MAYO CLINIC LABORATORIES

# Test Definition: MPS4B

Mucopolysaccharidosis IV Enzyme Panel, Blood Spot

## Overview

### Useful For

Supporting the biochemical diagnosis of mucopolysaccharidosis type IVA and IVB

This test is **not useful for** carrier detection.

### Reflex Tests

| Test Id | Reporting Name | Available Separately | Always Performed |
|---|---|---|---|
| MPSBS | Mucopolysaccharidosis, BS | Yes | No |

### Genetics Test Information

This test provides diagnostic testing for individuals with clinical signs and symptoms suspicious for mucopolysaccharidosis type IVA or IVB. If an enzyme deficiency is detected by this screening test, additional biochemical or molecular testing is required to confirm a diagnosis.

### Testing Algorithm

If results are normal, testing is complete.

If results indicate mucopolysaccharidoses IVA or IVB, quantitation of heparan sulfate, dermatan sulfate and keratan sulfate may be performed at an additional charge.

### Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Blood Spot Collection Card-Spanish Instructions
- Blood Spot Collection Card-Chinese Instructions
- Informed Consent for Genetic Testing (Spanish)
- Lysosomal Disorders Diagnostic Algorithm, Part 1
- Blood Spot Collection Instructions

### Method Name

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

### NY State Available

Yes

## Specimen

## Specimen Type

Whole blood

## Necessary Information

**1. Patient's age is required.**

**2. Reason for testing is required**

## Specimen Required

**Submit only 1 of the following specimen types:**

**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 ACD or 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. At least 2 spots should be complete, ie, unpunched.
3. Let blood dry on filter paper at room temperature in a horizontal position for a minimum of 3 hours.
4. Do not expose specimen to heat or direct sunlight.
5. Do not stack wet specimens.
6. Keep specimen dry.

**Specimen Stability Information:** Refrigerated (preferred) 60 days/Ambient 7 days/Frozen 60 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 (preferred) 7 days/Ambient 48 hours

## 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
Blood spot: 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
Mucopolysaccharidosis IVA, (MPS IVA; Morquio A syndrome) is caused by reduced or absent *N*-acetylgalactosamine-6-sulfate sulfatase (GALNS) enzyme activity. The glycosaminoglycans (GAGs), keratan and chondroitin sulfate, accumulate in multiple tissues but mainly bone, cartilage, heart valves, and cornea. Clinical features and severity of symptoms of MPS IVA are widely variable affecting multiple body systems, in particular the skeletal system. Other clinical features may include short stature, dental anomalies, corneal clouding, respiratory insufficiency, and cardiac disease. Cognitive abilities are generally unaffected.

Mucopolysaccharidosis type IVB (MPS IVB or Morquio syndrome B) is caused by reduced or absent beta-galactosidase activity leading to the accumulation of GAGs, particularly keratan sulfate. MPS IVB typically manifests as a systemic skeletal disorder with variable severity ranging from early severe disease to a later onset attenuated form. Virtually all patients have dysostosis multiplex and short stature along with other symptoms that may include coarse facies, hepatosplenomegaly, hoarse voice, stiff joints, cardiac disease, but no neurological involvement.

GM1 gangliosidosis is also caused by reduced or absent beta-galactosidase activity, however the clinical features include

neurological involvement in addition to the skeletal and other systemic findings associated with MPS IVB. The disorder can be classified into 3 subtypes that vary with respect to age of onset and clinical presentation.

Galactosialidosis is associated with a combined deficiency of beta-galactosidase and neuraminidase secondary to a defect in the cathepsin A protein. The disorder can be classified into 3 subtypes that vary with respect to age of onset and clinical presentation. Typical clinical presentation is coarse facial features, cherry-red spots, and skeletal dysplasia. The early infantile form is associated with fetal hydrops, skeletal dysplasia, and early death, while the late infantile form is characterized by short stature, dysostosis multiplex, coarse facial features, corneal clouding, hepatosplenomegaly, and heart valve problems.

