## Condition Description

Multiple epiphyseal dysplasia is a group of skeletal disorders with heterogeneous genetic causes. MED has seven subtypes with a continuum of clinical severity among these types. Clinical and radiographic features continue to be used reliably to assign patients to this general disease category. Identification of the precise genetic defect is important, however, to permit carrier testing and early prenatal diagnosis. Molecular analysis is likely to expand the clinical spectrum of MED and may also provide data relevant to prognosis and future therapeutic intervention. The overall incidence of MED is estimated to be 1 in 10,000 births. Although the phenotype range is broad, MED is mainly characterized with short stature and early-onset osteoarthrosis. Radiographic findings for MED show a generalized abnormality of epiphyseal ossification without significant vertebral involvement. MED can be inherited in an autosomal dominant or autosomal recessive manner. The autosomal recessive form of MED includes features such as club foot and bilateral double-layered patellae.

### References:

- GeneReviews

### Genes

- COL2A1
- COL9A1
- COL9A2
- COL9A3
- COMP
- MATN3
- SLC26A2

### Indications

This test is indicated for individuals with:

- Short stature and early-onset osteoarthrosis.
- An abnormal radiographic findings show a generalized abnormality of epiphyseal ossification without significant vertebral involvement.

### Methodology

**Next Generation Sequencing:** In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

### Detection

**Clinical Sensitivity:** 80%-90%. Pathogenic variants in the promoter region, some pathogenic variants in the introns and other regulatory element pathogenic variants cannot be detected by this analysis. Large deletions will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Analytical Sensitivity:** ~99%

### Specimen Requirements

Submit only 1 of the following specimen types

**Type: Whole Blood**

Specimen Requirements:

- In EDTA (purple top) tube:
  - Infants (2 years): 3-5 ml
  - Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

Specimen Requirements:
In microtainer: 60 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

**Special Instructions**

Radiographic results can help interpretation.

**Related Tests**

- Multiple Epiphyseal Dysplasia: Deletion/Duplication Panel