Research Interim Inspection Report

Date of Inspection: 27 July 2011
Purpose of inspection: Interim Inspection of Research Licence
Length of inspection: 5 hours
Inspectors: Wil Lenton
Sara Parlett

Inspection details:
The report covers the pre-inspection analysis, the visit and information received between 28 April 2009 and 4 November 2011.

Date of Executive Licensing Panel: 18 November 2011

Centre details

Project Title	Analysis of Chromosomes in Human Preimplantation embryos using FISH and CGH
Centre Name	London Fertility Centre
Centre Number	0088
Research licence Number	R0169/4/d
Centre Address	53 Portland Place London W1B 1QJ
Person Responsible	Miss Samantha Knight
Licence Holder	Dr Brendan Ball
Treatment centres donating to this research project	0068 Leicester Fertility Centre
Date Licence Issued	01/01/2009
Licence expiry date	31/12/2011
Additional conditions applied to this licence	None

Contents

Purpose of the Inspection report

The purpose of the inspection is to assess whether research using human embryos is carried out in compliance with the Human Fertilisation and Embryology (HF&E) Act 1990 (as amended) and the Code of Practice and that progress is made towards achieving the stated aims of the project. The report summarises 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 Authority's Executive Licensing Panel which makes the decision about the centre's licence.

Report to Executive Licensing Panel

Brief description of the centre and its licensing history:
The centre has seen much organisational change over the past eighteen months, most notably the change of ownership which occurred on 29 March 2010. The centre is now part of the Spire Healthcare group. There have also been significant staff changes over the same time period, including the laboratory manager, research Person Responsible (PR), Licence Holder (LH) and centre manager.

Miss Samantha Knight was approved as PR for research project R0169 by the Executive Licensing Panel (ELP) on 11 March 2010, having successfully completed the PR Entry Programme (PREP number R/1163/8).

An interim inspection took place on 28 April 2009, at which time no regulatory non-compliances were noted.

Although this inspection was initially scheduled to be a licence renewal inspection, shortly prior to the date of inspection, the Executive were informed by senior management at the centre that they would no longer be seeking the renewal of the research licence at the present time, but would allow the licence to lapse, upon expiry on 31 December 2011.

The inspection team were directed to undertake an interim-style inspection and inform the ELP of the centre's wish to allow research licence R0169 to lapse, as part of the inspection/licensing process.

Variation to Licence.
During the post-inspection period the Executive was informed that the centre wishes to vary its licence in order to change its current Licence Holder (LH), associated with;

i. the treatment and storage licence (L0088/17/e; which expires on 31 August 2013)
ii. the research licence (R0169/4/e; which expires on 31 December 2011)

The Executive has received an application form and all other required documentation as specified by General Direction 0008. An Executive Summary together with all required documentation is included with the inspection papers for consideration by the ELP.

Title of research project: Analysis of Chromosomes in Human Preimplantation Embryos using (FISH) and (CGH)

Summary for licensing decision

In considering overall compliance, the inspection team considers that it has sufficient information drawn from documentation submitted by the centre prior to inspection and from observations and interviews conducted during the inspection visit to draw a conclusion on the continuation of the centre's licence, until it expires on 31 December 2011. The PR has indicated that they will not be seeking renewal of the licence at the present time.

The Executive Licensing Panel (ELP) is asked to note that at the time of the inspection there was one critical area of non-compliance that required improvement.

Critical area of concern.

- **The embryo storage consent monitoring process has been reviewed and amended**

Since the inspection visit the PR has confirmed that this recommendation has been fully implemented.

As requested within the report the PR has also provided an action-plan and time-line which addresses the following issues;

Patient-donated embryos presently within storage at the centre for use in research will be either;

- Used in embryo-biopsy training at the centre if appropriate consents are in place
- Transferred to another HFEA-licensed centre for use in associated research work if appropriate consents are in place
- Allowed to perish if requested by the donating patients or if the storage consent expires.

The PR will also provide a fully referenced final report with results, conclusions and references to any publications arising from the research project by 31 December 2011.

