Research Licence Inspection Report

Project Title Research licence Number Person Responsible Nominal Licensee Inspection type Licence expiry date Date Renewal fee paid	**Correlation of embryo morphology with ability to generate embryonic stem cell lines and subsequent growth and differentiative characteristics** R0133 Peter Braude Yacoub Khalaf **Renewal** 30/04/2011 N/A
Centre Number	0102
Centre Name	Guy's Hospital
Centre Address	Stem Cell and Embryology Research Laboratories Assisted Conception Unit, Guy's and St Thomas' Hospital NHS Trust, 11th Floor Tower Wing, Guy's Hospital St Thomas Street London SE1 9RT
Treatment centres donating to these research projects	0102 (Guy's Hospital) 0144 (The Woking Nuffield Hospital) 0006 (The Lister Fertility Clinic) 0208 (South East Fertility Clinic) 0086 (BMI Chelsfield Park ACU) 0030 (Herts and Essex Fertility Centre) 0070 (The Bridge Centre) 0158 (Chelsea & Westminster Hospital)
Inspection date	26th February 2009
Licence Committee Date	20th May 2009
Inspector(s)	Miss Sarah Hopper Mrs Ellie Suthers

About the Inspection:
The purpose of the inspection is to ensure that research is carried out in compliance with the HF&E Act 1990, Code of Practice, licence conditions and directions and that progress is made towards achieving the stated aims of the project.

The report is used to summarise the findings of the inspection highlighting areas of firm compliance and good practice, as well as areas where improvement may be required to meet regulatory standards. It is primarily written for the Licence Committee who makes the decision about the centre's licence renewal application. The report is also available to patients and the public following the Licence Committee meeting.

This report covers the period between 6th February 2008 and 27th February 2009.

Brief Description of the Projects

Project **R0133** entitled "**Correlation of embryo morphology with ability to generate embryonic stem cell lines and subsequent growth and differentiative characteristics**" has been licensed since 2005.

The lay summary is as follows:

Stem cells are unique cell populations which are able to undergo both self renewal and specialisation into new cell types. Although stem cells have been found in a wide variety of adult tissues, embryonic stem (ES) cells, which have been isolated from the inner cell mass (ICM) of blastocyst stage (Day 5) embryos are thought to maintain a higher potential for specialisation into many different cell types which may be of use in treating some serious degenerative diseases such as Parkinson disease, diabetes, or repair organs following stroke or heart attacks. In order to achieve this aim, stem cells need to made reliably and safely for use. Not only does this require an assessment of which embryos are more likely to produce stem cell lines and the conditions likely to facilitate stem cell growth, but there is also the requirement for them to be produced under conditions suitable for use in human therapy. This will require a methodical study of embryo quality and potential of individual cells which make up the early embryo, and also trial and error of conditions that facilitate safe stem cell production. It is also important that any such information gleaned is shared internationally to minimize the number of embryos used. In addition, stem cell lines derived from embryos from patients who have undergone PGD to avoid transmission of serious genetic disease, may be useful in studying mechanisms of how those genetic diseases progress and cause symptoms. Studies of stem cells derived from embryos carrying clinically-relevant mutations, e.g. with the Huntington's or cystic fibrosis mutation, will be useful not only in understanding how the mutation affects various tissues, but also in developing molecules which may be used in the treatment or amelioration of symptoms caused by these serious genetic conditions

The licence was granted under the following purposes:

- Increasing knowledge about the development of embryos
  Human Fertilisation and Embryology (Research Purposes) Regulations 2001 s2(a)

- Increasing knowledge about serious disease

Human Fertilisation and Embryology (Research Purposes) Regulations 2001 s2(b)

- Enabling any such knowledge to be applied in developing treatments for serious disease *Human Fertilisation and Embryology (Research Purposes) Regulations 2001 s2(c)*

		R0133
Research activities	Research on human embryos	✓
	Storage of licensed material	✓
	Creation of embryos for research	
	Derivation of human embryonic stem cells	✓
	Cell nuclear replacement	

Changes/ improvements since last inspection

Since the last inspection a new research facility has been built on the 11th floor of the Tower Wing, Guy's Hospital. The new premises were inspected on the 5th June 2008 and the licence varied to reflect the new address of the premises on the 18th June 2008. The new research facility comprises of two dedicated research laboratories situated within the new assisted conception unit. New equipment has also been bought for use in the new laboratories.

