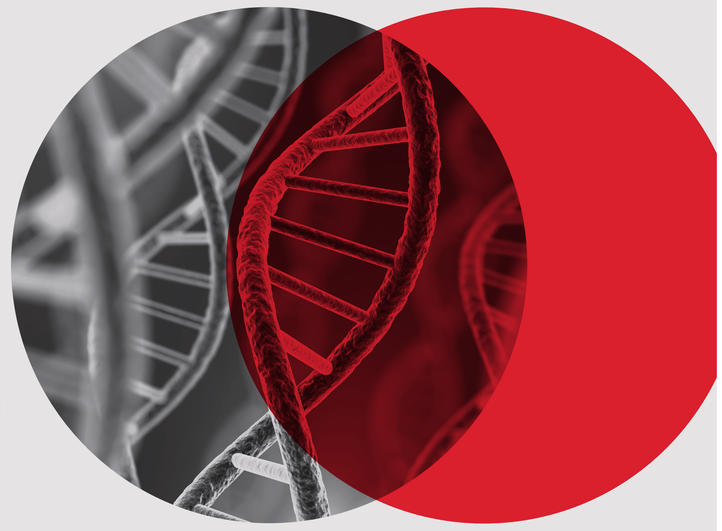
A Five-year Review: External Quality Assurance of Hereditary Haemochromatosis Testing



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Introduction

The hereditary haemochromatosis (HH) EQA has been offered by the RCPAQAP since 2003. The majority of participants are in Australia, with participants ranging from Hong Kong, India, New Zealand and Oman (Figure 1). HH is an autosomal recessive disorder that is associated with variants in the *HFE* gene and iron overload[1]. Three *HFE* gene variants (c.845G>A, c.187C>G and c.193A>T) have been characterised and associated with HH. For this EQA program, participants were provided with 8-10 DNA samples per year and are required test each sample for c.845G>A, c.187C>G and c.193A>T if performed in their laboratory. Here we report the overall results from 2014 to 2018. Participants were assessed according to the consensus values based on a target value obtained from reference and source laboratory results.

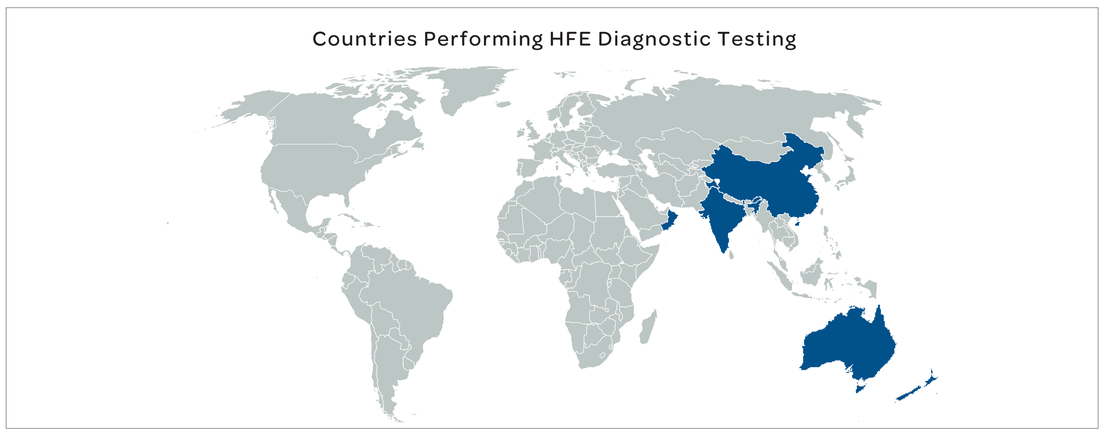

Figure 1: DNA samples were distributed to five different countries.

Methods

An EQA was developed to assess inter-laboratory performance on *HFE* genotyping. A total of 44 DNA samples were distributed to 37 laboratories during the years 2014-2018 (Figure 2). Participants were requested to report on the gene variant detected and the zygosity status in each sample tested.