Summary of project

Lay summary of the research project:

Certain in vitro fertilisation (IVF) patient groups have been identified as being at high risk of producing embryos with chromosomal abnormalities. These chromosomal abnormalities usually cause failure of implantation following repeated IVF embryo transfers, or miscarriages. In a minority of cases the embryos can develop to cause a pregnancy affected by a chromosomal abnormality such as trisomy 21 (Down's syndrome). Preimplantation genetic screening (PGS) is a technique, which allows embryos produced during an IVF treatment cycle to be tested for specific chromosomal abnormalities. Following the screening procedure only embryos that are identified as being normal for the chromosomes being analysed are considered for embryo transfer. Due to the increased selective power provided by this procedure, PGS may reduce miscarriage rates and improve both implantation rates and live birth rates in specific patient groups. The screening process involves looking at the chromosomes present in a single cell taken from a 3 day old embryo (named biopsy).
PGS relies on the fact that chromosomally, this cell should be an identical copy of the remaining cells in the embryo. By inference if the cell is normal, it likely came from a normal embryo, and if it was abnormal from an abnormal embryo. Previous studies have shown that many human embryos are not made up of chromosomally identical cells. These embryos are called mosaic embryos. Mosaicism can affect the reliability and hence the benefits of PGS. Our study aims to analyse single biopsied cells using comparative genome hybridization (CGH) or microarray techniques both of which can detect all the chromosomes in the cell. The results will be compared with the results obtained from the remaining embryo using fluorescence in-situ hybridisation (FISH: a simpler technique able to reliably detect between 5 and 9 chromosomes in a single cell). This strategy will allow us to further investigate the incidence of mosaic embryos and the degree of mosaicism. In this way, we may be able to determine whether mosaicism is linked with a specific patient profile, such as age or IVF techniques such as embryo freezing and what degree of mosaicism an embryo can tolerate. This will ultimately improve the management of patients requesting PGS and help our understanding of early human development Furthermore, we would like to analyse the metabolic activity during embryo development. This can be achieved by utilising innovative technologies which are non-invasive to the embryo and are performed in the media the embryos are cultured in. It has been very recently suggested that there is correlation between embryonic metabolic activity and embryo implantation. This means that by assessing an embryo's metabolic activity we can predict its implantation rate. This can help IVF clinics accurately select the best embryo for transfer which would give a desired pregnancy. Such result can reduce multiple births and provide patients with higher pregnancy rates. During this multi-step study we propose to investigate the possible correlation between morphology, genetic status and metabolic activity of an embryo. We aim to combine our experience in analysing genetic abnormalities at the embryonic level with the metabolic results. If such correlation exists it might be possible to predict the embryos' genetic status by assessing morphology and metabolic activity. This will eliminate the invasive examination of embryos by biopsy and reduce the cost of selecting the embryo with the greatest potential of implanting and giving a healthy pregnancy.

Lay summary of the research undertaken since the last inspection on: 28 April 2009

From May 2009 until April 2011, 85 embryos have been thawed for research.
For the analysis of chromosomes in human preimplantation embryos using FISH and CGH, 51 embryos were thawed with 32 surviving and these being used for research. These embryos were used to validate trophectoderm biopsy and then had chromosome analysis performed on them by CGH array and FISH.
Thirty-two biopsied embryos and biopsied cells were sent to a diagnostic laboratory and six were sent to a collaborative centre. These were used to compare the two methods.

For the metabolomic analysis and comparing that to FISH and CGH, 34 embryos were thawed. 20 survived. Four embryos were biopsied at the six to eight cell stage and the cells and embryos were spread for validation and sent to a collaborative centre. The remaining 16 were sent to a collaborative centre with the corresponding culture fluid. Fifteen of these embryos were degenerate and there was a problem with embryo development. There was no problem with other embryos in our commercially prepared culture fluid. This lack of embryo development meant no growth to the blastocyst stage and this was found to be the metabolomic culture fluid used, which had been made and supplied from another licensed centre, but had not previously been used for human embryos. For this reason from April 2010 the thawing of embryos for this study was suspended until the September of that year, when the culture fluid problem had been investigated fully. Since that time no further embryos donated to research have been thawed and used for research. The work carried out on this study so far shows that by selecting the morphologically best embryo for embryo transfer, does not mean that the embryo is viable. If morphology is combined with FISH or CGH analysis, then this gives more information.

Objectives of the research:

The objectives of the proposed research project are the same as they were at the interim inspection of 2009.

