

Plasma Cell Proliferative Disorder, FISH, Tissue

## **Overview**

### **Useful For**

Supporting the diagnosis of plasmacytoma or myeloma when coordinated with a surgical pathology consultation

Detecting, at diagnosis, recurrent common chromosome abnormalities in patients with a plasmacytoma or myeloma in paraffin-embedded tissue specimens

#### **Reflex Tests**

Test Id	Reporting Name	Available Separately	Always Performed
_1099	Interphases, 25-99	No, (Bill Only)	No
_1300	Interphases, >=100	No, (Bill Only)	No
_IL25	Interphases, <25	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
_PBCT	Probe, +2	No, (Bill Only)	No

## **Testing Algorithm**

This test includes a charge for the probe application, analysis, and professional interpretation of results for one probe set (2 individual fluorescence in situ hybridization [FISH] probes). Additional charges will be incurred for all reflex or additional probe sets 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.

A minimum of 35% plasma cell involvement is required for a successful paraffin plasma cell FISH evaluation. If a bone marrow clot specimen is submitted with less than 35% plasma cell involvement, testing will be canceled.

The plasma cell high-risk FISH panel for paraffin-embedded tissue includes testing for the following abnormalities, using the FISH probes listed:

1p deletion/1q gain, CDKN2C/1q22 probe set t(14q32;var) or *IGH* rearrangement, IGH break-apart probe set -17/17p-, TP53/D17Z1 probe set

If an IGH rearrangement is identified, appropriate reflex testing will be performed in an attempt to identify the translocation partner using the FISH probes listed:

t(4;14)(p16.3;q32) IGH::FGFR3 fusion, FGFR3/IGH probe set

t(11;14)(q13;q32) or IGH::CCND1 fusion, CCND1/IGH probe set

t(14;16)(q32;q23) IGH::MAF fusion, IGH/MAF probe set

t(14;20)(q32;q12) IGH::MAFB fusion, IGH/MAFB probe set

For decalcified (bone) specimens, one FISH probe set (break-apart IGH) will be attempted. If this FISH probe is unsuccessful, testing will be canceled due to lack of hybridization as a result of the decalcification process. If the IGH



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FISH probe is successful, the remaining FISH probes will be evaluated.

Appropriate ancillary probes may be performed at consultant discretion to render comprehensive assessment. Any additional probes will have the results included within the final report and will be performed at an additional charge.

#### **Method Name**

Fluorescence In Situ Hybridization (FISH)

### **NY State Available**

Yes

### Specimen

# **Specimen Type**

Tissue

# **Ordering Guidance**

This test does not include a pathology consultation. If a pathology consultation is requested, order PATHC / Pathology Consultation and the appropriate fluorescence in situ hybridization test (FISH) test will be added and performed at an additional charge.

For the **most complete** genetic evaluation on fresh bone marrow specimens (collected within 96 hours of receipt), order MSMRT/ Mayo Algorithmic Approach for Stratification of Myeloma and Risk-Adapted Therapy Report, Bone Marrow.

For evaluation of high-risk abnormalities in addition to *IGH*::*CCND1* fusion on fresh bone marrow specimens (received within 96 hours of collection), order PCPDS / Plasma Cell Proliferative Disorder, High Risk with Reflex Probes, Diagnostic FISH Evaluation, Bone Marrow. If the specimen received for this test is fresh bone marrow received within 96 hours of collection, this test will be canceled and automatically reordered by the laboratory as PCPDS.

For evaluation of high-risk abnormalities in addition to *IGH*::*CCND1* fusion on a fixed cell pellet specimen or a fresh bone marrow specimen received greater than 96 hours after collection, order MFCDF / Myeloma, High Risk with Reflex Probes, Diagnostic FISH Evaluation, Fixed Cell Pellet. If the specimen received for this test is a fixed cell pellet or fresh bone marrow sample greater than 96 hours post-collection, this test will be canceled and automatically reordered by the laboratory as MFCDF.

