

**MINUTES OF THE FOURTEENTH MEETING OF THE SCIENTIFIC AND  
CLINICAL ADVANCES GROUP HELD ON THURSDAY 24TH NOVEMBER  
2005  
AT BLOOMSBURY STREET**

**PRESENT:**

**Members**

Neva Haites- Chair  
Maybeth Jamieson  
Suzi Leather  
Chris Barratt  
Peter Braude (co-optee)  
Clare Brown  
Roger Pedersen (co-optee)

**Executive**

Tim Whitaker  
Hannah Darby  
Katy Berry  
Juliet Tizzard

**1. Apologies**

1.1 Apologies were received from David Barlow, Iain Cameron, Charles Lister, Ted Webb for their absence and Peter Braude for being late.

1.2 Members were invited to declare any conflicts of interest they had in relation to the agenda items. No conflicts of interest were declared.

**2. Minutes of the meeting of 13<sup>th</sup> September 2005**

2.1 The minutes of the last meeting were taken as read, subject to clarifying the wording of point 6.3 to emphasise that banking of stem cells is not within the remit of the HFEA.

**Action: Hannah Darby**

**3. Matters arising**

3.1 It was noted that all the matters arising were to be actioned at this meeting or the February 2006 meeting.

**4. Chair's business**

4.1 The Chair informed members that this meeting would be Roger Pederson's last meeting as he has decided to leave the group due to work commitments. Roger was thanked for his highly valued contribution to the group.

4.2 The Chair gave feedback from Authority and licence committee meetings.

4.3 It was noted that in the future SCAG should consider the results of the success rates project and should consider some learning points from licence committee meetings.

**Action: Charles Lister**

## **5. Taking forward horizon scanning issues – work plan. SCAG (11/05)01**

5.1 This item was introduced by Katy Berry. This paper outlines issues for consideration in next year's business plan and issues for earlier consideration. It was noted that there are three issues which have been prioritised and to be considered before next year's business plan. Members were asked to note the recommendation and approve the proposed work plan.

5.2 Issues for consideration for 2006/7:

5.2.1 It was noted that in relation to in vitro maturation, the process for clinical trials in ART should be considered. The monitoring, co-ordination and regulation of clinical trials is a separate issue which requires clarification from the clinical trials unit.

5.2.2 It was noted that trials for IVM would involve looking at in vitro development but not necessarily the transfer of embryos to patients.

5.2.3 Members considered the possible use of microarrays for PGD and it was decided that developments are likely to arise in this field which need to be monitored.

**Action: Katy Berry**

5.2.4 Consideration was given to the level of work which will be needed regarding possible developments in deriving stem cell lines from individual blastomeres. Members were of the opinion that as the destruction of embryos in certain research is legal in the UK then this technique (which is a way of obtaining stem cells without destroying embryos) may not be widely used. However, this technique could be useful for individual banking of stem cells. It was decided that this issue should also be considered by ELC and it is hoped that the Chair of ELC will be a member of SCAG from June 2006.

**Action: Juliet Tizzard**

5.2.5 Regarding sperm sorting for sex selection it was agreed that no further work should be done on this issue until the data from clinical trials is available.

5.3 Issues for earlier consideration:

5.3.1 Members discussed the use of somatic cells to create embryonic stem cell lines ('stembrids'). It was decided that SCAG should keep an eye on the literature regarding stembrids but use of this technique may not be as immediate as first thought.

**Action: Katy Berry**

5.4 Subject to the comments above members agreed the proposed work plan.

5.5 The group was updated regarding the Horizon Scanning Panel. It was noted that the December meeting was cancelled because many panel members were unable to attend. It was noted that new issues are put to the panel every month via the web forum. SCAG members suggested that video conferencing could be used if panel members cannot meet in person. Also, due to the relatively low number of comments received on the web forum it may be more successful if individual panel members are phoned when specific issues arise which are relevant.

## **6. In vitro maturation of oocytes. SCAG (11/05)02.**

6.1 This paper was introduced by Katy Berry, on behalf of Chris O'Toole. It was noted that this paper was for decision and that members would need to make a recommendation on the safety of in vitro maturation of oocytes and the category of patients it should be offered to. No applications for the clinical use of IVM have yet been received but it is expected that one will be received in the near future.

