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Ústav lekárskej biológie, genetiky a
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Guideline for Screening / Diagnostics of Reproductive Losses

Project: GIFD — Genetical Spectrum of Intrauterine Fetal Death Causes in Slovakia

Ethical Committee of the University Hospital Bratislava: Approval EK 1/92003

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1. Purpose and Scope

1.1 Purpose

The GIFD project's core diagnostic algorithm reflects the technical capacity of the coordinating institute. Not every laboratory or clinical department in Slovakia that encounters reproductive losses has access to the same equipment, budget or specialist staff. This guideline translates „GIFD diagnostic algorithm,, into modifiable, resource-tiered pipelines so that workplaces with different technical, financial and personnel capacity can implement an appropriate version of genetic screening, in line with the WP4 objective of enabling nationwide implementation of the algorithm.

1.2 Scope

- Applies to: any Slovak workplace (genetics laboratory, pathology department, or obstetrics/gynaecology department with laboratory access) that manages reproductive losses and wishes to offer or refer for genetic screening.
 - Applies to reproductive losses from second and third trimester of gestation.
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2. Defining Workplace Capacity Tiers

Three indicative tiers are proposed below. They are a starting point for discussion, not a finished classification — the specific equipment, staffing and turnaround thresholds should be validated against the actual profile of Slovak genetics laboratories and pathology departments.

Tier	Typical capability	In-house genetic tests	Illustrative setting
Tier 1 — Basic	PCR thermocycler + capillary electrophoresis access; no in-house microarray/NGS	QF-PCR (aneuploidy screen) only	e.g. regional hospital genetics/laboratory unit
Tier 2 — Intermediate	Tier 1 capability + MLPA workflow	QF-PCR + MLPA (subtelomeric/microdeletion panels)	e.g. larger regional or university-affiliated laboratory
Tier 3 — Advanced / Reference	Tier 1–2 capability + aCGH/NGS, Sanger sequencing	Full Deliverable 11 algorithm	GIFD coordinating institute (IoMBGCG)

3. Universal Minimum Recommendation (All Tiers)

Regardless of tier, every workplace is recommended to apply the same anamnestic risk-factor screen before — or instead of, where testing capacity is constrained — laboratory analysis. This step requires no additional equipment or budget and is the single highest-yield triage tool currently validated within the project.

Risk factors: positive prenatal screening result; maternal age 40 years or over; previous pregnancy affected by aneuploidy; hydrops fetalis; congenital anomaly on prenatal ultrasound.





Evidence base: in a GIFD-affiliated cohort of 55 second- and third-trimester losses, overall QF-PCR diagnostic yield was 5% (3/55), rising to 14.3% (3/21; 95% CI 3.0–36.3%) when restricted to the 21 cases (38%) with at least one of the above risk factors; no aneuploidy was detected among risk-factor-negative cases in this cohort. As the source study notes, these figures come from a single-centre cohort with a wide confidence interval, so larger prospective cohorts are needed before risk status is used to withhold testing outright — at every tier it should be used to prioritise limited capacity, not to exclude cases from testing altogether.

Recommended use by tier:

- Tier 3 (full capacity): apply risk screening to set testing order/urgency; all cases still receive first-line QF-PCR.
- Tier 1–2 (constrained capacity): apply risk screening to decide which cases are tested in-house first and which are referred to a higher tier when local QF-PCR/MLPA capacity or budget is limited.

4. Referral Network, Sample Transport

Transport arrangement is determined by expected transit time to the receiving workplace. Where delivery can be completed within a few hours, the sample is transported at laboratory (ambient/room) temperature without additional cooling. Where transit will exceed this window, the sample is frozen to -20°C prior to dispatch and kept frozen throughout transport, consistent





with the long-term storage condition already defined in the Sampling & Storage Guideline (Deliverable 4).

5. Minimum Reporting and Central Database Standards

To keep cases comparable across all workplace tiers, every case entered into the central GIFD database should carry two layers of minimum data: the case-report information collected at sample submission, and the testing/interpretation data generated once analysis is complete.

6.1 Case-level minimum dataset (recorded at sample submission)

This corresponds to the information already collected on the project's patient information form and should accompany every sample regardless of which tier submits it:

- Maternal age
- Gestational age at loss (completed weeks)
- Date and time of fetal loss / delivery
- Date and time of sample collection
- Material submitted (tissue type, per the material categories defined in the Sampling & Storage Guideline, Deliverable 4)
- Results of prenatal screening
- Clinical diagnosis and course of the pregnancy
- Reproductive history (anamnesis)
- Family history of congenital malformations, stillbirth, recurrent reproductive loss, intellectual disability, genetic disorders, and consanguinity (both maternal and paternal side)
- Other known risk factors





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6.2 Testing and interpretation minimum dataset (recorded after analysis)

- Outcome of the risk-factor screen
 - Test(s) performed and platform/method used
 - Result(s), including ACMG/AMP or ACMG/ClinGen classification tier for any finding
 - Causality category assigned
 - Referral tier/pathway, if the case was referred to a higher-capacity workplace
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