Template for Reporting Results of Biomarker Testing of Specimens from Patients with Non-Small Cell Carcinoma of the Lung

Version: 2.2.0.0
Protocol Posting Date: September 2025
This biomarker template is not required for accreditation purposes but may be used to facilitate compliance with CAP Accreditation Program Requirements.

Version Contributors
Authors: Brett W. Baskovich, MD*, Kirtee Raparia, MD, FCAP*
Other Expert Contributors: Patrick L. Fitzgibbons, MD, FCAP, George G. Birdsong, MD, Joseph D. Khoury, MD, Raja R. Seethala, MD, Frank Schneider, MD, Alexander Baras, MD, PhD
* Denotes primary author.

For any questions or comments, contact: cancerprotocols@cap.org.

Glossary:
Author: Expert who is a current member of the Cancer Committee, or an expert designated by the chair of the Cancer Committee.
Expert Contributors: Includes members of other CAP committees or external subject matter experts who contribute to the current version of the protocol.

Accreditation Requirements

Completion of the template is the responsibility of the laboratory performing the biomarker testing and/or providing the interpretation. When both testing and interpretation are performed elsewhere (eg, a reference laboratory), synoptic reporting of the results by the laboratory submitting the tissue for testing is also encouraged to ensure that all information is included in the patient's medical record and thus readily available to the treating clinical team. This template is not required for accreditation purposes.

Summary of Changes

v 2.2.0.0

- Updates to EGFR, ALK, ROS1, RET, BRAF, NTRK, and PD-L1 sections
- Addition of NRG1 section
- Addition of optional Specify Fusion Partner question to ROS1, RET NTRK1, NTRK2, and NTRK3 Molecular Methods
- Addition of BRAF:p.V600K, BRAF:p.V600R, and BRAF:p.V600D answers to BRAF Mutational Analysis question
- Addition of specific PD-L1 markers to include PD-L1 22c3, PD-L1 228-8, PD-L1 SP142, and PD-L1 SP263

Reporting Template

Protocol Posting Date: September 2025

Select a single response unless otherwise indicated.

CASE SUMMARY: (Lung Biomarker Reporting Template)

Completion of the template is the responsibility of the laboratory performing the biomarker testing and / or providing the interpretation. When both testing and interpretation are performed elsewhere (e.g., a reference laboratory), synoptic reporting of the results by the laboratory submitting the tissue for testing is also encouraged to ensure that all information is included in the patient's medical record and thus readily available to the treating clinical team.
Gene names should follow recommendations of The Human Genome Organisation (HUGO) Nomenclature Committee (www.genenames.org; accessed September 2, 2025).
All reported gene sequence variations should be identified following the recommendations of the Human Genome Variation Society (www.http://varnomen.hgvs.org;accessed September 2, 2025).

SPECIMEN

+Adequacy of Sample for Testing

___ Adequate

+Specify Estimated Percent of Tumor Cellularity (area used for testing): _____ %

___ Suboptimal (explain): _____

Please refer to original laboratory report for explanation.

+Specimen Type

___ Untreated diagnostic specimen

___ Relapse specimen (after treatment; specify)#: _____

 # When data is available, specify treatment type. This is most relevant to targeted inhibitors associated with specific genomic changes conferring treatment resistance.

RESULTS

EGFR

+Mutational Analysis

___ No EGFR mutation detected

___ Mutation(s) identified

Select all that apply

___ EGFR:p.G719X

___ EGFR Exon 19 deletion (specify, if known): _____

___ EGFR Exon 20 insertion (specify, if known): _____

___ EGFR:p.S768I

___ EGFR:p.T790M

___ EGFR:p.L858R

___ EGFR:p.L861Q

___ Other (specify): _____

___ Cannot be determined (explain): _____

+EGFR L858R by Immunohistochemistry (clone 43B2)

___ Negative

___ Positive
___ Equivocal (explain): _____
___ Cannot be determined (explain): _____

+EGFR Exon 19 Deletion (E746_A750del) (clone 6B6)
___ Negative
___ Positive
___ Equivocal (explain): _____
___ Cannot be determined (explain): _____

