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Template for Reporting Results of Biomarker Testing of Specimens From Patients With Myeloproliferative Neoplasms

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The College of American Pathologists (CAP) offers these templates to assist pathologists in providing clinically useful and relevant information when reporting results of biomarker testing. The CAP regards the reporting elements in the templates as important elements of the biomarker test report, but the manner in which these elements are reported is at the discretion of each specific pathologist, taking into account clinician preferences, institutional policies, and individual practice.

The CAP developed these templates as educational tools to assist pathologists in the useful reporting of relevant information. It did not issue them for use in litigation, reimbursement, or other contexts. Nevertheless, the CAP recognizes that the templates might be used by hospitals, attorneys, payers, and others. The CAP cautions that use of the templates other than for their intended educational purpose may involve additional considerations that are beyond the scope of this document.

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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.

Biomarker Reporting Template

Myeloproliferative Neoplasms (MPNs)

Select a single response unless otherwise indicated—*Note:* Use of this template is optional.*

*Reporting on the data elements in this template is not required.

Specimen Type

- ☐ Peripheral blood
- ☐ Bone marrow
- ☐ Isolated granulocytes from peripheral blood
- ☐ Other (specify): _____

Results

Cytogenetic Testing Results (Karyotype)

- ☐ No abnormalities detected
- ☐ Abnormal karyotype detected
- (specify): _____

Fluorescence In Situ Hybridization Testing

- ☐ *BCR-ABL1*
- ☐ No *BCR-ABL1* fusion detected
- ☐ *BCR-ABL1* fusion detected (specify percentage of positive cells): _____%
- ☐ *PDGFRA*
- ☐ No *PDGFRA* fusion detected
- ☐ *FIP1L1-PDGFRA* fusion detected (specify percentage of positive cells): _____%

___ Other *PDGFRA* fusion detected (specify percentage of positive cells):
 ___ %

___ *PDGFRB*

___ No *PDGFRB* fusion detected

___ *ETV6-PDGFRB* fusion detected (specify percentage of positive cells):
 ___ %

___ Other *PDGFRB* fusion detected (specify percentage of positive cells):
 ___ %

___ *FGFR1*

___ No *FGFR1* rearrangement detected

___ *FGFR1* rearrangement detected (specify percentage of positive cells):
 ___ %

***BCR-ABL1* Transcript Reverse Transcription–Polymerase Chain Reaction (RT-PCR) Testing**

___ No *BCR-ABL1* fusions detected

___ *BCR-ABL1* fusions detected

If quantitative testing performed:

___ *BCR-ABL1* normalized copy number (*BCR-ABL1*/reference gene):

Percent *BCR-ABL1* on International Scale (e13/14a2 (p210) fusions only):
 ___ %

***JAK2* p.V617F (c. 1849G.T) Mutation Testing**

___ No mutation detected

___ Mutation detected

For *JAK2* p.V617F, if test is quantitative, specify quantitative value:

Reported as:

___ Percent mutant allele burden

___ Percent transcript levels

___ Normalized copy number (V617F transcripts/ reference gene)

Additional Mutation Testing

___ *JAK2* exon 12

___ No *JAK2* exon 12 mutation detected

___ *JAK2* exon 12 mutation detected (specify mutation):

___ *MPL*

___ No *MPL* mutation detected

___ *MPL* mutation detected (specify mutation):

___ *CALR* (calreticulin)

___ No *CALR* mutation detected

___ *CALR* mutation detected (specify mutation):

___ *KIT*

___ No *KIT* mutation detected

___ *KIT* mutation detected (specify mutation):

___ Other (specify gene): _____

___ No mutation detected

___ Mutation detected (specify mutation):

Methods

BCR-ABL1 Transcript RT-PCR Testing

Assay sensitivity: _____

JAK2 p.V617F (c. 1849G.T) Mutation Testing

Assay sensitivity: _____

Assay method:

___ Allele-specific PCR

___ Sanger sequencing

___ Pyrosequencing

___ Next-generation sequencing

___ Other (specify): _____

Other Mutation Testing (Specify Gene): _____

Assay sensitivity: _____

Assay method:

- ☐ Allele-specific PCR
☐ Sanger sequencing
☐ Pyrosequencing
☐ Next-generation sequencing
☐ Other (specify): _____

Exon(s)/codon(s) covered: _____

Explanatory Notes

Myeloproliferative neoplasms are clonal disorders characterized by the expansion of one or more myeloid lineages, leading to increased bone marrow cellularity and elevated peripheral blood myeloid cell counts. The latter may manifest as granulocytosis, erythrocytosis, thrombocytosis, or a combination of these, depending on the disease subtype. The diagnosis and classification of MPNs require synthesis of the clinical, morphologic, immunophenotypic, and molecular genetic findings. During the course of the last few years, the spectrum of genetic mutations identified in MPNs has expanded, and PCR and/or sequence-based mutation testing is now routinely incorporated into the diagnostic workup. However, the diagnosis still relies heavily on the peripheral blood and bone marrow morphologic findings and the clinical features of the disease, particularly for those patients who do not have a disease-defining genetic abnormality.

In the 2008 World Health Organization classification system, the category of MPNs includes chronic myelogenous leukemia; chronic neutrophilic leukemia; polycythemia vera; primary myelofibrosis; essential thrombocythemia; chronic eosinophilic leukemia; mastocytosis; and MPN, unclassifiable; and the clinical and pathologic findings may overlap with the category of myeloid and lymphoid neoplasms with eosinophilia and abnormalities of *PDGFRA*, *PDGFRB*, and *FGFR1*.¹ Classical cytogenetic karyotyping and fluorescence in situ hybridization testing are often used in the evaluation of patients to test for the presence of t(9;22)(q34;q11.2); *BCR-ABL1*—particularly for those who present with neutrophilic leukocytosis—and for abnormalities of *PDGFRA*, *PDGFRB*, and *FGFR1* for those patients who present with eosinophilia. Otherwise, patients with MPNs may have a variety of cytogenetic abnormalities. Various trisomies, such as +8 and/or +9, are often identified. Given the degree of standardization and specialization that has occurred in *BCR-ABL1* testing, and the repeated nature of the analyses, CAP has published a separate chronic myelogenous leukemia monitoring template for those patients known to have chronic myelogenous leukemia.

When the cytogenetic and/or fluorescence in situ hybridization testing results are nonspecific or negative, it may be necessary to use additional molecular genetic tests. The *JAK2* p.V617F (c.1849G.T) somatic point mutation is present in almost all patients with polycythemia vera and in a large proportion (40%–50%) of patients with essential thrombocythemia or primary myelofibrosis. Both qualitative and quantitative testing methods are employed, although the utility of quantitation of the mutant *JAK2* allele burden remains somewhat controversial. A small percentage of patients with polycythemia vera who

lack evidence of a *JAK2* p.V617F mutation may have a mutation in exon 12 of *JAK2*, and these are often insertions or deletions.² Different testing methods are often used for *JAK2* p.V617F and *JAK2* exon 12 mutations, and it should be noted that different methods—for example, Sanger sequencing and allele-specific PCR—may have markedly different sensitivities. Mutations in the *CALR* (calreticulin) gene were recently identified in most patients with essential thrombocythemia or primary myelofibrosis who lack *JAK2* mutations.^{3,4} Less commonly, mutations in the *MPL* gene are present in a subset of essential thrombocythemia/primary myelofibrosis patients without *JAK2* or *CALR* mutations.³ *KIT* mutation testing is helpful for the diagnosis and subclassification of mastocytosis and is important for determining the likely response to tyrosine kinase inhibitor therapy.⁵

Given the pace of recent findings, additional pathologically relevant mutations are likely to be identified and/or clinically validated in the near future. With this in mind, the template includes space for reporting other mutation testing, and future template updates will reflect additional molecular genetic findings that may be incorporated into the World Health Organization classification system.

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