Scheme 5B – Interpretative HFE Genotyping and Hereditary Haemochromatosis

General Comments Scenarios 3 & 4 /2015 **Distributed June 2015**

General comments

The overall standard of reports was good with very few clerical or typographical errors noted. Some reports still include only minimal statements about the genotyping method used, without supplying specific information (e.g. a reference, or other information about primer or probe sequences, or specificity and sensitivity of the method) and therefore the statement may be of little use. Once again less than half of the labs submitting reports included full HGVS nomenclature and have received a comment on this as in previous years.

Participating laboratories may be interested to know of recently published best practice guidelines for the molecular genetic diagnosis of hereditary hemochromatosis from the European Molecular Quality Network (EMQN): Porto et al. European Journal of Human Genetics (2015), 1–17

Scenario 3

This scenario described a 51 year old male with raised ferritin (serum ferritin concentration 500 µg/L) and a non-fasting transferrin saturation of 40%. Genetic testing had shown him to be homozygous for the H63D mutation, C282Y not detected. The risk of iron overload in relation to H63D homozygosity is low. The genotype may explain the patient's raised ferritin concentration but a Tsat under 45% is suggestive that the raised ferritin may not be related to iron overload but may have another cause requiring further investigation. Some reports suggested repeating testing ferritin on a fasting sample; however fasting is not relevant to serum ferritin concentration, but to serum iron and transferrin saturation. Some reports recommended regular monitoring of ferritin levels but did not suggest that other causes of the raised ferritin (e.g. infection, inflammatory disorders or malignancy for example) should be investigated. In summary relatively few labs clearly gave the key advice that although the genotype might contribute in part to increased ferritin, the priority is to identify the major cause which is likely to be more serious, i.e. first do no harm by not allowing the genotype or haemochromatosis to distract the GP.

Scenario 4

This scenario concerned a patient whose brother is a HFE compound heterozygote. The patient was found to be heterozygous for H63D with C282Y not detected.
The value of this test result is in excluding risk and this was not clear in many reports. There is no need to assume that the brother has anything other than a genotype. It would have been helpful to clarify that only the brother's genotype indicates family testing. Several reports correctly indicated the minimal risk associated with the patients genotype but then went on to suggest that iron indices should be tested. The assessors agreed that this was contradictory advice and unwarranted, a penalty point was awarded accordingly.

On a more general note, reports should be more inclined towards sensible and economical advice that allows GPs to do as much as possible rather than covering every remote possibility with referrals.