+Interpretation (select all that apply)
___ An EGFR mutation is present that is associated with response to EGFR tyrosine kinase inhibitors
___ An EGFR mutation is present that is associated with resistance to EGFR tyrosine kinase inhibitors
___ Two EGFR mutations are present, one of which is associated with resistance to EGFR tyrosine kinase inhibitors
___ EGFR L858R immunohistochemical staining is positive, which is associated with response to EGFR tyrosine kinase inhibitors
___ EGFR E746_A750del immunohistochemical staining is positive, which is associated with response to EGFR tyrosine kinase inhibitors

ALK

+Rearrangement by Molecular Methods
___ No ALK rearrangement detected
___ Rearrangement identified
  ___ EML4::ALK (specify variant type, if known): _____
  ___ KIF5B::ALK
  ___ KLC1::ALK
  ___ Other ALK rearrangement (specify, if known): _____
___ Cannot be determined (explain): _____

+ALK Immunohistochemistry
___ Negative
___ Positive
___ Equivocal (explain): _____
___ Cannot be determined (explain): _____

+Interpretation (select all that apply)
___ An ALK fusion is identified that is associated with response to ALK tyrosine kinase inhibitors
___ ALK immunohistochemical staining is positive which is associated with response to ALK tyrosine kinase inhibitors

ROS1

+Rearrangement by Molecular Methods

___ No ROS1 rearrangement detected
___ ROS1 rearrangement identified
+Specify Fusion Partner: _____
___ Cannot be determined (explain): _____

+ROS1 by Immunohistochemistry
___ Negative
___ Positive
___ Equivocal (explain): _____
___ Cannot be determined (explain): _____

+Interpretation (select all that apply)
___ A ROS1 fusion is present, which is associated with response to ROS tyrosine kinase inhibitors
___ ROS1 immunohistochemical staining is positive, which is associated with response to ROS1 tyrosine kinase inhibitors

RET

+Rearrangement by Molecular Methods
___ No RET rearrangement detected
___ RET rearrangement identified
+Specify Fusion Partner: _____
___ Cannot be determined (explain): _____

+Interpretation
___ A RET fusion is present which is associated with response to RET tyrosine kinase inhibitors
___ No RET fusions are detected

KRAS

+Mutational Analysis
___ No KRAS mutation detected
___ Mutation(s) identified
Select all that apply
___ KRAS:p.G12C
___ KRAS:p.G12D
___ KRAS:p.G12V
___ KRAS:p.G12S
___ KRAS:p.G12A
___ KRAS:p.G12R
___ KRAS:p.G13D
___ KRAS:p.G13C
___ KRAS:p.Q61L
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Interpretation (select all that apply)
___ A KRAS mutation is identified which is associated with resistance to tyrosine kinase inhibitor therapy
___ A KRAS mutation is identified which is associated with response to specific inhibitors

BRAF

+Mutational Analysis
___ No BRAF mutations detected
___ Mutation(s) identified
Select all that apply
___ BRAF:p.V600E
___ BRAF:p.V600K
___ BRAF:p.V600R
___ BRAF:p.V600D
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Interpretation
___ A BRAF mutation is present which is associated with response to BRAF inhibitors
___ No BRAF mutations are detected

ERBB2

+Mutational Analysis
___ No ERBB2 mutations detected
___ Mutation(s) identified
Select all that apply
___ ERBB2:p.S310F
___ ERBB2:p.L755S
___ ERBB2:p.Y772_A775dup insertion
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Copy Number Analysis
___ No ERBB2 (HER2) amplification detected
___ ERBB2 (HER2) amplification identified
Select all that apply
___ Specify Copy Number: _____
___ Specify Ratio to Centromere 17: _____
___ Cannot be determined (explain): _____

+HER2 Immunohistochemistry
___ Negative (0-1)

