INTRODUCTION
Painful channelopathies are a phenotypically and genetically heterogeneous group of autosomal dominant or sporadic disorders, which include small-fibre neuropathy, inherited erythromelalgia, familial episodic pain syndrome & paroxysmal extreme pain disorder. These disorders have been associated with gain of function mutations in the SCN9A, SCN10A, SCN11A or TRPA1 genes, which encode sodium ion / cation channels expressed in nociceptors. Pathogenic mutations in these genes are reported to account for 9-29% of patients with small-fibre neuropathy. Mutations in the coding region and exon-intron boundaries of SCN9A are reported to account for approx. 62% of paroxysmal extreme pain disorder, and appear to account for the majority of inherited erythromelalgia. The proportion of cases of familial episodic pain syndrome due to mutations in these genes is unknown.

TESTING
Diagnostic: Clinically affected patients
Presymptomatic: Relatives of clinically affected patients

REFERRALS
- From Hospital Consultants, mainly Neurology or Clinical Genetics
- Presymptomatic referrals are only accepted from Clinical Genetics

STRATEGY
- Sequencing of SCN9A, SCN10A, SCN11A and TRPA1 as a gene panel, with all results reported together.
- Presymptomatic testing for the known familial pathogenic variant(s)

TECHNICAL INFORMATION
- Next generation sequencing of the coding region and exon-intron boundaries of SCN9A, SCN10A, SCN11A and TRPA1, covered to a minimum of 30 reads or by Sanger sequencing. All potentially pathogenic variants are confirmed by Sanger sequencing.
- Sanger sequencing of the relevant region(s) for presymptomatic testing.

TARGET REPORTING TIMES
Diagnostic test: 40 working days
Presymptomatic test: 10 working days

N.B Details are correct for the date of printing only – last updated 15/06/2015