BACKGROUND:
Somatic mutations of codons 515 and 505 in exon 10 of the “myeloproliferative leukemia virus oncogene” (MPL) represent clonal markers in essential thrombocytemia (ET) and primary myelofibrosis (PMF), and serve as WHO major criteria for the diagnosis of these diseases. MPL codon 515 (W515) mutations are found in an estimated 3-4% of patients with ET and 7% of patients with PMF, including approximately 8.5% and 13% of JAK2 V617F-negative ET and PMF patients. In addition, MPL W515 mutations have been detected in patients who fall within the provisional WHO category of refractory anemia with ring sideroblasts associated with marked thrombocytosis (RARS-T).

A germline mutation in MPL codon 505 (S505N) was first identified in hereditary thrombocytemia but has also been reported to be somatic in both ET and PMF.

MPL is located at chromosome 1p34 and encodes for the thrombopoietin receptor. MPL exon W515 and S505N mutations appear to result in ligand independent activation of the thrombopoietin receptor and its downstream cell signaling pathways.

MPL W515/S505N MUTATION ANALYSIS:
MPL W515/S505N Mutation Analysis can be ordered separately or as part of our myeloproliferative neoplasm suite of tests. When ordered as part of a reflex panel, if ET or PMF are suspected, patients in whom JAK2 V617F mutations are not detected will automatically undergo CALR. If CALR mutations are not detected, they will automatically undergo MPL W515/S505N. MPL W515 and S505N analysis will detect the MPL W515L/K/A/R mutations, as well as variants present in these and other exon 10 codons.

MPL W515/S505N mutation analysis can also be ordered in patients in whom hereditary thrombocytemia is suspected or in family members of individuals with hereditary thrombocytemia in whom a germline mutation has been identified.

REASONS FOR REFERRAL:
• Diagnosis of essential thrombocytemia and primary myelofibrosis.
• Diagnosis of hereditary thrombocytemia.

METHOD:
MPL W515/S505N mutations are detected and characterized by PCR amplification and direct sequencing of the coding and junctional regions of MPL exon 10 in the absence and presence of a probe that suppresses amplification of wild-type MPL codon 515.

LIMITATIONS:
The lower limit of detection of the assay is approximately 2% (allele burden) for MPL codon 515 and approximately 20% for all other MPL exon 10 codons and splice junctions.
REFERENCE INTERVAL:
Somatic mutations are reported as mutation detected or mutation not detected. Germline mutations are reported as heterozygous or not detected. All sequence variations are reported using standard nomenclature.

SPECIMEN REQUIREMENTS:
3-5 ml EDTA (lavender top) whole blood or 2-5 ml EDTA bone marrow aspirate or DNA, high quality, ≥500ng at 25 ng/ul

SHIPPING REQUIREMENTS:
Place the room temperature specimen and requisition in plastic bags, seal and insert in a Styrofoam container. Seal the Styrofoam container, place in a sturdy cardboard box and tape securely. Ship the package in compliance with your overnight carrier guidelines. Address package to:

Client Services/Molecular Oncology Laboratory
BloodCenter of Wisconsin
638 N. 18th Street
Milwaukee, WI 53233
800-245-3117, ext. 6250

TURNAROUND TIME: 14 days

CPT CODES: 81403

REFLEX ORDERING:
MPN (Myeloproliferative Neoplasms) Reflex - ET/PMF
JAK2 V617F Mutation Analysis  CPT Codes: 81270  Turnaround Time: 5-7 days
CALR Mutation Analysis (if indicated)  CPT Codes: 81479  Turnaround Time: additional 5-7 days
MPL 505/515 Mutation Analysis (if indicated)  CPT Codes: 81403  Turnaround Time: additional 14 days

REFERENCES: