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Workshop on QMS in PCR PGD

Introduction to session

- **Section 1 Personnel**
- Training and staff development — Sioban SenGupta (UK)
- Staff assessment and competency logs — Pam Renwick (UK)
- **Section 2 Pre-examination Process and Post Examination Process**
- Information: couples, IVF labs, PGD labs — Martine De Rycke (Belgium)
- **Section 3 Pre-examination Process (for labs)**
- PGD protocol strategies / mutation detection — Celine Montou (France)
- PGD protocol linkage / validation — Francesco Fiorentino (Italy)
- **Section 4 Examination Process**
- Receiving samples, SOPs, risk assessments — Jan Traeger-Synodinos (Greece)
- **Section 5 Evaluation and Quality**
- Follow-up and misdiagnosis — Gary Harton (USA)
- EQA – monogenic disorders — Sandi Deans (UK)

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Personnel, Training and Staff Development

Sioban SenGupta
University College London Centre for PGD

Clinical Pathology Accreditation

References from International Organiziation for Standarization

- ISO 15189:2007
  - Medical Laboratories
    - Particular requirements for quality and competence
- ISO/IEC 17025:2005
  - General requirements for the competence of testing and calibration labs
- ISO 9001:2000
  - Quality Management systems
    - Requirements
- ISO 9000:2005
  - Quality Management systems
    - Fundamentals and vocabulary
- ISO 22870:2006
  - Point of care testing (POCT)
    - Requirements for Quality and competence

CPA standards for Personnel

- Professional direction
- Staffing
- Personnel management
- Staff orientation and induction
- Job descriptions and contracts
- Staff records
- Staff annual joint review
- Staff meetings
- Staff training and education

Professional Direction

- Laboratory Director
  - Executive accountability and competence to assume responsibility for the service
    - Medical Consultant status / Member Royal College of Pathologists
- Continued professional development
- Departmental meeting to review service

Royal College of Pathologists

The Royal College of Pathologists
Pathology: the science behind the cure

- Two routes for FRCPath
  (cytogenetics/molecular genetics)
  - Examination
    - Part 1 – 2 papers, practical, oral
    - Part 2 – written component, oral
  - Publication
    - 30 peer reviewed papers (10 first or senior author)

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Staffing

- State registration as clinical scientist
  - In UK nothing specific for PGD
  - Trying to set up a system
- Other roles
  - Quality management
  - Training and education
  - Health and safety

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State registration as Clinical Scientist

- Need certificate of attainment from Association of Clinical Scientists
- Apply to Health Professionals Council (HPC) for state registration
  - Sections for Cytogenetics and Molecular genetics
  - Nothing specific for PGD
  - Trying to get new section established for PGD

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Association of Clinical Scientists

- Two routes
- Route 1
  - Approved Training programme
    - 2 years training / 2 years experience
    - 3 years training / 1 year experience
- Route 2
  - No Approved Training programme
    - 3 years PG degree / 3 years experience

- Portfolio of competencies
  - Scientific
  - Clinical
  - Technical
  - Research and Development
  - Communication
  - Problem Solving
  - Management

Personnel Management

Staff orientation and induction

- Introduction to staff
- Job description
- Quality manual and accreditation information
- Fire training/health and safety/occupational health
- Data protection
- Training programme established

Job Description and Contracts

- Job title
- Line of accountability
- Purpose of job
- Main duties and responsibilities
- Staff annual joint review
- Signatures of staff and manager

Staff records

- Personal details
- Employment details
- Job description
- Terms and conditions of employment
- Record of staff induction and orientation
- Record of attendance at fire lectures
- Record of education, training, CPD
- Educational and professional qualifications
- Certificate of registration
- Absence record
- Accident record
- Record of Annual joint review
- Record of occupational health
- Record of disciplinary action

Staff annual joint review

- For every staff member
- Staff fills in first section and gives to manager in advance
- Manager and staff discuss - write summary of discussion
- Any training needs clearly identified and time lines recorded
- Any disagreements recorded
- Both sign form

Annual review

- A summary of your main achievements in relation to your aims, objectives for the review period and any significant changes in your responsibilities since the last review (or in the previous 12 months if there has not been a previous review).
- A summary of any factors affecting achievement of your aims and objectives or your contribution to the work of the department over the review period.
- Major activities, tasks and priorities anticipated in the coming review period and any training or other support that you will need to assist you in achieving them.