The microarray analysis is the next part of the project which will kick off and provide results regarding the embryos' full chromosomal complement as well as smaller gene defects from one single cell or from a handful of cells. Blastocyst biopsy will be perfected which will allow more cells to be removed to achieve higher rates of results from array-CGH. Recent unpublished data from Wells et al (personal communication) have shown 75% pregnancy rate for women in advanced maternal age and/or recurrent IVF failure undergoing PGS whilst performing blastocyst biopsy and subsequently carrying out array-CGH. The new area of metabolomics is proposed to be investigated. Using metabolic activity measurements we will be able to provide a rapid, non-invasive procedure during IIVF cases. Current metabolomics instruments are designed to aid in the assessment of viable embryos with the greatest reproductive potential. Through the use of a highly sensitive method of biomarker identification, metabolic analysis can be performed in just minutes, requiring only a small amount of spent culture media. Metabolic activity measurement provides objective assessment of viability without compromising the embryo, helping guide treatment options for patients undergoing IVF. Advantages of the metabolic activity measurements include:

- Non-invasive assessment of embryo viability
- Complete analysis in less than one minute
- Requires small sample size (10μL) of spent culture media
- Small, user friendly instrumentation (proposed commercial instrument to be used)
- Assimilates easily into current laboratory practice

There have been some studies indicating the use, practicality and positive results by combining embryo morphology assessment with metabolic activity measurements (Botros et al, 2008; Seli et al, 2008; Scott et al, 2008; Vergouw et al, 2008). We propose to take the above mentioned studies a step further and attempt to combine our experience with genetic analysis using FISH and CGH along with the metabolic activity measurements using the commercial instrument and investigate the correlations (if any) between embryo morphology, metabolic activity of embryos and genetic status of embryos. This will enable us to achieve better and more accurate selection of embryos that will give rise to pregnancy. Hopefully, the addition of metabolic activity measurements in clinical patients (following our study) can promote elective single embryo transfer (eSET) since the embryo selected would be most viable one. The correlation between morphology, genetic analysis and metabolomics has to be established before the analysis of metabolytes can be used in a clinical environment. This would be carried out on donated frozen research embryos, initially to continue the correlation work with metabolytes versus genetic analysis with CGH and FISH.

Donation and use of embryos:

Data supplied by the centre as per General Direction 0002; 1 January to 31 December 2010.

	Fresh	Frozen
Total donated	0	37
Total received or thawed	0	10
Total used in research	0	4
Total disposed of	0	57

(Only four embryos were used in 2010, which is less than originally predicted)

During the review of the research database, research notes and from discussions between the research PR and the inspection team, concerning the use of embryos within the current project, it was concluded that;

From May 2009 until April 2011, 85 embryos were thawed for use in the research project.

For chromosome analysis (trophectoderm biopsy validation, followed by CGH array or FISH):

- 51 embryos were thawed, of which 32 survived.
- 26 spread embryos/cells were sent to a diagnostic laboratory and a further 6 spread embryos/cells sent to a collaborative centre, for comparative analysis.

For metabolomics studies:

- 34 embryos were thawed, of which 20 survived.
- 4 embryos were biopsied at the 6-8 cell stage and the cells/embryos spread for methodology validation.
- 16 spread embryos plus culture fluid were used for the metabolomics study. Fifteen of these embryos degenerated. An investigation at the centre concluded that this was due to an issue with the culture medium used.

- Due to the culture medium issue no research work has been undertaken since April 2010 and no further research work is planned.

- Due to organisational and personnel changes within the centre, and the lack of resources available to pursue the research work, the senior management at the centre have indicated that they will not be renewing the research licence at the present time. The research licence will be allowed to lapse upon expiry of the present licence on 31 December 2011.

The research PR informed the Executive that the centre has a total of 102 frozen embryos donated to research currently in storage. Of these;

- 77 embryos have specific research consents in place
- 15 embryos are without specific research consents
- 10 embryos are due to be discarded due to the expiry of the storage consent period

Following discussions with the inspection team, it was agreed that the research PR would ensure that;

- any embryos donated to research, which had appropriate training and/or research consents in place, would either be utilised for the purpose of training laboratory staff in embryo biopsy , or transferred to its HFEA-licensed collaborative centre for use in consented research work (HFE Act Schedule 3; (2)1; SRLC R19 R23)

- patients who donated their embryos to research, but do not have either training or specific research consents in place, would be contacted in order to ask whether they would like to provide training or specific research consent, in order for their embryos to be used in training or research, prior to the expiry of the storage consent period (SRLC R19 R23)

Details of inspection findings

Inspection findings

Ensure that all licensed research by the centre meets ethical standards, and is done only where there is both a clear scientific justification and no viable alternative to the use of embryos
(Guidance note 29, 30, 31)

What the centre does well.