There have been no significant staff changes since the last inspection.

Additional licence conditions and recommendations and actions taken by centre since last inspection

Additional Licence Condition	N/A
A	

Recommendations	**Action Taken**
An SOP should be created for the induction of new staff as required by CoP Standard S.6.6.3 and S.6.2.7. N.B The Committee endorsed this recommendation and asked that the SOP be submitted to the Executive by 12th May 2008.	This policy was not submitted to the Executive by 12th May 2008 but evidence that it is in place was seen at this inspection. A Trust and local induction policy, which was seen to have been in place since 2005 and has been reviewed on an annual basis**,** is stored on the main quality management system database. This included Trust

	requirements: mandatory training (annual) local induction and requirements. Local requirements included having read and understood local policies and procedures: the Code of Practice (7th Edition): Alerts and adverse incident policies (seen to include the HFEA reporting requirements) The quality manager confirmed that researchers are included in this induction process.

Summary for Licence Committee

Overall the inspectorate was satisfied that the centre demonstrated compliance with regulatory requirements for: the security of premises, procedures for recruitment of donors and the research governance framework. The inspectorate therefore recommends the continuation of the centre's licence without additional conditions. Subject to the agreement of the peer reviewer it is also recommended that the licence be varied to include creation of embryos.

However, the Committee are asked to note two issues that were raised on inspection.

1) Progress reports have not been submitted in the timeframes specified in General Direction D2006/4. The PR was reminded of the requirements for submission of progress reports.

2) During the inspection it was found that in the past year licensed research work on this project, and the other project conducted at centre 0102 (R0075) has been conducted in premises no longer licensed for that activity. Due to delays in building work the PR had not commenced research work in the premises which had been granted a licence by Licence Committee in June 2008. Instead, work had continued in laboratories within the assisted conception unit[1] on the 4th floor of the same building. These laboratories had previously been licensed for research but not since the 18th June 2008. This is a breach of Section 12 of the Human Fertilisation and Embryology Act which states that "The following shall be conditions of every licence granted under this Act- that the activities authorised by the licence shall be carried on only on the premises to which the licence relates and under the supervision of the person responsible". The PR stated that as a contingency measure, in the event that they experienced technical problems on the 11th floor, he had maintained the laboratories on the 4th floor. The PR informed the inspectorate that he took steps to ensure that at no time any embryos were at risk and so continued to use the licensed treatment and storage assisted conception unit (centre 0102), to which their previously licensed research laboratory area is attached and functioning, for research purposes.

Information about the breach, which concerned research projects R0133 and R0075, was considered by the Licence Committee on the 11th March 2009[2]. The Licence Committee considered the breach as related to project R0075 and noted the centre's good history of regulatory compliance and on these grounds decided to take no further regulatory action.

[1] Premises which held a treatment and storage licence only.

[2] An application to vary the centre's licence to include premises on the 4th and 11th floor of the building was also considered as this Committee meeting. The Committee agreed that it was appropriate to vary the licences for the research projects with immediate effect, to state that the licences cover "ACU premises on the 4th and 11th floors, Tower Wing, Guy's Hospital".

They also noted that the breach may be taken into account in future in the event of any future breach of regulatory requirements. However, the Committee does not appear to have considered the breach with regard to research project R0133. The Licence Committee are therefore asked again to consider the breach and to consider what, if any, regulatory response is required.

Proposed licence variations

The PR has applied for the licence to be varied to include the following activity:

- creation of embryos *in vitro*

The PR's rationale for this variation is that where donor consent is in place they wish to use unfertilised eggs (this would include eggs which have not fertilised following IVF/ICSI or eggs which were not used because they were immature at the time of ICSI) to create embryos for use within the research project. The HFEA Executive are currently awaiting comments from the Peer Reviewer on this additional activity.