A diagnostic workup for MPS typically also includes glycosaminoglycan determination in urine (MPSQU / Mucopolysaccharides Quantitative, Random, Urine) or blood (MPSBS / Mucopolysaccharidosis, Blood Spot, or MPSER / Mucopolysaccharidosis Quantitative, Serum) and molecular genetic analysis of the relevant gene. For MPS IVA, molecular analysis of the *GALNS* gene (CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies; specify Gene List ID: EMCP-JUFPRX) and for MPS IVB and GM1 gangliosidosis, molecular analysis of the *GLB1* gene (CGPH; specify Gene List ID: EMCP-D5F3YS) allows for detection of disease-causing variants in affected patients and subsequent carrier detection in relatives.

A diagnostic workup for galactosialidosis traditionally includes determination of beta-galactosidase enzyme activity in leukocytes or fibroblasts and molecular analysis of *CTSA* (CGPH; specify Gene List ID: IEMCP-D1J7U5). Analysis of urine mucopolysaccharides, oligosaccharides, ceramide trihexoside, and sulfatides (LSDS / Lysosomal Disorders Screen, Random, Urine) can help differentiate between galactosialidosis, MPS IVA, and MPS IVB/GM1 to guide physicians in choosing the best confirmatory molecular testing option. See Lysosomal Disorders Diagnostic Algorithm, Part 1.

## Reference Values

N-acetylgalactosamine-6-sulfatase: >0.70 nmol/mL/hour
Beta-galactosidase: >1.30 nmol/mL/hour

An interpretive report will be provided.

## Interpretation

Abnormal results are not sufficient to establish a diagnosis of a particular disease. To verify a preliminary diagnosis based on this assay, additional biochemical or molecular genetic analyses are required.

When abnormal results are detected, a detailed interpretation is given, including an overview of the results and of their significance, a correlation to available clinical information, elements of differential diagnosis, recommendations for additional biochemical testing, and in vitro, confirmatory studies (enzyme assay, molecular genetic analysis), and a phone number to reach one of the laboratory directors in case the referring physician has additional questions.

## Cautions

Beta-galactosidase is also reduced in patients with galactosialidosis. Those patients will also demonstrate deficient activity of neuraminidase which is not evaluated on this panel. If there was clinical suspicion of galactosialidosis, please order follow up testing to include test OLIGU / Oligosaccharide Screen, Random, Urine.

Individuals with pseudodeficiency alleles can show reduced enzyme activity.

Carrier status (heterozygosity) for these conditions cannot be reliably detected.

Enzyme levels may be normal in individuals receiving enzyme replacement therapy or who have undergone hematopoietic stem cell transplant.

### Clinical Reference

1. Neufeld EF, Muenzer J. The mucopolysaccharidoses. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; Accessed September 11, 2025. https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225544161
2. Hopwood JJ, Ballabio A. Multiple sulfatase deficiency and the nature of the sulfatase family. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; Accessed September 11, 2025. https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225546905

## Performance

### Method Description

One dried blood spot sample (DBS) is incubated with a mix of substrate and internal standard (IS) for iduronate 2-sulfatase, heparan N-sulfatase, alpha-N-acetylglucosaminidase, N-acetylgalactosamine-sulfate, beta-galactosidase, arylsulfatase B, beta-glucuronidase, and tripeptidyl peptidase 1. A second DBS sample is incubated with a mix of substrate and IS for acetyl-CoA:alpha-glucosaminide N-acetyltransferase; and third DBS sample with a mix of substrate and IS for palmitoyl-protein thioesterase 1. Following overnight incubation, the samples are combined, extracted by liquid-liquid extraction, and analyzed by tandem mass spectrometry.(Unpublished Mayo method)

### PDF Report

No

### Day(s) Performed

Thursday

### Report Available

3 to 9 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

82657
83864 (if appropriate)

## LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| MPS4B | MPS IV Panel, BS | 104112-8 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| BG753 | Reason for Referral | 42349-1 |
| 618424 | N-acetylgalactosamine-6-sulfatase | 88019-5 |
| 618425 | Beta-galactosidase | 55916-1 |
| 618426 | Interpretation | 59462-2 |
| 618423 | Reviewed By | 18771-6 |