Scheme 5B – Interpretative HFE Genotyping and Hereditary Haemochromatosis

General Comments Scenarios 3 and 4 /2021 **Distributed December 2021**

Report format

The laboratories that are using HGVS nomenclature are using it to various degrees. Comprehensive HGVS nomenclature includes the Sequence ID for both cDNA and Protein Reference sequences.

Case Number 3:

Amarjit Singh, male, D.O.B. 12/12/1988; Unique identifier 878 321 9000
Patient's address: 55 Marlborough Crescent, Farstone FL33 9YY
Referral from GP Dr Ian Greene, The Surgery, Main Road, Farstone, FL34 8EE

Amarjit has been diagnosed with diabetes and has had both hips replaced. His serum ferritin is 5000µg/l. The GP wanted to eliminate haemochromatosis as a possible explanation. The HFE genotype came back as normal. The p.C282Y mutation was absent. The GP wants to know whether there is any further action required to rule out other forms of inherited iron overload.

1. **A number of laboratories assumed that H63D analysis was performed and found to negative**
2. **Confirm the High Ferritin and Rule out a possible Acute Phase Response:** Repeat Ferritin and TS% to confirm Biochemical overload and/or to rule out Acute phase response (recent surgery).
3. **Rule out other possible secondary causes** of hyperferritinaemia. (Note: Amarjit has DM, which could also be indication of another different secondary cause of iron-overload).
4. **Proceed to specialist genetic testing:** with reference to Ethnicity in terms of rare HFE variants, other Primary Iron Metabolism Disorders (HJV, Ferroportin, and TFR2)
5. **Referral as per appropriate results**

Case Number 4:

Poric O'Brien, male, D.O.B. 16/5/1965; Unique identifier 867 534 3223
Patient's address: 8 Chestnut Villas, Nuneham NZ12 4RG
Referral from GP Dr Marie Ellory, The Nuneham Health Centre, Nuneham NZ12 7RR

Poric has seven siblings. He has had a zoom meeting with his GP because one of his sisters have been diagnosed with haemochromatosis. They have discussed the possibility of genetic testing and what the implications are for his children. The GP wants to know what blood samples are required and what tests would need doing, in what order the tests need to be done and who would need to be tested and how they would go about being tested.

1. **Sample types:**
   1.1. Serum for Ferritin & Transferrin saturation% (Biochemical Iron Indices)
   1.2. EDTA Plasma for HFE genotyping.
2. **Order of testing:**
   2.1. A routine laboratory investigation for haemochromatosis involves firstly the assessment of the biochemical Iron Indices followed by HFE genotyping.
   2.2. Not specifically stated if Poric's sister has a genetic or clinical diagnosis or Both. Knowledge of Poric's sister HFE status at this point can determine if HFE genotyping prioritised/precedes/ done concurrently with Biochemical Iron studies
3. **Genotyping & Biochemical Iron Indices Results:** Dictates Specialist referral
4. **Family Testing:**
   4.1. Adult offspring
   4.2. Siblings
   4.3. Partner/Spouse
   4.4. No testing in Minors
5. **Contact information for referral if different from Laboratory**