Pre- and Post Examination Process

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PGD centre: implementing QAS

- Right people
  (trained, competent)
- Right way
  (best practice for policies and procedures)
- Right results
  (accurate, unbiased)

PGD in practice

- Pre-examination process (clinical genetics unit, IVF unit)
- Pre-examination process (lab)
- Examination process (lab)
- Post-examination process/follow-up (lab, clinical genetics unit, IVF unit)

Pre-examination process: critical elements

- Evaluation of PGD request/ acceptance
- Genetic counselling
- Informed consent

under applicable legal, ethical and professional standards

Evaluation of the PGD request

- Preliminary evaluation before initial consultation (mail)
- By who?
  - Team of 'right' people:
    - Clinical geneticist
    - IVF clinician
    - Molecular geneticist/cytogeneticist
    - Specialist physician
    - Local ethical committee
    - Plus national regulations

Evaluation of the PGD request

- Is PGD acceptable?
  - Condition
  - Age of the female partner (basal FSH)
- Is PGD possible?
  - Available molecular/cytogenetic information (original testing reports)

Consultation at the IVF unit

- IVF clinician
  - Reproductive history
  - Pre-IVF tests and examination
- IVF counsellor
  - IVF treatment/ results/ benefits/ limitations/ (short and long-term) risks/ costs/ time line
  - Informed consent for IVF
    - Information part and consent part
    - Written authorisation by each partner
    - Before treatment
    - Different languages
    - Document deposit in patient's file

Consultation at the genetics unit

- Genetic counselling
  - Who?
    - Clinical geneticist
  - When?
    - Initial consultation
    - After pre-examination lab workup
    - After clinical cycle
    - Prenatal follow-up
    - Postnatal follow-up

Consultation at the genetics unit

- Genetic counselling
  - Genetic information (language)/non-directive
  - Help understand genetic basis/risks
  - Explain reproductive options
  - Support in decision making
  - Check diagnosis upon referral
  - Pedigree

Consultation at the genetics unit

- Genetic counselling
  - PGD procedure/ results/ benefits/ limitations/ cost/ time line
  - Pre-PGD sampling of probands/family members
    - Karyotypes, CF, specific genetic condition

Consultation at the genetics unit

- Genetic counselling: checklist
  - Risk for OHSS
  - Cancellation cycle if insufficient oocytes
  - no unprotected sex around oocyte retrieval/ during preclinical workup for custom made tests
  - Only testing for genetic condition
  - Theoretical % embryos genetically transferable vs reality
  - Principle and efficiency of test => embryos remain without diagnosis
  - Take home baby rate, specified for condition

Consultation at the genetics unit

- Genetic counselling: checklist continued
  - Risk for misdiagnosis
  - Decision making about fate of carrier embryos (X-linked reces)
  - Decision making about fate of non-compatible healthy embryos in case of HLA typing
  - Decision making about prenatal diagnosis
  - Embryo transfer policy: no transfer for non-biopsied or non-diagnosed or abnormal/affected embryos
  - Cryopreservation policy and live birth rate after transfer of frozen/thawed embryos
  - Contact person/coordinator

Consultation at the genetics unit

- Genetic counselling
  - Fate of non-transferred/non-cryopreserved embryos (at our centre in a separate informed consent for scientific research)
  - Informed consent for PGD (+ informed consent for research on embryos)
    - Information part and consent part
    - Written authorisation by each partner
    - Before treatment
    - Different languages
    - Document deposit in patient's file

Example informed consent


SCIENTIFIC RESEARCH
PATIENT INFORMATION
AND CONSENT

Example informed consent

In particular, research is carried out into:

1. improving IVF techniques;
2. male infertility;
3. optimisation of in vitro maturation methods of immature oocytes;
4. factors that play a role in in vitro fertilisation and the embryo's development;
5. implantation disorders: the interaction between the embryo and the womb;
6. the freezability of oocytes and embryos
7. pre-implantation genetic diagnosis: the development and validation of diagnostic genetic testing;
8. obtaining and cultivating embryonic stem cell lines: research into the safety of using these cells for stem cell therapy;

the right to withdraw your consent to the use of your gametes and/or embryos up to the moment that the research commences without having to give any explanation for this. Your refusal shall in no way affect your treatment.