The research licence was previously renewed in July 2009. It received ethical approval by an independent Ethical Review Board, which will remain in place until the licence expires.

The project's licence renewal application was reviewed by a peer reviewer and the HFEA RLC in July 2009. Both considered that the centre met appropriate ethical standards and had clear justification for, and no viable alternative to, the use of human embryos in research. The licensed activities approved were: the storage of embryos and the use of embryos in research. The licence was approved to allow research for the following purposes, as defined in Schedule 2, 3A (2) to the HFE Act 1990 (as amended):

- increasing knowledge about the causes of miscarriages
  Human Fertilisation and Embryology Act 1990 Schedule 2 3(2)(c)
- developing methods for detecting the presence of gene or chromosome abnormalities in embryos before implantation
  Human Fertilisation and Embryology Act 1990 Schedule 2 3(2)(e)
- increasing knowledge about the development of embryos
  Human Fertilisation and Embryology (Research Purposes) Regulations 2001 s2(a)
- promoting advances in the treatment of infertility
  Human Fertilisation and Embryology Act 1990 Schedule 2 3(2)(a)

What they could do better.

The present inspection was originally scheduled to be part of the licence renewal process. As such the centre's licence renewal application and other submitted documentation were forwarded for scrutiny via peer review. The peer reviewer observed that very little work had been undertaken during the lifetime of the licence, due mainly to organisational changes and technical difficulties. The peer reviewer also questioned the likelihood of any future success of the proposed research project. Partially due to the peer reviewer's comments and the honest acknowledgment by centre senior management that appropriately resourcing the research project, was an issue going forward, the Executive were informed shortly before the inspection that the centre would not be seeking to renew the research licence at this point in time, but would allow it to lapse on its expiry in December 2011. The peer reviewer's

comments have been included below in order to give background to this difficult but important decision by the centre. They have been included in the, 'could do better' section of the report, but are no longer an issue due to the centre's decision not to renew the research licence.

Peer review concerns over results and scientific justification.
The peer reviewer states that, '34 frozen embryos yielded no results because of technical problems with culture medium' and that, 'Overall, the productivity from the existing research licence is poor.' The research PR agreed that the more recent results from the work were disappointing, but explained that the work had been hampered by the supply of culture medium which had led to very poor embryo development in the metabolomics study. Due to this problem, further work had been suspended between April and September 2010, whilst the issue was investigated. No further research work was undertaken after this date.
The peer reviewer also notes that, 'There is a lack of clarity throughout over exactly what has been done, and what will be done.' The research PR recognised that with the re-organisation of the centre and loss of research staff (including the previous research PR), it had been difficult to commit appropriate time to the research project. The peer reviewer identifies that, 'There is a significant amount of published information on mosaicism and it is not clear that this centre can usefully add to that.'

In conclusion the peer reviewer states, 'The research undertaken has addressed the purposes of the existing research licence, but the productivity has been close to zero. This is partly explained by ownership and other changes in the centre, and partly by technical difficulties in the culture of embryos. Nevertheless, this is not a good track record, and does raise concerns about the likely success of the future proposed research.'

Have respect for the special status of the embryo when conducting licensed activities
(Guidance note 15, 18, 22, 25, 26)

What the centre does well.

All research activities are carried out on licensed premises which are located within the same building (SRLC R1).

The centre has a documented procedure in place which ensures that embryos are not kept in culture for more than 14 days. This practice was observed during an audit of patient records the research documentation on the day of inspection (SRLC R28).

A designated individual, who is not directly involved in the patient's own treatment is available to discuss the research project, prior to donation of any licensed material (SRLC R22).

From the review of patients' notes on the day of inspection, it was determined that appropriate consents are in place for the use of embryos in the research project. Embryos donated from centre 0068 are supplied with consents which are checked by staff prior to the embryos being stored and the information entered onto the research database (SRLC R18).

