Bristol Genetics Laboratory is a UKAS accredited medical laboratory No.9307.

North Bristol NHS Trust

R68 Huntington Disease – *HTT* gene

Contact details:
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Sample Required
See Sample requirements page at www.nbt.nhs.uk/genetics **for full details**

Samples should be accompanied by a FULLY completed request form (available as download at www.nbt.nhs.uk/genetics or from the laboratory).

Please include details of test, family history, address and postcode, NHS number, referring clinician and unit/hospital.

Consent and Storage:
All genetic testing requires consent. **It is the responsibility of the referring clinician to ensure that appropriate consent has been obtained.**

DNA is stored from **ALL** patients unless consent for this is specifically denied.

Stored samples may be used for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

Clinical Background and Genetics

- Huntington disease (HD) (OMIM 143100) is a progressive neurodegenerative disorder that is inherited in an autosomal dominant manner.
- Common symptoms include behavioural changes and psychosis, involuntary movements, chorea, rigidity, dementia and seizures.
- Death occurs on average 15-17 years after onset of symptoms, often due to heart disease or pneumonia. Severe, juvenile-onset cases have reduced life expectancy.
- HD is caused by an expansion of a CAG polyglutamine repeat tract in the first exon of the Huntingtin gene (*HTT*) at 4p16.3 (OMIM 613004).
- Normal individuals have alleles between 8 and 35 CAG repeats. A repeat size of 36 or greater is diagnostic for HD.
- The severity and age of onset of symptoms correlates strongly with the size of the CAG expansion. The average age of onset is 35-40 years. Alleles with 36 to 39 repeats are associated with later onset of symptoms.
- The repeat is unstable and can expand between generations causing a more severe presentation with earlier onset in the offspring of an affected individual (anticipation). HD shows a parent of origin effect with large increases in expansions occurring at paternal meiosis.

Service offered

- **Direct HD1/HD3 PCR** incorporates the CAG expansion and is used for accurate sizing of the triplet repeat – up to approximately 70 repeats.
- **Triplet primed PCR (TP-PCR)** is a test that indicates the absence or presence of an expansion, but cannot be used to determine the expansion size. It is used to distinguish true homozygous cases from cases where the expanded allele failed to amplify on the direct PCR.

National Genomics Test Directory R68: Huntington disease

Referrals

- **Diagnostic testing:** Molecular confirmation of a clinical diagnosis of HD. Requests are accepted from Clinical Geneticists and Consultant Neurologists. Diagnostic referrals from other specialisms may be accepted but must be accompanied by a completed consent form (available to print at the end of this document or obtainable from the Bristol Genetics Laboratory, Tel: 0117 414 6168).
- **Predictive testing:** For individuals with a family history of HD who request carrier testing. Requests are only accepted from Clinical Genetics after appropriate genetic counselling.
- **Prenatal testing:** For the foetus of a parent with a confirmed molecular diagnosis of HD. Involvement of Clinical Genetics is essential. Prenatal referrals must be arranged with the laboratory well in advance.

Clinical Advice

- If clinical discussion is required, we would recommend contact with Dr Andrew Norman, Consultant Clinical Geneticist, St Michael's Hospital, Bristol (Tel: 0117 342 5231)

Target Reporting Times

Diagnostic testing	42 days
Predictive testing	14 days
Prenatal testing	3 days

Quality

- BGL participates in the GenQA scheme for this service

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https://www.nbt.nhs.uk/severn-pathology/pathology-services/bristol-genetics-laboratory-bgl

CONSENT FORM FOR GENETIC TESTING FOR HUNTINGTON DISEASE

I understand that it is possible to have a genetic test to determine whether Huntington Disease is a likely cause of *my/my relative's* clinical symptoms and I wish to proceed with this test.

I understand that the test will show one of the following:

- That *I do/he or she does* have the condition and that *my/their* children are at risk of carrying the abnormal gene
- That *I do not/he or she does not* have Huntington Disease
- In very rare cases the test can be difficult to interpret

I acknowledge that a positive result may have important implications for other family members.

I *(name)*……..……of…….

…… agree to having a genetic test for Huntington Disease.

This has been explained to me by……of ……

Patient

Signed……...Date……..……..

Consultant

Signed……...Date……...…….

Clinical specialty…..…….

If the patient is unable to give written consent to this test, **VERBAL** consent has been witnessed by:

(Name)…….…… of…….

……..……..

Relationship to the patient……..……