Test Definition: PKUBS

Phenylalanine and Tyrosine, Blood Spot

Overview

Useful For

Monitoring effectiveness of therapy in patients with hyperphenylalaninemia

This test is **not sufficient** for follow-up for abnormal newborn screening results or for establishing a diagnosis of a specific cause of hyperphenylalaninemia

Genetics Test Information

This test provides evaluation of patients with hyperphenylalaninemia or monitoring effectiveness of therapy.

This test **does not provide** sufficient follow-up for abnormal newborn screening results because other causes of hyperphenylalaninemia (eg, tetrahydrobiopterin deficiency) cannot be excluded by this test alone.

Special Instructions

- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Blood Spot Collection Instructions

Method Name

Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Ordering Guidance

For follow-up of an abnormal newborn screen for potential phenylketonuria, order PKU / Phenylalanine and Tyrosine, Plasma.

Necessary Information

Patient's age is required.

Specimen Required

Submit only 1 of the following specimens:

Preferred:

Specimen Type: Blood spot
Supplies: Card-Blood Spot Collection (Filter Paper) (T493)
Container/Tube:
Preferred: Blood Spot Collection Card
Acceptable: Whatman Protein Saver 903 Paper, PerkinElmer 226 filter paper, Munktell filter paper, or blood collected in tubes containing EDTA and dried on filter paper.
Specimen Volume: 2 Blood spots
Collection Instructions:
1. An alternative blood collection option for a patient older than 1 year is a fingerstick. For detailed instructions, see How to Collect a Dried Blood Spot Sample.
2. Let blood dry on filter paper at room temperature in a horizontal position for a minimum of 3 hours.
3. Do not expose specimen to heat or direct sunlight.
4. Do not stack wet specimens.
5. Keep specimen dry.
Specimen Stability Information: Ambient (preferred) 90 days/Refrigerated 90 days/Frozen 90 days
Additional Information:
1. For collection instructions, see Blood Spot Collection Instructions
2. For collection instructions in Spanish, see Blood Spot Collection Card-Spanish Instructions (T777
3. For collection instructions in Chinese, see Blood Spot Collection Card-Chinese Instructions (T800)

Acceptable:
Specimen Type: Whole blood
Container/Tube:
Preferred: Lavender top (EDTA)
Acceptable: Yellow top (ACD)
Specimen Volume: 2 mL
Collection Instructions: Send whole blood specimen in original tube**. Do not aliquot.**
Specimen Stability Information: Refrigerate 6 days

Forms

If not ordering electronically, complete, print, and send a Biochemical Genetics Test Request (T798) with the specimen.

Specimen Minimum Volume

Blood spots: 1; Whole blood: 0.5 mL

Reject Due To

Blood spot specimen that shows serum rings or has multiple layers	Reject
Insufficient specimen	Reject
Unapproved filter papers	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Varies		

Clinical & Interpretive

Clinical Information

Phenylketonuria (PKU) is the most frequent inherited disorder of amino acid metabolism (occurring in about 1:10,000-1:15,000 births) and was the first successfully treated inborn error of metabolism. It is inherited in an autosomal recessive manner and is caused by a defect in the enzyme phenylalanine hydroxylase (PAH), which converts the essential amino acid phenylalanine to tyrosine. Deficiency of PAH results in decreased levels of tyrosine and an accumulation of phenylalanine in blood and tissues. Untreated, PKU leads to severe brain damage with intellectual impairment, behavior abnormalities, seizures, and spasticity. The level of enzyme activity differentiates classic PKU (PAH activity <1%) from other milder forms; however, all are characterized by increased levels of phenylalanine (hyperphenylalaninemia). Treatment includes the early introduction of a diet low in phenylalanine. Some patients may also benefit from adjuvant tetrahydrobiopterin (BH4) supplementation (a cofactor for PAH), or enzyme substitution therapy.

Tetrahydrobiopterin is a cofactor of not only PAH but also of the tyrosine and tryptophan hydroxylases. Approximately 2% of patients with hyperphenylalaninemia have a deficiency of BH4, which causes a secondary deficit of the neurotransmitters, dopamine and serotonin. There are 4 autosomal-recessive disorders associated with BH4 deficiency plus hyperphenylalaninemia: guanosine triphosphate cyclohydrolase deficiency, 6-pyruvoyl tetrahydropterin synthase deficiency, dihydropteridine reductase deficiency, and pterin-4 alpha carbinolamine dehydratase (PCD) deficiency. This group of disorders, except for PCD, is characterized by progressive dystonia, truncal hypotonia, extremity hypertonia, seizures, and intellectual disability though milder presentations exist. PCD has no symptoms other than transient alterations in tone. Treatment may include administration of BH4, L-dopa (and carbidopa) 5-hydroxytryptophan supplements, and a low phenylalanine diet.

Tyrosine is a nonessential amino acid that is derived from dietary sources, the hydroxylation of phenylalanine, or protein breakdown. Primary (PKU) and secondary (defects of BH4 metabolism) hyperphenylalaninemia can cause abnormally low levels of tyrosine. Measurement of the phenylalanine:tyrosine ratio is helpful in monitoring appropriate dietary intake.

Reference Values

Phenylalanine: 27-107 nmol/mL

Tyrosine:
<4 weeks: 40-280 nmol/mL
> or =4 weeks: 25-150 nmol/mL

Interpretation

The quantitative results of phenylalanine and tyrosine with age-dependent reference values are reported without added

interpretation. When applicable, reports of abnormal results may contain an interpretation based on available clinical information.

A phenylalanine:tyrosine ratio higher than 3 is considered abnormal.

Cautions

No significant cautionary statements

Clinical Reference

1. Mitchell GA, Grompe M, Lambert M, Tanguay RM. Hypertyrosinemia. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA. eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw Hill; 2019. Accessed January 2, 2026. Available at https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225082825
2. Donlon J, Sarkissian C, Levy H, Scriver CR. Hyperphenylalaninemia: Phenylalanine hydroxylase deficiency. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed January 2, 2026. Available at https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225081923
3. Arnold G, Vockley J. Phenylalanine hydroxylase deficiency. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews [Internet]. University of Washington, Seattle; 2000. Updated November 20, 2025. Accessed January 2, 2026. Available at www.ncbi.nlm.nih.gov/books/NBK1504/

Performance

Method Description

A 3-mm disk is punched out of the dried blood spot into a 96-well plate. The amino acids are extracted by the addition of acetonitrile and known concentrations of isotopically labeled amino acids as internal standards. The extract is moved to another 96-well plate, dried under a stream of nitrogen, and derivatized. Analytes are measured by liquid chromatography tandem mass spectrometry. The concentrations of the phenylalanine and tyrosine are established by computerized comparison of ion intensities of these analytes to that of the respective internal standards.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

3 to 5 days

Specimen Retention Time

1 year

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

84030
84510
82542 (if appropriate for government payers)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PKUBS	Phenylalanine and Tyrosine, BS	79621-9

Result ID	Test Result Name	Result LOINC® Value
92405	Phenylalanine, BS	29573-3
92406	Tyrosine, BS	35571-9
92407	Reviewed By	18771-6