

# Research Licence Committee Meeting

28 November 2007

21 Bloomsbury Street London WC1B 3HF

## MINUTES Item 1

**Research Project R0180: Generation of disease specific human embryonic stem cell lines by somatic cell nuclear transfer**  
**Stem Cell Biology Laboratory Wolfson Centre for Age-Related Diseases,**  
**Kings College London (0297)**  
**Initial Application**

### Members:

Emily Jackson – Chair, Lay Member  
Richard Harries, Lay Member  
Clare Brown, Lay Member  
Maybeth Jamieson, Consultant Embryologist, Glasgow Royal Infirmary  
Neva Haites, Professor of Medical Genetics, University of Aberdeen

### In Attendance:

Trish Davies, Director of Regulation/  
Deputy Chief Executive  
Chris O'Toole, Head of Research Regulation  
Claudia Lally, Committee Secretary

### Observing:

David Gomez, legal adviser to the HFEA

### Providing Clinical Advice:

William Ledger, Professor of Obstetrics and Gynaecology, University of Sheffield

### Providing Legal Advice:

Graham Miles, Morgan Cole Solicitors

Conflicts of Interest: members of the Committee declared that they had no conflicts of interest in relation to this item.

The following papers were considered by the Committee:

- papers for Licence Committee (128 pages)
- the following papers were tabled:
  - written legal advice by Morgan Cole (5 pages)
  - decision tree (2 pages)
  - invited comments on the creation of human-animal Cytoplasmic hybrid embryos (16 pages)
  - documents submitted in support of the application (7 pages)
    - i. proposed patient information
    - ii. proposed patient consent sheet
  - responses from Dr Minger to the comments of the Peer Reviewers (3 pages)

1. The papers for this application for a research licence were presented by Debra Bloor, HFEA Inspector. Dr Bloor reminded the Committee that the title of the proposed research project is: "Generation of disease specific human embryonic stem cell lines by somatic cell nuclear transfer". The project would involve isolating fibroblasts from patients suffering from genetic neurodegenerative and other diseases and transferring nuclei from these fibroblasts into enucleated non-human oocytes. The resulting cells would be cultured in an attempt to produce cytoplasmic hybrid embryos and the researchers would then attempt to derive stem cells from these embryos. Any stem cells derived would be characterised and ultimately be made available to the wider scientific community for the advancement of research into serious genetic disease.
2. Dr Bloor informed the Committee that the proposed Person Responsible for the project, Dr Stephen Minger, is an experienced scientist with an appropriate publishing history and significant experience of working with human embryos. Dr Bloor further informed the Committee that the other researchers are also suitably experienced and that the premises are suitable and secure. She added that the proposed Person Responsible acknowledges that further equipment and staff will be needed pending approval of the application and subsequent funding decisions.
3. Dr Bloor summarised the findings of the inspection report and highlighted that the Person Responsible has a clear understanding of the requirement to properly track and document the fate of any embryos created through the proposed methods.
4. Dr Bloor informed the Committee that Dr Minger has partially completed the Person Responsible Entry Programme (PREP) assessment for prospective Persons Responsible for research projects. Dr Bloor further informed the Committee that some parts of the completed sections of this assessment are not in line with suggested answers and some parts of the programme remain outstanding. Dr Bloor reported that she will be following this up with Dr Minger and on the basis of his previous involvement and experience in embryos research was confident of his suitability.
5. Dr Bloor informed the Committee that the patient information and consent forms for use in the project have now been submitted and reviewed by the Executive who found them to comply with the requirements of the standard conditions for stem cell research licences.
6. Dr Bloor informed the Committee that Dr Minger has now submitted his responses to the peer reviews. These responses had been tabled for the Committee but have not yet been sent back to the reviewers for their final comment. Dr Bloor also reported that Dr Minger has requested that the licence

application be considered by the Licence Committee before the project is considered by the Local Research Ethics Committee (LREC).

7. The Committee asked Professor Ledger to address the adverse comments from the peer reviewer at page 43 of the Committee papers. Professor Ledger commented on the question asking whether families in which genetic forms of the neurodegenerative diseases occur have been identified and whether family members are likely to give informed consent. Professor Ledger advised the Committee that in his opinion it was quite right that individuals have not been approached prior to the licensing of the project as those individuals might then be disappointed if the licence application is not successful and the research does not take place. Professor Ledger also considered the question asking how the researchers plan to characterize the neural cells from the mutant human embryonic stem cell lines. Professor Ledger stated that this was a reasonable point by the peer reviewer and agreed that this should perhaps have been worked out prior to submission of the application.