Breaches of the Act, Standard Licence Conditions or Code of Practice:

The table below sets out matters which the Inspection Team considers may constitute breaches of the Act, Standard Licence Conditions and/or the Code of Practice, and their recommended improvement actions and timescales. The weight to be attached to any breach of the Act, Standard Licence Conditions or Code of Practice is a matter for the Licence Committee;-

Breach	Action required	Time scale
Licensed research work on project R0133 has been conducted on the premises which are not licensed for research. Section 12 of the Human Fertilisation and Embryology Act states that The following shall be conditions of every licence granted under this Act- that the activities authorised by the licence shall be carried on only on the premises to which the licence relates and under the supervision of the person responsible.	The PR must ensure that licensed work is only conducted on appropriately licensed premises.	With immediate effect
Progress reports have not been submitted on 6 monthly intervals. Standard Licence Condition 19.5 requires that the centre shall provide the Authority with a progress report as specified in Directions. The relevant General Direction, D2006/4, requires that progress reports be submitted on a 6 monthly basis.	Timely submission of progress reports.	6 monthly intervals as per General Direction D2006/4.

Non-Compliance

Area for improvement	Action required	Time scale
None		

Recommendations

Area for improvement	Action required	Time scale
None		

Report of Inspection findings

1. **Organisation**

Desired Outcome: The research is well-organised and managed and complies with the requirements of the HFE Act.

Summary of findings from inspection
Evidence of:

- Organisation of the centre
- Leadership and management
- Staffing
- Funding
- Resource management
- Research governance

Staff

Principal investigator	Professor Peter Braude
Scientists	1
Laboratory technicians	
Support staff (receptionists, record managers, quality and risk managers etc)	

Highlighted areas of firm compliance
The PR who has managed this project since its inception in 1994 has completed the HFEA PR entry programme. The PhD student who is working on elements of this project has relevant and valuable embryology experience and has had access to continuing professional education. Evidence of the various courses and training sessions attended by the student was provided during the inspection. The project is funded MRC grants and a Wellcome Trust Strategic Award Meetings between the research staff are held. A record is maintained of these meetings and evidence of five formal meetings which took place in the past year was provided during the inspection. The quality management system in place for the licensed treatment and storage activities at this centre also supports the research activities. Documents submitted before and during the inspection had evidence of version control. The inspectorate were informed that research staff follow the assisted conception's unit incident handling policy. A copy of this policy was seen on inspection and was seen to meet HFEA requirements with regard to reporting timelines.

The PR has put into place all requirements outlined at the last inspection: a staff induction policy is in place and a copy of this was provided to the inspectorate.
Issues for consideration
Progress reports have not been submitted in accordance with the timelines outlined in General Direction D2006/4. In the past year, the HFEA Executive received progress reports only on the 21 June 2007 and the 16 January 2009. The PR is reminded of Standard Licence Condition 19.5 which requires that the centre shall provide the Authority with a progress report as specified in Directions. The General Direction which is currently in force and relates to progress reports, D2006/4, requires that the PR shall submit a progress report to the HFEA every six months from the date the licence was granted.
Executive recommendations for Licence Committee
Note potential breaches of General Direction D2006/4
Areas not covered in this inspection
None

2. Premises and equipment

Desired Outcome: The premises and equipment are safe, secure and suitable for their purpose.

Summary of findings from inspection:

- Suitability of premises
- Storage facilities
- Safety of equipment

Highlighted areas of firm compliance
At the time of inspection, the building work on the new premises had not been fully completed but equipment to be used for this project had been installed within the research laboratory. The research laboratories were inspected and were seen to be secure with access restricted to authorised personnel using a swipe card system. The room which will be used as the cryostore was seen to be fitted with low oxygen sensors and an alarm system. This room was also secured via the swipe card system. Records relating to research which contain patient information are stored in lockable administration offices which are situated in a restricted area of the assisted conception unit. The research team reported that they will have the necessary equipment required to undertake their stated objectives. Key equipment used in the research project will be connected to a system which will continuously monitor environmental parameters. Maintenance records and equipment logs were seen to be up to date and complete on the centres electronic quality management system. The centre has begun to validate its equipment following the Association of Clinical Embryologists (ACE) guidance. A completed validation form was seen for one of the centres class II hoods. There is a plan in place to validate all existing and new equipment as part of the transfer to the new facility.
Issues for consideration
The current licence for this research projects lists the 11th floor, Tower Wing, Guy's Hospital, St Thomas Street, London, SE1 9RT as the licensed premises. This licence was granted on the 18th June 2008 in response to an application made by the PR to reflect new premises, which would encompass the new assisted conception unit[3] and the research laboratories.

