to the HHSEP in October.

#### October 2004 horizon scanning questionnaire

2. The questionnaire, as recommended by SCAG, was kept to three questions; two general horizon scanning questions and one about *in vitro* maturation (IVM). The questionnaire was sent out in October and panel members were given about four weeks to respond although we made it clear that because horizon scanning was an ongoing process we would be happy to receive their response whenever they could return it.

**HFEA horizon scanning expert panel  
Questionnaire- October 2004**

1. What do you consider to be the biggest issue on the scientific horizon that could impact on assisted reproductive medicine and/ or technology in the future (in the next 1 year to five years)?
2. Are you aware of any techniques that are being developed in animal models that will be potentially transferable to human ART in the future? On what time-scale do you think this will occur?
3. What are your views on *in vitro* maturation of oocytes? In your opinion, do you think that there is sufficient knowledge about embryos created using *in vitro* matured oocytes to allow these embryos to be used in treatment services?

### **Response rate**

3. To date, eleven responses have been received out of 18 questionnaires sent out (61% response rate). Although some of the newer members of the panel did not receive questionnaires until later than the original HHSEP members. A full list of all the current HHSEP members can be found in Annex A.

### **Summary of responses**

4. The responses to the first two questions have been summarised according to topic because there was some overlap in the issues and topics raised. The third question about *in vitro* maturation of oocytes was summarised separately. Direct quotes from the experts can be found in Annex B.

### **Questions 1 and 2**

#### Issues relating to gametes

5. Several of the experts commented that the development of germ cells *in vitro* was an issue that could have an impact on ART in the future. This was specifically brought up in association with development of both sperm and oocytes from embryonic stem cells. It was noted that generation of oocytes from embryonic stem cells could potentially overcome a shortage of oocytes for use in derivation of further embryonic stem cell lines, if the embryos from the stem-cell derived oocytes were able to develop to the blastocyst stage.

6. One member of the panel mentioned that *in vitro* sperm maturation is being developed in animals and could potentially be transferable to humans within five years.
7. Another issue raised was that of germ cell transplantation which, in the opinion of the expert, could potentially have an impact on ART within 5 years. It was noted that *in vitro* maturation and cryopreservation of oocytes will require risk assessment for higher rates of chromosomal anomalies.

#### Issues relating to embryos

8. Controlling differentiation of embryos to maintain proliferation of a cleaving embryo to gain large numbers of cells for embryo splitting was an issue raised by one of the panel members. This would seem contrary to the idea of selecting the best embryos to put back because splitting an embryo could compromise the chances of embryo implantation and/or survival.
9. The production of human chimeras was mentioned in two contexts. The first, stem cells with desirable characteristics can be added to the inner cell mass of an embryo to enhance the genetic 'quality' of an embryo. The second reason for potentially producing chimaeras would be to allow lesbian partners to have equivalent genetic contribution to a child by combining embryos created from fertilised eggs from each partner.
10. It was suggested that expression analysis of developmentally important genes in embryos *in vitro* could predict the implantation potential of an embryo prior to implantation. This would allow selection of embryos with high chances of implantation on characteristics other than morphology. Many of the expert panel stressed the importance of research in the area of embryo culture, with regards both the use of automated culture systems and also the effect of sub-optimal culture conditions on embryos. Research in this area would potentially produce more sophisticated techniques to select the best embryo to transfer. Improved assessment of the best embryos to transfer will improve success rates so that single embryo transfer will be more attainable. New technology such as comparative genome hybridisation<sup>1</sup> or microarray<sup>2</sup> technology (gene chips) could have an impact on screening of pre-implantation embryos for chromosomal abnormalities or developmental gene expression.

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<sup>1</sup> An *in situ* hybridisation technique which is used in the characterisation of chromosomal abnormalities where there is a net loss (deletion) or gain (duplication, insertion or amplification) of genetic (chromosomal) material.

<sup>2</sup> A very small, two dimensional array, typically on a glass, filter, or silicon wafer, upon which genes or gene fragments are deposited, in a predetermined spatial order. Labelled DNA from a sample is then allowed to hybridise to the array allowing the expression analysis of a large number of genes.

## Ethical issues

11. Two experts commented on ethical issues in terms of the future with embryos selection; the use of IVF for selecting characteristics of embryos in fertile couples and how far 'scientific perfection' should be allowed and regulated.

## **Question 3**

### Use of IVM in treatment

12. When asked to consider the use of *in vitro* matured oocytes in treatment, panel members considered there to be insufficient research and information on the procedure for it to be used in treatment. However, it was pointed out that there had been successful pregnancies from IVM oocytes and the technique is promising. It was suggested by one member that it could be possible to resolve the major issues surrounding IVM within five years.

13. It was noted that before IVM be used in treatment, further research would need to be carried out. The research would need to focus on the effects of imprinting<sup>3</sup> or epigenetic reprogramming<sup>4</sup>. Maternal imprinting occurs during the maturation of the oocyte; if maturation occurs *in vitro*, it may have an impact on this process and could lead to an increase in the cases of rare imprinting diseases. A study of the potential of embryos derived from IVM oocytes to form embryonic stem cells was suggested as a way to understand more about the potential of these embryos.

14. The general feeling from the expert panel was that further research into the effect of IVM on oocytes and the potential of the embryos was needed before being offered as treatment to patients.

## **PGD & Susceptibility Genes**

15. The Executive has identified a strand of horizon scanning work on PGD and susceptibility genes which was discussed and approved at the November Authority meeting. We propose to gather views from the Panel on how this technology may be developed in the next 2-3 years and for views on specific genes that may be identified during that period.

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<sup>3</sup> A genetic phenomenon that determines, for certain genes, which one of the pair of alleles, the mother's or the father's, will be active in the development of the individual.

<sup>4</sup> Refers to factors affecting the development of an organism other than the primary sequence of the target genes. Imprinting is a type of epigenetic reprogramming.

### **Next steps**

16. Subject to comments from members, the issues raised here will be fed into the horizon scanning process, along with information gathered by the executive, as set out in paper SCAG/ELC (12/04)01. The outcome of the selection and filtering process will be reported back to the committee in February.

### **Conclusion**

- 17 Members are asked to:
- note the responses of the experts to the horizon scanning questions;
  - comment on any issue that they feel is of particular concern to the Authority and whether there are any follow-up questions to put up to the panel;
  - note the concerns of the expert panel with regard the use of *IVM* oocytes on treatment;
  - suggest questions on PGD and susceptibility genes that it would be helpful to put to the Panel.