



# Test Definition: MBLF

Mannan Binding Lectin Complement Pathway,  
Functional, Serum

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## Overview

### Useful For

[Investigating recurrent meningococcal disease in young children](#)

Investigating recurrent or severe infections in adults

Investigating glomerular kidney diseases

Additionally, deficiencies or dysregulation within the complement system may be identified in patients when this test is used in combination with related tests.

### Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

### NY State Available

Yes

## Specimen

### Specimen Type

Serum Red

### Ordering Guidance

The most appropriate primary assays to use as screening methods for complement deficiencies are COM / Complement, Total, Serum and AH50 / Alternative Complement Pathway, Functional, Serum. Abnormal results in one or the other, none, or both assays will help direct further testing. If total complement and AH50 are both normal but the suspicion of a complement deficiency remains, this test for the lectin pathway function is recommended. After the initial 3 pathways of complement functional status are evaluated, the analysis of individual components and regulators may uncover functional or quantitative defects in certain components.

This test is rarely useful when ordered in isolation.

As the heat-labile fraction of the immune system, complement activation in vitro has been a challenge for researchers and scientists. Because of the thermal instability of complement proteins, it is often necessary to repeat testing to rule out a possible pre-analytical issue with a sample type, real complement consumption, or dysregulation.

### Specimen Required

#### Patient Preparation:

1. Fasting: 8 hours, preferred but not required

2. Specimen **should not** be collected earlier than 48 hours following plasma exchange.

**Supplies:** Sarstedt Aliquot Tube, 5 mL (T914)

**Collection Container/Tube:** Red top (serum gel/SST are **not acceptable**)

**Submission Container/Tube:** Plastic vial

**Specimen Volume:** 1 mL

**Collection Instructions:**

1. Immediately after specimen collection, place the tube on wet ice.
2. After sample has clotted on wet ice, centrifuge at 4 degrees C and aliquot serum into plastic vial.
3. Freeze specimen within 30 minutes of centrifugation. Specimen must be placed on dry ice if not frozen immediately.

**Additional Information:** If a refrigerated centrifuge is not available, it is acceptable to use a room temperature centrifuge, provided the specimen is kept on ice before centrifugation, and immediately afterward, the serum aliquoted and frozen.

**Specimen Minimum Volume**

0.4 mL

**Reject Due To**

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

**Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Serum Red	Frozen	14 days	

**Clinical & Interpretive**

**Clinical Information**

Complement proteins are components of the innate immune system. There are 3 pathways to complement activation: the classical pathway, the alternative (or properdin) pathway, and the lectin (or mannan binding lectin: MBL) pathway.

The total complement assay (COM / Complement, Total, Serum) is the best screening assay for complement abnormalities of the classical complement pathway (C1qrs, C4, C2, C3, C5, C6, C7, C8, C9). The COM assay will be abnormal if there are specific hereditary or acquired C1-C9 complement component deficiencies or if there is consumption of complement due to immune (or autoimmune) complexes.

Abnormalities in the alternative pathway may be evaluated with the AH50 functional assay (AH50 / Alternative Complement Pathway, Functional, Serum). The alternative pathway shares C3 and C5 through C9 components but has unique early complement components designated factors D, B, and P, as well as regulatory factors H and I. This pathway can be activated by hydrolysis of C3 or by microbial polysaccharides and does not require immune complex formation as

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a trigger. Patients with deficiencies in the alternative pathway factors (D, B, P, H, and I) or late complement components (C3, C5-C9) are unusually susceptible to recurrent *Neisserial* meningitis. Dysregulation of the alternative pathway is also observed in cases of atypical hemolytic uremic syndrome and rare kidney diseases such as C3 glomerulopathies.(1)

MBL is an acute phase protein, one of several lectins and collectins that initiate lectin pathway complement activity. These proteins play a role in host defense, recognizing pathogen- and damage-associated molecular patterns. MBL associates with MBL-associated serine proteases (MASP-1, -2, and -3) to activate complement components C2 through C9. MBL deficiency is a common finding worldwide due to the broad genetic distribution of deficient *MBL2* alleles (5%-30% or higher in isolated populations).(1-3) Seven haplotypes are commonly observed, with a potential for 28 possible combinations.(4)

MBL activity of less than 10% may be found in a normal population at frequencies of 20% to 30%, a finding confirmed by Mayo Clinic during validation studies.