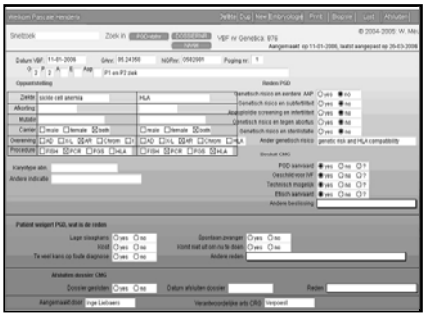
You are also free to object to (a) certain form(s) of the scientific research described above.

The research does not benefit you financially, nor does it incur any additional costs for you.

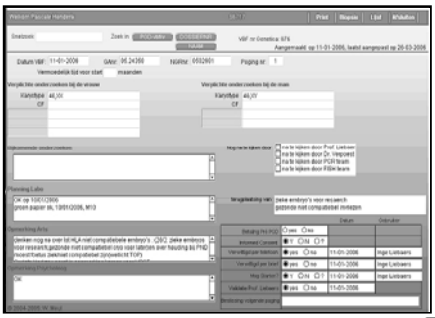
Registration and data managing of patients, cycles, outcome

- Electronic database
  - Genetic file
  - IVF file
  - Embryology
  - Biopsy
  - Genetic testing FISH/PCR
  - Pregnancy/children follow-up
- Requirements:
  - Personal login
  - Registration/validation is restricted
  - Audit trail system (who and when)

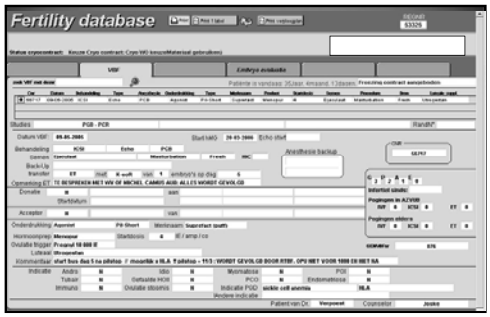
Example genetic file



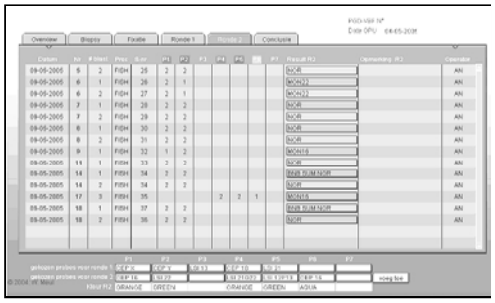
Example genetic file



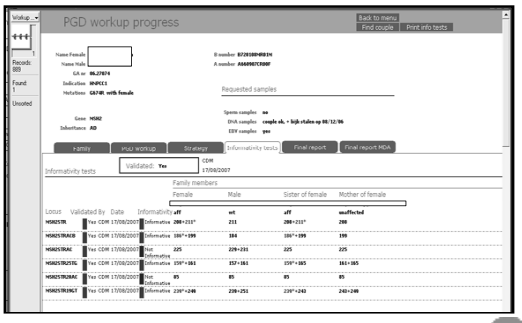
Example IVF file



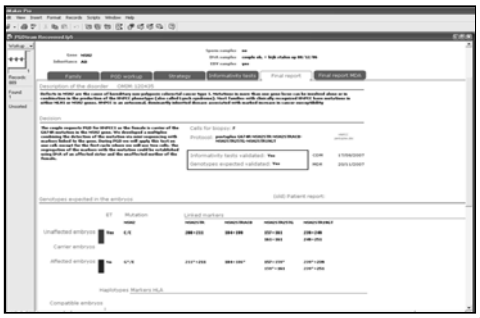
Example clinical cycle: FISH (second round)



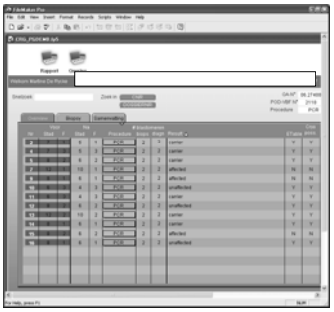
Example pre-clinical workup PCR: informativity and segregation analysis