[3] The application for treatment and storage licence was considered by a licence committee on the 25th June 2008. The Committee agreed to vary the centre's licence to reflect the new address which would cover both the 4th and the 11th floor of the building (the premises being named as Assisted Conception Unit Guy's and St Thomas Hospital NHS Trust, Guy's Hospital). The Committee asked that no licence be issued to the centre (and thus no patient treatment be commenced under the terms of the licence) until the Executive has received confirmation that all the recommendations have been complied with. This confirmation has not been received and therefore treatment and storage activities have continued to be conducted in the original premises on the 4th floor under licence L0102/14/a.

However, on inspection it was noted that research work on both research projects held by the centre, R0075 and R0133, had been conducted in premises (4th floor of the same building) which had a licence for treatment and storage activities but were no longer licensed for research work. While no written evidence was seen that research work on R0133 had been undertaken on these unlicensed premises, the PR himself stated that some work had recently been conducted on the unlicensed 4th floor premises due to problems with the gas supply on the 11th floor. The inspectorate did observe that embryos stored for future use in research were stored on the 4th floor.

This issue was raised with the PR, who was reminded that licensed activities may only be conducted on licensed premises. To act otherwise is a breach of Section 12 (a) of the HFE Act (1990) which states: The following shall be conditions of every licence granted under this Act- that the activities authorised by the licence shall be carried on only on the premises to which the licence relates and under the supervision of the person responsible.

The PR was also asked to submit an incident report to the HFEA about this breach. This was received on the 11th March 2009.

The PR explained that he and his team have experienced significant and unanticipated delays in moving to the new licensed premises on the 11th floor. The PR stated that as a contingency measure, in the event that they experienced technical problems on the 11th floor, as has happened recently, he maintained the laboratories on the 4th floor. The PR informed the inspectorate that he took steps to ensure that at no time any embryos were at risk and so continued to use the licensed treatment and storage assisted conception unit (centre 0102), to which their previously licensed research laboratory area is attached and functioning, for research purposes. However, the PR acknowledges that they should have taken the precaution of licensing both premises to anticipate any such delay.

Executive recommendations for Licence Committee

The Licence Committee are asked to note the potential breach of Section 12 (1a) which states: The following shall be conditions of every licence granted under this Act--(a) [except to the extent that the activities authorised by the licence fall within paragraph (aa), that those activities] shall be carried on only on the premises to which the licence relates and under the supervision of the person responsible.

Information about this breach, which concerned both research projects R0133 and R0075, was considered by the Licence Committee on the 11th March 2009. The Licence Committee considered the breach as related to project R0075 and noted the centre's good history of regulatory compliance and on these grounds decided to take no further regulatory action. They also noted that the breach may be taken into account in future in the event of any future breach of regulatory requirements. However, the Committee does not appear to have considered the breach with regard to research project R0133. The Licence Committee are therefore asked again to consider the breach and to consider what, if any, regulatory response is required.

Areas not covered in this inspection

None

3. Donation of material

Desired outcome: Donors are recruited appropriately and any research carried out on their embryos is in accordance with their consent.

Summary of findings from inspection:

- Recruitment of donors
- Ensuring prospective donors have access to further guidance
- Ensuring prospective donors have time to consider donation properly
- Ensuring patient consent is not breached
- Prevention of coercion of prospective donors

Highlighted areas of firm compliance
Embryo donation to both projects is coordinated by a 0.2 WTE research nurse who has responsibility for donor centre coordination and support: embryo collection: verification of donor consent; documentation completion and embryo collection from the donor centres. The research nurse is employed by the Guys and St Thomas' NHS Foundation Trust which is reimbursed by the MRC for her time devoted to the individual MRC funded research project. Her remit it is to ensure all donated material is compliant with regulation and professional guidelines not the specific needs of the individual research projects. Donors from a number of donating centres across the UK are recruited to this project. The research nurse explained the procedures involved in this: At the time of clinical consultation the clinical doctor at the donor centre will approach the potential donor about the concept of donating embryos to stem cell research. If the potential donor is expresses an interest the centre will then contact the research nurse at centre 0102 and pass on contact details. The research nurse will mail information and consent forms to the potential donor and make herself available for any questions, discussions or explanations required. A contact telephone number if the embryo donor wants to change their mind is on all information including the research consent form. They are told at the time of consent that they are free to change their mind about donation at any time before the embryo is used. They are told verbally and in writing that they can't benefit in anyway from individual donation and that they will not be told of the outcome of their donation i.e. where and when the embryo is used. They are also informed on the consent form that they can not derive any financial benefit from any research. Consent forms are returned to the research nurse in the mail and are initially filed in a folder. The research nurse collects the embryos at the discretion of the donating centre. The research nurse informed the inspectorate that the equipment is relatively new and that it is fit for purpose. There is a witnessing and transfer protocol for the movement of embryos from the donor centre, in transit and acceptance by the researcher at centre 0102. At the time of inspection all consent forms reviewed were seen to be complete and in line with regulatory requirements. Staff from donating centres visit 0102 on a regular basis to see how research is going and staff are encouraged to call or contact the centre at any time for information or if there is a concern or difficulty.

