

## Overview

### Useful For

Preferred test for the diagnosis of biotinidase deficiency

Follow-up testing for certain organic acidurias

### Genetics Test Information

Preferred test to rule out biotinidase deficiency.

### Special Instructions

- [Informed Consent for Genetic Testing](#)
- [Biochemical Genetics Patient Information](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)

### Highlights

Enzymatic testing for the diagnosis of biotinidase deficiency, usually in follow-up to an abnormal newborn screen.

### Method Name

Colorimetric

### NY State Available

Yes

## Specimen

### Specimen Type

Serum

### Ordering Guidance

Molecular testing is available, see *BTDZ / Biotinidase Deficiency*, *BTD Full Gene Analysis*, *Varies*.

If measurement of biotin concentration is requested, order *BIOTN / Biotin, Serum*.

### Specimen Required

#### Collection Container/Tube:

**Preferred:** Serum gel

**Acceptable:** Red top

**Submission Container/Tube:** Plastic vial

**Specimen Volume:** 1 mL

**Collection Instructions:** Centrifuge immediately and aliquot serum into plastic vial.

## 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 \(T602\)](#)

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

## Specimen Minimum Volume

0.5 mL

## Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	OK

## Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen (preferred)	21 days	
	Refrigerated	5 days	

## Clinical & Interpretive

### Clinical Information

Biotinidase deficiency is an autosomal recessive disorder caused by variants in the biotinidase gene (*BTD*). Age of onset and clinical phenotype vary among individuals depending on the amount of residual biotinidase activity. Profound biotinidase deficiency occurs in approximately 1 in 137,000 live births and partial biotinidase deficiency occurs in approximately 1 in 110,000 live births, resulting in a combined incidence of about 1 in 61,000. The carrier frequency for biotinidase deficiency within the general population is about 1 in 120.

Untreated profound biotinidase deficiency typically manifests within the first decade of life as seizures, ataxia, developmental delay, hypotonia, sensorineural hearing loss, vision problems, skin rash, and alopecia. Partial biotinidase deficiency is associated with a milder clinical presentation and may include cutaneous symptoms without neurologic involvement. Certain organic acidurias, such as holocarboxylase synthase deficiency, isolated carboxylase synthase deficiency, and 3-methylcrotonylglycinuria, present similarly to biotinidase deficiency. Serum biotinidase levels can help rule out these disorders.

Treatment with biotin is successful in preventing the clinical features associated with biotinidase deficiency. In symptomatic patients, treatment will reverse many of the clinical features except developmental delay, vision, and hearing complications. As a result, biotinidase deficiency is included in most newborn screening programs. This enables

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early identification and treatment of presymptomatic patients.

Molecular tests are useful for confirmation of diagnosis or carrier testing. When biotinidase enzyme activity is deficient, sequencing of the entire *BTB* gene (BTBZ / Biotinidase Deficiency, *BTB* Full Gene Analysis, Varies) allows for detection of disease-causing variants in affected patients. Identification of familial variants allows for testing of at-risk family members (FMTT / Familial Variant, Targeted Testing, Varies).

While genotype-phenotype correlations are not well established, it appears that certain genetic variants are associated with profound biotinidase deficiency, while others are associated with partial deficiency.

### Reference Values

3.5-13.8 U/L

### Interpretation

An interpretive report is provided.

Values below 3.5 U/L are occasionally seen in specimens from unaffected patients.

### Cautions

A diet high in biotin may result in normal clinical presentation even when the biotinidase level is low.

Assay interference may occur for specimens collected when the patient is being treated with a sulfa drug.

### Clinical Reference

1. ACMG Newborn Screening ACT Sheets. Accessed January 19, 2024. Available at [www.acmg.net/ACMG/Medical-Genetics-Practice-Resources/ACT\\_Sheets\\_and\\_Algorithms/ACMG/Medical-Genetics-Practice-Resources/ACT\\_Sheets\\_and\\_Algorithms.aspx?hkey=9d6bce5a-182e-42a6-84a5-b2d88240c508](http://www.acmg.net/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms.aspx?hkey=9d6bce5a-182e-42a6-84a5-b2d88240c508)
2. Zempleni J, Barshop BA, Cordonier EL, et al. Disorders of biotin metabolism. In: Valle D, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Diseases. McGraw-Hill; Accessed January 19, 2024. Available at <https://ommbid.mhmedical.com/content.aspx?sectionid=225548571>
3. Wolf B. Biotinidase Deficiency. In: Adam MP, Mirzaa GM, Pagon RA, et al., eds. GeneReviews [Internet]. University of Washington, Seattle; 1993-2023. Updated May 25, 2023. Accessed January 19, 2024. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK1322/>

### Performance

#### Method Description

Biotinidase activity is determined colorimetrically by measuring p-aminobenzoate liberation from N-biotinyl-p-aminobenzoate at 546 nm. Activity is determined from a standard curve of p-aminobenzoic acid. Modified Sigma substrate is used. (Wolf B, Grier RE, Allen RJ, et al. Biotinidase deficiency: the enzymatic defect in late-onset carboxylase deficiency. Clin Chim Acta. 1983;131(3):273-281; Cowan T, Pasquali M. Laboratory investigations of inborn errors of metabolism. In: Sarafoglou K, Hoffman GF, Roth KS, eds. Pediatric Endocrinology and Inborn Errors of Metabolism. 2nd ed. McGraw-Hill; 2017:1139-1158)

**PDF Report**

No

**Day(s) Performed**

Monday, Thursday

**Report Available**

2 to 5 days

**Specimen Retention Time**

30 days

**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**

82261

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
BIOTS	Biotinidase, S	1982-8

Result ID	Test Result Name	Result LOINC® Value
50672	Biotinidase, S	1982-8
50673	Interpretation	59462-2
50675	Reviewed By	18771-6