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Supporting information for establishing IVF Laboratory

Quality Assurance and Quality Control

Working within a quality management system is increasingly important for IVF centres, it helps to minimise risk and encourages best practice and safe effective patient care. This document prepared by the IFSS provides basic guidance with regard to what should be included in a quality management system. Information and examples are given which can be used by centres to build their quality manual and quality control and assurance protocols. The document covers the basics of a quality manual, aspects of clinical governance, examples of quality control and quality assurance, tools for assessing competence, basic validation for equipment and suggestions for audit. The information is not exhaustive and is not designed specifically to meet any regulatory or published standards.

Quality Manual:

Suggested index to use:

1. Introduction

2. Quality Policy

3. Documented Information

4. Training and competence

5. Audits, monitoring and measurement

6. Risk management

7. Laboratory QC and QA

1. Introduction: The introduction in the quality manual should contain the following information as a minimum:

- General introduction to the centre
- Centre location / site details
- Services provided
- The types of treatments carried out
- Management arrangements.
- Simple flow chart of processes carried out (i.e. pathway from referral to treatment outcome detailing appointments)
- Simple organisational chart detailing line management for staff employed
- How communication occurs within your unit e.g. frequency of meetings and how they are recorded.
- How the patient treatment is planned and reviewed.
- Scope of the quality system

2. Quality Policy: A quality policy is a short simple document which reflects your centre's aims and ethos and is held within the quality manual. The document can also be displayed for patients to read, is usually signed by management and includes a small set of quality principles such as

Commitment to listening to patients needs to improve the service

Ensuring utmost confidentiality

Providing treatments in a safe environment

Ensuing staff are training and competent in all their duties

Maintain an ethos of continual improvement

Learn from positive and negative events within an open and honest environment

3. Documented Information:

This should be a description to how all the documented information is managed in the centre.

Sat within the quality management system should be a range of standard operating procedures (SOP) for each task undertaken. A standard format should be used. Each SOP should be clearly written with a title, a reference number, date issued, version number, author and review date. For example a simple footer can be used for example:

An effective SOP describes;

who will perform the task,

what materials are necessary,

where the task will take place,

when the task shall be performed,

how the person will exactly execute the task,

how and where any generated information is recorded.

A tracking system needs to be in place to ensure there is control of documentation. A simple and effective way is to hold a master document database which lists all documents in use. Using a policy of only printing documents as and when required will ensure only the most up to date version is in circulation. All documents can be hyperlinked from the master database. If a change is required it is reviewed, agreed, the current version archived and the changed version saved as a new version number. All documented information should be reviewed after an agreed period of time (e.g. annually).

4. Training and Competence

Training logs should be maintained by all new staff and formal competency assessment should be undertaken before a member of staff is allowed to practice independently (appendix 1). Once trained annual competency reviews can be undertaken on every member of staff to ensure the task (appendix 2 details an example of an SOP review for an embryo transfer)

5. Audit, monitoring and measurement

Audits are used to systematically assess evaluate and improve patient care. They are used to measure current practice to highlight where improvements can be made. Any practice or process can be audited following the audit cycle which involves 5 stages;

- prepare
- select criteria to measure,

- measure performance level,
- reflect, plan, change and make improvements
- re-audit to ensure improvements are sustained

An annual schedule of audits should be planned (appendix 3). Once completed they should be reported on a standard form (appendix 4), and there should be documented evidence that the findings are shared with the team.

Examples of audits which can be conducted include:

- OHSS: All cases of OHSS reviewed on an annual basis. The percentage of all cases reviewed to assess if an increase or decrease has occurred from the previous year.
- Consent procedures: 100% of all patients should have appropriate consent prior to procedures commencing. Notes audit to assess accuracy of consent taking. Fifty sets of notes audited to check if all consents were signed and in place prior to treatment. Report non-conformances and re audit if necessary.
- Embryo transfer: Each individual operator to be assessed for clinical pregnancy rate, biochemical rate and ectopic pregnancy rate. If an operator falls >5% of clinics average figure then further investigation required.

Key Performance Indicators are used to measure and monitor service provided. A very useful resource to understand KPIs and how to use them is the Vienna consensus report of an expert meeting on the development of ART laboratory performance indicators (ESHRE specialist interest group of embryology and Alpha scientists in Reproductive Medicine). The paper defines the appropriate performance indicators for monitoring 'fresh' cycles. Other professional bodies such as the Association of Embryologists (UK) have defined various KPIs which can be measured and set suggested benchmarks (Hughes and ACE 2012). If a KPI falls below expected levels a troubleshooting exercise should be conducted.

