**Measure Description**

Percentage of non-small cell lung cancer (NSCLC) surgical pathology reports that include anaplastic lymphoma kinase (ALK), epidermal growth factor receptor (EGFR), AND tyrosine protein kinase ROS1 mutation status.

**Denominator Statement**

All surgical pathology reports with documentation of lung biopsy or resection that have diagnosis of NSCLC

CPT®: 88305 (Lung, transbronchial biopsy)  
88307 (Lung, wedge biopsy)  
88309 (Lung, total/lobe/segment resection)  
AND  
ICD-10  
- C34.00: Malignant neoplasm of unspecified main bronchus  
- C34.01: Malignant neoplasm of right main bronchus  
- C34.02: Malignant neoplasm of left main bronchus  
- C34.10: Malignant neoplasm of upper lobe, unspecified bronchus or lung  
- C34.11: Malignant neoplasm of upper lobe, right bronchus or lung  
- C34.12: Malignant neoplasm of upper lobe, left bronchus or lung  
- C34.2: Malignant neoplasm of middle lobe, bronchus or lung  
- C34.30: Malignant neoplasm of lower lobe, unspecified bronchus or lung  
- C34.31: Malignant neoplasm of lower lobe, right bronchus or lung  
- C34.32: Malignant neoplasm of lower lobe, left bronchus or lung  
- C34.80: Malignant neoplasm of overlapping sites of unspecified bronchus and lung  
- C34.81: Malignant neoplasm of overlapping sites of right bronchus and lung  
- C34.82: Malignant neoplasm of overlapping sites of left bronchus and lung  
- C34.90: Malignant neoplasm of unspecified part of unspecified bronchus or lung  
- C34.91: Malignant neoplasm of unspecified part of right bronchus or lung  
- C34.92: Malignant neoplasm of unspecified part of left bronchus or lung

**Denominator Exclusions**

Squamous cell carcinoma

**Denominator Exceptions**

Specimen contains metastatic carcinoma (not a primary neoplasm)  
Insufficient tissue for testing  
Necrotic tissue
No residual carcinoma
Not a lung specimen (e.g. lymph nodes, incl hilar lymph nodes; pleural fluid)

**Numerator Statement**
Surgical pathology reports that contain impression or conclusion of, or recommendation for biomarker mutation testing for each of the three biomarkers, ALK, EGFR and ROS1.

Information must be provided about each biomarker; a non-specific note about “biomarker testing” or other documentation that does not conclusively identify each biomarker by name does not meet the measure.

**Numerator Exclusions**
None

**Guidance**
This measure is to be reported each time a non-small cell lung cancer specimen pathology report is finalized during the performance period. This measure may be submitted by eligible clinicians who perform the quality actions described in the measure based on the services provided and the measure-specific denominator coding.

A short note on mutation status can be made in the final report, such as:
- Mutation(s) identified/positive
- No mutation(s) identified/ negative
- ALK, EGFR and ROS1 testing previously performed
- ALK, EGFR and ROS1 mutation testing recommended
- ALK, EGFR and ROS1 mutation cannot be determined or is not possible
- ALK, EGFR and ROS1 mutation testing not indicated

Mutation status may be derived from either the primary or a reference laboratory. The status does NOT have to be the same for all three biomarkers as long as each is recorded.

**Measure Information**

**NQS Domain**
Communication and Care Coordination

**Meaningful Measures Area(s)**
Transfer of Health Information and Interoperability

**Meaningful Measure Rationale**
Various gene alterations have been identified as oncogenic drivers for NSCLC, including mutations of EGFR, ALK and ROS1. The Lung Cancer Mutation Consortium found that two thirds of NSCLC patients have an oncogenic driver and that overall survival improves if patients receive matched targeted therapy (1).

Referring physicians depend on both the pathologists’ interpretations of and any recommendations for tests in order to provide quality patient care. If the status is not indicated in each pathology report for the patient, unnecessary repeat testing may be performed delaying treatment and increasing cost. This...
measure monitors the success of pathologists in effectively communicating this important information for the purpose of care coordination and efficient use of resources.

Knowledge of mutation status of ROS1, ALK and EGFR is thus necessary for appropriate clinical decision-making in advanced NSCLC. Alternative treatments are considered when any one or more of these rearrangements are discovered before or during first-line chemotherapy. ROS1 rearrangement occurs in 1% to 2% of non-small cell lung carcinomas and predicts response to crizotinib and ceritinib therapy, which are first-line treatments. Response rates, including complete responses, approach 70% (2-4). For ALK1, in addition to identifying tumors that are likely to respond to targeted therapies, knowledge of ALK rearrangement status typically predicts inferior response to immunotherapies. Approximately 5% of lung adenocarcinomas have a chromosomal rearrangement involving the ALK gene and associated with ALK protein overexpression. Patients with such tumors respond to therapy with ALK tyrosine kinase inhibitors, such as crizotinib (2, 5). Finally, approximately 20% of lung adenocarcinomas contain an EGFR activating mutation that predicts response to therapy with EGFR tyrosine kinase inhibitors such as erlotinib (2, 6-10).