___ Equivocal (2+)
___ Positive (3+)
___ Cannot be determined (explain): _____

+Interpretation (select all that apply)
___ An ERBB2 (HER2) mutation is present which is associated with response to anti-HER2 therapy
___ ERBB2 (HER2) amplification is present which is associated with response to anti-HER2 therapy
___ HER2 is positive by immunohistochemistry (3+) which is associated with response to anti-HER2 therapy

MET

+Mutational Analysis
___ No MET mutation detected
___ Mutation(s) identified
Select all that apply
___ MET:p.D963_splice mutation
___ MET:p.D1010N
___ MET:p.D1010_splice mutation
___ MET exon 14 deletion
___ Other (specify): _____
___ Cannot be determined (explain): _____

+Copy Number Analysis
___ No MET amplification detected
___ MET amplification identified
Select all that apply
___ Specify Copy Number: _____
___ Specify Ratio to Centromere 7: _____
___ Cannot be determined (explain): _____

+Interpretation (select all that apply)
___ A MET alteration is present which is associated with response to MET tyrosine kinase inhibitors
___ MET amplification is present which is associated with response to MET tyrosine kinase inhibitors

NTRK

+NTRK1 by Molecular Methods
___ No NTRK1 rearrangement detected
___ NTRK1 rearrangement identified
+Specify Fusion Partner: _____
___ Cannot be determined (explain): _____

+NTRK2 by Molecular Methods
___ No NTRK2 rearrangement detected
___ NTRK2 rearrangement identified

+Specify Fusion Partner: _____
___ Cannot be determined (explain): _____

+NTRK3 by Molecular Methods
___ No NTRK3 rearrangement detected
___ NTRK3 rearrangement identified
+Specify Fusion Partner: _____
___ Cannot be determined (explain): _____

+NTRK by immunohistochemistry
___ Negative
___ Positive
___ Equivocal
___ Cannot be determined (explain): _____

+Interpretation (select all that apply)
___ An NTRK fusion is present which is associated with response to NTRK inhibitors
___ NTRK immunohistochemical staining is present. Fusion testing by NGS or FISH will be performed
___ NTRK immunohistochemical staining is present but fusion testing is negative. This is not associated with response to NTRK inhibitors
___ Other (specify): _____

NRG1

+Rearrangement by Molecular Methods
___ No NRG1 rearrangement detected
___ NRG1 rearrangement identified
+Specify Fusion Partner: _____
___ Cannot be determined (explain): _____

+Interpretation
___ An NRG1 fusion is present which is associated with response to NRG1 inhibitors
___ No NRG1 fusions are detected

Mismatch Repair

+Immunohistochemistry (IHC) Testing for Mismatch Repair (MMR) Proteins (select all that apply)

___ MLH1
MLH1 Result
___ Intact nuclear expression
___ Loss of nuclear expression
___ Cannot be determined (explain): _____
___ MSH2

MSH2 Result
___ Intact nuclear expression
___ Loss of nuclear expression
___ Cannot be determined (explain): _____
___ MSH6
MSH6 Result
___ Intact nuclear expression
___ Loss of nuclear expression
___ Cannot be determined (explain): _____
___ PMS2
PMS2 Result
___ Intact nuclear expression
___ Loss of nuclear expression
___ Cannot be determined (explain): _____
___ Background non-neoplastic tissue / internal control with intact nuclear expression

+Microsatellite Instability (MSI)
___ MSI-Stable (MSS)
___ MSI-Low (MSI-L)
___ MSI-High (MSI-H)
___ Cannot be determined: _____

+Interpretation (select all that apply)
___ The case is MSI-H which is associated with response to immune checkpoint inhibitors
___ The case is mismatch repair deficient which is associated with response to immune checkpoint inhibitors

Tumor Mutational Burden

+Specify Tumor Mutational Burden: _____

+Tumor Mutational Burden Level
___ Low
___ High
___ Equivocal
___ Cannot be determined (explain): _____

+Interpretation
___ The case is TMB-high which is associated with response to immune checkpoint inhibitors
___ The case is TMB-low which is not associated with response to immune checkpoint inhibitors