MBL function assessment is recommended as second-tier testing when total complement and alternative complement analyses are both within reference intervals, and the clinical presentation of recurrent infections, along with suspicion of complement dysregulation, remains in the differential.

### Reference Values

> or =10%

### Interpretation

Low (<10%) mannan-binding lectin (MBL) pathway activity is consistent with very low or absent MBL protein in the context of normal alternative pathway and normal classical pathway activity. Not all individuals with decreased MBL function will manifest with clinical symptoms. MBL pathway function test results must be interpreted with clinical presentation, other comorbidities (autoimmune disease, infection, malignancy), and the overall status of the immune system (primary and secondary immunodeficiencies). In addition, identification of an MBL deficiency does not exclude other etiologies that would predispose individuals to an increased risk of infection.

### Cautions

This assay is a functional test and is dependent on correct sampling, storage, and shipping conditions. Both degradation by temperature and consumption of complement components will lead to falsely low function results. These are difficult to differentiate from real complement dysregulation.

While preanalytic handling can lead to falsely low results, it is far less likely that it would lead to falsely normal results.

Complement testing may be ordered in several circumstances where standard treatment includes plasmapheresis or plasma exchange. The procedure itself, if traumatic, may activate complement so may not reflect what is going on with the patient's complement system. In addition, the plasma exchange may include donor complement proteins. The recommendation is to collect blood prior to the plasma exchange whenever possible.

Functional results inconsistent with the clinical history should be verified with a new blood draw.

Specimens should be frozen immediately after collection.

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The use of complement C5 inhibitor therapies such as eculizumab and ravulizumab will result in the blocking of C5. C5 is necessary for the complement function to progress until the formation of the membrane attack complex. Hence, in the presence of eculizumab or ravulizumab, results for CH50, AH50, or MBLF will be decreased or undetectable.

**Clinical Reference**

1. Willrich MAV, Braun KMP, Moyer AM, Jeffrey DH, Frazer-Abel A. Complement testing in the clinical laboratory. *Crit Rev Clin Lab Sci.* 2021;58(7):447-478. doi:10.1080/10408363.2021.1907297
2. Heitzeneder S, Seidel M, Forster-Waldl E, Heitger A. Mannan-binding lectin deficiency - Good news, bad news, doesn't matter? *Clin Immunol.* 2012;143(1):22-38. doi:10.1016/j.clim.2011.11.002
3. Kalia N, Singh J, Kaur M. The ambiguous role of mannan-binding lectin (MBL) in human immunity. *Open Med (Wars).* 2021;16(1):299-310. doi:10.1515/med-2021-0239
4. Eisen DP, Osthoff M. If there is an evolutionary selection pressure for the high frequency of MBL2 polymorphisms, what is it? *Clin Exp Immunol.* 2014;176(2):165-171. doi:10.1111/cei.12241

**Performance****Method Description**

The Wieslab enzyme-linked immunosorbent assay complement assay for the mannan-binding lectin (MBL) pathway combines principles of the hemolytic assay for complement activation with the use of labeled antibodies specific for neoantigens produced as a result of complement activation. The micro titer plate strips are coated with mannan. Patient serum is diluted in diluent containing specific blocker to ensure that only the MBL pathway is activated. During the first incubation, the diluted patient serum in the wells is activated by the coating. The wells are then washed and C5b-9 membrane attack complex (MAC) is detected with a specific alkaline phosphatase labeled antibody to the neoantigen expressed during MAC formation. After a final wash, an alkaline phosphatase substrate is added. The amount of MBL pathway complement activity correlates with the color intensity of the solution and is measured by absorbance (optical density). (Mollnes TE, Jokiranta TS, Truedsson L, et al. Complement analysis in the 21st century. *Mol Immunol.* 2007;44[16]:3838-49; Willrich MAV, Braun KMP, Moyer AM, Jeffrey DH, Frazer-Abel A. Complement testing in the clinical laboratory. *Crit Rev Clin Lab Sci.* 2021:1-51)

**PDF Report**

No

**Day(s) Performed**

Wednesday

**Report Available**

2 to 8 days

**Specimen Retention Time**

14 days

**Performing Laboratory Location**

Mayo Clinic Laboratories - Rochester Superior Drive

## 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

86161

### LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
MBLF	MBL Complement Path, Func, S	74522-4

Result ID	Test Result Name	Result LOINC® Value
MBLF	MBL Complement Path, Func, S	74522-4