Appendix D: Scenarios in which genetic testing for *HFE*-HH is not indicated

The following scenarios do not warrant genetic testing for *HFE*-HH:

- Screening the general population.
- Testing individuals of non-European descent for *HFE*-HH as the C282Y variant is exceedingly rare in the non-European population; thus, a negative *HFE*-HH genetic test has no clinical utility. See Appendix C: Epidemiology of HFE hemochromatosis for the prevalence of hereditary hemochromatosis in different populations. Non-European patients with evidence of iron overload (persistently high ferritin AND TSAT ≥45%) should be referred to a specialist.
- Patients with clinical findings (see Appendix B: Nonspecific signs and symptoms of extreme iron overload by organ) that are found in iron overload but who do not have a TSAT ≥45%.
- As *HFE*-HH is an adult-onset disorder, genetic testing is not generally indicated in children and so can be deferred until the child is able to exercise autonomy regarding decision making.[14,15]
- Parents of individuals homozygous for C282Y (i.e., C282Y;C282Y genotype) who do not themselves have hyperferritinemia and a TSAT ≥45%.
- First-degree relatives (parents, siblings and children) of individuals identified to be heterozygous for C282Y (whether C282Y/wild type or C282Y/H63D) who do not have hyperferritinemia and a TSAT ≥45%.
- First-degree relatives (parents, siblings and children) of individuals with non-C282Y *HFE* genotypes who do not themselves have hyperferritinemia and a TSAT ≥45%.[16]