PD-L1 IHC

+PD-L1 22c3 IHC Interpretation
___ Positive
___ Negative

___ Cannot be determined
+Specify Percentage of Tumor Cells with Staining (TPS): _____ %
+Specify Combined Number of Tumor and Immune Cells with Staining per 100 Tumor Cells (CPS): _____ cells
+Specify Percentage of Tumor-associated Immune Cells with Staining: _____ %
+Specify Percentage of Tumor Area Occupied by Tumor-associated Immune Cells: _____ %

PD-L1 22c3 IHC Methods

+Controls (select all that apply)
___ Internal control cells present; expected immunoreactivity
___ Internal control cells present; no immunoreactivity of either tumor cells or internal controls
___ External controls available; expected immunoreactivity
___ External controls available; no immunoreactivity in expected cells

+Assay Information
___ Food and Drug Administration (FDA) cleared test / vendor (specify): _____
___ Laboratory-developed test

+Specify Quantitative Imaging Analytics Performed: _____

+PD-L1 28-8 IHC Interpretation
___ Positive
___ Negative
___ Cannot be determined
+Specify Percentage of Tumor Cells with Staining (TPS): _____ %
+Specify Combined Number of Tumor and Immune Cells with Staining per 100 Tumor Cells (CPS): _____ cells
+Specify Percentage of Tumor-associated Immune Cells with Staining: _____ %
+Specify Percentage of Tumor Area Occupied by Tumor-associated Immune Cells: _____ %

PD-L1 28-8 IHC Methods

+Controls (select all that apply)
___ Internal control cells present; expected immunoreactivity
___ Internal control cells present; no immunoreactivity of either tumor cells or internal controls
___ External controls available; expected immunoreactivity
___ External controls available; no immunoreactivity in expected cells

+Assay Information

___ Food and Drug Administration (FDA) cleared test / vendor (specify): _____
___ Laboratory-developed test

+Specify Quantitative Imaging Analytics Performed: _____

+PD-L1 SP142 IHC Interpretation
___ Positive
___ Negative
___ Cannot be determined
+Specify Percentage of Tumor Cells with Staining (TPS): _____ %
+Specify Combined Number of Tumor and Immune Cells with Staining per 100 Tumor Cells (CPS): _____ cells
+Specify Percentage of Tumor-associated Immune Cells with Staining: _____ %
+Specify Percentage of Tumor Area Occupied by Tumor-associated Immune Cells: _____ %

PD-L1 SP142 IHC Methods

+Controls (select all that apply)
___ Internal control cells present; expected immunoreactivity
___ Internal control cells present; no immunoreactivity of either tumor cells or internal controls
___ External controls available; expected immunoreactivity
___ External controls available; no immunoreactivity in expected cells

+Assay Information
___ Food and Drug Administration (FDA) cleared test / vendor (specify): _____
___ Laboratory-developed test

+Specify Quantitative Imaging Analytics Performed: _____

+PD-L1 SP263 IHC Interpretation
___ Positive
___ Negative
___ Cannot be determined
+Specify Percentage of Tumor Cells with Staining (TPS): _____ %
+Specify Combined Number of Tumor and Immune Cells with Staining per 100 Tumor Cells (CPS): _____ cells
+Specify Percentage of Tumor-associated Immune Cells with Staining: _____ %
+Specify Percentage of Tumor Area Occupied by Tumor-associated Immune Cells: _____ %

PD-L1 SP263 IHC Methods

+Controls (select all that apply)
___ Internal control cells present; expected immunoreactivity
___ Internal control cells present; no immunoreactivity of either tumor cells or internal controls
___ External controls available; expected immunoreactivity
___ External controls available; no immunoreactivity in expected cells

+Assay Information
___ Food and Drug Administration (FDA) cleared test / vendor (specify): _____
___ Laboratory-developed test

+Specify Quantitative Imaging Analytics Performed: _____

Variants with Potential Pathologic Relevance

+Specify Marker and Results (repeat up to 20 times): _____

Other Variants of Unknown Significance (VUS)

+Specify Marker and Results (repeat up to 20 times): _____

COMMENTS

Comment(s): _____