Guidelines for the Genetic Analysis of Solid Tissue Samples

Available Genomic Tests

1) **Microarray (SNP based microarray platform)** - this is the principal test and will detect whole chromosome gains or losses, segmental imbalances throughout the genome to a high resolution, and other genomic conditions observed in pregnancy loss referrals (e.g. triploidy, molar pregnancies, uniparental isodisomy, degrees of maternal cell contamination).
2) **Conventional karyotyping** - this is no longer a routine test for solid tissue referrals, however, it is available on request.
3) **Cell culture** - viable cells can be propagated in culture to facilitate biochemical assays or long-term storage.

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.
- R412/R27 - Fetal anomalies with a likely genetic cause (non-urgent).

Please note that we do <u>not</u> 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 R412 indications which may be eligible for WGS (R27), WES or Large Panel testing in the future, following multidisciplinary review and Clinical Geneticist approval).
- Samples received following sudden unexplained infant death, including coroner cases, will have DNA extracted and stored but will not be processed for testing unless testing has been specifically requested or a likely genetic cause indicated.

Microarray

- 3rd or subsequent unexplained miscarriage (*previous obstetric history <u>must</u> 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).

WES/WGS/Large panel (*Consultant Clinical Geneticist referrals only)*

- Where MDT review consider a monogenic malformation disorder is likely (R412/R27).

Conventional karyotype

- Familial cytogenetic rearrangements where determination of balanced carrier status is deemed essential (R297).

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

**Tissue culture media is available from the laboratory on request

Referral Information

Please ensure that a **completed genetic referral form** accompanies the sample(s) and that **full clinical information** is provided, including a full list of any malformations. This may assist the interpretation of results.

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).