Staff meetings

- Regular staff meetings; weekly, monthly
  - Minutes taken to ensure actions carried out

Staff training and education

- Key for all staff involved in PGD
- Several areas of competence:
  - Scientific
  - Clinical
  - Technical
  - Research and development
  - Communication
  - Problem solving
  - Management

Scientific Competence

- Knowledge of
  - suitability of diagnostic tests for single cell analysis
  - limitations of commonly used diagnostic tests in molecular PGD
  - genetic disorders, mutations and DNA markers
- Training
  - lecture course
    - techniques /disorders / IVF/ preimplantation embryo development
  - designing protocols for PGD
    - Workbook of optimised protocols / lab meetings - progress reports
  - writing SOPs and HFEA Licence applications

Clinical competence

- Need to
  - interpret results of a diagnostic test
  - understand clinical problems of genetic disorders
  - develop tests according to clinical picture
- Training
  - Observation / shadowing of cases
  - audits with embryologists and clinicians
  - work-up for PGD cases
  - Observation days
    - Scientists, embryologists, doctors and nurses

Technical competence

- Experience of
  - performing diagnostic procedures
  - trouble shooting
  - use of quality control and quality assurance
- Training
  - Witness audits
  - Single cell isolation / PCR – Efficiency / ADO / Contamination
  - Blastomere tubing – embryologists – spares / cases
  - Protocol design and optimisation - PGD work-ups, follow-ups
  - Presentations at lab meeting, writing SOPs
  - EQA

Research and Development competence

- Ability to
  - critically appraise literature, develop a project
  - develop and apply new technique / protocol
  - present the research finding
- Training
  - Journal Club
  - MSc, PhD, MRCPath
  - PGD work –ups , new disorders, new techniques
  - Seminars and courses
  - Presentations at conferences

Communication competence

- Ability to
  - Respond to enquires regarding the service
  - Communicate effectively with colleagues
  - Communicate with patients, healthcare professional, public
- Training
  - Observation days / Understanding course of treatment
  - Organisational chart / Responsibilities / Contact details
  - Presentations in lab meetings, clinical meetings, conferences

Problem solving competence

- Need to
  - Interpret quality control and quality assurance data
  - Recognise diagnostic problems
  - Understand underlying cause of diagnostic problems
  - Have experience in problem solving
- Training
  - Vertical and horizontal audits
  - Follow –up of spare embryos
  - Clinical audit / diagnosis rate

Management competence

- Ability to understand
  - legal and ethical boundaries
  - limits of knowledge / skills
  - principles of clinical governance
  - need for accreditation
  - importance of effective communication in a multidisciplinary team
  - principles of appraisal and be able to supervise staff
  - Importance of continuing professional development
  - health and safety requirements
  - structure / organization / finance

Training targets

- Year 1
  - Completion of workbook
  - Work up for 3 cases
  - Design and optimisation of 1 case
  - Observation of 6 cases
- Year 2
  - Work up for 6 cases
  - Design and optimisation of 3 cases
  - Shadowing of 6 cases
  - PGD of 2 cases
- Year 3
  - Workup for 10 cases
  - Design and optimisation of 6 cases
  - PGD for 10 cases

Conclusion

- Need to have written policies for each aspect
- Clearly defined staff records
- Regular meetings
- Annual appraisals
- Essential to keep staff up to date

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Personnel: Competency

Pamela Renwick

PGD Centre, Guys Hopsital NHS Foundation Trust, London

UK

ISO 15189:2007 Medical laboratories – Particular requirements for quality and competence.