No evidence of coercion of prospective donors was seen from a review of returned HFEA patient questionnaires submitted by patients at centre 0102.

Consent for use of embryos in research is checked, witnessed and documented before embryos are actually used in the project. Evidence of this check was seen in the two research records audited by the inspection team.

A documented standard operating procedure is in place which outlines the steps to be taken when transferring embryos from the clinical sphere to the research project. A copy of this procedure was reviewed by the inspectorate and seen to include a reminder to staff that embryos generated from donor eggs/sperm cannot be used in research unless the donor has also given consent. A documented procedure is also in place which describes the process for transferring embryos donated to research by patients at other units. Both protocols are supported by a detailed flow chart which outlines the processes involved.

Donated material is given an individual and unique identifier for use in research; therefore once it has been transferred for use in the research the material is anonymous. Use of this unique identifier was seen in the laboratory log books maintained by the research team.

Researchers receive information regarding the expiry date of stored embryos. This information was seen to be clearly documented on the transfer sheets provided to the research team.

Issues for consideration
None
Executive recommendations for Licence Committee
None
Areas not covered in this inspection
None

4. Patient information and consents

Desired outcome: Patients are provided with appropriate information which allows them to give informed consent.

Summary of findings from inspection:

- Patient information
- Consent forms
- Patient information for projects deriving embryonic stem cells
- Consent forms for projects deriving embryonic stem cells
- Donor and patient records

Highlighted areas of firm compliance
The patient information was considered by the inspectorate to be clear and lay intelligible. Patient information and the consent forms contain the requirements of regulatory compliance in the Code of Practice (7th Edition) The PR explained that the patient information and consent forms were developed in conjunction with the Human Embryonic Stem Cell Coordinators' network (hESCCO). The research nurse responsible for recruiting donors was able to demonstrate that she was using the latest version of patient information and consents. These documents were seen to be subjected to document version control.
Summary of audit of patient records
Two sets of records from patients who donated embryos to this project were reviewed and were seen to contain valid consent forms. Witnessing of the transfer of embryos to research was documented appropriately in all of the records reviewed. The transfer of embryos to research is witnessed, with the operator and witness signing to confirm have completed appropriate consents to research. The audit of donor records also revealed that the witnessing mechanisms in place prevented the use of embryos where consent from both gamete providers was not evident.
Issues for consideration
None
Executive recommendations for Licence Committee
None
Areas not covered in this inspection
None

5. Scientific practice

Desired outcome: Research is carried out in accordance with licence conditions and makes progress towards achieving stated aims

Summary of:

- Use of material
- Progress in setting and achieving aims and objectives
- Standard operating procedures
- Minimisation of material loss and wastage

Use of material
101 fresh embryos have been supplied for this project in the last year and thirty seven of these were suitable for inclusion in the project. All the fresh embryos donated to this project were donated by patients receiving treatment at centre 0102. In total 88 frozen embryos have been supplied to the project in the last year and 33 of these have been used so far. The frozen embryos have been supplied by eight different licensed treatment and storage centres: Guy's Assisted Conception Unit, Woking Assisted Conception Unit, Lister Hospital Assisted Conception Unit, South East Fertility Unit, Chelsfield Park Fertility Unit, Herts and Essex Fertility Unit, Bridge Centre and the Chelsea and Westminster Assisted Conception Unit. The PR estimates that they will use 150 fresh embryos and 150 frozen embryos in the next 12 month period.
Project objectives
Renewed objectives and methods: (i) Derivation of hES with clinically relevant genetic mutations and assess the suitability of such lines as disease in a dish models The generation of lines with clinically significant mutations has demonstrated proof-of-principle that these lines can be derived, and with the mutations as expected. Preliminary results with KCL008_HD2 suggest that these cells are a valuable and clinically-relevant cell source for the study of disease pathogenesis. Future work with the astroglial progenitor populations will focus on characterising aggregate formation and the role of glial cells in HD pathogenesis in a human disease model. Collaborations with HD experts have been forged to examine clinically relevant lines further and to seek funding for these approaches. We will attempt to derive additional lines with disorders such as spinal muscular atrophy, myotonic dystrophy and inherited motor neurone disease amongst others as such embryos become available. (ii) Investigation of derivation of stem cells from single blastomeres and understanding of human blastomere puliripotency. No definitive conclusions can be made at this juncture regarding the origin, timing and