#### **Shipping Instructions**

Advise Express Mail or equivalent if not on courier service.

## **Necessary Information**

- **1.** A pathology report is required for testing to be performed. If not provided, appropriate testing and/or interpretation may be compromised or delayed. Acceptable pathology reports include working drafts, preliminary pathology, or surgical pathology reports.
- 2. The following information must be included in the report provided:
- -Patient name



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- -Block number must be on all blocks, slides, and paperwork
- -Date of collection
- -Tissue source
- **3.** A reason for testing must be provided. If this information is not provided, an appropriate indication for testing may be entered by Mayo Clinic Laboratories.
- **4.** A list of probes is required if select probes are necessary or if the patient is being tracked for known abnormalities. See Table in Clinical Information.

### **Specimen Required**

Submit only 1 of the following specimens:

**Preferred:** 

**Specimen Type:** Tissue block **Collection Instructions:** 

- 1. Submit a formalin-fixed, paraffin-embedded tumor tissue block. Blocks prepared with alternative fixation methods will be attempted but are less favorable for successful results.
- 2. Provide fixation method used.

#### **Additional Information:**

- 1. Paraffin embedded specimens can be from any anatomic location (skin, soft tissue, lymph node, etc).
- 2. Bone specimens that have been decalcified will be attempted for testing, but the success rate is approximately 50%.

#### Acceptable:

**Specimen Type:** Tissue slides

Slides: 1 Hematoxylin and eosin-stained and 10 unstained

Collection Instructions: Submit 10 consecutive unstained, positively charged, unbaked slides with 5 micron-thick

sections of the tumor tissue and 1 slide stained with hematoxylin and eosin.

#### **Forms**

If not ordering electronically, complete, print, and send a <u>Hematopathology/Cytogenetics Test Request</u> (T726) with the specimen.

## **Specimen Minimum Volume**

Slides: 1 Hematoxylin and eosin stained and 7 unstained

## Reject Due To

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

# **Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Tissue	Ambient (preferred)		
	Refrigerated		

# **Clinical & Interpretive**



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### **Clinical Information**

A plasmacytoma is a localized proliferation of plasma cells that are cytologically and immunophenotypically identical to the plasma cell clones seen in myeloma. There are 2 primary types of plasmacytomas, solitary plasmacytoma of bone (SPB) and extramedullary plasmacytoma (EP).

The SPBs are a localized bone tumor comprised of plasma cells and account for about 5% of all plasma cell neoplasms. Common sites for SPBs are the vertebrae, ribs, skull, pelvis, femur, clavicle, and scapula. Patients often present with pathological fracture or bone pain near the lesion. Treatment is typically radiation therapy; at 10 years, 35% of patients appear to be cured, 55% develop myeloma, and 10% have local recurrence.

The EPs are tumors of plasma cells that form in areas away from the bone and account for 3% to 5% of all plasma cell neoplasms. Approximately 80% of EPs occur in the upper respiratory tract. Less common locations include the gastrointestinal tract, bladder, testis, central nervous system, and skin. Treatment consists of radiation therapy. Regional recurrence develops in about 25% of patients, but development of myeloma is less frequent, occurring in only about 15% of patients.

Genetics of both types of plasmacytomas, while not extensively studied, appear to be the same as plasma cell myeloma.

Paraffin plasma cell fluorescence in situ hybridization evaluation of bone marrow clot specimens is also important when a fresh bone marrow specimen is not available or is unsuccessful in the initial/diagnostic evaluation to document the genetic abnormalities associated with a patient's plasma cell clone.

#### Reference Values

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 a given probe set.

A positive result is not diagnostic of a plasmacytoma or myeloma but may provide relevant prognostic information.

A negative result does not rule out the presence of plasmacytoma, myeloma, or another neoplastic disorder.

## **Cautions**

This test is not approved by the US Food and Drug Administration and is best used as an adjunct to existing clinical and pathologic information.