6.2 Members were of the opinion that there have been no significant new developments in the area since IVM was considered by the Working Group on New Developments in Reproductive Technologies. There is no more additional information which would contraindicate allowing it for certain categories of women, by groups that have the expertise.

6.3 It was noted that an important study by a Finnish group (which has published in Human Reproduction) is missing from this paper. This study reported high pregnancy rates following egg collection with no drug stimulation, IVM then either IVF or ICSI. The results of this study would argue against restricting patient groups.

6.4 The group concluded that no studies on IVM have suggested that the technique is dangerous and there is no evidence of abnormalities. However, there is insufficient evidence to be absolutely certain of its safety and no long term follow up. The risk of IVM treatment needs to be considered in relation to the risk of drug use. However, if the technique is offered to patients it should be offered with warnings.

6.5 Members were of the opinion that currently the HFEA does not have the power to make groups carry out clinical trials and that imposition of a requirement to carry out clinical trials may prevent them from carrying out the technique due to costs and delays. However it would be good practice for any new team, when introducing in vitro maturation into clinical practice, to include careful monitoring and follow up. Clinical trials would need to follow EU guidelines to ensure data is collected properly etc.

6.6 The HFEA has already issued a research licence for creating embryos using IVM and the media to mature eggs is available commercially.

6.7 Members expressed concerns regarding previous recommendations from the Working Group that centres should be required to have an IVM research license before they can use IVM clinically.

6.8 It was decided that the HFEA should recommend that clinics should prove they have suitable experience of creating embryos from IVM oocytes (through a research license or otherwise) before using it clinically.

6.9 The wording in the second bullet point in point 9 of this paper should be changed from 'on site' to 'demonstrate expertise'.

6.10 It was noted that if oocytes are exposed to HCG and gonadotrophins then they cannot be classed as undergoing IVM. So clinics who use oocytes from patients who have been injected with HCG and gonadotrophins cannot claim to have had IVM experience.

6.11 It was concluded that there is little evidence of harm but good evidence of pregnancy rates following IVM. SCAG should inform future licence committee meetings that centres should be able to use IVM for oocytes of any women, if they have experience of practicing IVM. The HFEA should recommend that it would be good practice for clinics to have experience of IVM (this could be included as a recommendation/requirement in order for a clinic to be licensed to carry out IVM).

6.12 The group decided that a statement should be produced for consideration by ACE, RCOG and BFS which will be circulated to SCAG members.

**Action: Chris O'Toole**

## **7. Vitrification. SCAG (11/05)03.**

7.1 This paper was presented by Hannah Darby. The group was asked to note the information and studies presented in the paper regarding clinical use of vitrification and form a view on its safety and efficacy.

7.2 Members were of the opinion that the issue should be approached like comparing two different culture mediums as vitrification is simply an adaptation of existing cryopreservation methods.

7.3 It was noted that although the majority of vitrification strategies bring the eggs or embryos into direct contact with liquid nitrogen (which increases the risk of contamination with pathogens), many clinics who carry out freezing also use techniques which expose directly to liquid nitrogen.

7.4 It was noted that clinics which carry out PGD may be particularly interested in vitrification. This is because following PGD there are a small number of embryos to store and because of the need to precisely time exposure to cryoprotectant vitrification can only be carried out on a few embryos at a time. Also, there is evidence showing improved survival of biosied embryos using vitrification. Following PGD embryos will be close to blastocyst stage.

7.5 Due to reports of greater success rates for blastocyst transfer compared to three day transfer more clinics may become interested in vitrification as the majority of reports for vitrification are with blastocysts.

7.6 As there is no way of getting data for possible effects of vitrification in later life animal embryologists should be consulted as the technique has been carried out for a long time in cows and other animals.

7.7 It was suggested that before the technique can be fully assessed studies need to be carried out on vitrification of cleavage stage embryos and on vitrification versus slow freezing. Also, it should be confirmed which clinics already carry out vitrification.

7.8 The group concluded that there are no particular concerns regarding this technique that are above those for freezing, other than direct contact with a non-sterile product, but training and protocols are essential.