OVERALL			
	KPI	Calculation (x 100 for %)*	Suggested benchmarks
1	IVF fertilisation rate	2PN + 3PN/No. inseminated	>65%
2	IVF abnormal fertilisation rate	≥3PN/No. inseminated	<5%
3	IVF 1PN rate	1PN/No. inseminated	<5%
4	ICSI fertilisation rate	2PN/No. injected	>65%

5	ICSI 1PN rate	1PN/No. injected	<5%
6	ICSI damage rate	No. degenerate/No. injected	<10%
7	Failed fertilisation rate	No. of cases with 0 fertilised/No. inseminated	<5%
8	Low fertilisation rate	No. of cases with <30% 2PN of Met II	<10%
9	Cleavage rate	No. cleaved/No. 2PN	>90%
10	IVF oocyte maturity	No. fert. + Unfertilised Met II/No. oocytes collected	>80%
11	ICSI oocyte maturity	No. of Met II/No. of oocytes collected (at time of injection)	>80%
12	Utilisation rate	No. transferred or frozen/No. 2PN	>50%
13	Blastocyst formation rate	No. 2PN with progression to D5/D6/Total no. of 2PN	>50%
14	Frozen embryo survival rate	No. survived/No. thawed	>70%
15	Follicle yield	No. of oocyte collected/No. follicles punctured	>80%

Based on patients under the age of 40 who had at least three oocytes collected or more

FRESH CYCLES		
Pregnancy rates (%)	Suggested benchmarks D2/3	Suggested benchmarks D5/6
Positive hCG per oocyte retrieval (OR)	40%	45%
Positive hCG per embryo transfer (ET)	45%	50%
Clinical preg. (FH on scan at 7 weeks)/OR	35%	40%
Clinical preg. (FH on scan at 7 weeks)/ET	40%	45%
Multiple birth rate/ET	<10%	<5%
FROZEN CYCLES		

Pregnancy rates (%)	Suggested benchmarks D2/3	Suggested benchmarks D5/6
Positive hCG per thaw cycle	35%	40%
Positive hCG per thaw cycle + ET	40%	45%
Clinical preg. (FH on scan at 7 weeks)/thaw	30%	35%
Clinical preg. (FH on scan at 7 weeks)/ET	35%	40%
Multiple birth rate/ET	<10%	<5%

Table 1. ACE laboratory key performance indicators. (modified from Hughes and ACE 2012). These are suggested benchmarks. Centres should calculate their own benchmarks and trigger points based on their patient population and data.

Patient satisfaction: There should be a measurement of patient satisfaction. This can range from a simple questionnaire asking how they rate the service to a more in-depth analysis of the patient pathway (appendix 5)

6. Risk management:

Creating an open honest environment in a no blame environment will ensure that all incidents and near misses are reported. Once reported an investigation should be undertaken to find out what was the root-cause of the incident. A simple form / data base can be used to record:

- Date of the incident / near miss
- Details of those involved (including any witnesses)
- Location of incident
- Description of the incident / near miss
- Any immediate action taken
- Detail of the investigation carried out (route cause analysis)
- Detail of any actions required / corrective actions

Any incidents / near misses should be discussed at clinic meetings and recorded in the meeting minutes.

Complaints should be logged and tracked. They should be discussed at management level. Once received the complaint should be investigated by consulting with members of the team, agreeing what action is necessary and formulating a response to the patient making the complaint. There should be a written policy to how complaints are dealt with including time frames for responding.

In an attempt to prevent incidents occurring Risk Assessments should be carried out. A consistent format should be used for each risk assessment. The systematic process involves

- Identifying a hazard which has the potential to cause harm to staff (or visitors). (This can be done by a *visual check, examining instruction books and analysing the incident book)*
- Assessing how the hazard could cause harm and the level of risk it posed (ie the likelihood that the hazard would hurt people). To do this consider the following: How often the task is done, how many staff are involved or near the hazard, how long the task takes, whether any incidents had occurred previously when carrying out the task and how effective the current controls are in place. Then consider how likely the incidence of harm is (certain to occur, very likely, possible, unlikely or rare).
- Work out how the problem could be prevented practically in the workplace (deciding the most effective risk controls).
- Recording the findings on the risk assessment form to describe the measures required to put the controls in place.
- Review the risk once the controls are put in place.

