

## Overview

### Useful For

Aiding in the diagnosis of new cases of multiple myeloma or other plasma cell proliferative disorders as a part of a profile

Identifying prognostic markers based on the anomalies found

This test **should not be used** to track the progression of disease.

### Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
_PBCT	Probe, +2	No, (Bill Only)	No
_PADD	Probe, +1	No, (Bill Only)	No
_PB02	Probe, +2	No, (Bill Only)	No
_PB03	Probe, +3	No, (Bill Only)	No
_IL25	Interphases,	No, (Bill Only)	No
_I099	Interphases, 25-99	No, (Bill Only)	No
_I300	Interphases, >=100	No, (Bill Only)	No

### Testing Algorithm

This test is only orderable as part of a profile, based on the flow cytometric analysis and presence of 0.1% or greater monotypic plasma cells. For more information see MSMRT / Mayo Algorithmic Approach for Stratification of Myeloma and Risk-Adapted Therapy Report, Bone Marrow.

This test is designed for diagnostic specimens from patients with multiple myeloma or other plasma cell proliferative disorders.

This test includes a charge for application of the first probe set (2 fluorescence in situ hybridization: FISH probes) and professional interpretation of results. Additional charges will be incurred for all reflex probes performed. Analysis charges will be incurred based on the number of cells analyzed per probe set. If no cells are available for analysis, no analysis charges will be incurred.

For diagnostic samples, all probes in the initial panel will be evaluated if sufficient plasma cells are identified. The initial panel includes testing for the following abnormalities using the probes listed:

17p-, *TP53/D17Z1*

1q gain, *TP73/1q22*

14q32 rearrangement, *IGH*

t(11;14), *CCND1/IGH*

8q24.1 rearrangement, *MYC*

-13/13q-, *RB1/LAMP1*

+9/+15, *D9Z1/D15Z4*

+3/+7, *D3Z1/D7Z1*

Based on the results from the initial panel, reflex testing may be performed to identify the following abnormalities using the probes listed:

t(14;16)(q32;q23) *IGH/MAF*

t(4;14)(p16.3;q32) *FGFR3/IGH*

t(14;20)(q32;q12) *IGH/MAFB*

t(6;14)(p21;q32) *CCND3/IGH*

For follow-up samples, only *TP73/1q22*, *TP53/D17Z1* and *MYC* probes along with a single probe that was abnormal in a previous study will be tested. If a previous sample was uninformative due to an insufficient number of plasma cells, analysis will begin with the initial panel (if sufficient plasma cells are identified).

Initial screening will be performed to determine if sufficient plasma cells are present within the provided specimen. If the standard algorithm is not desired, indicate which probes should be used.

### Method Name

Only orderable as part of a profile. For more information see MSMRT / Mayo Algorithmic Approach for Stratification of Myeloma and Risk-Adapted Therapy Report, Bone Marrow.

Fluorescence In Situ Hybridization (FISH)

### NY State Available

Yes

## Specimen

### Specimen Type

Bone Marrow

### Specimen Required

Only orderable as part of a profile. For more information see MSMRT / Mayo Algorithmic Approach for Stratification of Myeloma and Risk-Adapted Therapy Report, Bone Marrow.

### Specimen Minimum Volume

2 mL

### Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

### Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Bone Marrow	Ambient (preferred)		
	Refrigerated		

## Clinical and Interpretive

### Clinical Information

Multiple myeloma is a hematologic neoplasm that generally originates in the bone marrow and develops from malignant plasma cells. There are 4 main categories of plasma cell proliferative disorders (PCPD): monoclonal gammopathy of undetermined significance (MGUS), monoclonal immunoglobulin deposition diseases (amyloidosis), plasmacytoma, and multiple myeloma. MGUS, which occurs in 3% to 4% of individuals over age 50 years, represents the identification of an asymptomatic monoclonal protein, yet approximately 1% per year will progress to multiple myeloma. Amyloidosis represents a rare group of deposition disorders including primary amyloidosis vs. light chain and heavy chain disease. Plasmacytomas represent isolated collections of bone or extramedullary plasma cells with a risk for development of multiple myeloma. Generalized bone pain, anemia, limb numbness or weakness, symptoms of hypercalcemia, and recurrent infections are all symptoms that may indicate multiple myeloma.

As myeloma progresses, the malignant plasma cells interfere with normal blood product formation in the bone marrow resulting in anemia and leukopenia. Myeloma also causes an overstimulation of osteoclasts, causing excessive breakdown of bone tissue without the normal corresponding bone formation. These bone lesions are seen in approximately 66% of myeloma patients. In advanced disease, bone loss may reach a degree where the patient suffers fractures easily.

Multiple myeloma is increasingly recognized as a disease characterized by marked cytogenetic, molecular, and proliferative heterogeneity. This heterogeneity is manifested clinically by varying degrees of disease aggressiveness. Multiple myeloma patients with more aggressive disease experience suboptimal responses to some therapeutic approaches; therefore, identifying these patients is critically important for selecting appropriate treatment options.

