Tubulo-interstitial Nephropathy:
Familial Juvenile Hyperuricemic Nephropathy (FJHN) & Medullary Cystic Disease Type 2 (MCKD)
Uromodulin (UMOD) and Renin (REN); OMIM 191845 and 179820

INTRODUCTION
Autosomal dominant tubulo-interstitial kidney disease refers to disorders characterised by slowly progressive chronic tubulo-interstitial kidney disease leading to end-stage renal disease (ESRD).

Subtypes include:
- **UMOD-associated kidney disease** (this is the collective term for the following conditions: familial juvenile hyperuricemic nephropathy type 1 (FJHN1); medullary cystic kidney disease type 2 (MCKD2); and uromodulin storage disease). Clinical findings for FJHN1 include hyperuricemia and gout usually in the teenage years, tubulo-interstitial kidney disease and ESRD. Clinical findings for MCKD2 additionally include development of kidney cysts, however FJHN1 and MCKD2 are widely considered variants of the same condition.
- **Familial Juvenile Hyperuricemic Nephropathy Type 2 (FJHN2)** (REN-associated kidney disease). In addition to the clinical features seen in FJHN1, affected individuals usually develop hypoproliferative anemia with low haemoglobin concentrations during childhood.

TESTING AND REFERRALS
All samples should be accompanied by a completed referral form (click here)

Diagnostic:
- Clinically affected patients (see strategy below). UK diagnostic referrals are accepted from Clinical Genetics, Endocrinology, Renal Physicians and Consultants from other relevant specialties
- Carrier/Presymptomatic/Test for Familial Mutation:
  - Relatives of clinically affected patients/Patients at risk of developing FJHN or MCKD2. Pathogenic mutation has been identified in **UMOD** or **REN** in a family member
  - Presymptomatic referrals should ideally be referred through/in collaboration with Clinical Genetics departments.

Prenatal: Prenatal testing referrals would only be accepted from Clinical Genetics.

STRATEGY
Molecular analysis of **UMOD** and **REN** is recommended in patients who meet the following criteria:
- a) low urate excretion or
- b) hyperuricemia and at least one of the following
c) medullary cysts  d) gout  e) anaemia in childhood  f) family history of tubulointerstitial kidney disease
g) polyuria, plus mildly elevated serum creatinine concentration  h) renal impairment (tubulointerstitial kidney disease)

Once a pathogenic mutation has been identified in an individual, testing for that variant is available to other at-risk or affected family members.

TECHNICAL INFORMATION
- Mutation screening in diagnostic referrals is undertaken by fluorescent sequencing of the entire coding region and intron/exon boundaries of the **UMOD** and **REN** genes (exons 2-11 and 1-10 respectively).
- Analytical sensitivity is expected to exceed 95%. Clinical sensitivity depends on definitive diagnosis.

TARGET REPORTING TIMES
Diagnostic test: 40 days
Presymptomatic/Familial Mutation test: 10 days

N.B. Details are correct for the date of printing only – last updated 24/1/2013