Scheme 5B – Interpretative HFE Genotyping and Hereditary Haemochromatosis

General Comments Scenarios 1 and 2/2023 **Distributed April 2023**

Case Number 1:
Janet Butler, Female, DOB: 27/06/1993, Unique Identifier: 17011971AE
Patient's Address: 15A Albert Court, Georgetown, GE79
Referring GP: Dr Alice Hope, "The Hope Surgery", 17 Victoria Ave, Georgetown GE79

Janet Butler was forwarded for HFE genetic testing as part of family testing. Her mother was previously tested as homozygous for the p.Cys282Tyr variant in the HFE gene. Janet has tested as compound heterozygous for the p.Cys282Tyr and p.His63 Asp variants in the HFE gene. Her serum Transferrin Saturation is 30%, with a ferritin level of 250µg/L. Her clinical details noted include fatty liver disease. Please prepare an interpretative report for Janet Butler with clear information on her risk of developing clinical Haemochromatosis, and any other actions that maybe required.

Case Number 2:
Jack Forde, Male, DOB: 17/03/1959, Unique identifier 15121837BF
Patients address: 30 Kenilworth Drive, Shepard's Hill, B23
Referring GP: Dr James Lee, "Main St Clinic", 12 Main St, Shepard's Hill B23

Clinical scenario
Mr Forde has tested homozygous for the p.Cys282Tyr variant in the HFE gene. He has a persistently high serum ferritin 500µg/L and an elevated fasting Transferrin Saturation of 60% which was confirmed upon repeat testing. He has clinical signs and symptoms of arthritis in both of his hands. Mr Forde is a widower and has three children: Matthew age 17, Isobel aged 15, and John age 9. His GP has contacted the laboratory and wishes to know what are the risks for Mr Forde's children and what further actions are necessary in terms of family testing. Please prepare an interpretative report for Mr Forde and also provide the GP with the information that he requested and any other considerations that may be required for further testing.

General feedback/advice from the assessors:

1. A few labs are still referring to the genotypes as CC, YY etc. rather than using the accepted HGVS nomenclature (some seem to use both as well as outdated HGVS nomenclature too [H63D etc.]).
2. The reasoning behind scoring for the compound heterozygote case (5B 01/2023):
   2.1. C282Y/H63D compound heterozygote = low risk for developing clinical signs of haemochromatosis.
   2.2. C282Y/H63D compound heterozygote & co-morbidity e.g. Fatty liver disease = Mild/moderate risk for developing clinical signs of haemochromatosis.