HFEA Licence Committee Meeting

1st December 2011

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

Minutes – Item 3

Centre 0035 (Oxford Fertility Unit) – Grade A Incident (IN02404)

Members of the Committee:	Committee Secretary:
David Archard (lay) Chair Sally Cheshire (lay) (videoconference) Rebekah Dundas (lay) (videoconference) Sue Price (professional) Mair Crouch (lay) Jane Dibblin (lay)	Lauren Crawford Legal Adviser: Tom Rider, Field Fisher Waterhouse

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

- Cover sheet
- Initial incident report form centre 0035
- HFEA's root cause analysis
- Centre's root cause analysis
- Centre's audit summary
- Executive Licensing Panel minutes – 12 August 2010
- Executive Licensing Panel minutes – 23 October 2009
- LC minutes - 21 September 2009
- LC minutes – 30 July 2009
- LC minutes – 11 September 2008
- LC minutes – 13 September 2007
- Tabled Item – Email from PR dated 30 November 2011 regarding "use of cabinets"

The Committee also had before it

- HFEA Protocol for the Conduct of Licence Committee Meetings and Hearings
- 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); and

- 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 Directions 0000 – 0012
- Guide to Licensing
- Compliance and Enforcement Policy
- Policy on Publication of Authority and Committee Papers
- HFEA Pre-Implantation Diagnostic Testing ("PGD") Explanatory Note For Licence Committee

Background

1. The Committee noted that it had received a report from centre 0035 following an incident in July 2011. During fertilisation checks on ISCI treated eggs on 30 July 2011, an embryologist noticed contamination, of low level, present in all dishes containing ICSI treated eggs/ embryos and recognised the possibility that the IVF produced embryos may also be contaminated. The Laboratory Director was informed of the non-conformity on the same day. In line with best practice new culture dishes were prepared and all the embryos were moved into these dishes following substantial washing.

2. At the time of the incident the centre's PR was on annual leave so the Clinical Director (CD) was notified and on 31 July 2011 attended the centre to speak directly with the embryologists. After discussions between the CD and the Laboratory Director, it was decided that even though there was considered to be only a negligible chance of the contamination affecting the embryos, that this chance still presented a risk the centre were not prepared to take. As a precautionary measure to eliminate any form of risk to the patients and their embryos the embryo transfers were cancelled. The patients involved were contacted.

3. The Committee noted the centre's investigations and their findings that this type of incident had not been seen before and that the level of contamination observed was very low. The centre's investigations found no obvious source of contamination in the processes or practices used. The Committee further noted that the Laboratory Director considered it plausible that the use of a pipette in an earlier sperm preparation may have contaminated the barrel, thus contaminating the media bottle used to

prepare the embryo culture dishes. The Committee accepted that this was the most likely explanation.

4. The Committee noted the incident was reported promptly in line with the HFEA's incident reporting requirements.

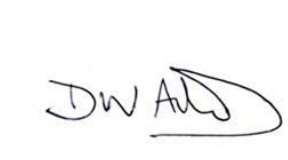
5. The Committee noted that the centre has as a result changed its practice and documented procedure for preparing dishes for embryo cultures to avoid any possibility of contamination, namely dishes will now be prepared in a facility, comprising a workstation with pipettes and pipette tips, dedicated to dish preparation, and that no other processes will be performed in the workstation or using the pipettes allocated to it. In addition, SOP's have been updated to emphasise the importance of decontaminating pipettes between processes and dealing with gametes and/ or embryos from different patients. Staff have been made aware of the changes.

6. The Committee noted that the CD invited all affected patients to the centre to explain the nature of the incident and its impact on their treatment. A refund package was offered, including a further treatment cycle free of charge. In addition, patients have been offered further discussions and counselling.

7. The Committee noted that the Case Officers analysis supported the centre's findings and that no other concerns were noted at the inspection.

8. The Committee hopes that at the renewal inspection next year, the centre provide clear evidence that the new SOP's are being adhered to and would also hope that other centres are following the same practices.

Signed: Date: 12/12/2011



David Archard (Chair)

Incident Investigation Report – IN02404

Background of the centre and the licence history

The Oxford Fertility Unit (the centre) was first established as a HFEA licensed clinic in 1992 and in 2009 re-located from the John Radcliffe Hospital, Oxford, to purpose built premises at the Oxford Business Park (North)[1].

The centre underwent a scheduled renewal inspection in June 2008 and an interim inspection in May 2010. The interim inspection report described four major and seven other areas of non-compliance seen on inspection which led to recommendations from the inspection team. The Person Responsible (PR) implemented corrective actions in response to all of these recommendations. The centre has no additional conditions on its licence.