The centre has a process in place to ensure that all licensed material used in research is uniquely coded (SRLC R26).

What they could do better.

During the inspection of patient records, it was discovered that two embryos, which had been donated to research and whose consent to storage had expired, had been kept in storage for a further two months prior to being discarded (SRLC R39).

Changes / improvements since the last inspection on 28 April 2009:

Area for improvement	Action required	Action taken as evidenced during this inspection
None.		

Areas of practice that require the attention of the Person Responsible

The section sets out matters which the Inspection Team considers may constitute areas of non compliance. These have been classified into critical, major and others. Each area of non compliance is referenced to the relevant sections of the Act, Regulations, Standard Licence Conditions, Directions or the Code of Practice, and the recommended improvement actions required are given, as well as the timescales in which these improvements should be carried out.

Critical area of non compliance

A critical area of non compliance is an area of practice which poses a significant direct risk of causing harm to a patient, donor or to an embryo. A critical area of non compliance requires immediate action to be taken by the Person Responsible

Area of practice and reference	Action required and timescale for action	PR Response	Executive Review
During the inspection of patient records, it was discovered that two embryos which had been donated to research and whose consent to storage had expired, had been kept in storage for a further two months prior to being discarded. (SRLC R39).	The PR should ensure that all embryos donated to research and currently in storage have effective consent in place. The PR also needs to review and revise current processes to ensure embryos are not stored past their consented storage period for the remainder of the length of licence/until transported to another licensed centre.	A new process for discarding has been put in place for clinical and research embryos in storage. Although this has still been difficult to implement due to staff shortages. Due to the present research project R0169 not being renewed, it is proposed that; 1. All patients with donated embryos in storage will be contacted before any of their remaining embryos are transferred to another HFEA licensed clinic. 2. If patients are willing for their embryos to be used in associated research, new consents relating to the proposed research work would be completed/submitted prior to their embryos being transferred to the associated research centre. 3. If patients have consented to training, they will be asked to complete a specific training consent, which would allow these to be used for biopsy training at LFC. 4. Any embryos whose storage consents expire	The embryos in question had been discarded prior to the inspection. With respect to the patient donated embryos remaining in storage, the Executive have received an action-plan and time-line from the research PR at the centre, which, if fully implemented would satisfy the Regulatory requirements (for details see ‘additional information from PR’ below)

		would be disposed of in the usual manner. 5. Any embryos donated to research and in storage for which the patients could not be contacted, will be kept on licensed premises at LFC until they reach their expiry date, at which point they too will be discarded.	With the current research project not being renewed, the Executive propose to closely monitor the present situation concerning the patient donated embryos remaining in storage and will expect the research PR to forward regular updates concerning the fate of these embryos, which coincide with the supplied action-plan and time-line. An 'end of research project' report is to be submitted by the research PR prior to 31 December 2011.

Major area of non compliance

A major area of non compliance is a non critical area of non compliance:

- which poses an indirect risk to the safety of a patient, donor or to an embryo through the procurement, use, storage or distribution of gametes and embryos, which do not comply with the centre's licence;
- which indicates a major shortcoming from the statutory requirements;
- which indicates a failure of the Person Responsible to carry out his/her legal duties
- a combination of several "other" area of non compliance, none of which on their own may be major but which together may represent a major area of non compliance.

Area of practice and reference	Action required and timescale for action	PR Response	Executive Review
None			

Other areas of practice that requires improvement

Areas of practice that requires improvement is any area of practice, which cannot be classified as either a critical or major area of non compliance, but which indicates a departure from good practice.

Area of practice and reference	Action required and timescale for action	PR Response	Executive Review
None			

Additional information from the Person Responsible

Time Line for Research Licence R169/4/e at London Fertility Centre

Date	Action
24th October 2011	Dr Joyce Harper contacted at the Centre for PGD at UCL to send copies of UCL Research consents. UCL are willing to accept any research embryos which have been specifically consented for their projects.
1st November 2011	UCL and Reprogenetics to be contacted regarding the outcome of previous research embryos biopsied material sent.
7th November 2011	Registered letters to be sent out to all patients with Research embryos in storage. Choices to be given to patients; Continue to store for training for biopsy, with the specific consent. Consent to research at UCL and consent to transport. Consent to discard the stored research embryos.
21st November 2011	Responses from all correspondence to be received by LFC. Paperwork to be checked and samples allocated to each option. Electronic data to be updated.
30th November 2011	Transport to be arranged to Research centre at UCL using dry shippers and a courier service. Any outstanding samples to be stored on storage licence until they reach expiry and then allowed to perish.
16th December 2011	End of Research report to be completed.
21st December 2011	End of Research Project report to be sent to the HFEA prior to the 31st December.