- **B9 Staff training and education**
  - **B9.3** Competency to perform assigned tasks shall be assessed following training and periodically thereafter. Retraining and reassessment shall occur when necessary. Records of competency assessments shall be kept (B6).
- Employer must demonstrate that their employees are adequately trained and experienced enough to carry out their job function(s)
  - Procedures
  - Equipment

Demonstrating Competency

- Assessment by:
  - Witness procedure
  - Written questions
  - Achieve set level of success: cell biopsy, cell collection, amplification.
- Levels of competency:
  - Not competent
  - Competent with supervision
  - Competent
  - Competent to troubleshoot and train others

Assessment: procedures (1)

Assessment record: Collection of biopsied blastomeres

Member of staff undergoing assessment .....

Grade .....

Name of assessor ..... Grade .....

SOP Number(s): LP.D.PGD.Blastomere Collection
LP.D.PGD.Case Set up
LF.D.PGD.CheckList.Case Set up

Risk assessment: RF.D.PGD.CellCult

Knowledge

- Use of bi-focal microscope
- If hand drawn glass pipettes are used: selection of pipette with appropriate diameter.
- Cell quality measures: cell number, embryo grade, visible nucleus, vacuoles, blebs, cell symmetry, zona quality.
- Understands the importance of minimal liquid volume transfer.
- Brussels collection method for removal of culture media through wash drops.
- Understands potential sources of DNA contamination and need for appropriate precautions.
- Sample checking procedure.
- What to do if a cell lyses or is 'lost' during collection.
- Health and safety issues associated with this procedure.
- Who to report to if there is a problem.

Competence - is able to: **Trainer's signature**

- If used, Set up mouth pipette ☐.....
- If used, Safe disposal of glass pipettes ☐.....
- Set up microscope ☐.....
- Collect cells and transfer through wash drops ☐.....
- Deposit & observe cell to 0.2ml tube containing lysis buffer ☐.....
- Achieve 90% amplification with no contamination in non template controls ☐.....

Assessment: procedures (2)

Assessment forms: equipment (1)

Assessment record: ABI3730 use and maintenance

Member of staff undergoing assessment .....

Grade .....

Name of assessor ..... Grade .....

Associated lab protocols; LP-D-ABI3730

Specific knowledge of the following has been assessed:

	Initial		Initial
ABI3730 maintenance		Understand odd/even/quadrant plate loading	
The 1 x buffer and are changed every 48hrs (Sigma water, ABI3730 buffer)		**Ensure all unused wells are filled with T.1E; FAILURE TO DO SO WILL DAMAGE THE ARRAY**	
Wash septas, reservoir, and buffer chamber with water and dry with white tissue every 48 hrs.		Use of heat sealer to seal plate; remove lids first from part used plates	
Replacement of buffer polymer when req.		Heat denature for genotype analysis	
Perform monthly maintenance routine		Check polymer and buffer levels and ensure there are no air bubbles	
Order consumables when required		Check PC is on and there is a green light on the ABI3730machine	
Able to change array and know when this is required.		Use correct base for plate i.e. Grey 96 and 384 bases	
Perform computer hard drive maintenance		Set up run sheet, select appropriate results group	
ABI3730 use		Aware of correct instrument protocol and analysis protocol to use	
Book use in red folder beside machine, including record of no.runs and type		How to remove data	
Load samples in T.1E for sequencing analysis		Aware of when to get help; red light on machine	
Load samples in formamide with size standard for genotype analysis			

Assessment forms: equipment (2)

Assessment of ABI3730 use and maintenance.

Write short answers to the following questions.

1. What does it mean and/or what action should you take if the light on the front of the ABI3730 is;

   a) Green
   b) Flashing green

   c) Flashing yellow

   d) Flashing red

   e) Not visible

2. What checks should you perform before you start running samples?

3. What do you need to do if you decide to re-run a sample plate?

Competency Log (1)

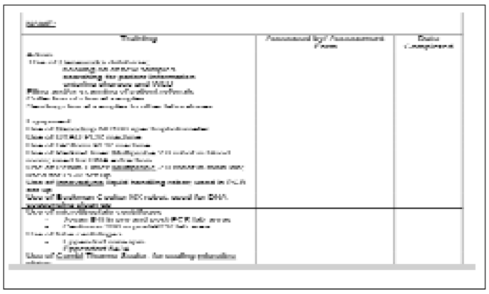
- Record each individual's formal qualifications, experiences and training episodes
- Mechanism to manage, review and identify additional training needs for an individual, team or organisation on a regular, systematic and timely basis
- Sourcing of suitable cover during the period of absence for employees.

