

## Overview

### Useful For

Diagnosis of galactose-1-phosphate uridyltransferase deficiency, the most common cause of galactosemia

Confirmation of abnormal state newborn screening results

### Genetics Test Information

Galactose-1-phosphate uridyltransferase (GALT) deficiency is the most common cause of galactosemia and requires lifelong restriction of dietary galactose.

Classic galactosemia can be diagnosed by analysis of GALT enzyme.

This test provides enzymatic testing for the diagnosis of GALT deficiency.

### Testing Algorithm

For more information see [Galactosemia Testing Algorithm](#).

### Special Instructions

- [Informed Consent for Genetic Testing](#)
- [Galactosemia Testing Algorithm](#)
- [Biochemical Genetics Patient Information](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)
- [Galactosemia-Related Test List](#)

### Method Name

Enzyme Reaction followed by Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

### NY State Available

Yes

## Specimen

### Specimen Type

Whole Blood EDTA

### Ordering Guidance

**This assay is not appropriate for monitoring dietary compliance.** If dietary monitoring is needed, order GAL1P / Galactose-1-Phosphate, Erythrocytes.

This test is for galactose-1-phosphate uridyltransferase (GALT) enzyme testing only. The preferred test to evaluate for possible diagnosis of galactosemia, routine carrier screening, and follow-up of abnormal newborn screening results is GCT / Galactosemia Reflex, Blood.

This assay will not detect galactokinase (GALK) deficiency or uridine diphosphate-galactose 4' epimerase (GALE) deficiency.

-To evaluate for GALK deficiency, order GALK / Galactokinase, Blood.

-To evaluate for GALE deficiency, order GALE / Uridine Diphosphate -Galactose 4' Epimerase, Blood.

-To evaluate for GALM deficiency, order GALP / Galactose, Plasma and molecular analysis of the *GALM* gene.

### Necessary Information

Patient's age is required.

[Biochemical Genetics Patient Information \(T602\)](#) is recommended, but not required, to be filled out and sent with the specimen to aid in the interpretation of test results.

### Specimen Required

Multiple whole blood tests for galactosemia can be performed on 1 specimen. Prioritize order of testing when submitting specimens. For a list of tests that can be ordered together see [Galactosemia-Related Test List](#).

### Container/Tube:

**Preferred:** Lavender top (EDTA)

**Acceptable:** Green top (sodium heparin) or yellow top (ACD)

**Specimen Volume:** 5 mL

### Forms

1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available:

-[Informed Consent for Genetic Testing \(T576\)](#)

-[Informed Consent for Genetic Testing-Spanish \(T826\)](#)

2. [Biochemical Genetics Patient Information \(T602\)](#) is recommended.

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

### Specimen Minimum Volume

2 mL

### Reject Due To

|                 |        |
|-----------------|--------|
| Gross hemolysis | Reject |
|-----------------|--------|

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---------------|-------------|------|-------------------|
|---------------|-------------|------|-------------------|

|                  |                          |         |  |
|------------------|--------------------------|---------|--|
| Whole Blood EDTA | Ambient                  | 14 days |  |
|                  | Refrigerated (preferred) | 28 days |  |

## Clinical & Interpretive

### Clinical Information

Galactosemia is an autosomal recessive disorder that results from a deficiency of any 1 of the 4 enzymes catalyzing the conversion of galactose to glucose: galactose-1-phosphate uridyltransferase (GALT), galactokinase (GALK), uridine diphosphate galactose-4-epimerase (GALE), and galactose mutarotase (GALM). GALT deficiency is the most common cause of galactosemia and is often referred to as classic galactosemia. The complete or near-complete deficiency of GALT enzyme is life threatening if left untreated. Complications in the neonatal period include failure to thrive, liver failure, sepsis, and death.

Galactosemia is treated by a galactose-restricted diet, which allows for rapid recovery from the acute symptoms and a generally good prognosis. Despite adequate treatment from an early age, individuals with galactosemia remain at increased risk for developmental delays, speech problems, and abnormalities of motor function. Female patients with galactosemia are at increased risk for premature ovarian failure. Based upon reports by newborn screening programs, the frequency of classic galactosemia in the United States is approximately 1 in 30,000, although literature reports range from 1 in 10,000 to 1 in 60,000 live births.

Galactose-1-phosphate (Gal1P) accumulates in the erythrocytes of patients with galactosemia. The quantitative measurement of Gal1P (GAL1P / Galactose-1-Phosphate, Erythrocytes) is useful for monitoring compliance with dietary therapy. Gal1P is thought to be the causative factor for development of liver disease in these patients and, because of this, patients should maintain low levels and be monitored on a regular basis.