HFEA Executive Licence Panel Meeting

18 November 2011

Finsbury Tower, 103-105 Bunhill Row, London EC1Y 8HF

Minutes – Item 4

Centre 0088 – (London Fertility Centre) – Interim Inspection Report (Research)

Members of the Panel:	Committee Secretary:
Peter Thompson, Director of Strategy & Information (Chair) Mark Bennett, Director of Finance & Facilities Ian Peacock, Analyst Programmer	Joanne McAlpine

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

The Panel also had before it:

- HFEA Protocol for the Conduct of Meetings of Executive Licensing Panel
- 8th edition of the HFEA Code of Practice
- Human Fertilisation and Embryology Act 1990 (as amended)
- Decision trees for granting and renewing licences and considering requests to vary a licence (including the PGD decision tree)
- Guidance for members of Authority and Committees on the handling of conflicts of interest approved by the Authority on 21 January 2009.
- Guidance on periods for which new or renewed licences should be granted
- Standing Orders and Instrument of Delegation
- Indicative Sanctions Guidance
- HFEA Direction 0008 (where relevant), and any other relevant Directions issued by the Authority
- Guide to Licensing
- Compliance and Enforcement Policy
- Policy on Publication of Authority and Committee Papers

Consideration of Application

1. The Panel noted that this centre has undergone considerable organisational change over the past eighteen months, most notably the change of ownership which occurred on 29 March 2010. The centre is now part of the Spire Healthcare group.

2. The Panel also noted that there have been significant staff changes over the same time period.

3. The Panel noted that Miss Samantha Knight was approved as the PR for research project R0169 by the Executive Licensing Panel on 11 March 2010, having successfully completed the PR Entry Programme.

4. The Panel noted that the centre has also made an application to vary the Licence Holder for the research project – which it approved earlier under Item 2.

5. The Panel noted that an Interim Inspection took place on 28 April 2009, at which time no regulatory non-compliances were noted.

6. The Panel noted that although this inspection (conducted in July 2011) was scheduled to be a licence renewal inspection, shortly prior to the date of inspection, the Executive was informed by senior management at the centre that they would no longer be seeking the renewal of the research licence, but would allow the licence to lapse, upon expiry on 31 December 2011.

7. The Panel noted that the inspection team was directed to undertake an interim-style inspection and to inform the Executive Licensing Panel of the centre's intention to allow research project R0169 to lapse.

8. The Panel noted the reasons why the centre decided not to apply to renew research project R0169, namely organisational and personnel changes and a lack of resource. It was also clear that no research work under this licence had taken place since April 2010.

9. The Panel noted that at the time of the inspection there was one critical area of non-compliance that required improvement, relating to the embryo and storage consent monitoring process.

10. The Panel noted that since the inspection the PR has confirmed that this critical area of non-compliance has fully been implemented.

11. The Panel noted that, as requested within the inspection report, the PR has also provided an action plan and time line which addresses the issue of patient –donated embryos presently within storage at the centre for use in research. These will be either:

- Used in embryo-biopsy training at the centre if appropriate consents are in place
- Transferred to another HFEA-licensed centre for use in associated research work if appropriate consents are in place
- Allowed to perish if requested by the donating patients or if the storage consent expires.

12. The Panel noted that the PR will also provide a fully referenced final report with results, conclusions and references to any publications arising from the research project by 31 December 2011.

13. The Panel noted that the Inspectorate recommends the continuation of the centre's licence with no additional conditions, and to allow the project to lapse from the 31 December 2011.

Decision

14. The Panel endorsed the Inspectorate's recommendation to continue the centre's licence, with no additional conditions and endorsed the recommendations made in the report.

15. The Panel requested the Inspectorate to ensure that a final report is submitted by the PR before the 31 December 2011.

Signed: Peter Thompson Date: 23/11/11.
Peter Thompson (Chair)