STANDARD OPERATING PROCEDURE

Title: Genetic Testing for Idiopathic Hypoparathyroidism
ERN Group: MTG2 Calcium and Phosphate Disorders
Platform: CPMS
Version: Final v2.0
Effective date: 1 June, 2026

1. Purpose

To define a standardized operating procedure (SOP) for requesting, performing, evaluating and communicating genetic testing for patient with idiopathic hypoparathyroidism, following CPMS discussion and recommendation within the ERN calcium and phosphate network.

2. Scope

This SOP applies to all healthcare providers (HCPs) participating in the ERN calcium and phosphate group who submit or discuss cases of idiopathic hypoparathyroidism via CPMS.

3. Responsibilities

- **Treating physician:** Case identification, patient consent for genetic testing, sample collection, patient/family communication, and implementation of management recommendations.
- **Network experts:** Participation in CPMS discussions, eligibility assessment, interpretation of genetic results, post-genetic counselling and management guidance.
- **Geneticist:** Interpretation of genetic variants, contribution to CPMS discussions, advice on clinical relevance, inheritance patterns, family screening, and variant reclassification where applicable.
- **ERN coordination:** Oversight of process consistency, documentation, and periodic review.

4. Procedure

4.1 Case Identification

A potential case of idiopathic hypoparathyroidism is identified by a clinician within the network. Secondary causes must be excluded according to current clinical standards prior to CPMS submission.

Funded by the European Union

4.2 Case Submission and CPMS Discussion

If a center has a case that may require genetic testing, they should first contact the working group for genetic testing in Hypoparathyroidism (**please contact Maria Yavropoulou at myavropoulou@med.uoa.gr).** A standardized checklist will be provided to ensure all necessary information is collected, including phenotype, biochemical data, imaging, family history, and prior investigations.

At the same time, the center will coordinate with the chairs of MTG2 **(please contact the Paediatric Chair, for patients under 18 years, or the Adult Chair, for patients over 18 years)** to arrange presentation of the case within the CPMS system with all the relevant clinical information to support multidisciplinary review.

Following CPMS consultation, if genetic testing is recommended, the center will reconnect with the working group for genetic testing in Hypoparathyroidism who will support the center in organizing and initiating the genetic testing process. Concurrently, the case should be registered in the appropriate registries platform.

4.3 Eligibility Assessment for Genetic Testing

During the CPMS discussion, predefined eligibility criteria for genetic testing are reviewed. Criteria may include:

- Idiopathic or early-onset hypoparathyroidism
- Atypical or syndromic features
- Positive family history
- Refractory disease course or unusual treatment response

Genetic testing is initiated only following CPMS consensus recommendation which is documented in CPMS.

4.4 Patient Information and Informed Consent

For eligible cases, the treating physician informs the patient about the rationale, scope, benefits and limitations and potential outcomes and implications of genetic testing. Written information is provided, and a standardized informed consent/agreement is obtained prior to testing.

4.5 Sample Collection and Shipment

A blood sample is collected locally in accordance with the agreed protocol. Samples are labelled and shipped to Blueprint Genetics following predefined logistical and quality requirements.

4.6 Genetic Analysis

Genetic analysis is performed by Blueprint Genetics in line with the agreed testing panel and standards. Results are returned to the referral/treating physician within the agreed turnaround time.

Funded by the European Union

Once genetic testing has been completed and results are available, it is the HCP responsibility to report the findings both in the CPMS system and back to the working group for genetic testing in Hypoparathyroidism. The genetic data will then be incorporated into the registries platform alongside the clinical case information.

4.7 Multidisciplinary Review of Result

Genetic results are reviewed and discussed in a subsequent CPMS meeting involving clinicians, geneticists, and other relevant experts. Variant classification, clinical relevance, and implications for patient care/surveillance and family screening are addressed.

4.8 Communication of Results to the Patient

The treating physician communicates the results to the patient and provides appropriate counselling, including discussion of uncertainties where relevant.
Referral for specialist genetic counselling is arranged when appropriate.

4.9 Patient Management and Treatment Guidance

Based on the genetic findings and CPMS discussion, recommendations for patient management and potential treatment adaptations are formulated. Where applicable, guidance toward genotype-informed therapy is provided.

4.10 Documentation

All relevant clinical, genetic, and management information is documented in CPMS using a standardized format, including CPMS summaries and follow-up plans.