An example risk assessment template is in appendix 6

7. Laboratory Quality Control and Assurance

Equipment:

A master spreadsheet should be held documenting all the equipment in the centre. This should include the model and serial number and dates when servicing is performed. All equipment should be covered by an appropriate service plan to ensure the equipment is well maintained and calibrated accordingly. All measuring and test equipment should be calibrated using approved sub-contractors and equipment used should be traceable to national standards. Records should be kept of servicing.

Critical equipment which can have direct or indirect impact on embryo quality should be subjected to independent quality control checks. Daily checks should be recorded for incubator temperature (unless specified differently by the manufacturer). pH if possible and carbon dioxide and oxygen should be measured at an agreed frequency if if the gas isn't pre mixed. Heated stage checks and fridge temperature checks should also be carried out. Ideally temperature checks should be conducted using a calibrated electronic thermometer with a thermocouple which can be placed in media within a dish. Examples of record sheets see appendix 7 and 8

Cleaning frequency should be defined and a record should be made (appendix 9)

Traceability of media and consumables:

Where ever possible consumables and culture media in the IVF lab should be fit for purpose and be certified for IVF use.

On receiving items a simple inward receipt can be carried out (appendix 10). Once a new batch is opened this should be recorded so that all consumables used are fully traceable. A electronic database can be used or simple paper records can be kept (appendix 11).

Any consumable used which is not certified for use in IVF and has not been subjected to an mouse embryo bioassay can be simply tested using a sperm survival test (Critchlow et al 1989)

Consistency and reproducibility:

Embryological assessments can be subjective and be variable in reliability and consistency. Best practice is to subscribe to an external quality assurance scheme such as NEQAS. NEQAS provides a comprehensive service for semen analysis and embryo morphological assessment. If it is not possible to subscribe effective internal quality assurance can be undertaken. Each quarter each team member should perform motility and concentration counts on the same sample. Morphological assessment can also be undertaken. Results should be collected by a nominated member of the team and analysed for differences in results.

References

Critchlow JD et al Quality control in an in-vitro fertilization laboratory: use of human sperm survival studies. 1989 Hum Reprod., 4:5: 545-549

ESHRE specialist interest group of embryology and Alpha scientists in Reproductive Medicine. The Vienna consensus: report of an expert meeting on the development of ART laboratory performance indicators. 2017. Hum Reprod Open pp 1-7

Hughes C. Association of clinical embryologists—guidelines on good practice in clinical embryology laboratories 2012. Hum Fertil (Camb), 15:174–89

Recommended further reading

Quality and Risk management in the IVF laboratory. Sharon Mortimer and David Mortimer. 2nd Edition 2015. Cambridge University Press isbn: 9781107421288

Organisation and management of IVF units. A practical guide for the clinician. Flemming and Varghese. 2016 Springer. ISBN 978-3-319-29373-8

Olofsson, Banker M and Sjoblom. Quality management systems for your in vitro fertilisation clinic's laboratory: Why bother? J Hum Reprod Science 2013; 6(1): 3-8

Appendix 1: Competency sign off sheet

- Personnel must be provided with training. Documented evidence of training must be kept.
- Working without supervision is not permissible until competency has been confirmed which involves demonstrating knowledge and understanding of the scientific/technical processes and principles relevant to their designated tasks.
- Training must be updated as required when procedures change

Ongoing competency is reviewed via audits and SOP competency reviews.

This document is to summarise the competencies achieved by an individual. Further evidence will be found in CPD files, Validation files and audit results

Embryologist / MLA: ………………………………………………………………

Job Title:

Line manager:

Competency assessed	SOP reference	Date Assessed	Assessed by
Sterile technique			
Traceability of media and consumables			
Dish preparation			
Principles of consent			
Basics of culture conditions			
Witnessing			

Partner sperm preparation			
Donor sperm preparation			
Preparation of frozen sperm samples			
Preparation of antisperm antibody positive sample			
Preparation of retrograde samples			
PESA / TESE			
Oocyte recovery			
Sperm cryopreservation			
IVF insemination			
Cumulus removal			
ICSI			
Fertilisation checks			
Embryo assessment			
Blastocyst assessment			
Embryo transfer			
Slow rate freezing of embryos			
Thawing of embryos			
Time lapse (embryoscope and Primo)			
Vitrification			
Re-warming			