influence of axes of polarity in the oocyte and early cleavage stage embryos. Some molecular experiments have been attempted with human embryos, although doubts over the methodology limits the value of the results. For example, the identification of polarised distribution of leptin and STAT3 in the oocyte has been shown, but there has been no systematic study of lineage specific gene expression in single early human cleavage embryos with the aim of analysing whether differences in expression exist between sister blastomeres. Furthermore, whilst chimeric proof of pluripotency after manipulation is clearly not possible in humans, the ability of all sister single blastomeres to generate stem cell lines would offer the most convincing proof available. Therefore future aims are to continue the derivation attempts with single blastomeres and also to validate a single cell PCR approach and use it to assess a panel of markers for ICM, TE and germline to investigate the pluripotent status of sister blastomeres.

(iii) Derivation of hES cells under GMP conditions.

Our new ACU with full GMP air handling and monitoring will be completed during the early part of 2009, and will enable methods for preparing stem cells under clinical grade conditions to be established. This will entail working closely with the UKSCB and others to try and unify approaches and to develop protocols that fulfil the EUTC directive and the road-map being coordinated by the various regulators involved. It is anticipated that it will take up to a year to develop the various protocols and procedures required. Once developed it is anticipated that embryos from in house, and those received frozen from collaborating unit will be used for this purpose.

Lay summary of research undertaken

Stem cells are unique cell populations which are able to undergo both self renewal and specialisation into new cell types. Although stem cells have been found in a wide variety of adult tissues, embryonic stem (ES) cells, which have been isolated from the inner cell mass (ICM) of blastocyst stage (Day 5) embryos are thought to maintain a higher potential for specialisation into many different cell types which may be of use in treating some serious degenerative diseases such as Parkinson disease, diabetes, or repair organs following stroke or heart attacks. In order to achieve this aim, stem cells need to made reliably and safely for use. Not only does this require an assessment of which embryos are more likely to produce stem cell lines and the conditions likely to facilitate stem cell growth, but there is also the requirement for them to be produced under conditions suitable for use in human therapy. This will require a methodical study of embryo quality and potential of individual cells which make up the early embryo, and also trial and error of conditions that facilitate safe stem cell production. It is also important that any such information gleaned is shared internationally to minimize the number of embryos used. In addition, stem cell lines derived from embryos from patients who have undergone PGD to avoid transmission of serious genetic disease, may be useful in studying mechanisms of how those genetic diseases progress and cause symptoms. Studies of stem cells derived from embryos carrying clinically-relevant mutations, e.g. with the Huntington's or cystic fibrosis mutation, will be useful not only in understanding how the mutation affects various tissues, but also in developing molecules which may be used in the treatment or amelioration of symptoms caused by these serious genetic conditions.

Peer reviewers comments
N/A interim inspection
Highlighted areas of firm compliance
There is a procedure in place to ensure embryos are not cultured beyond 14 days, this system was seen to be detailed in the laboratory protocol: transfer of embryos to research licence. There is a system in place which records each time material is handled. Evidence of this was seen during review of the laboratory log books. The procedure for disposal of material has been documented in a protocol. This was provided to the inspection team. Staff were able to demonstrate their procedures to ensure that embryos are not stored beyond the statutory storage period. Two systems are in use; the first is a database system which, the researchers informed the inspectorate, is checked by the assisted conception unit personnel as well as the research team. A file is also maintained which includes records for all embryos awaiting use in research. This was seen to be organised chronologically and a clear log is also kept at the end of the file which listed all embryos awaiting use and their statutory storage date. Review of the log and the file indicated that no embryos are being stored outside the statutory storage period and the next embryos to reach their expiry date will do so on the 23rd March 2009. An audit of all stored material has been conducted in the past year. A record of this audit was provided and this stated that only minor administration discrepancies had been found during the audit.
Issues for consideration
None
Executive recommendations for Licence Committee
None
Areas not covered in this inspection
Peer review

Report compiled by:

Name……Sarah Hopper …….