The centre provides a full range of licensed treatments to self-funded and NHS patients including: In vitro fertilisation (IVF); Intracytoplasmic sperm injection (ICSI); embryo transfer; Frozen embryo transfer (FET); intrauterine insemination (IUI); sperm, oocyte and embryo storage; donor sperm and oocyte procurement and processing; treatment with donor gametes and embryos; oocyte sharing; preimplantation genetic screening (PGS) and preimplantation genetic diagnosis (PGD). The centre is the only one in the UK currently providing in-vitro maturation of oocytes with IVF or ICSI treatment.

The centre performed 1452[2] licensed treatment cycles in the year 1 February 2009 – 31January 2010 and is currently open 7 days a week, 08.00 to 16.30 Monday to Friday and 08.00 to 12.00 on Saturday and Sunday. A member of medical staff is contactable 24 hours a day, 7 days a week via an emergency number provided in patient information and also by the centre answer phone. There have been no significant changes in activity or patient demographics since the last inspection.

Summary Incident Description & Consequences

28 July 2011 – Dishes for embryo culture for the next day were prepared (i.e. labelled, filled with appropriate volumes of specific media and placed in an incubator to equilibrate) according to the centre's standard operating procedure (SOP) for this activity.

29 July 2011 – Post ICSI treated eggs were moved into embryo culture drops. This procedure was performed with the aid of a low power microscope. Fertilised eggs following conventional IVF were also moved into embryo culture drops.

30 July 2011 - Using a microscope to carry out fertilisation checks on ICSI processed eggs (ICSI performed on 29 July 2011) an embryologist noticed contamination,[3] of low level, present in all dishes containing ICSI treated eggs/embryos and recognised the possibility that

[1] These new premises were inspected by the HFEA on 25 August 2009 and a new treatment and storage licence was granted on the 21 September 2009.

[2] This data were extracted from the HFEA register for the period indicated above. The data may be subject to change as errors are notified to us by clinics, or picked up through our quality management systems.

[3] Further investigation revealed that the contamination consisted of fragments of immotile (dead) sperm cells.

the IVF produced embryos may also be contaminated. The embryologist informed the Laboratory Director of this non-conformity. In line with best practice new culture dishes were prepared and all the embryos were moved into these dishes following substantial washing. The PR was on annual leave so their delegated substitute was notified of the findings and the actions taken. The delegated substitute is the centre's Clinical Director (CD) who was also the centre's PR for some years until 21 September 2009.

31 July 2011 – The CD attended the centre to speak directly with the embryologists, then telephoned the Laboratory Director (who was also on leave) to discuss the situation. It was decided that even though there was considered to be only a negligible chance of the contamination affecting the embryos, that this chance still presented a risk the centre were not prepared to take. As a precautionary measure to eliminate any form of risk to the patients and their embryos the embryo transfers were cancelled. The patients (eleven couples) were requested to attend the centre so the CD could discuss the situation with them directly. The Laboratory Director attended the centre to begin the investigation.

Actions taken by the centre to determine the source of contamination
The PR and the Laboratory Director confirmed that only one procedure involving gametes/embryos is carried out in a workstation at any given time. All dishes are prepared under aseptic conditions using sterile sealed consumables. Various sources of cross contamination were considered including the barrel of the pipettor, poor workstation hygiene allied with poor pipette technique, prior contamination of the embryo culture medium, oil or dishes, and the mechanism and technique used to change the disposable plastic pipette tips.

During the site visit, discussions with the PR and Laboratory Director confirmed that each of the possibilities above and the relevant laboratory processes and staff competence to perform them, have all been examined in some detail. The report of the investigations carried out by the centre indicates that no evidence was found to suggest that either of the possibilities– a list the HFEA inspection team find to be exhaustive – appeared to be a likely or consistent source of contamination. As a precautionary measure following the incident the centre had already implemented a major change to the plating out procedure. A hood within the laboratory is now dedicated to be used solely for the plating out procedure. Following this change in practice a senior member of staff not directly involved in the incident, carried out an audit of the plating out procedure[4]. The audit finding confirmed that no major changes to the procedure were required.