8. In reference to the legal advice prepared by Morgan Cole the Committee considered whether this research project is one for which a licence may be granted under the Human Fertilisation and Embryology Act 1990. The Committee took into account that a licence may be granted which authorises bringing about the creation of embryos *in vitro* or keeping or using embryos for the purposes of a project of research. The Committee noted that the question before them was whether the organism that would be created by inserting human nuclei into enucleated animal oocytes would be an embryo covered by the Human Fertilisation and Embryology Act 1990.

9. Following consideration of the written legal advice and advice from Professor Ledger and Professor Haites, the Committee concluded that that this precise project of research involves the creation and use in research of a “live human embryo” within the meaning of section 1 of the Human Fertilisation and Embryology Act 1990, and that, consequently, this research project is prohibited except in pursuance of a licence granted by the Authority.

10. In reaching this decision, the Committee followed the approach set out by the House of Lords in the case of *R(Quintavalle) v the Secretary of State for Health [2003] UKHL 13*. In particular, the Committee took into account the following points:

a) in enacting the 1990 Act, Parliament opted for a strict regime of control in this area, and did not intend any activity within this field to be unregulated: there was to be no free for all;

b) an embryo created by this method falls within the same genus of fact as other embryos covered by the 1990 Act, in particular, such an embryo has a full human nuclear genome and is live.

11. The Committee next considered whether the proposed research is prohibited by any of the provisions of the 1990 Act. The Committee agreed that it was satisfied that the proposed project is not prohibited as the law now stands.

12. The Committee considered whether the project of research appears either necessary or desirable for one or more of the purposes as set out in paragraph 3(2) of Schedule 2 to the 1990 Act or in paragraph 2(2)(a) of the Human Fertilisation and Embryology (Research Purposes) Regulations 2001. The Committee considered the stated aims of the project and evaluation of the project by three peer reviewers. They also considered the fact that the project had not yet been considered by a Local Research Ethics Committee. Taking into account these three aspects of the application, members of the Committee came to the conclusion that they did not have sufficient information to reach a decision at this time. In reaching this conclusion the Committee took into account the following considerations:

a) the Committee noted that the application had been submitted over a year ago and agreed that that this is a considerable amount of time in this fast moving area of research. In particular, the Committee noted the possible relevance to the proposed project of the emergence of new technologies for the reprogramming of somatic cells. The Committee concluded that it would be useful if the prospective Person Responsible could be invited to submit an addendum to section 11 of the application which states how the project fits into the current state of knowledge on the subject;

b) of the three peer reviewers, two had stated that the application should be resubmitted. The proposed Person Responsible had responded to their comments but this response had not been resubmitted to the peer reviewers. Accordingly it was not yet known by the Committee whether the reviewers would be satisfied with these responses. In addition, the Committee asked that any addendum to section 11 submitted by the prospective Person Responsible should be forwarded to the peer reviewers to be taken into account by them in their decision;

c) the Committee agreed that it was not usual for them to consider a research proposal without Local Research Ethics Committee approval.

13. The Committee accordingly decided to adjourn the meeting to allow the above points to be addressed. The Committee also asked that during the intervening period Dr Bloor report back on progress in relation to the issues raised in the inspection report, in particular the PREP assessment. In the meantime, the Committee took into account the fact that the Local Research Ethics Committee would be scrutinising the consent forms and patient information proposed for the project. The Committee accordingly decided that it

might be useful to the LREC for the Licence Committee to consider, and provide some feedback on, patient information and consent forms even though it was not able to make a decision on the application today.

14. The Committee considered the patient information sheet and noted that the use of non-human eggs is not mentioned until half way down the third page. The Committee agreed that as this aspect is one of the most salient aspects of the research and possibly of great interest to potential donors it should be mentioned in the title to the information sheet. The Committee also felt that the information should be slightly modified to take into account the fact that donors cannot be assumed to have any knowledge of IVF. Thirdly the Committee agreed it might be useful if the patient information included the website address for the UK Stem Cell Bank Steering Committee. The Committee decided that, following changes to the information to address these points, they are satisfied that the patient information and consent form meet the requirements set out in the standard conditions for stem cell research licences.

15. The Committee expressed its hope that the applicant would be able to take on board the Committee's comments sufficiently quickly to enable the application to be brought back before the Committee at its meeting on 9 January 2008.

