**Condition Description**

Congenital hypothyroidism occurs when the thyroid gland fails to develop or function properly. In 80-85% of cases, the thyroid gland is absent (agenesis), ectopically located, and/or severely reduced in size (hypoplasia) [1]. In the remaining cases, a normal-sized or enlarged thyroid gland is present, but production of thyroid hormones is decreased or absent. If treatment begins in the first month after birth, infants usually develop normally. However, if thyroid hormone therapy is not initiated within the first two months of life, congenital hypothyroidism can cause severe neurological, mental, and motor damage (cretinism). In the United States and many other countries, all newborns are tested for congenital hypothyroidism.

Studies have shown that 2% of congenital hypothyroidism patients with thyroid dysgenesis have a positive familial history [2]. A segregation analysis led to the conclusion that thyroid developmental abnormalities are compatible with an autosomal dominant mode of inheritance with a low penetrance [3]. Mutations in many genes are known to cause congenital hypothyroidism. Multiple affected individuals have been shown to be heterozygous for mutations in the Paired Box Gene 8 (PAX8 2q12-q14), including individuals with positive family histories [4-8].

**References:**

**Genes**

**PAX8**

**Indications**

This test is indicated for:

- Confirmation of a clinical/biochemical diagnosis of congenital hypothyroidism.

**Methodology**

PCR amplification of 11 exons contained in the PAX8 gene is performed on the patient's genomic DNA. Direct sequencing of amplification products is performed in both forward and reverse directions using automated fluorescence dideoxy sequencing methods. The patient's gene sequences are then compared to a normal reference sequence. Sequence variations are classified as mutations, benign variants unrelated to disease, or variations of unknown clinical significance. Variants of unknown clinical significance may require further studies of the patient and/or family members. This assay does not interrogate the promoter region, deep intronic regions, or other regulatory elements, and does not detect large deletions.

**Detection**

Clinical Sensitivity: unknown. Mutations in the promoter region, some mutations in the introns, other regulatory element mutations, and large deletions will not be detected by this analysis.

Analytical Sensitivity: ~99%. Results of molecular analysis should be interpreted in the context of the patient's biochemical phenotype.

**Specimen Requirements**

Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**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: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Special Instructions**

Please submit copies of diagnostic biochemical test results along with the sample. Contact the laboratory if further information is needed.

**Related Tests**

- [Known Mutation Analysis (KM)](#) is available to family members if mutations are identified by sequencing.
- Prenatal Custom Diagnostics is available to couples who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.