This type of incident has not been seen before at the centre and the level of contamination observed was very low. The centre's investigations have found no obvious source of contamination in the processes or practices used. The centre has concluded therefore that this incident is related to a low frequency and unforeseeable failure in practice which allowed cross contamination to occur. Specifically, the Laboratory Director considers it plausible that the use of a pipette in an earlier sperm preparation may have contaminated the barrel thus contaminating the media bottle used to prepare the embryo culture dishes. For this to occur however it required poor pipetting technique during the sperm preparation, poor cleaning of the pipette after that process, then poor pipetting technique during the plate preparation. This concordance of events would explain why this type of incident has not occurred at the centre before as the chance occurrences necessary are unlikely to occur together. It should also be noted that this scenario is only postulated and little evidence was seen during the centre's investigation to support it.

[4] Audit summary attached as an appendix to this document

However as a result the centre has changed its practice and documented procedure used to prepare dishes for embryo culture, to completely remove any possibility of contamination: dishes will in future be prepared in a facility, comprising a workstation with pipettes and pipette tips, dedicated to dish preparation. No other processes will be performed in this workstation or using the pipettes allocated to it. This arrangement removes any potential cellular source of contamination from the dish preparation process, which is the most effective risk control measure which could be implemented to prevent another incident of this kind.

SOPs have also been updated to emphasise the importance of decontaminating pipettes between processes and dealing with gametes and/or embryos from different patients. Staff have been informed of these changes.

Terms of Reference of the investigation

- To determine that the licensable activities relating to the centre's laboratory processes complied with the HFEA Code of Practice 8th edition
- To establish whether failings occurred in the ICSI preparation processes resulting in contamination
- To provide a report as a record of the investigation process
- To provide a means of sharing learning from the incident sector wide

Specialty/ Location:	Preparing dishes for embryo culture in the clinical embryology laboratory
Effect on patients:	Psychological distress Eleven patients prepared for embryo transfers that did not take place and will therefore have to undergo further treatment at a later date
Severity level:	Pre-investigation scoring of the incident: (A) likelihood of recurrence : 3 (B) Consequence: 5 (C) risk rating (C = A x B): 15

Scope and Level of Investigation

Site visit – 18 August 2011- Paula Nolan (Clinical Governance Lead/Inspector), Dr Andrew Leonard (Scientific Inspector). Present from the centre – Person Responsible and Laboratory Director.
Document review
Root Cause Analysis

Involvement and support of Patient and Relatives

The HFEA has not received any patient complaints relating to this incident.

The CD invited all the patients affected to the centre so that he could explain the nature of the incident and how this would impact on their current treatment. Further to this all patients have been offered a refund package that includes a further treatment cycle free of charge. All patients have been offered the opportunity to have further discussions with the PR and/or the CD. Counselling has also been offered to all patients.

The PR provided a further update on 01 November 2011 explaining that 9 of the 11 affected couples have returned for consultations or have been in contact and are continuing on with further treatment with the centre. One couple are going abroad for egg donation and one couple are going for further IVF in another Unit.

Chronology of events – see centre's root cause analysis

Notable Practice
The incident was reported in line with the HFEA's incident reporting requirements.

The CD was out of the country when the incident site visit was scheduled but offered to fly back to attend in person. The inspection team considered that it was not necessary for the CD to attend as the Laboratory Director and the PR were both present during the site visit. Further to this the CD was contactable via telephone during the course of the site visit.

Once the centre's incident investigation was complete and corrective actions implemented. The centre initiated an audit of practice by a senior member of staff not directly involved in the incident or the incident investigation.

Care and Service Delivery Problems (Themed and prioritised)
None noted

Contributory Factors
Possible contamination of pipette shafts

Standard Operating Procedure not comprehensive enough regarding the repeated use and cleaning of pipettes

Root Causes
Repeat use of pipettes for more than one process or sample

Incomplete cleaning of pipettes between different processes and samples

Discussion

A review of the HFEA incident database has revealed that in the previous five years two incidents of a similar nature have been reported. Although the severity impact for these two incidents was not as severe, in both cases a thorough investigation was initiated with findings broadly similar to those described in this report.