Signed..... Date.....  
Emily Jackson (Chair)

# Research Licence Committee Meeting

9 January 2008

21 Bloomsbury Street London WC1B 3HF

## MINUTES Item 1

**Research Project R0180: Generation of disease specific human embryonic stem cell lines by somatic cell nuclear transfer**

**Stem Cell Biology Laboratory Wolfson Centre for Age-Related Diseases,  
Kings College London (0297)**

### Initial Application

#### Members:

Emily Jackson – Chair, Lay Member  
Clare Brown, Lay Member

#### Present via teleconference phone:

Maybeth Jamieson, Consultant  
Embryologist, Glasgow Royal  
Infirmary

Neva Haites, Professor of Medical  
Genetics, University of Aberdeen

#### Providing Clinical Advice:

William Ledger, Professor of  
Obstetrics and Gynaecology,  
University of Sheffield

#### In Attendance:

Trish Davies, Director of Regulation/  
Deputy Chief Executive

Chris O'Toole, Head of Research  
Regulation

Claudia Lally, Committee Secretary

#### Observers from the Regulation

#### Department:

Joanne McAlpine

Barbara Lewis

Elaine Suthers

#### Providing Legal Advice:

Graham Miles, Morgan Cole Solicitors

Conflicts of Interest: members of the Committee declared that they had no conflicts of interest in relation to this item.

The following tabled papers were considered by the Committee:

- research application considered on 28 November 2007 (15 pages)
- peer reviews considered on 28 November (24 pages)
- minutes of Licence Committee meeting on 28 November 2007 (5 pages)
- summary for Licence Committee by Dr O'Toole and Ms Davies dated 8 January 2008 (2 pages)
- letter from Dr Minger received on 8 January 2008 (1 page)
- revised patient information and consent form (total 8 pages)
- addendum to section 11.1 of the application form (2 pages)
- recent comments from Peer Reviewers in response to addendum (5 pages).

1. The papers for this application for a research licence were presented by Chris O'Toole, Head of Research Regulation. Dr O'Toole reminded the Committee that this project would involve isolating fibroblasts from patients suffering from genetic neurodegenerative and other diseases and transferring nuclei from these fibroblasts into enucleated non-human oocytes. The resulting cells would be cultured in an attempt to produce cytoplasmic hybrid embryos and the researchers would then attempt to derive stem cells from these embryos. Any stem cells derived would be characterised and ultimately be made available to the wider scientific community for the advancement of research into serious genetic disease. Dr O'Toole further reminded the Committee that the inspection of the centre found the premises to be suitable and secure and the researchers to be suitably experienced.

2. Dr O'Toole drew the Committee's attention to the information that had been submitted since the Licence Committee previously considered this application, on 28 November 2007. This was:

- an addendum to the application submitted by the proposed Person Responsible for the project, Dr Stephen Minger, stating how the project fits into the current state of knowledge on the subject
- responses to the addendum from the peer reviewers
- patient information and consent form which have been changed to incorporate the Committee's comments on 28 November
- a letter from Dr Minger pointing out that Local Research Ethics Committee (LREC) approval is unlikely to be forthcoming prior to an HFEA licence being granted, and suggesting that a licence be granted subject to subsequent LREC approval.

3. The Committee asked the Executive whether there had been any progress with respect to the Person Responsible Entry Programme (PREP) assessment, which had not been fully completed by Dr Minger prior to the Licence Committee meeting on 28 November. Dr O'Toole acknowledged that this was still outstanding. In considering past practice of the Committee in relation to the completion of PREPs prior to the granting of a licence, the Committee recognised that, where the proposed PR on a research project has previous experience as a PR, the Committee has previously granted a licence subject to satisfactory completion of the PREP within a reasonable timeframe. In addition the Committee recognised that it would have the power to impose a licence condition requiring the completion of PREP before the commencement of any licensable activity, if a licence should be granted. Accordingly, the Committee agreed that this issue did not prevent further consideration of the application.

4. The Committee considered the absence of LREC approval, which will have to be obtained before any patients can be recruited to this research project. The

Committee took into account the fact that, even if a licence is granted by the Authority, research could not commence without LREC approval, and further that it could impose a condition requiring LREC approval before any research commenced. The Committee agreed that the absence of LREC approval should not prevent further consideration of the application.

5. The Committee carefully considered all of the written material submitted, including the addendum to section 11 setting out how the applicant considers the proposed research fits into the current state of knowledge, particularly in the light of developments in relation to reprogramming of somatic cells that have taken place since the application was submitted. The Committee noted that the peer reviewers had been given the opportunity to comment on the addendum.

6. The Committee again considered the issue of whether this research project is one for which a licence may be granted under the Human Fertilisation and Embryology Act 1990. Taking into account that a licence may be granted which authorises bringing about the creation of embryos *in vitro* or keeping or using embryos for the purposes of a project of research, the Committee considered the question whether the organism that would be created by inserting human nuclei into enucleated animal oocytes would be an embryo covered by the Human Fertilisation and Embryology Act 1990.

### **The decision of the Committee**

7. The Committee affirmed that that this precise project of research does involve the creation and use in research of a “live human embryo” within the meaning of section 1 of the Human Fertilisation and Embryology Act 1990, and that, consequently, this research project is prohibited except in pursuance of a licence granted by the Authority.

