BACKGROUND:
Somatic mutations in exon 12 of the Janus Kinase 2 gene (JAK2) are found in approximately 2-3% of patients with polycythemia vera (PV). JAK2 exon 12 mutations represent clonal markers in PV, and serve as a WHO major criterion for the diagnosis of this disorder. Mutations predominantly cluster within the region of codons 537 - 544.

JAK2 is located on chromosome 9q24 and encodes for "Tyrosine-protein kinase JAK2" (JAK-2), an intracellular tyrosine kinase associated with the cytoplasmic domains of type 1 and type 2 cytokine receptors. Exon 12 is the first encoding exon of the autoinhibitory JH2 pseudokinase domain. Mutations in exon 12 are predicted to result in a loss of normal autoinhibition, producing cytokine independent activation of JAK-2 and its downstream cell signaling pathways.

JAK2 EXON 12 MUTATION ANALYSIS:
This analysis can also be ordered separately or as a reflex test as part of our myeloproliferative neoplasm suite of tests. When ordered as a reflex test, JAK2 exon 12 sequencing will be performed for patients suspected of having polycythemia vera in whom a JAK2 V617F mutation is not detected.

REASONS FOR REFERRAL:
• Diagnosis of polycythemia vera.

METHOD:
JAK2 exon 12 mutations are detected and characterized by a combination of PCR amplification, fragment analysis, and direct sequencing of the coding and junctional regions of the exon.

LIMITATIONS:
The lower limit of detection of the assay is approximately 20%. The assay is expected to detect >99% of somatic variants within the JAK2 exon 12 coding and junctional regions that are present at an allele burden of ~ 20% or greater.

REFERENCE INTERVAL:
Mutation detected or mutation not detected. Sequence variations are reported using standard nomenclature.
SPECIMEN REQUIREMENTS:
3-5 ml EDTA (lavender top) whole blood or EDTA bone marrow

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: 10-14 days

CPT CODES: 81403

REFLEX ORDERING:
MPN (Myeloproliferative Neoplasms) Reflex - PV
  JAK2 V617F Mutation Analysis CPT Codes: 81270 Turnaround Time: 5-7 days
  JAK2 Exon 12 Mutation Analysis (if indicated) CPT Codes: 81403 Turnaround Time: additional 10-14 days

REFERENCES: