Scheme 5B – Interpretative HFE Genotyping and Hereditary Haemochromatosis

General Comments Scenarios 1 and 2 /2019 **Distributed May 2019**

Scenario 1

In this scenario the patient known to be homozygous for the p.C282Y mutation. Reports must state that this genotype is consistent with a diagnosis of HFE-related HH in the presence of raised iron indices. It is useful to acknowledge that serum ferritin and tSat are still outstanding. Specialist referral should be advised if iron indices indicate iron overload and annual monitoring of serum ferritin should be advised.

Information on testing for other family members should include first degree relatives (particularly siblings) to be advised of the benefits of screening. Reports could include the information that the patients offspring will be obligate carriers of C282Y, however, screening of children <16 years of age should in most cases be deferred until they reach 16.

A total of 21 penalty points were awarded for this scenario.

Number of Penalty Points	Number of Participants
0	11
1	3
2	5
3	0
4	2

Scenario 2

In this scenario the patient is identified as a compound heterozygote for C282Y (c.845G>A, p.(Cys282Tyr)) and H63D (c.187C>G p.(His63Asp)) which gives her an increased risk of developing HH (higher than general population but lower than C282Y homozygosity). The submitted reports dealt with this risk in variety of ways, but some overstated the risk associated with this genotype. A number of penalty points were also awarded in this scenario for inadequate advice about family screening.

A total of 18 penalty points were awarded for this scenario.

Number of Penalty Points	Number of Participants
0	10
1	7
2	2
3	1
4	1

Report Comment
Some of the reports were excellent. These were the ones that

1. Summarised the information provided
2. Explained what the risks were to family members and who needed to be screened and why
3. What further biochemical tests were needed and what actions would need to be taken regarding monitoring and referral to an expert
4. These reports also used the correct HGVS nomenclature
5. They also picked up on the points that some of the information was not currently available but in the pipeline and certain other results were borderline

It is important to consider that when a report is being written the person receiving the report will probably not be an expert in haemochromatosis and this may be the first time that they have had to deal with a patient with haemochromatosis. It is also key in writing a report that there should be sufficient information for the patient to understand the implications for his or her relatives as it may be them who are explaining why other family members may need to have a blood or genetic test.

The nomenclature used should be consistent throughout the report. HGVS-based nomenclature is preferable - C282Y or p.(Cys282Tyr) are the terms that are clearly understood by requestors, and most likely to be used in relevant literature or guidelines. The use of YY, HD based nomenclature etc should be avoided – or if used, an explanatory footnote is advised. As genetic reports, these should ideally include a description of the variant at nucleotide level and the reference sequence – this information could potentially be included in a footnote so that the message of the report is clear and concise.