MAYO CLINIC LABORATORIES

# Test Definition: METF

MET (7q31), FISH, Tissue

## Overview

### Useful For

Providing prognostic information and guiding treatment primarily for patients with lung, gastric, and colorectal tumors as well as other tumor types

### 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 includes a charge for the probe application, analysis, and professional interpretation of results for one probe set (2 individual fluorescence in situ hybridization probes). No analysis charges will be incurred if an insufficient number of representative cells are available for analysis.

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 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

## Additional Testing Requirements

Confirmation testing by Microarray testing to resolve atypical fluorescence in situ hybridization results is available, order CMAPT / Chromosomal Microarray, Tumor, Formalin-Fixed Paraffin-Embedded

## 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.?**

1. Patient name
2. Block number - must be on all blocks, slides, and paperwork?
3. Date of collection
4. 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.

## Specimen Required

**Submit only 1 of the following specimens:**

**Preferred**

**Specimen Type:** Tissue block

**Collection Instructions:** 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 by FISH 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 an 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

*MET* is a proto-oncogene and its overexpression is associated with disease progression. Recent studies have shown *MET* amplification to be a major mechanism of acquired resistance to epidermal growth factor receptor tyrosine kinase domain inhibitor (EGFR-TKI). *MET* amplification has been reported in approximately 5% of patients not treated with EGFR-TKI and up to 20% of patients with acquired resistance to gefitinib or erlotinib. *MET* amplification has also been identified in several other cancers including colorectal adenocarcinoma, gastric adenocarcinoma, and gastroesophageal adenocarcinoma.

### Reference Values

An interpretive report will be provided.

### Interpretation

*MET* will be clinically interpreted as positive, negative or equivocal.

Establishment of a clear definition of *MET* amplification has been challenging with the evolution of criteria, as the need to differentiate between true MET amplification and chromosome 7 polysomy has become clear.

For this assay, *MET* will be reported as amplified (positive) when there is a MET:D7Z1 ratio greater than 2.0 and an average of greater or equal to 5 MET signals/nucleus based on current scientific literature.

Because various other definitions have been proposed, results indicating a greater or equal to 5 MET signals/nucleus with a MET:D7Z1 ratio less than 2.0 will be reported as an equivocal result as this finding likely reflects chromosome 7 polysomy but may represent an unusual mechanism of *MET* amplification. Similarly, results indicating a MET:D7Z1 ratio greater than 2.0 and less than 5 MET signals/nucleus will be reported as equivocal. Chromosomal microarray studies (TEST: CMAPT) may be considered in these instances to clarify the FISH results.

A result with a MET:D7Z1 ratio less than or equal to 2.0 and an average of less than 5 MET signals/nucleus will be considered negative for amplification of *MET*.

Patients with 5 or more copies of *MET* have a poor prognosis.

A negative result does not exclude the presence of a neoplastic disorder.

### Cautions

This test is not approved by the U.S. 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%.

FISH 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. Cappuzzo F, Marchetti A, Skokan M, et al. Increased *MET* gene copy number negatively affects survival of surgically resected non-small-cell lung cancer patients. J Clin Oncol. 2009;27(10):1667-1674
2. Karamouzis MV, Konstantinopoulos PA, Papavassiliou AG. Targeting MET as a strategy to overcome crosstalk-related resistance to EGFR inhibitors. Lancet Oncol. 2009;10(7):709-717
3. Engelman JA, Zejnullahu K, Mistudomi T, et al. MET amplification leads to gefitinib resistance in lung cancer by activating ERBB3 signaling. Science. 2007;316(5827):1039-1043
4. Zhang M, Li G, Sun X, Ni S, et al. MET amplification, expression, and exon 14 mutations in colorectal adenocarcinoma. Hum Pathol. 2018;77:108-15
5. An X, Wang F, Shao Q, Wang FH, et al. MET amplification is not rare and predicts unfavorable clinical outcomes in patients with recurrent/metastatic gastric cancer after chemotherapy. Cancer. 2014;120(5):675-82
6. Lai GGY, Lim TH, Lim J, et al. Clonal MET amplification as a determinant of tyrosine kinase Inhibitor resistance in epidermal growth factor receptor–mutant non–small-cell lung cancer. J Clin Oncol. 2019;37(11):876-884
7. Recondo G, Che J, Janne PA, Awad MM. Targeting MET dysregulation in cancer. Cancer Discov 2020;10(7):922-934

## Performance

### Method Description

This test is performed using a commercially available MET probe set with an MET probe and a chromosome 7 centromere probe (D7Z1). 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 30 interphase nuclei (60 total) with the results expressed as a ratio of MET:D7Z1 signals.(Unpublished Mayo method)

### PDF Report

No

### Day(s) Performed

Monday through Friday

### Report Available

7 to 10 days

### Specimen Retention Time

Slides and H&E 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)

### LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| METF | MET (7q31), FISH, Ts | 90926-7 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 55203 | Result Summary | 50397-9 |
| 55204 | Interpretation | 69965-2 |
| 55206 | Result | 62356-1 |
| CG938 | Reason for Referral | 42349-1 |
| 55207 | Specimen | 31208-2 |
| 55208 | Source | 31208-2 |
| 55209 | Tissue ID | 80398-1 |
| 55210 | Method | 85069-3 |
| 55211 | Additional Information | 48767-8 |
| 55212 | Disclaimer | 62364-5 |

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|---|---|---|
| 55224 | Released By | 18771-6 |