During the course of the investigation no concerns were raised by the Executive regarding the centre's laboratory procedures and practices, which were considered to be compliant with the HFEA's Code of Practice. At the time of the incident the laboratory was adequately and appropriately staffed. Although the source of the contamination has not been identified with any certainty, the centre has taken the necessary steps to try and identify it. By examining and ruling out other factors it seems likely that the contamination was on the barrel of a pipettor. The centre has documented its investigations appropriately and has taken immediate corrective actions to prevent a recurrence by isolating the plate preparation process to a

dedicated facility away from any source of contamination.			
Recommendations Pipettes to be identified for use for either medium or sperm			
Action Plan – see centre's RCA (already implemented)			
Author	Paula Nolan (Clinical Governance Lead/Inspector)	**Date**	26 September 2011

HUMAN FERTILISATION & EMBRYOLOGY AUTHORITY

Incident Investigation Report -

Summary Incident Description & Consequences	
Incident type:	
Specialty:	
Effect on patient:	Embryo transfer did not proceed
Severity level:	
Scope and Level of Investigation	
Involvement and support of Patient and Relatives All patients brought into clinic and seen personally by Clinic Director to explain what had happened. Subsequently all patients have been written to and offered future treatment and access to the clinics' services.	
Chronology of events - See table overleaf	
Notable Practice Making up of dishes for embryo culture	
Care and Service Delivery Problems (Themed and prioritised) No underlying care or service delivery problem have been identified. Most likely this was human error in a fully staffed unit with a robust quality management system in place	
Contributory Factors Using different pipettors for different procedures may have contributed to this, hence an immediate action plan was put into place	
Root Causes As far as we can ascertain, the most likely explanation is that the barrel of a Pipettor seems to have been contaminated. The barrel of the pipette is not sterile but can come into contact with the inside of a bottle of medium and in this way contamination could theoretically occur. Procedures are never carried out in the same hood at the same time, hoods are always cleaned out and down after a procedure. A new procedure is always started with fresh tips. All members of staff are aware of the importance of good tissue culture practice	
Lessons Learned We have now dedicated one flow hood and associated pipettors to the process of making up dishes. All staff have been reminded of the importance of applying good tissue culture techniques. The barrel of all pipettors are now cleaned with sterilising wipes after and particularly before use	
Recommendations .	
Action Plan – Dedicated flow hood for this procedure set up immediately after incident occurred.	

Implementation, monitoring and evaluation arrangements Implementation was immediate. SOP altered. Audit has been done by Quality Management Manager which concluded that the measures implemented should prevent any re-occurrence
Arrangements for sharing and learning • Isolate dish preparation from work areas where other procedures may have been performed (even if these do not happen at the same time) eg have a dedicated flow hood • Ensure everyone aware and reminded of good tissue culture practice • Supplier of electronic witnessing system is now looking at a way to link electronically witnessed procedures to a particular workstation as this would be an additional traceability tool for all IVF units.

Author		**Date**	*26/08/11*

Chronology of events	
Date & Time	**Event**
28/07/11	Dishes for embryo culture made
29/07/11	Injected eggs after ICSI procedures moved into embryo culture drops under low power microscope Fertilised eggs after conventional IVF moved into embryo culture drops. Nothing unusual noted at this time.
30/07/11	Fertilised eggs after conventional IVF moved into embryo culture drops. Nothing unusual noted at this time. Fertilisation checks done on ICSI eggs from 29/07. Contamination noted at this point as this is not expected following ICSI. Contamination was extremely low. Lab Director notified by embryologists. New dishes made. All embryos moved into fresh drops following substantial washing Acting PR notified
31/07/11	Acting PR (who is also the Clinic director) went into unit and discussed situation direct with embryologists and then with Lab Director by telephone More difficult to determine contamination in conventional IVF dishes but felt these needed to be treated the same way as dishes made at the same time Decision to cancel all embryo transfers of patients involved and bring all patients affected into the unit to speak to directly Lab Director came into the unit to start the investigation Able to identify that contamination involved embryo culture dishes only by checking other dish types made at the same time but before those in question
01/08/11	Members of staff involved spoken to in order to try to understand what had happened and kept from lab duties whilst coming to terms with situation and whilst trying to piece together what happened Other staff also spoken to who may have been able to contribute to understanding what happened

	HFEA notified
02/08/11 – 04/08/11	The Witness Point Report (Electronic Witnessing system) provided clarification on what procedures were taking place that day but unfortunately did not allow determination of which workstations these occurred at. Given that there are a lot of procedures that go through the laboratory on a daily basis, staff have been unable to determine with complete certainty what procedures happened at which stations. However, it is a policy of the laboratory that two procedures involving gametes/embryos do not take place at the same workstation at the same time. Various sources of the contamination considered and tested, including the barrel of the pipettor, workstations not being cleaned down adequately after use and 'freak' occurances. Different volume range pipettors are used for different procedures which enabled certain procedures/processes to be eliminated as the source of the contamination.
04/08/11	It is concluded that it is extremely difficult to determine with any certainty the source of the contamination. Taking all things into consideration, contamination of the barrel of the pipettor seems the most likely explanation.