



# Test Definition: MPNML

MPL Exon 10 Sequencing, Reflex, Varies

## Overview

### Useful For

Aiding in the distinction between a reactive cytosis and a myeloproliferative neoplasm when *JAK2* V617F testing result is negative

Evaluating for variants in *MPL* in an algorithmic process for MPNCM / Myeloproliferative Neoplasm, *CALR* with Reflex to *MPL*, Varies

### Method Name

Only orderable as a reflex. For more information see MPNCM / Myeloproliferative Neoplasm, *CALR* with Reflex to *MPL*, Varies.

Sanger Sequencing

### NY State Available

Yes

## Specimen

### Specimen Type

Varies

### Specimen Required

Only orderable as a reflex. For more information see MPNCM / Myeloproliferative Neoplasm, *CALR* with Reflex to *MPL*, Varies.

### Submit only 1 of the following specimens:

**Specimen Type:** Whole Blood

**Container/Tube:** Lavender top (EDTA) or yellow top (ACD-B)

**Specimen Volume:** 3 mL

#### Collection Instructions:

1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**
3. Label specimen as whole blood.

**Specimen Stability Information:** Ambient (preferred)/Refrigerate

**Specimen Type:** Bone marrow

**Container/Tube:** Lavender top (EDTA) or yellow top (ACD-B)

**Specimen Volume:** 2 mL

**Collection Instructions:**

1. Invert several times to mix bone marrow.
2. Send bone marrow specimen in original tube. **Do not aliquot.**
3. Label specimen as bone marrow.

**Specimen Stability Information:** Ambient (preferred)/Refrigerate

**Specimen Type:** Extracted DNA from blood or bone marrow

**Container/Tube:** 1.5 to 2 mL tube

**Specimen Volume:** Entire specimen

**Collection Instructions:**

1. DNA must be extracted from blood or bone marrow within 7 days of collection.
2. Label specimen as extracted DNA and source of specimen.
3. Provide volume and concentration of the DNA.

**Specimen Stability Information:** Frozen (preferred) 1 year/Refrigerate/Ambient

**Additional Information:** DNA must be extracted in a CLIA-certified laboratory or equivalent and must be extracted from a specimen type listed as acceptable for this test (including applicable anticoagulants). We cannot guarantee that all extraction methods are compatible with this test. If testing fails, one repeat will be attempted, and if unsuccessful, the test will be reported as failed and a charge will be applied.

**Reject Due To**

Gross hemolysis	Reject
Paraffin-embedded bone marrow aspirate clot or biopsy blocks	Reject
Slides	Reject
Paraffin shavings	Reject
Moderately to severely clotted	Reject

**Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

**Clinical & Interpretive**

**Clinical Information**

The *JAK2* V617F variant is present in 95% to 98% of patients with polycythemia vera, 50% to 60% of patients with

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primary myelofibrosis (PMF), and 50% to 60% of patients with essential thrombocythemia (ET). Detection of the *JAK2* V617F variant helps establish the diagnosis of a myeloproliferative neoplasm (MPN). However, a negative *JAK2* V617F result does not indicate the absence of MPN. Other important molecular markers in *BCR::ABL1*-negative MPN include *CALR* exon 9 alterations (20%-30% of PMF and ET) and *MPL* exon 10 alterations (5%-10% of PMF and 3%-5% of ET). Variants in *JAK2*, *CALR*, and *MPL* are essentially mutually exclusive. A *CALR* variant is associated with decreased risk of thrombosis in both ET and PMF and confers a favorable clinical outcome in patients with PMF. A triple negative (*JAK2* V617F, *CALR*, and *MPL*-negative) genotype is considered a high-risk molecular signature in PMF.

### Reference Values

Only orderable as a reflex. For more information see MPNCLM / Myeloproliferative Neoplasm, *CALR* with Reflex to *MPL*, Varies.

An interpretive report will be provided.

### Interpretation

The results will be reported as 1 of the 3 following states:

- Positive for *CALR* variant
- Positive for *MPL* variant
- Negative for *CALR* and *MPL* variants

Positive variant status is highly suggestive of a myeloid neoplasm and clinicopathologic correlation is necessary in all cases.

Negative variant status does not exclude the presence of a myeloproliferative neoplasm or other neoplasms.

### Cautions

A positive result is not specific for a particular subtype of myeloproliferative neoplasm and clinicopathologic correlation is necessary in all cases.

A negative result does not exclude the presence of a myeloproliferative neoplasm or other neoplastic process.

### Clinical Reference

1. Klampfl T, Gisslinger H, Harutyunyan AS, et al. Somatic mutations of calreticulin in myeloproliferative neoplasms. *N Engl J Med*. 2013;369(25):2379-2390
2. Nangalia J, Massie CE, Baxter EJ, et al. Somatic *CALR* mutations in myeloproliferative neoplasms with nonmutated *JAK2*. *N Engl J Med*. 2013;369(25):2391-2405
3. Rotunno G, Mannarelli C, Guglielmelli P, et al. Impact of calreticulin mutations on clinical and hematological phenotype and outcome in essential thrombocythemia. *Blood*. 2014;123(10):1552-1555
4. Tefferi A, Lasho TL, Finke CM, et al. *CALR* vs *JAK2* vs *MPL*-mutated or triple-negative myelofibrosis: clinical, cytogenetic and molecular comparisons. *Leukemia*. 2014;28(7):1472-1477
5. Pikman Y, Lee BH, Mercher T, et al. *MPLW515L* is a novel somatic activating mutation in myelofibrosis with myeloid metaplasia. *PLoS Med*. 2006;3(7):e270
6. Pardanani AD, Levine RL, Lasho T, et al. *MPLW515* mutations in myeloproliferative and other myeloid disorders: a study of 1182 patients. *Blood*. 2006;108(10):3472-3476
7. Greenfield G, McMullin MF, Mills K. Molecular pathogenesis of the myeloproliferative neoplasms. *J Hematol Oncol*. 2021;14(1):103

## Performance

### Method Description

Genomic DNA is extracted, and Sanger sequencing is used to evaluate for alterations in *MPL*, exon 10. The sensitivity of this assay is approximately 20%, such that samples containing lower percentages of altered DNA will appear negative. (Unpublished Mayo method)

### PDF Report

No

### Day(s) Performed

Monday through Friday

### Report Available

7 to 10 days

### Specimen Retention Time

Whole blood/Bone marrow: 2 weeks; Extracted DNA: 3 months

### 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

81339-MPL (myeloproliferative leukemia virus oncogene, thrombopoietin receptor, TPOR) (eg, myeloproliferative disorder), exon 10 sequence