

Guidelines for the Genetic Analysis of Solid Tissue Samples

Available Genomic Tests

- 1) **QF-PCR** – this test will detect whole chromosome gains or losses for chromosomes 13, 15, 16, 18, 21, 22, X and Y.
- 2) **Array-CGH** – this test will detect imbalances throughout the genome to a high resolution.
- 3) **Conventional karyotyping** – this is no longer a routine test for solid tissue referrals, however, is available when required (e.g. some familial cytogenetic rearrangements, or the investigation of tissue specific cytogenetic mosaicism).
- 4) **Cell culture** – viable cells can be propagated in culture to facilitate biochemical assays.

Referral Eligibility (Pregnancy Loss Referrals)

Testing acceptance and methodology is provided in accordance with the National Genomics Test Directory for rare and inherited disease*, with reference to the following clinical indication codes:

- R318 - Recurrent miscarriage with products of conception available for testing (third or subsequent miscarriage).
- R22 - Fetus with a likely chromosomal abnormality.
- R21 - Fetal anomalies with a likely genetic cause

Please note that we do not process:

- Confirmation of an abnormal cytogenetic prenatal diagnosis.
- First or second trimester unexplained 1st or 2nd miscarriages with no fetal malformations.

* Please refer to the 'National Genomic Test Directory for rare and inherited disease' www.england.nhs.uk/publication/national-genomic-test-directories/ for full details of eligibility criteria, indication definitions, requesting specialities and testing methods.

Summary of Test Provision

DNA extraction / storage

- All processed samples will have DNA extracted and stored (this will include R21 indications which may be eligible for WES or Large Panel testing in the future, following multidisciplinary review including Clinical Geneticist).
- Samples received following sudden unexplained infant death, including coroner cases, will have DNA extracted and stored but will not be processed for testing unless a likely genetic cause is indicated.

QF-PCR / Array-CGH

- 3rd or subsequent unexplained miscarriage (*previous obstetric history must be detailed on the referral form*) (R318).
- Fetal loss, termination of pregnancy or miscarriage, where the malformations or clinical history are indicative of a likely chromosomal abnormality (R22).

Conventional karyotype

- Familial cytogenetic rearrangements, where appropriate (R297).
- Children and adults suspected of having a mosaic chromosome abnormality - *Consultant Clinical Geneticist referrals only* (R265).

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Instructions for Sending Samples

I. General requirements

- Please **do not** place samples in fixative.
- Please forward as soon as possible following collection, but if there is delay, store at 4°C. Do not freeze, expose to excess heat or store in fixative.
- Please ensure that packaging conforms to HSE packing Instructions P650 (see www.hse.gov.uk/cdg/pdf/infect-subs.pdf).
- Tests are principally DNA based.
- For cell culture or conventional karyotyping viable cells are required. Suspend samples in tissue culture media* or sterile isotonic saline and send without delay.

II. Pregnancy loss referrals

For ERPC (Evacuation of Retained Products of Conception) samples, separate the solid tissues and transfer to a dry, sterile, leakproof container. Please do not send in the procedure evacuation container.

POC	Solid tissues only	In dry, sterile, leakproof container
Placental biopsy (chorionic villi)	At least 2cm ³ taken adjacent to the cord insertion site to ensure it is the fetal side	In dry, sterile, leakproof container
Fetal tissues (skin, muscle, cord)	At least 1cm ³	In dry, sterile, leakproof container
Cord blood	1- 2ml	In EDTA tube

- Multiple samples may increase the success rate of testing.
- The laboratory can decide which samples will be most appropriate for processing from the samples received.
- A fetal skin biopsy is not always essential as the fetal genetic constitution can often be established from extra-embryonic tissue.

III. Biopsies from child and adult referrals

Biopsies from live patient	Skin: full depth needle punch biopsy	In tissue culture medium*, NOT DRY
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*Tissue culture media is available from the laboratory on request

Referral Information

As for all genetic test requests, please ensure that a completed genetic referral card accompanies the sample(s) and that full clinical information is provided, including a full list of the malformations.

Laboratory staff are always available to provide guidance on sample suitability and clarify acceptance criteria for higher levels of testing, if required (tel. 01722 429080 or e-mail: shc-tr.WRGLdutyscientist@nhs.net).