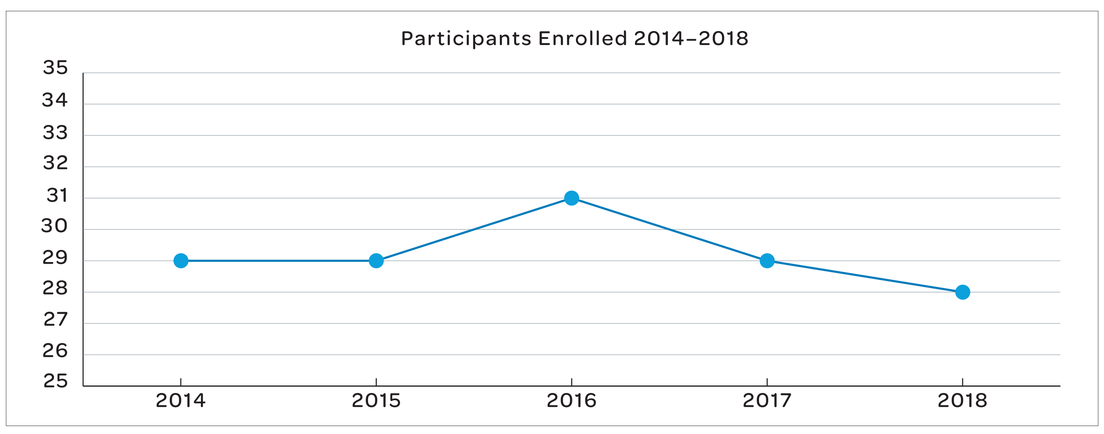

Figure 2: Total number of participants enrolled in the HH EQA during the years 2014-2018.

Different types of technology were used to perform the detection of variants in the *HFE* gene. From 2015, participants were requested to report the specific methodology used. The majority of participants used real-time PCR as their method of choice (Figure 3).

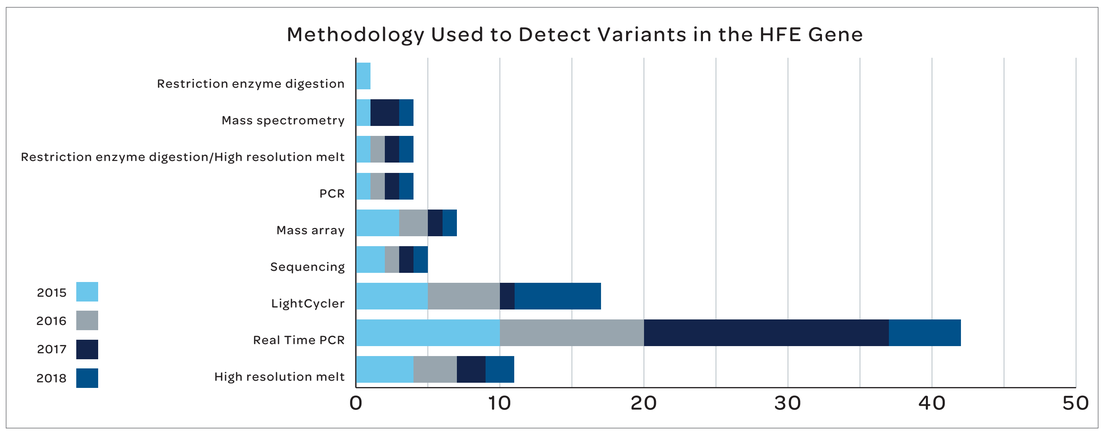

Figure 3: Methods employed by participants to perform *HFE* diagnostic testing.

Results

The EQA data from 2014-2018 are presented below (Figures 4, 5 & 6) and represent the levels of genotype reporting for the three *HFE* gene variants; c.845G>A, c.187C>G and c.193A>T.

Participant results were assessed as:

Concordant - if the participant's result matched the consensus result.

Discordant - for a participant result which does not match the consensus result or is incorrect and if the participant failed to obtain a result where one would be expected and no comparison could be made.

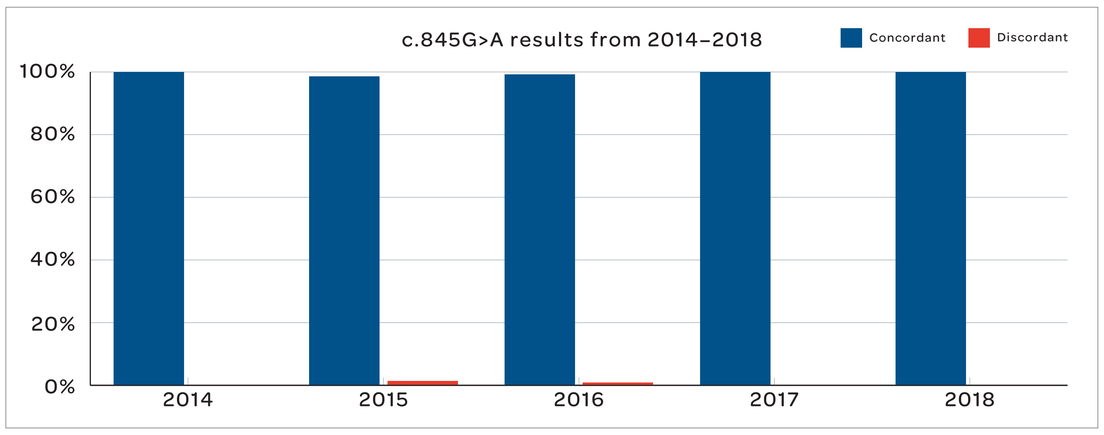

Figure 4: Assessment of participant results from 2014-2018 for the detection of NM_000410.3(HFE):c.845G>A (p.Cys282Tyr).

