Phenylketonuria (PKU): PAH Gene Deletion/Duplication

**Test Code:** DPAHX  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1

### Condition Description

Phenylketonuria (PKU) results in an inability to metabolize the amino acid phenylalanine to tyrosine. If dietary phenylalanine is not metabolized, the amino acid accumulates to neurotoxic levels resulting. If untreated, the condition results in mental retardation, seizures, microcephaly and behavior abnormalities. PKU is among the disorders tested by newborn screening and treated by dietary restriction. The incidence of PKU is approximately 1 in 10,000 live births. PKU is autosomal recessive disorder and caused by mutations in the *PAH* (12q22-q24) leading to deficiency of phenylalanine hydroxylase. Disease severity, clinical phenotype, and effectiveness of treatment differs among the different *PAH* mutations and correlates with the level of *PAH* enzyme activity. Complete or near complete absence of enzyme activity results in classical phenylketouria (PKU), which requires strict dietary restraint of phenylalanine for life. Milder enzyme deficiencies can result in non-PKU hyperphenylalaninemia (non-PKU HPA) or variant PKU. Carriers of PKU are unaffected.


**References:**

- GeneReviews Clinical Summary

### Genes

**PAH**

### Indications

This test is indicated for:

- Patients with a biochemical diagnosis of PKU.
- Individuals with biochemical test results indicating carrier status of PKU.
- Individuals who are at risk to be carriers of PKU, when the proband is unavailable for testing.

Sequencing is not appropriate for prenatal samples in which familial mutations have not been identified.

### Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient's phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

### Detection

Detection is limited to duplications and deletions. Array CGH will not detect point mutations or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

### Specimen Requirements

Submit only 1 of the following specimen types

* **Preferred specimen type:** Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:
Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Special Instructions**

Submit copies of diagnostic biochemical test results with the sample. Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside EGL Genetics, please submit a copy of the sequencing report with the test requisition. Contact the laboratory if further information is needed.

**Related Tests**

- Organic Acid Analysis (OA) and Plasma Amino Acid (AA) Analysis are used in the diagnoses of a patient with PKU.
- Prenatal testing is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.