Duarte-variant galactosemia (compound heterozygosity for the Duarte variant, N314D and a classic variant) is generally associated with higher levels of enzyme activity (5%-20%) than classic galactosemia (<5%); however, this may be indistinguishable by newborn screening assays. Previously, it was unknown whether children with Duarte-variant galactosemia were at an increased risk for adverse developmental outcomes due to milk exposure and were often treated with a low galactose diet during infancy. More recently, the outcomes data suggest a lack of evidence for developmental complications due to milk exposure, therefore treatment recommendations remain controversial. The Los Angeles variant, which consists of N314D and a second variant, L218L, is associated with higher levels of GALT enzyme activity than the Duarte-variant allele.

Newborn screening for galactosemia is performed in all 50 US states, though the method by which potentially affected individuals are detected varies from state to state and may include the measurement of total galactose (galactose and Gal1P) and/or determining the activity of the GALT enzyme. The diagnosis of galactosemia is established by follow-up quantitative measurement of GALT enzyme activity. If biochemical testing has confirmed the diagnosis of galactosemia, sequencing of the *GALT* gene (GALZ / Galactosemia, *GALT* Gene, Full Gene Analysis, Varies) is available to identify private variations.

For more information see [Galactosemia Testing Algorithm](#).

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**Reference Values**

> or =24.5 nmol/h/mg of hemoglobin

**Interpretation**

Results below 24.5 nmol/h/mg of hemoglobin in properly submitted specimens have different causes from carrier status for a disease-causing variant in the *GALT* gene (typically reduced galactose-1-phosphate uridyltransferase [GALT] activity close to the normal activity range) to "Classic Galactosemia" due to biallelic disease-causing variants in the *GALT* gene that abolish GALT activity. Further differentiation requires additional biochemical and molecular genetic analyses as well as correlation with clinical signs and symptoms.

Normal results (> or =24.5 nmol/hour/mg of hemoglobin) are not consistent with galactosemia due to GALT deficiency.

For more information see [Galactosemia Testing Algorithm](#).

**Cautions**

The results of testing performed in erythrocytes, including analysis of enzymes, biochemical phenotyping, or galactose-1-phosphate are invalid following a transfusion. Patients should wait 3 to 4 months post transfusion before collecting whole blood for galactose-1-phosphate uridyltransferase testing.

**Clinical Reference**

1. Berry GT. Classic galactosemia and clinical variant galactosemia. In: Adam MP, Feldman J, Mirzaa GM, et al. eds. GeneReviews [Internet]. University of Washington, Seattle; 2000. Updated March 11, 2021. Accessed September 12, 2024. Available at [www.ncbi.nlm.nih.gov/books/NBK1518/](http://www.ncbi.nlm.nih.gov/books/NBK1518/)
2. Walter JH, Fridovich-Keil JL. Galactosemia. In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019. Accessed September 12, 2024. Available at <https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=%20225081023>
3. Carlock G, Fischer ST, Lynch ME, et al. Developmental outcomes in Duarte galactosemia. *Pediatrics*. 2019;143(1):e20182516. doi:10.1542/peds.2018-2516
4. Anderson S. GALT deficiency galactosemia. *MCN Am J Matern Child Nurs*. 2018;43(1):44-51. doi:10.1097/NMC.0000000000000388

**Performance****Method Description**

An aqueous mixture containing water, uridine diphosphate (UDP)-glucose, (13)C2-labeled galactose-1-phosphate, and UDP-N-acetylglucosamine (internal standard) is added to a hemolysate aliquot. The mixture is then vortexed briefly and incubated at 37 degrees C for 15 minutes.

After incubation the reaction is quenched, extracted, and centrifuged. The top layer is then transferred to a 96-well plate. Then injected onto a liquid chromatography tandem mass spectrometry (LC-MS/MS). The ratio of the extracted peak area of (13)C2-labeled UDP-galactose to its internal standard UDP-N-acetylglucosamine as determined by LC-MS/MS is used to calculate the concentration of product analyte in the sample. The concentration of the product is then normalized using the calculated hemoglobin concentration to determine the patient's enzyme level in nmol/h/mg

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of hemoglobin.(Unpublished Mayo method)

**PDF Report**

No

**Day(s) Performed**

Monday, Wednesday, Friday

**Report Available**

4 to 7 days

**Specimen Retention Time**

Processed RBC: 2 months

**Performing Laboratory Location**

Rochester

**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**

82775

**LOINC® Information**

| Test ID | Test Order Name                | Order LOINC® Value |
|---------|--------------------------------|--------------------|
| GALT    | Gal-1-P Uridyltransferase, RBC | 24082-0            |

| Result ID | Test Result Name               | Result LOINC® Value |
|-----------|--------------------------------|---------------------|
| 8333      | Gal-1-P Uridyltransferase, RBC | 24082-0             |
| 2296      | Interpretation (GALT)          | 59462-2             |
| 58115     | Reviewed By                    | 18771-6             |