All Wales Medical Genomics Laboratory
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To whom it may concern,

RE: Requests for hereditary haemochromatosis genetic testing

HFE-related Hereditary Haemochromatosis (HH) causes iron overload which presents clinically as raised transferrin saturation and/or serum ferritin. The most common form of HH in people of North European ancestry is caused by a variant in the HFE gene, HFE:c.845G>A, p.(Cys282Tyr), also known as C282Y. HH caused by the HFE:c.845G>A, p.(Cys282Tyr) variant is an adult onset disorder with low penetrance that is inherited in an autosomal recessive pattern.

In accordance with the EMQN 2016 best practice guidelines for HH*, genetic testing for the HFE:c.845G>A, p.(Cys282Tyr) variant should be carried out in adult patients with raised transferrin saturation and/or serum ferritin, or in adult first degree relatives of a patient who is homozygous for the HFE: c.845G>A, p.(Cys282Tyr) variant.

In the absence of elevated iron indices or a family history of HH there is no evidence to support genetic testing for the HFE:c.845G>A, p.(Cys282Tyr) variant. Testing in minors is not normally recommended.

Testing is not recommended in relatives of a patient who has the HFE:c.187C>G, p.(His63Asp), also known as H63D.

Requests for HH genetic testing where the referral form doesn't clearly state that the patient meets the above criteria will not be accepted for testing.

To request genetic testing for Hereditary Hemochromatosis:

For diagnostic testing please complete a genetics request form** confirming:

- That the patient has raised transferrin saturation and/or serum ferritin
- That the patient is at least 18 years old†
- Name and location of the referring clinician

†If the patient is under the age of 18 and there is a clear clinical need (elevated iron indices or evidence of liver disease) requests can be accepted from haematology or clinical genetics.

For predictive testing (family history) please complete a genetics request** form confirming:

- The relationship to the patient of the family member with confirmed hereditary haemochromatosis (e.g. mother, father, sibling etc)
- That the affected family member is homozygous for the HFE:c.845G>A, p.(Cys282Tyr) variant
- That the patient is at least 18 years old
- Name and location of the referring clinician

If it is not possible to confirm the relationship or genotype of the affected family member the patient should be referred to clinical genetics.

Requests for predictive testing in patients who are under the age of 18 will not be accepted.

Any request where the details required above are not clearly stated on the referral form will not be accepted for testing. DNA from these samples will be extracted and stored.

Should you wish to discuss testing for hereditary haemochromatosis please contact the laboratory at Lab.genetics.cav@wales.nhs.uk.

*Porto *et al.* (2016) EMQN best practice guidelines for the molecular genetic diagnosis of hereditary hemochromatosis (HH). Eur J Hum Genet, 24(4):479-95. PMID 26153218
**Request forms are available from: https://medicalgenomicswales.co.uk/images/awmgsdownload/PurpleLabFormNonUKASaccredited.pdf