Anophthalmia/Microphthalmia/Anterior Segment Dysgenesis/Anomaly: Sequencing Panel

**Test Code:** MM139  
**Turnaround time:** 6 weeks  
**CPT Codes:** 81404 x2, 81479 x1

### Condition Description

Anophthalmia generally refers to an absence of the globe while the eyelids, conjunctiva, and lacrimal glands remain. Microphthalmia is a heterogeneous group of malformations with reduction in the size of the eyeball that is anatomically intact with only axial length reduction (simple form), or can also include anterior segment dysgenesis (complex form). Both anophthalmia and microphthalmia can occur as isolated or syndromic and can be bilateral or unilateral. Anterior segment dysgenesis generally refers to a complex spectrum of anomalies such as Axenfeld-Rieger anomaly and Peters anomaly where axial length may not be severely compromised. Syndromic forms can include Fraser syndrome, microphthalmia with linear skin defects, and Manitoba oculotrichoanal syndrome (MOTA).

### References:
- OMIM
- GeneReviews

### Genes

- B3GLCT
- BCCOR
- BMP4
- COL4A1
- CYP1B1
- FOXC1
- FOXE3
- FRAS1
- FREM1
- FREM2
- GRIP1
- HCCS
- MFRP
- NDP
- OTX2
- PAX6
- PITX2
- PITX3
- SMOC1
- SOX2
- STRA6
- VAX1
- VSX2

### Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of anophthalmia, microphthalmia, or anterior segment dysgenesis/anomaly.
- Carrier testing in adults with a family history of anophthalmia, microphthalmia, or anterior segment dysgenesis/anomaly.

### 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:** Unknown. Pathogenic variants in the promoter region, some pathogenic variants in the introns and other regulatory elements 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: DNA, Isolated

**Specimen Requirements:**
- Microtainer
- 8µg
- Isolation using the PerkinElmer™Chemagen™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

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

#### Type: Whole Blood (EDTA)

**Specimen Requirements:**
- EDTA (Purple Top)
- Infants and Young Children (2 years of age to 10 years old): 3-5 ml
- Older Children & Adults: 5-10 ml

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Autopsy: 2-3 ml unclotted cord or cardiac blood

**Specimen Collection and Shipping:**
Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

**Type: Saliva**

**Specimen Requirements:**
Oragene™ Saliva Collection Kit
Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

**Specimen Collection and Shipping:**
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

**Special Instructions**
Please include fundus photographs, electroretinogram (ERG) findings, visual field findings, and visual acuity, if available, for expert review and clinical correlation with test results.

**Related Tests**
- Eye Disorders: Comprehensive Sequencing and Deletion/Duplication Panels
- Anophthalmia/Microphthalmia/Anterior Segment Dysgenesis/Anomaly: Deletion/Duplication Panel