# Test Definition: MSDW

Multiple Sulfatase Deficiency, Leukocytes

## Overview

### Useful For

Supporting the biochemical diagnosis of multiple sulfatase deficiency in whole blood specimens

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

### Genetics Test Information

This test is a screening panel for individuals with clinical signs and symptoms suspicious for multiple sulfatase deficiency. If an enzyme deficiency is detected by this screening test, additional biochemical or molecular testing is required to confirm a diagnosis.

### Special Instructions

- Informed Consent for Genetic Testing
- Biochemical Genetics Patient Information
- Informed Consent for Genetic Testing (Spanish)

### Method Name

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

### NY State Available

Yes

## Specimen

### Specimen Type

Whole Blood ACD

### Shipping Instructions

**For optimal isolation of leukocytes, it is recommended the specimen arrive refrigerated within 6 days of collection to be stabilized**. Pre-analytical processing is performed Monday through Friday and Sunday. This test may be canceled if specimens are outside of stability when processing occurs. Collect and package specimens for arrival on days when processing is performed.

### Necessary Information

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

**2. Reason for testing is required.**

### Specimen Required

**Container/Tube:**

**Preferred:** Yellow top (ACD solution B)

**Acceptable:** Yellow top (ACD solution A) or lavender top (EDTA)
**Specimen Volume:** 6 mL
**Collection Instructions:** Send whole blood specimen in original tube. **Do not aliquot**.

### 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

5 mL

### Reject Due To

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

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Whole Blood ACD | Refrigerated (preferred) | 6 days | |
| | Ambient | 6 days | |

## Clinical & Interpretive

### Clinical Information

Multiple sulfatase deficiency (MSD) is a rare autosomal recessive lysosomal disorder caused by mutations in the sulfatase-modifying factor 1 (SUMF1) gene. SUMF1 encodes for a formylglycine-generating enzyme that performs a critical posttranslational modification necessary for activation of all human sulfatases, including arylsulfatase A and B. The clinical features of MSD encompass symptoms of every single sulfatase deficiency, including metachromatic leukodystrophy (MLD), the mucopolysaccharidoses, X-linked ichthyosis, and chondrodysplasia punctata type I. Age of onset and clinical severity are variable and correspond with the level of residual enzyme activity. A severe neonatal form of MSD closely overlaps the clinical presentation of the mucopolysaccharidoses, but it is often fatal within 1 year. Late-infantile MSD (onset 0-2 years) accounts for most cases and is characterized by a clinical presentation similar to MLD.

A diagnostic workup for MSD demonstrates reduced enzyme activity of several sulfatase enzymes including those on this panel (iduronate-2-sulfatase, heparan sulfate sulfatase, galactosamine-6-sulfate sulfatase, and arylsulfatase B). Individuals with MSD typically have an increased urinary excretion of sulfatides as well as increased urinary glycosaminoglycans, therefore a combined analysis of urine ceramide trihexoside, mucopolysaccharides,

oligosaccharides, and sulfatides (LSDS/ Lysosomal Disorders Screen, Random, Urine) may support a diagnosis. Molecular genetic analysis of the *SUMF1* gene (CGPH / Custom Gene Panel, Hereditary, Next-Generation Sequencing, Varies; specify Gene List ID: IEMCP-PCUBX1) allows for detection of disease-causing variants in affected patients and subsequent carrier detection in relatives.

### Reference Values

Iduronate-2-sulfatase: >2.20 nmol/h/mg protein
Heparan-N-sulfatase: >0.13 nmol/h/mg protein
N-acetylglucosamine-6-sulfatase: >0.03 nmol/h/mg protein
N-acetylgalactosamine-6-sulfatase: >1.60 nmol/h/mg protein

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 analysis), a phone number to reach one of the laboratory directors in case the referring physician has additional questions.

### Cautions

Individuals with pseudodeficiency alleles can show reduced enzyme activity.

Carrier status (heterozygosity) cannot be reliably detected.

### 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 10, 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 10, 2025. https://ommbid.mhmedical.com/content.aspx?bookid=2709&sectionid=225546905
3. Schlotawa L, Adang LA, Radhakrishnan K, Ahrens-Nicklas RC. Multiple Sulfatase Deficiency: A Disease Comprising Mucopolysaccharidosis, Sphingolipidosis, and More Caused by a Defect in Posttranslational Modification. Int J Mol Sci. 2020;21(10):3448. doi:10.3390/ijms21103448

## Performance

### Method Description

Leukocytes are incubated with four cocktail mixes in 96-well plates: 1) 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; 2) substrate and IS for acetyl-CoA:alpha-glucosaminide N-acetyltransferase; 3) substrate and IS for N-acetylglucosamine-6-sulfatase ; and 4) substrate and IS for palmitoyl-protein thioesterase 1. Following overnight incubation, the plates are combined and purified by liquid-liquid extraction. The extracts are evaporated, reconstituted with mobile phase, and analyzed by tandem mass spectrometry.(Unpublished Mayo method)

### PDF Report
No

### Day(s) Performed
Preanalytical processing: Monday through Friday, Sunday
Testing performed: Tuesday

### Report Available
3 to 9 days

### Specimen Retention Time
WBC homogenate: 1 month

### 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

### LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| MSDW | Multiple sulfatase deficiency, WBC | 104073-2 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| BG771 | Reason for Referral | 42349-1 |
| 618466 | Iduronate-2-sulfatase | 24089-5 |
| 618467 | Heparan-N-sulfatase | 24086-1 |

| | | |
|---|---|---|
| 620156 | N-acetylglucosamine-6-sulfatase | 24098-6 |
| 618468 | N-acetylgalactosamine-6-sulfatase | 24096-0 |
| 618469 | Interpretation | 59462-2 |
| 618465 | Reviewed By | 18771-6 |