## **8. Germinal vesicle transfer. SCAG (11/05)04.**

8.1 This paper was introduced by Katy Berry. The group was asked to consider the data and views presented in the report by Justin St John and come to a view regarding the use of GVT in treating infertility in older women and mitochondrial disease.

8.2 The group was informed that in this paper Justin concludes that this technology is useful for developmental biologists but there is not enough evidence for clinical use.

8.3 Members agreed that currently there is not enough evidence for the safety and efficacy of the technique in order to use it clinically. It is not known what the long term consequences of being a tri-mitochondrial person are and more evidence is needed from animal studies. The risk of being tri-mitochondrial versus the effects of mitochondrial disease need to be weighed up.

8.4 Important studies to consider include a study on monkeys and a study on cytoplasmic transfer in humans (three babies were born with abnormalities – 2 with Turner's syndrome and 1 with multiple abnormalities).

8.5 The group concluded that the clinical use of this technique needs to be reviewed at regular intervals. New research needs to be monitored.

**Action: Katy Berry and Hannah Darby**

8.6 Members suggested that the technique could potentially be tested/assessed by deriving stem cells from GVT embryos and examining heteroplasmy in replications.

**9. Assisted hatching. SCAG (11/05)05.**

9.1 This paper was introduced by Hannah Darby. Members were asked to consider the summary of studies regarding the effectiveness of assisted hatching and advise the group of any concerns.

9.2 It was noted that a study is soon to be published which will suggest that the use of assisted hatching has no effect on pregnancy rates.

9.3 Members were of the opinion that as yet there is no evidence for assisted embryo hatching having harmful/negative effects. However, there is no evidence that the use of the technique is advantageous and this issue needs to be kept under review.

9.4 It was decided that SCAG is not in a position to disagree with NICE guidance.

9.5 It was noted that the size of the hole in the zona may affect the rate of monozygotic twinning and this needs to be assessed.

**Action: Hannah Darby**

9.6 An Italian study has suggested that if embryos are cultured for an extended time, this may cause hardening of the zona.

9.7 The group expressed concerns regarding the use of the technique for all frozen-thawed cycles. It is currently not a licensing condition for assisted

hatching to only be offered to certain patient groups and there is nowhere on HFEA forms to indicate whether assisted hatching was carried out.

9.8 It was decided that an assisted hatching fact sheet, for the website, would be produced which will be considered at the next SCAG meeting.

**Action: Hannah Darby**

9.9 It was also decided that a licence committee should be asked if assisted hatching data can be collected at inspections to check which patients groups are being offered assisted hatching.

**Action: Hannah Darby**

## **10. SCAG membership and terms of reference**

10.1 This paper was tabled and presented by Katy Berry. Members were asked to comment on the selected topics that SCAG may require further expertise on and suggest any other areas and agree on which co-optees to invite.

10.2 The group was informed that SCAG may have to take on the residual work of the Safety and New Technologies Group (SANT).

10.3 Members considered that it would be useful to invite co-opted members with the following areas of expertise:

- SANT
- Imprinting and epigenetics
- Animal embryology
- Clinical embryology
- Molecular genetics
- In vitro derived gametes

10.4 It was decided that 6 additional permanent co-opted SCAG members need to be identified. It was agreed that the following people could be considered:

- Robin Lovell-Badge – Sex determination and stem cells
- Richard Gardner – Many areas of embryology and stem cells
- Daniel Brison - SANT
- Lorraine Young – Epigenetics, imprinting and stem cells
- Melanie Davies – Ran RCOG guidelines, works at UCH, Head of Women's Medical Federation and has not been involved with the Authority.
- Sue Pickering – Molecular biology and embryology
- Keith Campbell – Animal embryologist, embryo development and manipulation.

10.5 In addition to those named in the paper a number of other experts were identified whose expertise could be called upon, where relevant, for individual SCAG meetings:

- Sid Chandran – Cambridge embryologist
- Peter Andrews – Member of Horizon Scanning panel
- Ian Wilmut – Animal embryology
- Harry Moore – Stem cells
- Alison Murdoch – past Chair of BFS, clinician

**11. Any other business**

11.1 There was no other business

**12. Date of next meeting**

12.1 The next meeting will be on 14<sup>th</sup> February 2006 at 21 Bloomsbury Street.