MAYO CLINIC LABORATORIES

# Test Definition: MESOF

Mesothelioma, CDKN2A FISH, Tissue

## Overview

### Useful For

Supporting the diagnosis of mesothelioma when used in conjunction with an anatomic pathology consultation

### 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, <25 | No, (Bill Only) | No |
| _I099 | Interphases, 25-99 | No, (Bill Only) | No |
| _I300 | Interphases, >=100 | No, (Bill Only) | No |

### Testing Algorithm

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

This test includes a charge for the probe application, analysis, and professional interpretation of results for one probe set (2 individual FISH] probes. 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.

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 is only performed on specimens for the purpose of differentiating mesothelioma from histologic mimics.

This test is not appropriate for identifying *CDKN2A* deletions when mesothelioma is not included in the differential diagnosis. If this test is ordered and the laboratory is informed that the purpose of testing is not to differentiate mesothelioma from histologic mimics, the laboratory will cancel the testing.

This test does not include a pathology consultation. If a pathology consultation is requested, order PATHC / Pathology Consultation, and appropriate testing will be added at the discretion of the pathologist and performed at an additional charge.

Multiple oncology (cancer) gene panels are also available. For more information see Hematology, Oncology, and Hereditary Test Selection Guide.

## 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
-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:** Submit a formalin-fixed, paraffin-embedded (FFPE) tumor tissue block. Blocks prepared with alternative fixation methods will be attempted but are less favorable for successful results by fluorescence in situ hybridization testing; 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 4 unstained
**Collection Instructions**: Submit 4 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 Oncology Test Request (T729) with the specimen.

### Specimen Minimum Volume
Slides: 1 Hematoxylin and eosin stained and 2 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

### Clinical Information
The histologic distinction of malignant mesothelioma from benign mesothelial proliferations can be challenging. Loss of both copies of *CDKN2A* has been described as a recurrent abnormality in 59% to 80% of pleural malignant mesotheliomas depending on histologic features.(1-3) Homozygous deletion of *CDKN2A* is less common in peritoneal mesothelioma, reported to occur in 25% to 35% of cases.(2,4,5) The detection of homozygous deletion of *CDKN2A* by fluorescence in situ hybridization has been suggested as a useful adjunct to histologic examination in the differentiation of malignant mesothelioma from other processes.(6,7)

### Reference Values
An interpretive report will be provided.

### Interpretation
*CDKN2A* will be clinically interpreted as positive or negative.

A neoplastic clone is detected when the percent of cells with an abnormality exceeds the normal cutoff for the CDKN2A/D9Z1 probe set. In the proper clinical and histologic context, a positive result may support a diagnosis of mesothelioma. However, homozygous loss of *CDKN2A* can be identified in many neoplasms. Therefore, clinical and pathologic correlation are required.

A negative result suggests no deletion of the *CDKN2A* gene region at 9p21. However, as homozygous deletion is not present in all mesotheliomas, this result does not exclude the diagnosis of malignant mesothelioma. In addition, due to limitations of the technology, fluorescence in situ hybridization cannot detect all *CDKN2A* deletions.

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

This fluorescence in situ hybridization (FISH) assay does not rule out other chromosome abnormalities.

Fixatives other than formalin (eg, Prefer, Bouin's) may not be successful for 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 tumor is present for analysis. The pathologist reviewing the hematoxylin and eosin-stained slide may find it necessary to cancel testing if insufficient tissue/tumor is available for testing.

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

### Clinical Reference

1. Illel P, Ladanyl M, Rusch V, Zakowski MF. The use of CDKN2A deletion as a diagnostic marker for malignant mesothelioma in body cavity effusions. Cancer. 2003;99:51-56
2. Chiosea C, Krasinkas A, Cagle P, Mitchell KA, Zander DS, Dacic S. Diagnostic importance of 9p21 homozygous deletion in malignant mesotheliomas. Mod Pathol. 2008;21:742-747
3. Hwang H, Pyott S, Rodriguez S, et al. BAP1 immunohistochemistry and p16 FISH in the diagnosis of sarcomatous and desmoplastic mesotheliomas. Am J Surg Pathol. 2016;40:714-718
4. Krasinskas A, Bartlett D, Cieply K, Dacic S. CDKN2A and MTAP deletions in peritoneal mesotheliomas are correlated with loss of p16 protein expression and poor survival. Mod Pathol. 2010;23:531-538
5. Singhi A, Krasinskas A, Choudry H, et al. The prognostic significance of BAP1, NF2, and CDKN2A in malignant peritoneal mesothelioma. Mod Pathol. 2016;29:14-24
6. Monaco S, Shuai Y, Bansal M, Krasinskas AM, Dacic S. The diagnostic utility of p16 FISH and GLUT-1 immunohistochemical analysis in mesothelial proliferations. Am J Clin Pathol. 2011;135:619-627
7. Wu D, Hiroshima K, Yusa T, et al. Usefulness of p16/CDKN2A Fluorescence in situ hybridization and BAP1 immunohistochemistry for the diagnosis of biphasic mesothelioma. Ann Diagn Pathol. 2017;26:31-37

## Performance

### Method Description

The test is performed using a commercially available *CDKN2A* enumeration probe set with a CDKN2A probe and a chromosome 9 centromere probe (D9Z1). 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. The probe set is hybridized to the appropriate target areas, and 2 technologists each independently analyze 50 interphase nuclei (100 total) with the results expressed as the percent of abnormal nuclei.(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.

### 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
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 |
|---|---|---|
| MESOF | Mesothelioma, FISH, Ts | 21614-3 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 609715 | Result Summary | 50397-9 |
| 609716 | Interpretation | 69965-2 |
| 609717 | Result | 62356-1 |
| GC086 | Reason for Referral | 42349-1 |
| 609718 | Specimen | 31208-2 |

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|---|---|---|
| 609719 | Source | 31208-2 |
| 609720 | Tissue ID | 80398-1 |
| 609721 | Method | 85069-3 |
| 609722 | Additional Information | 48767-8 |
| 609723 | Disclaimer | 62364-5 |
| 609724 | Released By | 18771-6 |