IUI			
Information provision to patients			
Breaking bad news			
Multiple births policy			
FMS			
Handling LN2			
Health and safety regulations			
IDEAS / Data input			
DNA fragmentation assessment			
Use of embryos in training and research			
Equipment maintenance (including cleaning)			

Comments

………

………

………

………

………

Appendix 2

Embryologist assessed: ……………………………… **DATE..............**

Grade	**Improvement required**	**Competent**	**Comments**
Is all the paper work in place for the embryo transfer?			
Is the Embryo Transfer Sheet in the patient's notes completed?			
Is the verbal witness procedure carried out with the doctor and nurse present in theatre?			
Are the details of the embryos clearly explained to the patient?			
Is the Embryo Freezing Advice Sheet completed if embryos are being cryopreserved?			
Is the type and batch number of catheter recorded?			
Has the embryo(s) been transferred to a glue dish just before the procedure?			
Is the catheter prepared correctly and warmed?			
Is the dish ID check performed through the hatch with the scan nurse and the IVF witness check completed?			
Are the embryos loaded correctly into the catheter?			
At the end of the procedure is the media flushed through the catheter to check for retained embryos?			
Is sterile technique used at all times during processing?			

Is the laboratory record completed and signed?			
Is the heated stage used throughout and are the dishes kept outside the incubator for a minimum time to maintain viability			
Overall performance			

Suggestions for development:

………

………

………

Any deviations observed from SOP

………

………

Agreed action

Assessor's signature:…………………………………………………Date:………………………

Assessor's Name:…………………………………………………………………………………….

SOP Assessed against (insert reference)

Appendix 3: Audit Matrix

Year: ………………..   Authorised By: ………………………….

Audit Title	Jan	Feb	Mar ch	April	May	June	July	Aug	Sept	Oct	Nov	Dec

Appendix 4

<u>Audit Report: ……………………………………………</u>

<u>Ref No (s) of Procedure (s) Audited:</u>

<u>Dept (s) / Section (s) Involved:</u>

<u>Name of Auditor:</u>

<u>Date of Audit</u>:

<u>Result of Audit</u> :- (Tick suitable Box)

Satisfactory ☐ Unsatisfactory ☐ Observation ☐

<u>REPORT :-</u>

<u>AC</u>
<u>IM</u>

Signature of Auditor:

DATE CORRECTIVE ACTION

TO BE TAKEN:

Is Re-audit necessary:

Close out date and signature:

Appendix 5: Patient satisfaction questionnaire

As we are committed to providing a quality service to all our patients we are continually looking at ways to improve what we do therefore we would like you to tell us about your experience. We would like to invite you to tell us where improvements can be made and where we meet or not meet your expectations and requirements.

We would appreciate you taking 5 minutes of your time to complete this questionnaire which will provide valuable feedback to the team. The questionnaire is anonymous, so your views and suggestions will be treated in the strictest of confidence and will not affect your current or any future treatment.

Thank you for taking part and for helping us to improve our service.

Please tick the appropriate box and write any helpful comments.

1. The clinic reception area provides a welcoming environment

Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly Disagree

2. The staff always introduced themselves and treated me with courtesy

Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly Disagree

3. **The staff are always approachable**

Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly Disagree

4. **I feel my dignity and privacy have been respected at all times.**

Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly Disagree

5. **Overall, how would you rate the quality of service provided by the staff on the unit?**

(Please circle your response)

Doctors	Excellent	good	fair	poor	N/A
Nurses	Excellent	good	fair	poor	N/A
Embryologists	Excellent	good	fair	poor	N/A
Reception staff	Excellent	good	fair	poor	N/A
Counsellors	Excellent	good	fair	poor	N/A

6. **How would you rate the surroundings and facilities?**

(*Please circle your response)*

Waiting Room	Excellent	good	fair	poor	N/A
Scan Room	Excellent	good	fair	poor	N/A
Consultation Room	Excellent	good	fair	poor	N/A
Counselling Room	Excellent	good	fair	poor	N/A
Sperm Production	Excellent	good	fair	poor	N/A
Recovery	Excellent	good	fair	poor	N/A
Theatre	Excellent	good	fair	poor	N/A