Example pre-clinical workup PCR: report



Example: direct result flow

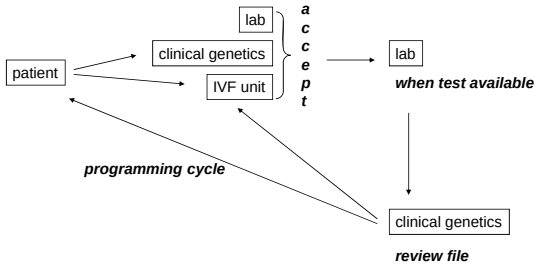


Example:summary, report

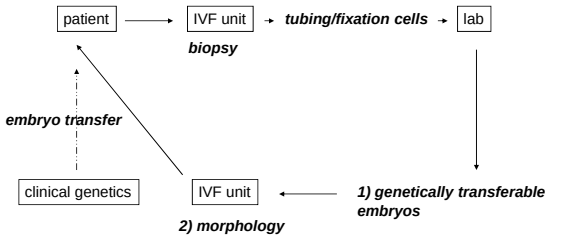
Registration and data managing of patients, cycles, outcome

- Electronic database
  - Benefits
    - Efficient data recording by “right” people through entire process
    - Minimise errors and discrepancies
    - Direct data flow to different units helps communication
    - Summaries and reports
    - Can allow virtual integration of physically seperated units

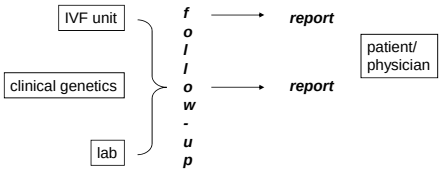
Pre-examination process



Examination process

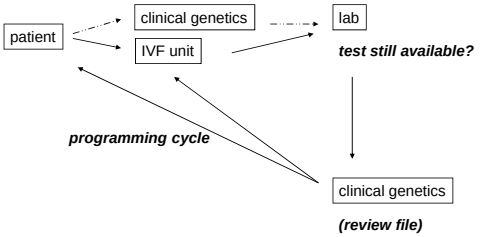


Post-examination process



If not pregnant ***=> new cycle (adaptations)***
=> other options
If pregnant ***=> follow-up of pregnancy/children***

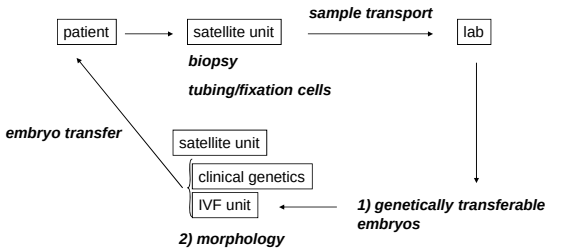
Pre-examination process



Pregnancy and baby follow-up

- Couples are asked to participate in follow-up studies before treatment
- Questionnaires for couple and their obstetrician are given to them at time of embryo transfer
- Questionnaires for couple and their pediatrician are send to them around delivery
- Children are asked to present at the clinic at 2 months, 1 year, 2 years,..

Transport PGD: examination process



Transport PGD

- Recommendations (1)
  - Before starting: arrange meetings and prepare written agreement between satellite and lab unit about procedures, contact persons, costs, time lines, responsabilities,...
  - Additional procedures on embryo biopsy for transport PGD, on sample transport, on reporting,...
  - Adequate, reliable courier service is essential
  - Relevant information on genetic condition, pedigree, accurate genetic analysis report, fertility status and pre-IVF results should be provided to the lab unit along with preclinical samples

Transport PGD

- Recommendations (2)
  - Satellite unit should train staff for biopsy/ fixation/ tubing
    - Training at lab unit / witness procedures at lab unit (adaptations)
    - Lab unit checks biopsy/ fixation/ tubing of satellite unit (site visit)
  - It is mandatory to carry out min 1 mock cycle before clinical cycles
    - Satellite unit sends tubed research blastomeres + report on biopsied sampes to lab unit
    - Lab unit: assessment of transport (timing), PCR amplification efficiency and contamination rate, and issues a report on the outcome
    - Satellite unit: assessment of lab report