### Reference Values

Only orderable as part of a profile. For more information see MSMRT / Mayo Algorithmic Approach for Stratification of Myeloma and Risk-Adapted Therapy Report, Bone Marrow.

An interpretive report will be provided.

### Interpretation

A neoplastic clone is detected when the percent of cells with an abnormality exceeds the normal reference range for any given probe.

### Cautions

This test is not approved by the FDA and is best used as an adjunct to existing clinical and pathologic information.

### Supportive Data

Each probe was independently tested and verified on bone marrow specimens. For each probe set a series of chromosomally abnormal specimens were evaluated to confirm each probe set detected the anomaly it was designed to detect.

### Clinical Reference

1. Swerdlow S, Campo E, Harris NL, et al: WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues.

IARC Press: Lyon. 2017

2. Kumar SK, Rajkumar SV: The multiple myelomas-current concepts in cytogenetic classification and therapy. *Nat Rev Clin Oncol.* 2018;15(7):409-421 doi:10.1038/s41571-018-0018-y

3. Rajkumar SV, Landgren O, Mateos MV: Smoldering multiple myeloma. *Blood.* 2015 May 14;125(20):3069-75. doi:10.1182/blood-2014-09-568899

4. Muchtar E, Dispenzieri A, Kumar S, et al: Interphase fluorescence in situ hybridization in untreated AL amyloidosis has an independent prognostic impact by abnormality type and treatment category. *Leukemia.* 2017 Jul;31(7);1562-1569 doi:10.1038/leu.2016.369

5. Lakshman A, Paul S, Rajkumar SV, et al: Prognostic significance of interphase FISH in monoclonal gammopathy of undetermined significance. *Leukemia.* 2018 Aug;32(8);1811-1815 doi:10.1038/s41375-018-0030-3

6. Bochtler T, Hegenbart U, Kunz C, et al: Prognostic impact of cytogenetic aberrations in AL amyloidosis patients after high-dose melphalan: a long-term follow-up study. *Blood.* 2016 Jul 28;128(4):594-602 doi.org/10.1182/blood-2015-10-676361

7. Treatment guidelines: multiple myeloma. mSMART 3.0. Accessed 01/16/2020. [www.msmart.org/mm-treatment-guidelines](http://www.msmart.org/mm-treatment-guidelines)

## Performance

### Method Description

This test is performed using both commercially available and laboratory-developed probes. Deletion or monosomy of chromosomes 13 and 17 and copy number gain of 1q are detected using enumeration strategy probes. Centromere probes are used to detect chromosomal gain of chromosomes 3, 7, 9, and 15. Translocations involving *IGH* with *FGFR3*, *CCND1*, *CCND3*, *MAF*, and *MAFB* are detected using dual-color, dual-fusion (D-fluorescence in situ hybridization: FISH) strategy probes. Rearrangements of *IGH* and *MYC* are detected using break-apart strategy (BAP) probes. For each probe set, 50 plasma cells (if possible) are scored and the result for each probe is reported. (Unpublished Mayo method)

### PDF Report

No

### Day(s) and Time(s) Test Performed

Specimens are processed Monday through Sunday.

Results reported Monday through Friday, 8 a.m.-5 p.m.

### Analytic Time

10 days

### Maximum Laboratory Time

11 days

### Specimen Retention Time

14 days

### Performing Laboratory Location

Rochester

## Fees and 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 Regional Manager. For assistance, contact [Customer Service](#).

### Test Classification

This test was developed using an analyte specific reagent. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

### CPT Code Information

88271x2, 88291-DNA probe, each (first probe set), Interpretation and report

88271x2-DNA probe, each; each additional probe set (if appropriate)

88271x1-DNA probe, each; coverage for sets containing 3 probes (if appropriate)

88271x2-DNA probe, each; coverage for sets containing 4 probes (if appropriate)

88271x3-DNA probe, each; coverage for sets containing 5 probes (if appropriate)

88274 w/modifier 52 - Interphase in situ hybridization, <25 cells, each probe set (if appropriate)

88274-Interphase in situ hybridization, 25 to 99 cells, each probe set (if appropriate)Â Â Â Â Â

88275-Interphase in situ hybridization, 100 to 300 cells, each probe set (if appropriate)

### LOINC® Information

Test ID	Test Order Name	Order LOINC Value
MPCDS	mSMART Eval, PCPDs, FISH	93357-2

Result ID	Test Result Name	Result LOINC Value
606091	mSMART Result Summary	62357-9
606092	mSMART Evaluation	57802-1
606093	Interpretation	69965-2
606094	Result Table	93356-4
606095	Result	62356-1
606096	Reason for Referral	42349-1
606097	Specimen	31208-2
606098	Source	85298-8
606099	Method	85069-3

---

Result ID	Test Result Name	Result LOINC Value
606100	Additional Information	48767-8
606101	Disclaimer	62364-5
606102	Released By	18771-6