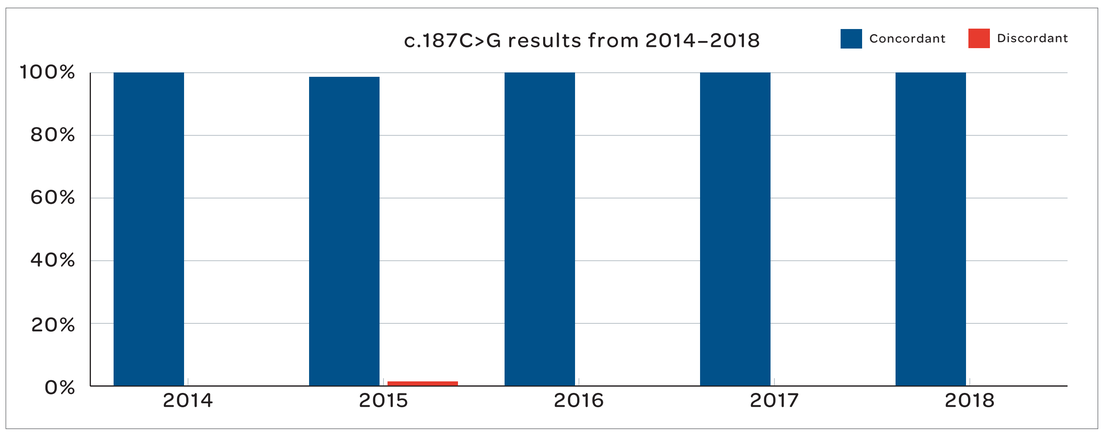

Figure 5: Assessment of participant results from 2014-2018 for the detection of NM_000410.3(HFE):c.187C>G (p.His63Asp).

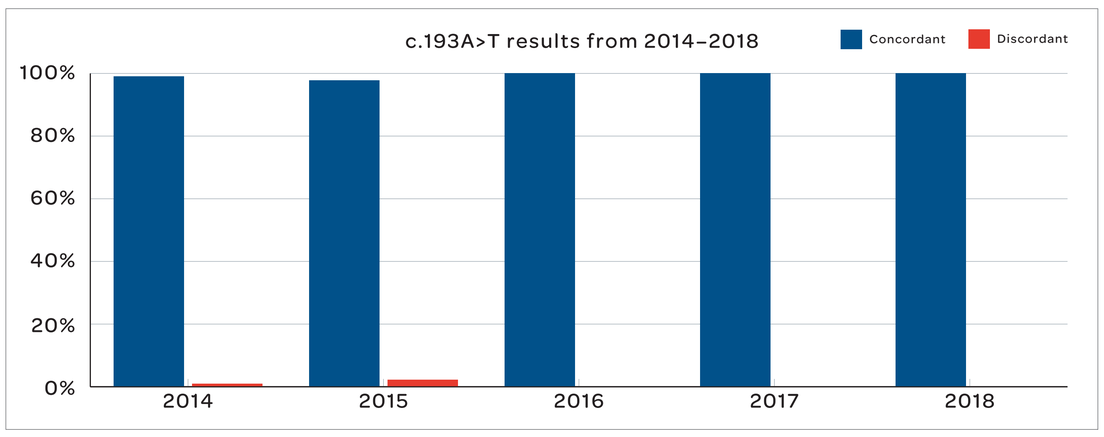

Figure 6: Assessment of participant results from 2014-2018 for the detection of NM_000410.3(HFE):c.193A>T (p.Ser65Cys).

Conclusion

The risk of iron overload is dependent on the type of variant detected. A homozygous c.845G>A, homozygous c.187C>G and compound heterozygote c.845G>A/c.187C>G variant have varying risks of iron overload which is associated with HH[1,2]. The significance of c.193A>T is currently unknown[1,2]. However, participants routinely perform this test if requested by the referring clinician. Participation in an EQA is essential to ensure that consistency of testing and reporting standards are maintained. This review has identified that over the last five years, participating laboratories have consistently produced good quality data for HH testing. Based on these data, patients are at a reduced risk of mis-diagnosis for HH.

Reference

1. Haemochromatosis.org.au. (2018). Genetics of haemochromatosis, Haemochromatosis Australia. Available at: https://haemochromatosis.org.au/genetics/ [Accessed 17 Aug. 2018].

2. Porto, G., Brissot, P., Swinkels, D., Zoller, H., Kamarainen, O., Patton, S., Alonso, I., Morris, M. and Keeney, S. (2018). EMQN best practice guidelines for the molecular genetic diagnosis of hereditary hemochromatosis (HH). https://www.nature.com/articles/ejhg2015128

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