<table>
<thead>
<tr>
<th>Measure Type</th>
<th>Process</th>
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<tbody>
<tr>
<td>Data Source</td>
<td>Laboratory Information Systems; pathology reports</td>
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</table>

**Summary of Performance Gap Evidence**

For performance year 2021, 15 reporting entities submitted data on this measure to CMS, although four were below the 20-case minimum. Case numbers ranged from 9 to 500. Performance scores ranged from 0% to 100% with an average performance of 62.56%.

For January 1st to July 1st 2022, 7 reporting entities have entered data into the Pathologists Quality Registry for this measure. Case numbers range from 4 to 314. Performance scores range from 80% to 100% with an average score of 96%.

Although ROS1 rearrangement predicts response to first line treatments, testing for ROS1 rearrangements occurs in as few as 20.6% of NSCLC cases or as many as 28% of cases (average 27.5%) (1, 5). Testing rates of ALK are higher, but recent study indicated as few as 58-64% of cases were tested for ALK rearrangement (1, 2, 5). Possibly due to the higher rate of EGFR mutation as compared to ROS1 or ALK rearrangement, rates of testing for EGFR mutation are higher than either ROS1 or ALK at approximately 75% (3), although EGFR testing varies depending on cancer stage (5).

Testing rates also vary across institutions and institution types. A 2021 study of sites in The US Oncology Network, which represents over 450 community oncology practices, found documentation of biomarker testing in the EHR was available in 35.5% of patients for EGFR, 32.9% for ALK, 5.7% for ROS1 (6)

Data regarding testing of all three mutation together are not as widely available, as ROS1 testing in particular has only recently been seen as standard. However, one study from 2019 indicated that 15.4% (875 out of 5688) of NSCLC patients who were tested for biomarkers received multigene panel sequencing (4).
<table>
<thead>
<tr>
<th>Measure Owner</th>
<th>College of American Pathologists</th>
</tr>
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<tbody>
<tr>
<td>NQF ID</td>
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<tr>
<td>Number of Performance Rates</td>
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<td>Improvement Notation</td>
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<td>Proportional Measure: Yes (Higher score indicates better quality)</td>
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<td>Continuous Variable Measure: No</td>
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<td>Ratio Measure: No</td>
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<td>Care Setting and Specialty</td>
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<td>Specialty: Pathology</td>
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<td>Submission Pathway</td>
<td>Traditional MIPS Only</td>
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<td>Current Clinical Guideline the Measure is Derived From</td>
<td>ROS1 testing must be performed on all lung advanced-stage adenocarcinoma patients, irrespective of clinical characteristics (Strong Recommendation) (1). The NCCN guideline for non-small cell lung cancer recommends testing for ROS1 rearrangements for nonsquamous NSCLC or NSCLS NOS (Category 2A evidence) (2).</td>
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</tbody>
</table>
ALK molecular testing should be used to select patients for ALK-targeted TKI therapy, and patients with lung adenocarcinoma should not be excluded from testing on the basis of clinical characteristics (Grade B evidence) (3). Testing for ALK gene rearrangements and EGFR gene mutations is recommended in the NSCLC algorithm for patients with nonsquamous NSCLC or NSCLC NOS so that patients with these genetic abnormalities can receive effective treatment with targeted agents (Category 1 evidence) (2).

EGFR molecular testing should be used to select patients for EGFR-targeted TKI therapy, and patients with lung adenocarcinoma should not be excluded from testing on the basis of clinical characteristics (Grade A Evidence) (3). EGFR mutation testing should be ordered at the time of diagnosis for patients presenting with advanced-stage disease (stage IV according to the 7th edition TNM staging system) who are suitable for therapy or at time of recurrence or progression in patients who originally presented with lower-stage disease but were not previously tested (Grade A Evidence) (3). Physicians may use molecular biomarker testing in tumors with histologies other than adenocarcinoma when clinical features indicate a higher probability of an oncogenic driver (Expert Consensus Opinion) (1, 2).


### CAP QCDR Measure
**Biomarker Testing - NSCLC**

**Measure Flow**

**Denominator**

- **Start**
- Procedure as listed in denominator (CPT 88305, 88307, 88309)
  - Not in Eligible Population/Denominator
  - Initial Population: 100 cases (a)
  - Diagnosis as listed in denominator (NSCLC)
  - Diagnosis of squamous cell carcinoma
    - Yes
    - Denominator Exclusion: 10 cases (x)
    - Eligible Population/Denominator (90 cases)
    - No
- Denominator Numerator = 90 cases

**Numerator**

- Surgical pathology report with ALK1, ROS1 and EGFR status documented
  - Yes
  - Numerator/Performance Met: 70 cases (b)
  - No
- Documentation of medical reason biomarker status not in pathology report
  - Yes
  - Denominator Exception: 10 cases (c)
  - No
  - No documentation of testing, reason not given
    - Yes
    - Performance Not Met: 10 cases (d)
  - No
- No/Missing Data—Data Completeness Not Met: 10 cases (d)

**SAMPLE CALCULATION:**

\[
\text{Numerator (b) = 70 reports} \\
\text{Denominator (a = 100 cases) - Denominator Exclusions (x = 10 cases) - Denominator Exceptions (c = 10 cases)} \\
\text{= 87.5%}
\]