5. Case Aggregation and Network Review

Eligible cases are aggregated and reviewed at regular intervals (e.g. monthly) to support close interaction within the network, shared learning, and harmonisation of clinical practice.

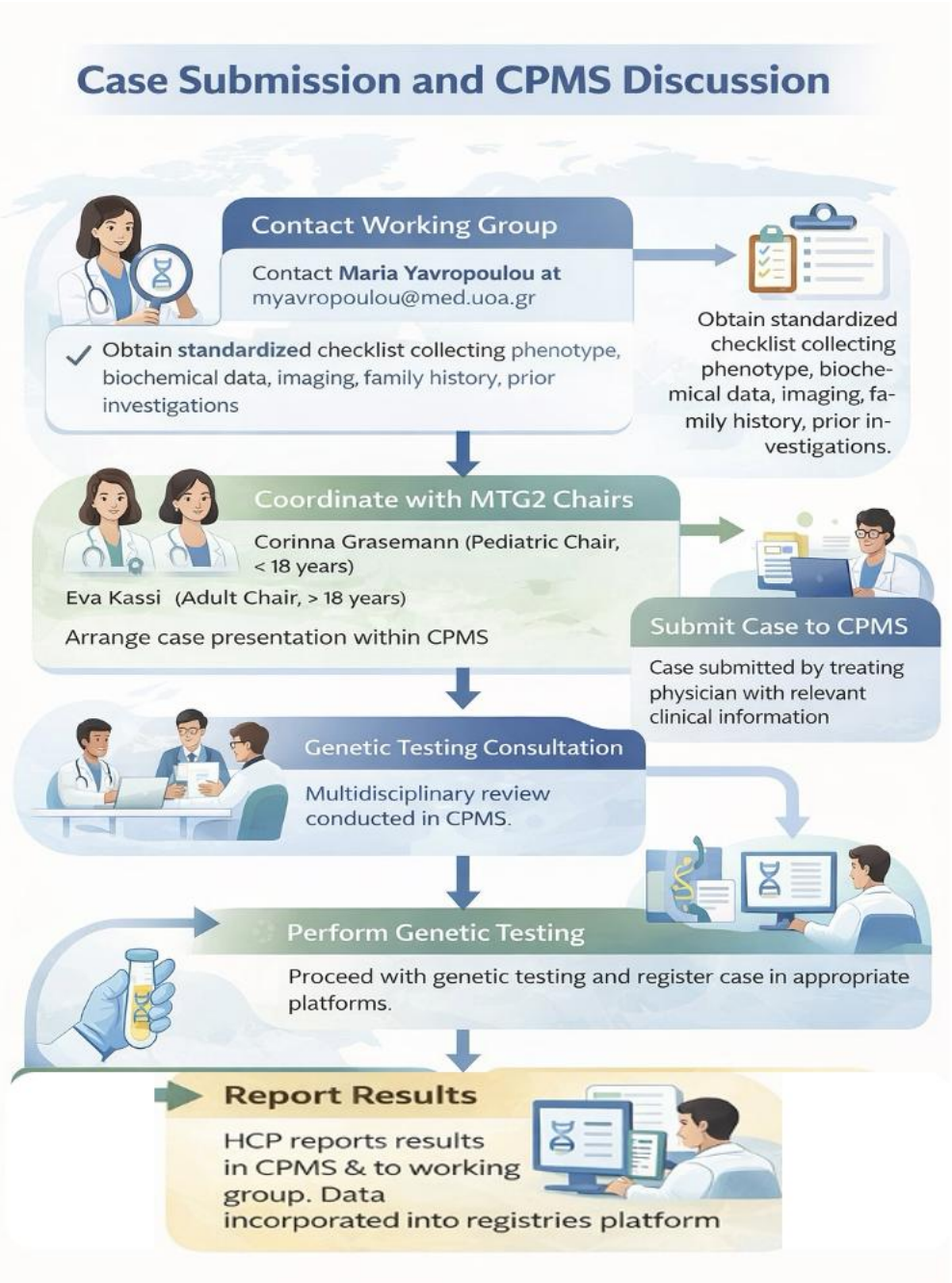
6. Governance and Compliance

This SOP complies with ERN principles and incorporates:

- GDPR and data protection requirements
- Defined roles and responsibilities
- Standard timelines for each procedural step
- Procedures for variant reclassification
- Management of incidental findings
- Quality assurance and periodic SOP review

Funded by the European Union

Case Submission and CPMS Discussion



Funded by the European Union