BACKGROUND:
RUNX1, also known as AML1, encodes the runt-related transcription factor 1 (core-binding factor subunit alpha-2). RUNX1 is located on chromosome 21 and comprises 8 exons. Somatic RUNX1 mutations are found in neoplastic cells from approximately 15% of patients with myelodysplastic syndromes (MDS), and approximately 13% of patients with acute myeloid leukemia (AML). In AML subtype FAB M0 the prevalence of RUNX1 mutations is as high are 40% or greater. In contrast to other AML subtypes, mutations in M0 are frequently biallelic, representing over 50% of cases. Mutations are chiefly distributed throughout exons 3 – 8. Frameshift and in-frame insertions and deletions, missense, nonsense, and splice site mutations have been reported. RUNX1 mutations appear to be associated with an adverse prognosis in MDS and de novo non-M3 AML. In addition, somatic RUNX1 mutations are clonal markers that can support the diagnosis of MDS.

REASONS FOR REFERRAL:
Risk stratification of patients with MDS or AML.

METHOD:
RUNX1 mutations are detected and characterized by PCR amplification, and direct sequencing of the coding and junctional regions of RUNX1 exons 1 - 8.

LIMITATIONS:
The lower limit of detection of the assay is approximately 20% allele proportion. The assay is expected to detect >99% of variants within RUNX1 exons 1 - 8 that are present at an allele proportion of approximately 20% or greater.

REFERENCE INTERVAL:
Somatic mutations are reported as mutation detected or mutation 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

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: 5-10 days

CPT CODES: 81479

REFERENCES:
- Chen CY et al, RUNX1 gene mutation in primary myelodysplastic syndrome—the mutation can be detected early at diagnosis or acquired during disease progression and is associated with poor outcome. (2007) British Journal of Haematology 139, 405-14.
- Christiansen DH et al, Mutations of AML1 are common in therapy-related myelodysplasia following therapy with alkylating agents and are significantly associated with deletion or loss of chromosome arm 7q and with subsequent leukemic transformation. (2004) Blood 104, 1474-81.