Summary of ESPN Research Project,
initiated by the ESPN WG CAKUT/UTI/Bladder dysfunction

Congenital anomalies of the kidney and the urinary tract (CAKUT) are one of the most frequent causes of chronic renal insufficiency and end-stage renal disease (ESRD) in children in Europe with significant ante- and perinatal mortality in severe bilateral cases. The socioeconomical burden is high. Though many CAKUT cases are sporadic, familial clustering is also common, suggesting that the pathogenesis is influenced by genetic factors. The results of genetic research have a major impact both for the understanding of the underlying pathophysiology as for clinical medicine. It is becoming increasingly evident that mutations in the same gene can cause very different phenotypes that range from single organ involvement starting in adolescence or even adulthood to lethal early embryonic multisystemic manifestations. Mutations in several renal developmental genes (including *PAX2*, *RET*, *HNF1B*, *BMP4* and many others) have been identified so far to be causative in a subset of children with congenital anomalies of the kidney and urinary tract. However, the mutation detection rate in most genes is rather low and the genetic basis in many children remains unidentified. New strategies involving next generation sequencing (NGS) techniques and whole exome and whole genome sequencing (WES, WGS) will have to be established in order to improve genetic testing in these children. The planned European Registry of Familial CAKUT Cases (ERFCC) will be dedicated to a systematic collection of clinical data in a multinational approach. Major intention is on one hand the collection of epidemiological and clinical data including family pedigrees, the results of renal imaging and funcional testing and the manifestation of extrarenal symptoms and one the other hand the establishment of a profound basis for genetic studies in this group of complex disorders of kidneys and urinary tract, leading to ESRD in many children and young adults. The application of new sequencing methods will revolutionize diagnostic algorithms and the constantly reducing costs per sample will provide a feasability for systematic genetic testing in many European countries. We believe that a focus on familial cases will largely enhance the likelihood to identify new genetic causes in CAKUT patients. We expect to generate a comprehensive collection of familial CAKUT cases throughout Europe by the means of this Registry initiative and the multinational approach of experts in the field strengthens the outcome of the study.