8. In reaching this decision, the Committee followed the approach set out by the House of Lords in the case of *R(Quintavalle) v the Secretary of State for Health [2003] UKHL 13*. In particular, the Committee took into account the following points:

a) in enacting the 1990 Act, Parliament opted for a strict regime of control in this area, and did not intend any activity within this field to be unregulated: there was to be no free for all;

b) an embryo created by this method falls within the same genus of fact as other embryos covered by the 1990 Act, in particular, such an embryo has a full human nuclear genome and is live.

9. The Committee applied the decision tree for research applications. The Committee identified the activities under consideration as the creation of human

embryos and the use of human embryos in research. The Committee agreed that as the law now stands these activities are not prohibited under the Human Fertilisation and Embryology Act 1990. The Committee recognised that the future of research, including research involving cytoplasmic hybrid embryos, may be affected by the Bill which is currently before Parliament. Although the law might change and the applicants need to be aware of that possibility, the Committee is under a legal duty to consider this application and apply the law as it stands.

10. The Committee considered whether the project of research appears either necessary or desirable for one or more of the purposes as set out in paragraph 3(2) of Schedule 2 to the 1990 Act or in paragraph 2(2)(a) of the Human Fertilisation and Embryology (Research Purposes) Regulations 2001. The Committee considered the stated aims of the project and the evaluation of the project by the three peer reviewers. The Committee noted that all three peer reviewers had stated that they considered this research project necessary or desirable in order to increase knowledge about serious disease, and to enable that knowledge to be applied in developing treatments for serious disease. One peer reviewer stated that if the project involved studying the mechanism of reprogramming then it would generate valuable information and the use of animal oocytes and somatic cell nuclear transfer would be justified. Because the research *would* involve the study of reprogramming, the Committee agreed that there was specific support for this project. In any event, the Committee was satisfied after considering the evidence as a whole that, in the context of the proposed project of research, these activities appear to be necessary or desirable for the following purposes:

- Human Fertilisation and Embryology (Research Purposes) Regulations 2001:  
2(2)(b) to increase knowledge about serious disease
- Human Fertilisation and Embryology (Research Purposes) Regulations 2001:  
2(2)(c) to enable any such knowledge to be applied in developing treatments for serious disease.

In reaching this decision the Committee took into account the fact that these two purposes were supported by all three peer reviewers. The Committee based its decision on the fact that scientific understanding of the process of cell differentiation and of reprogramming is still at an early stage yet these processes are fundamental to our understanding of the optimal way of producing pluripotent cells and of then driving differentiation safely down specific routes. The Committee agreed that until scientific knowledge in this area is more complete it is important for researchers to have the ability to use different model systems to obtain a fuller understanding of the molecular and cellular events involved. The Committee were of the view that increasing understanding in this area is an important step to increasing understanding about how diseases develop and

opening up new avenues for treatment. For these reasons, the Committee were satisfied that the proposed research is, in fact, both necessary and desirable for the specified purposes.

11. The Committee agreed that they were satisfied that the proposed creation and use of embryos was necessary for the purposes of this research. The Committee were satisfied that the proposed work could not be undertaken without the use of human embryos, and were also satisfied that the proposed work justified the creation of human- animal cytoplasmic embryos given the lack of available human oocytes. The Committee considered the emergence of new technologies for the reprogramming of adult somatic cells and agreed that, while very promising, these new technologies do not obviate the need for the basic research into differentiation of pluripotential embryonic stem cells as envisaged in this application.

12. The Committee agreed that they were satisfied with the patient information and consent forms submitted by the centre in response to the suggestions made by the Committee on 28 November 2007. The Committee agreed, however, that one further amendment would be desirable: the project title which currently heads the patient information sheet should also be used as a heading on the patient consent form. This change will make it absolutely clear to patients that the proposed research involves the use of non-human oocytes.

13. The Committee agreed that the requirements for the grant of a licence under Section 16 of the Human Fertilisation and Embryology Act 1990 were satisfied.. The Committee took into account the evidence before it, and the statement of Dr Bloor made on 28 November 2007 to the effect that, in her opinion, the proposed person responsible is suitable and the Committee was satisfied about the other requirements of section 16. The Committee decided to grant a licence for the research for a period of one year. The following condition is to apply to the licence:

Research work must not commence until such time as the Executive has received:

- a satisfactorily completed Person Responsible Entry Programme (PREP) assessment from the Person Responsible; and
- evidence that the research project has been approved by a Local Research Ethics Committee.

14. The Committee noted that the centre has not paid a licence fee and therefore stated that a final licence must not be issued until this fee has been received.

Signed..... Date.....  
Emily Jackson (Chair)