7. **The written information I was given was clear and easy to understand**

Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly Disagree

8. **During the the consultation I was given sufficient information**

Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly Disagree

9. During the consultation I could understand the information I was given

Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly Disagree

10. My treatment plan was clear to me at the end of the consultation

Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly Disagree

11. I was well cared for by team during the egg collection

Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly Disagree	N/A

12. The information I received after the egg collection was clear and helpful

Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly Disagree	N/A

13. I was well cared for during my embryo transfer / IUI

Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly Disagree	N/A

14. I understood all the information given to me during the embryo transfer / IUI

Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly Disagree	N/A

15. The instructions and information I was given during my treatment were clear and easy to understand

Strongly agree	Agree	Neither agree or disagree	Disagree	Strongly Disagree	N/A

Finally, please feel free to make any other comments about the treatment you have received. For example, what was done well and what could have been improved upon?

………

………

………

………

Many thanks for giving your time to complete this questionnaire

Appendix 6: Risk Assessment template

<table>
<tr><td>Title:</td><td colspan="4"></td></tr>
<tr><td>Description of risk</td><td colspan="4"></td></tr>
<tr><td>Existing controls in place when risk was identified</td><td colspan="4"></td></tr>
<tr><td colspan="2" rowspan="3">Initial Risk Score i.e. with existing controls in place</td><td>Consequence (1-5)</td><td colspan="2"></td></tr>
<tr><td>Likelihood (1–5)</td><td colspan="2"></td></tr>
<tr><td>Risk Score
(consequence x likelihood)</td><td colspan="2"></td></tr>
<tr><td colspan="5">Action Plan to reduce the risk to an acceptable level</td></tr>
<tr><td colspan="2">Description of actions</td><td colspan="2">Responsibility
(Job title)</td><td>Completion
Date</td></tr>
<tr><td colspan="2"></td><td colspan="2"></td><td></td></tr>
<tr><td colspan="2"></td><td colspan="2"></td><td></td></tr>
<tr><td colspan="2"></td><td colspan="2"></td><td></td></tr>
<tr><td colspan="2"></td><td colspan="2"></td><td></td></tr>
<tr><td colspan="2" rowspan="4">Target Risk Score i.e. after full implementation of action plan</td><td>Consequence (1-5)</td><td colspan="2"></td></tr>
<tr><td>Likelihood (1–5)</td><td colspan="2"></td></tr>
<tr><td>Risk Score</td><td colspan="2"></td></tr>
<tr><td>Date for completion</td><td colspan="2"></td></tr>
<tr><td colspan="2">Assessment undertaken by:
Name</td><td colspan="3">Job title</td></tr>
<tr><td colspan="2"></td><td colspan="3"></td></tr>
<tr><td>Date of assessment</td><td></td><td>Date of next review</td><td colspan="2"></td></tr>
</table>

Appendix 7: Incubator QC checks

Incubator: …………………………………….. Month: ……………………………………

Day	Temperature	CO2 level	Oxygen level	pH	Signature
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
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26					
27					
28					
29					
30					
31					

Appendix 8: Heated stage check

Date / initial	**Stage:**	**Stage:**	**Stage:**
	L Side .... °C R Side .... °C Centre .... °C	L Side .... °C R Side .... °C Centre .... °C	L Side .... °C R Side .... °C Centre .... °C
Comments / Action required			
	L Side .... °C R Side .... °C Centre .... °C	L Side .... °C R Side .... °C Centre .... °C	L Side .... °C R Side .... °C Centre .... °C
Comments / Action required			

Appendix 9: Cleaning rota

	Date and Initial	Date and Initial	Date and Initial	Date and Initial	Date and Initial	Date and Initial
Clean centrifuge						
Clean flow hoods						
Clean Microscopes						
Clean Gilsons						
Top up dewars and Charge dry shipper						
Mop and wash floors						
Re stock lab						
Incubator maintenance						

Appendix 10: Inward receipt of consumables

		Embryologist
Date of delivery		
Order number		
Item description		
Is delivery note present	**Yes No**	
Staff member signing for delivery		
Is package in good condition	**Yes No**	
Is item for refrigeration	**Yes No**	
Are goods in an acceptable condition	**Yes No**	
Does the amount supplied match those on delivery note (detail if not)	**Yes No**	
Is this item on the approved consumable list	**Yes No**	
Did product come with certification	**Yes No**	

Staple delivery note to this form and file

Appendix 11: Consumable batch record

Record date and batch number when opening a new box of consumables.

Date:……………………….

Item	**Date Opened**	**Batch Number**	Expiry date	**Initial**