

## Autosomal Recessive Polycystic Kidney Disease: *PKHD1* Gene Deletion/Duplication

**Test Code:** WG

**Turnaround time:** 2 weeks

**CPT Codes:** 81228 x1

### Condition Description

The majority of individuals with autosomal recessive polycystic kidney disease (ARPKD) present in the neonatal period with enlarged echogenic kidneys. Clinical diagnostic criteria of autosomal recessive polycystic kidney disease (ARPKD) are:

Typical findings on renal imaging

AND

One or more of the following:

- Clinical/laboratory signs of hepatic fibrosis that leads to portal hypertension and may be manifested by hepato-splenomegaly and/or esophageal varices
- Hepatic pathology demonstrating a developmental ductal plate abnormality
- Absence of renal cysts in both parents, as demonstrated by ultrasound examination
- Pathoanatomical proof of ARPKD in an affected sib
- Parental consanguinity suggesting autosomal recessive inheritance

At initial presentation, approximately 45% of infants have liver abnormalities, including hepatomegaly, dilated intrahepatic biliary ducts, and increased echogenicity. Pulmonary hypoplasia resulting from oligohydramnios occurs in a number of affected infants. Approximately 30% of affected neonates die, primarily of respiratory insufficiency. More than 50% of affected children progress to end-stage renal disease (ESRD), usually in the first decade of life. With neonatal respiratory support and renal replacement therapies, the ten-year survival of those who live beyond the first year of life has improved to 82%. Fifteen-year survival is estimated to be 67%-79%. A minority of individuals present as older children, usually with hepatosplenomegaly as the presenting feature.

*PKHD1* (6p21.1-p12) is the only gene known to be associated with ARPKD. Mutation detection rates for sequence analysis of the coding region and flanking intronic regions have not been reported; they are expected to be as high or higher than those reported for mutation scanning analyses. Mutation scanning by denaturing high-performance liquid chromatography (DHPLC) has demonstrated an overall mutation detection rate of 82%-85% when diagnostic criteria of ARPKD are met either prenatally or postnatally.

The incidence of ARPKD is estimated at 1:10,000 to 1:40,000. The true incidence may be underestimated because children may die in the neonatal period without a definitive diagnosis, and previously undetected young adults are being diagnosed by molecular genetic testing. The carrier frequency for a *PKHD1* mutation in the general population is estimated to be 1:70.

For patients with suspected ARPKD, sequence analysis is recommended as the first step in mutation identification. For patients in whom mutations are not identified by full gene sequencing, deletion/duplication analysis is appropriate.

[Click here](#) for the GeneTests summary on this condition.

### Genes

[PKHD1](#)

### Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of ARPKD in individuals who have tested negative for sequence analysis
- Carrier testing in adults with a family history of ARPKD who have tested negative for sequence analysis

### Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region.

### Detection

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

### Specimen Requirements

**Submit only 1 of the following specimen types**

### Type: DNA, Isolated

#### Specimen Requirements:

Microtainer

3µg

Isolation using the Perkin Elmer™ 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

Autopsy: 2-3 ml unclotted cord or cardiac blood

#### Specimen Collection and Shipping:

Ship sample at room temperature for receipt at EGL within 72 hours of collection. Do not freeze.

### Special Instructions

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

### Related Tests

- Sequencing analysis of the *PKHD1* gene is available (WF) and is required before deletion/duplication analysis.
- Prenatal testing 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.