Designation……HFEA inspector…….

Date……27th February 2009……

Appendix A: Centre Staff interviewed

The PR and 4 other members of staff

Appendix B: Licence history for previous 3 years

R0133

Status	Licence	Type	Active From	Expires
Active	R0133/3/b	Research Project	18/06/2008	30/04/2011
Replaced by New Version	R0133/3/a	Research Project	01/05/2008	30/04/2011
Expired	R0133/2/c	Research Project	01/09/2006	30/04/2008
Expired	R0133/2/b	Research Project	29/06/2005	30/04/2008
Offer licence sent but not acknowledged	R0133/2/a	Research Project	01/05/2005	30/04/2008
Replaced by New Version	R0133/1/a	Research Project	15/04/2002	30/04/2005

There are no conditions on the current licence

Appendix C:

RESPONSE OF PERSON RESPONSIBLE TO INSPECTION REPORT

Research Licence: 0133
Centre Number: 0102
Name of PR: Prof Peter Braude
Date of Inspection: 26th February 2009
Date of Response 11th May 2009

I have read the inspection report and agree to meet the requirements of the report.

Name: Peter Braude
Date: 11th May 2009

1. Correction of factual inaccuracies

Page 5, Breach 1: refers to licence 0075, which although is factually correct, in this case should refer to 0133.

Page 11. Our research nurse although now employed by the Guy's and St Thomas Trust, has 0.2 WTE devoted to the HFEA licensed projects, for which the Trust receives reimbursement from my relevant MRC grants. Hence the statement should read - The research nurse is employed by the Guys and St Thomas' NHS Foundation Trust **which is reimbursed by the MRC for her time devoted to the individual MRC funded research project.**

2. Comments and additional information.

Having read carefully the papers received in response to my request for licence variation, I appreciate that the Committee have handled the unwitting breach of premises licence with understanding and consideration. However it is my submission that the handling of the variation request put us in breach conditionally on its issue:

1. Having sought advice on conditions for our new premises, I applied for a licence variation in good time and in good faith, appreciating that it would be necessary to have the 11th floor research laboratories and storage licensed, in order to continue research activity without hiatus.
2. The fact that the licence was issued on the 18th June, more than 10 weeks before any intended move to the new premises, gave the reassurance that application for licensing of the new premises, had been done in a timely fashion.
3. If revocation of the 4th floor premises licence was conditional on issue of the 11th floor licence, it would have meant that all research work, which was continuing as usual prior to the intended move, and storage of embryos would have been made illegal by default.
4. Since the 11th floor premises were neither ready, nor intended to be ready, by the date of issue of the variation, it would have meant that all stored embryos would have had to be destroyed thenceforth.
5. To the best of my awareness there was no information provided with the notice of the variation to the effect that the 4th floor licence was to be revoked on its issue.

6. If such information had been received, I would immediately have contested the obligatory nature of the breach and dealt with it by requesting both premises to be licensed in the variation.
7. I am sure that, in the same way that the effect of the variation was not fully appreciated by me at the time, its effect might not have been immediately apparent to the Licence Committee issuing the variation.

I ask that these facts be taken into account by the committee in their intention to record this as a breach in the unit's licence history, as immediate breach on issue of the variation was inevitable without due warning.

3. Actions taken:

(a) Breach 1: Use of 4th floor following licence variation. This was attended to with immediate effect and application made so that both floors would be considered as licensed premises. An incident report was submitted on and received by HFEA on 11th March 2009. I now understand that the circumstances of the breach, as outlined in my incident report, were not seen by the Licence Committee and therefore have been presented above.

Having made the final move to the new unit for all clinical and research purposes, work now only takes place in 11th floor premises, and the 4th floor is being dismantled.
A request is hereby made to revoke the 4th floor as licensed premises.

Breach 2: We contest that we have not produce 6 monthly reports for R0133.
According to our records licences are *due 6 monthly (from the date the licence was granted),* and accepting that a full report of activities has accompanied each request for renewal, or in documents submitted for inspection visits, we believe we have fulfilled our obligation.

Licence granted: 1st Sept 06
Licence due: 30th April 2008

- Progress report completed 5th Dec 2006
- Progress report completed 19th June 2007
- Application for new licence completed in Dec 07, which included full report of work to date.

