Multiple endocrine neoplasia type 1 (MEN 1) is a familial cancer syndrome characterised by parathyroid hyperplasia, pituitary adenomas, and neuroendocrine tumours of the pancreas and duodenum. In 1997, the MEN1 tumour suppressor gene was identified, and since then numerous germline mutations have been reported to be distributed throughout the gene (PMID:15714081, PMID:10090472, PMID:16595707, PMID:17342152). These mutations include missense, nonsense, and frameshift mutations, as well as mutations potentially responsible for abnormal RNA splicing, and highlight the need to investigate the entire MEN1 gene when characterizing new MEN 1 families. Coding sequence mutations that may disrupt the MEN1 gene can be screened for by direct sequence analysis of PCR-amplified fragments encompassing each of the exons, including flanking 5’(20bp) and 3’(10bp) intronic sequence, comprising the coding region of the MEN1 gene. Less common deleterious mutations consisting of genomic rearrangements of the MEN1 gene may be detected by the Multiplex Ligation-dependent Probe Amplification method (MLPA)5, which may be confirmed by LR-PCR, (unless the genomic deletion occurs at the extreme 5’ or 3’ ends of the gene), or by gene dosage determination (e.g. using a
MULTIPLE ENDOCRINE NEOPLASIA: TYPE 1

MLPA copy number analysis. All variants interpreted as either ACMG category 1, 2, or 3 (pathogenic, likely pathogenic, VUS; PMID: 25741868) are confirmed using Sanger sequencing, MLPA, or other assays. ACMG category 4 and 5 variants (likely benign, benign) are not reported, but are available upon request. This assay has been validated at a level of sensitivity equivalent to the Sanger sequencing and standard copy number analysis (>99%; PMID: 27376475).

Critical Information:
Pedigree required.

Storage and Shipment:
Must be received within 5 days of collection, shipped at room temperature by courier/overnight delivery.

Test Schedule:
As required,
Monday to Friday 0800-1600 hours