Competency Log (2)

	A	C	D	E	F	G	H	I	J	K	L	M	N
1	**Lab Methods & Analysis & Equipment**	Dr Emma Ashton	Lina Brodd	Dr Jo Campbell	Miss Victoria Cloke	Mr Tom Cullup	Dr David Ellis	Mr Adu Gyamfi	Miss Sue Lillis	Miss Jenny May	Mrs Jo McCauley	Mrs Rachael Mein	Mr David Moore
2													
3	T = Trainer												
4	C = Fully Competent												
5	S= Competent with Supervision												
6	U = Not competent												
7	R= Re-training required												
8													
9													
10													
11													
12	Post	CS	MTO1	CS	TS	PreCS	CS	MTO1	CS	Admin	CS	CS	CS
13	Start Date	01/10/2001	05/03/2008	01/10/2000	08/10/2007	03/10/2005	01/10/1998	01/04/2006	22/09/2003	18/10/2004	16/07/2002	02/07/2001	22/09/2003
14	End Date												
15	**Professional Qualifications**												
16	Grade A Certificate of Competency	Y	N	Y	N	Y	N	N	Y	N	Y	Y	Y
17	State Registered Clinical Scientist (SRCS)	Y	N	Y	N	N	Y	N	Y	N	Y	Y	Y
18	DipRCPath	Y	N	Y	N	N	Y	N	Y	N	N	Y	Y
19	MRCPath	N	N	N	N	N	N	N	N	N	N	N	N
20	Disease Specialism	Yes	No	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes
21	**DNA Diagnostic Laboratory Procedures**												
31	**Sample Processing;**												
32	Collecting clinical specimens from specimen reception	U	C	U	C	C	C	C	U	U	U	U	U
33	Test selection procedure	C	U	C	U	U	C	U	C	U	C	C	C
34	Sample checking and tube transfers	C	C	C	C	C	C	C	C	U	C	C	C
35	Sending DNA samples by post	C	C	C	C	C	C	C	C	U	C	C	C
36	Sending blood samples to SEEGEN labs by courier	U	C	U	C	U	C	C	U	C	U	U	U
37	Sending samples by non-SEEGEN courier	C	S	C	U	U	C	U	C	C	C	C	C
38													
39	DNA/RNA Extraction												
40	DNA extraction from blood - Chemagen kit;	U	C	U	C	R	U	C	R	U	U	U	U
41	DNA extraction from CVS	C	U	C	U	C	C	U	U	U	C	C	C
42	DNA extraction from amniotic fluid	C	U	C	U	C	C	U	U	U	C	C	C
43	DNA extraction for solid tissue - manual extraction	U	U	R	U	C	C	U	U	U	C	U	U
44	DNA extraction from solid tissue - Chemagen kit	U	U	U	U	U	U	U	U	U	U	U	U
45	DNA extraction from saliva - Oragene kit	U	U	U	U	C	U	U	U	U	U	U	U
46	DNA clean-up using phenol/chloroform	C	U	C	C	C	C	U	C	U	C	C	C
47	DNA clean-up by ethanol re-precipitation	C	U	C	C	C	C	U	C	U	C	C	C
48													
49	**Equipment;**												
50	Gilson use	C	C	C	C	C	C	C	C	U	C	C	C
51	Gilson maintenance	C	U	C	U	C	C	U	C	U	C	C	T
52	Gilson Calibration	C	U	C	U	C	R	U	C	U	C	R	T
53	Use of Perkin-Elmer Mulitiprobe 2 DNA extraction	U	C	U	C	C	U	C	R	U	U	U	U
54	Use of NanoDrop DNA quantifier	C	C	C	C	C	U	C	C	U	C	C	C

DNA Lab log / PGD lab log /

Training plans



Maintaining competency (1)

- Mechanism when a change is implemented (procedure/equipment) all appropriate people have been informed and assessed as required.