Licence granted: 1st May 2008
Licence due: 30 April 2011

- Progress report submitted Jan 2009 as part of information for our formal inspection.

Applying this system we believe that our next report is due around November 2009. We would appreciate clarification on this please.

HFEA Research Committee Meeting
20 May 2009

21 Bloomsbury Street London WC1B 3HF

Minutes – Item 2

Guy's Hospital (0102; R0133) – Interim inspection

Members of the Committee:	Committee Secretary:
Emily Jackson (lay) – Chair Richard Harries (lay) Neva Haites (geneticist) Hossam Abdalla (clinician) David Archard (lay)	Kristen Veblen Legal Adviser: Graham Miles, Morgan Cole

Declarations 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 (59 pages)
- tabled papers (3 pages).

The Committee also had before it:

- HFEA Protocol for the Conduct of Licence Committee Meetings and Hearings
- 7th edition of the HFEA Code of Practice
- Human Fertilisation and Embryology Act 1990 (as amended)
- HFEA (Licence Committees and Appeals) Regulations 1991 (SI 1991/1889)
- Decision Tree for Application for a Research Licence
- Guidance for members of Authority and Committees on the handling of conflicts of interest approved by the Authority on 21st January 2009.

1. The Committee noted that the purpose of this project was to generate greater knowledge to inform the development of human therapeutic applications for stem cells by assessing the correlation of embryo

morphology, subsequent growth with the potential of stem cells derived from these embryos to have different abilities to differentiate .

2. The Committee noted the decision of a previous Committee on 11 March 2009 concerning the breach of section 12(1)(a) of the HFE Act 1990 (as amended), which states: the following shall be conditions of every licence granted under this Act – that the activities authorised by the Licence shall be carried on only on the premises to which the licence relates and under the supervision of the Person Responsible.

3. The Legal Adviser confirmed that the identified breach had been dealt with by the Committee on 11 March 2009 by that Committee noting the breach but determining that no further action should be taken. On that occasion the Committee also agreed to vary the licence to include both the 4th and 11th floors whilst the transition was taking place. Accordingly, it was unnecessary to deal with that issue further apart from clarifying the scope of the licensed premises in the licence to be renewed.

4. The Committee noted the further explanation made by the Person Responsible about the unwitting nature of the breach. The Committee also noted that the 4th floor is no longer required to be used and that the licensed premises should now be restricted to the 11th floor.

5. The Committee considered the dates of submission of progress updates for this project, as described in the response of the Person Responsible (PR), and wished to remind the PR of the requirement to submit an update every six months, as described in Direction 2006/4. The Committee noted, and thanked the PR for, the progress report dated January 2009 and observed that in keeping with the Direction noted above, the next progress report should be submitted in July 2009.

6. The Committee further considered the application to vary the licence to include the creation of embryos in vitro and noted that it was not in possession of a project-specific peer review for this application.

<u>The Committee's Decision</u>

7. The Committee agreed that they were content for this licence to continue with no additional conditions and that for the purposes of R0133, the Licence should be varied with immediate effect to state that the licence covers "ACU premises on the 11th floor, Tower Wing, Guy's Hospital".

8. When considering the variation to add the creation of embryos in vitro, the Committee was satisfied on the basis of all of the information available that the creation of embryos is necessary or desirable for the following purposes:
    - Increasing knowledge about the development of embryos
      HFE (Research Purposes) Regulations 2001 2(a)
    - Increasing knowledge about serious disease
      HFE (Research Purposes) Regulations 2001 2(b)
    - Enabling any such knowledge to be applied in developing treatments for serious disease
      HFE (Research Purposes) Regulations 2001 2(c)

9. The Committee was also satisfied that the proposed use of embryos is necessary for the purposes of the project of research because of the increased efficiency with which stem cells may be derived from fresh, instead of frozen, embryos.

10. The Committee decided that, subject to receipt of a project specific peer review confirming that, in the opinion of the peer reviewer, the creation of embryos is necessary or desirable for the purposes specified above and that the proposed use of such embryos is necessary for the project of research, the variation of the licence could be granted. In the event that the peer reviewer expresses a different opinion, the matter should be referred back to the Research Licence Committee for further evaluation.

Signed…… Date 29.5.09.
Emily Jackson (Chair)