Fixatives other than formalin (eg, Prefer, Bouin's) may not be successful for fluorescence in situ hybridization (FISH) assays. Non-formalin fixed specimens will not be rejected.

Paraffin-embedded tissues that have been decalcified may not be successful for FISH analysis. The success rate of FISH studies on decalcified tissue is approximately 50%, but FISH will be attempted if sufficient tumor is present for analysis.

Fluorescence in situ hybridization studies will be attempted if sufficient plasma cells are present for analysis. The pathologist reviewing the hematoxylin and eosin-stained slide may find it necessary to cancel testing if the paraffin-embedded specimen contains less than 35% plasma cells.



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If no FISH signals are observed post-hybridization, the case will be released indicating a lack of FISH results.

#### **Clinical Reference**

- 1. WHO Classification of Tumours Editorial Board, eds. Haematolymphoid Tumours. 5th ed. IARC Press; 2024:603-630. WHO Classification of Tumours. Vol 11
- 2. Arber DA, Orazi A, Hasserjian RP, et al, eds. The International Consensus Classification of Myeloid and Lymphoid Neoplasms. Wolters Kluwer: 2025:384-396
- 3. 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
- 4. Lu X, Andersen EF, Banerjee R, et al. Guidelines for the testing and reporting of cytogenetic results for risk stratification of multiple myeloma: a report of the Cancer Genomics Consortium Plasma Cell Neoplasm Working Group. Blood Cancer J. 2025;15(1):86. Published 2025 Jun 18. doi:10.1038/s41408-025-01286-w
- 5. Gagnon MF, Midthun SM, Fangel JA, et al. Superior detection rate of plasma cell FISH using FACS-FISH. Am J Clin Pathol. 2024;161(1):60-70. doi:10.1093/ajcp/aqad108

#### **Performance**

## **Method Description**

This test is performed using both commercially available and laboratory-developed probes. Deletion of the *TP53* locus from chromosome 17 or monosomy 17 and deletion of the *CDKN2C* locus or gain of the 1q22 locus are detected using enumeration strategy probe sets. An *IGH* rearrangement is detected using a dual-color break-apart (BAP) strategy probe set. Dual-color, dual-fusion fluorescence in situ hybridization (D-FISH) strategy probe sets are used when a rearrangement of the *IGH* gene is detected.

Paraffin-embedded tissue samples are cut at 5 microns and mounted on positively charged glass slides. The selection of tissue and the identification of target areas on the hematoxylin and eosin (H and E)-stained slide are performed by a pathologist. Using the H and E-stained slide as a reference, target areas are etched with a diamond-tipped engraving tool on the back of the unstained slide to be assayed. For each probe set, 100 total cells are scored and the result for each probe is reported. (Unpublished Mayo method)

#### PDF Report

No

### Day(s) Performed

Monday through Friday

#### Report Available

7 to 10 days

#### Specimen Retention Time

Slides used for analysis are retained by the laboratory in accordance with regulatory requirements. Client provided paraffin blocks and extra unstained slides (if provided) will be returned after testing is complete.



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## **Performing Laboratory Location**

Mayo Clinic Laboratories - Rochester Main Campus

#### Fees & Codes

#### **Fees**

- Authorized users can sign in to <u>Test Prices</u> 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 <u>Customer Service</u>.

#### **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**

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)

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

# **LOINC®** Information

Test ID	Test Order Name	Order LOINC® Value
PLASF	Plasma Cell Prolif, FISH, Ts	In Process

Result ID	Test Result Name	Result LOINC® Value
52219	Result Summary	50397-9
52221	Interpretation	69965-2
52220	Result Table	93356-4
54593	Result	62356-1
CG753	Reason for Referral	42349-1
52222	Specimen	31208-2
52223	Source	31208-2
52224	Tissue ID	80398-1
52225	Method	85069-3
55033	Additional Information	48767-8
52226	Released By	18771-6
53823	Disclaimer	62364-5