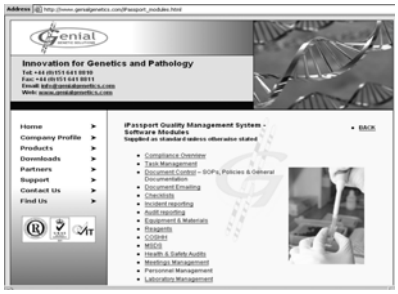
- Compliance
  - Evidence updated SOPs have been read and are in use (document control:excel spreadsheets, commercial software)
  - Assessments
  - Examination Audits

Compliance: updated SOPs

Section	SOP	Description	Read by	Date
Lab + Equipment	LF-D-PGD-Floor-Plans-level4-V1.1	PGD floor plans		
	LF-D-PGD-Fridge+Freezers-V2.0	PGD contents of fridges and freezers		
	LF-D-PGD-Kit_tube-colours-V1.0	Colours of PCR kits and tubes		
	LF-D-PGD-Forms-chemicals-V1.0	Form recording all chemicals entering lab		
	LF-D-PGD-Forms-DNA-boxes-V1.0	Form recording the DNAs stored in boxes in fridge 1		
	LF-D-PGD-Forms-gilsons-V1.0	Form recording the maintenance of the gilsons		
	LF-D-PGD-Forms-MDA-enzyme-V1.0	Form recording the MDA enzyme		
	LF-D-PGD-Forms-solutions-V1.0	Form to record all solution made in the lab		
	LF-D-PGD-Forms-temperatures-V1.0	Form recording the temperatures of the fridges and freezers		
	LF-D-PGD-Forms-UV-Hood-V1.0	Form recording the maintenance of the UV Hoods		
	Equip_Service Contracts_Repairs	PGD Excel doc of all equipment + servicing and repairs		
	Orders	PGD Excel doc of all ordered items		
	Catalogues	PGD Excel doc of all ordered items		
	Pipette records	PGD Excel doc of all pipettes		
	MF-P-EquipInv-V1.0	Excel doc of equipment inventory for PGD lab		
General	LP-D-PGD-General-V2.0	PGD general information		
	LP-D-PGD-Sample Identifiers-V1.2	PGD sample identifiers		
	LP-D-PGD-Databases-V1.1	PGD databases		
	LP-D-PGD-ACU PGD Referrals-V1.1	ACU flow chart of PGD referral processing		
	LP-D-PGD-ACU PGD case schedule-V1.1	ACU flow chart of PGD case scheduling		
	LP-D-PGD-ACU PGD Case flowchart-V1.1	ACU flow chart of PGD case		
Oragene DNA extract	LP-D-PGD-ExtractOragene-V1.0	DNA extraction from saliva		
	LF-D-PGD-checklist-oragene-V1.0	Checklist for oragene DNA extraction		
PGD case	LF-D-PGD-checklist-case-PGH-V1.0	Checklist for case lysis, MDA and PCR		
	LF-D-PGD-checklist-case-samples-PGH-V1.0	Sample checklist for PGH case		
	LP-D-PGD_Case Set Up-V1.0	Setting up for a case		
	LF-D-PGD- checklist- case-set up.V1.0	Setting up for a case checklist		
	LP-D-PGD-Archive-Store-Dispose-V1.2	PGD archiving storing and disposing of case PCR samples		
	All Cases - results	PGD excel doc of case outcomes		
	LP-D-PGD-COD-V1.1	PGD confirmation of diagnosis		
	LF-D-PGD-checklist-COD-V1.0	Checklist for COD		

Document control: commercial software (1)

IPassport



Document control: commercial software (2)

Q Pulse

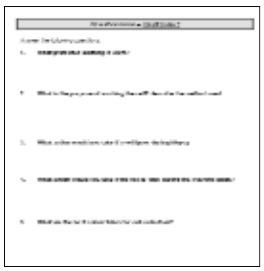
Maintaining competency (2)

- When someone is assessed and deemed to be competent –for how long is this valid?

  Does it depend on:
  - Frequency of performing procedure?
  - Complexity of the procedure?
  - Change in personal circumstances?

- Need to re-assess if technique not performed in X months?

Re-assessment



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