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

North Bristol NHS Trust

Cystic Fibrosis (CF)

Contact details:
Bristol Genetics Laboratory
Pathology Sciences
Southmead Hospital
Bristol, BS10 5NB
Enquiries : 0117 414 6174
FAX: 0117 414 6168
Email address:
nbn-tr.geneticsenquiries@nhs.net

Head of department:
Rachel Butler FRCPath

Consultant Lead for Molecular Genetics:
Maggie Williams FRCPath

Service Lead:
Catherine Delmege
Email:
Catherine.Delmege@nbt.nhs.uk

Sample Required:

Adult: 5mls blood in EDTA
Paediatric: at least 1ml EDTA (preferably >2ml)

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 DNA 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

- Cystic fibrosis (CF) is the most frequent severe autosomal recessive genetic disorder in the Caucasian population.
- Incidence in the Northern European Caucasian population is 1:2500 births and carrier frequency is 1:25.
- CF is caused by pathogenic variants in the Cystic Fibrosis Transmembrane Conductance Regulator gene (*CFTR*, located at 7q31.2) which lead to abnormalities in the structure, function and production of a chloride channel.
- Clinical severity is variable but in its classical form CF is characterised by chronic lung disease and pancreatic insufficiency.
- Referrals for CF analysis are accepted in patients with a clinical diagnosis of CF, a possible diagnosis of CF, cases of foetal echogenic bowel, CFTR related disease (CFTR-RD) such as bronchiectasis, and also in cases of male infertility where obstructive azoospermia associated with CBAVD or severe oligospermia associated with CUAVD is suspected (see Y chromosome microdeletion analysis)
- Carrier testing is offered to “at risk” adult family members, as appropriate. Genetic counselling, prior to testing, is recommended for these families.
- Please refer to the BSGM guidelines on carrier testing in children http://www.bsgm.org.uk/media/678741/gtoc_booklet_final_new.pdf
- Since 2007 all newborns in the UK population are screened for cystic fibrosis at 5 days on neonatal blood spots. Patients with raised IRT are then screened for the four most common *CFTR* pathogenic variants in the Northern European Caucasian population. This laboratory screens for p.Phe508del, p.Gly542X, p. Gly551Asp and c.489+1G>T, using Real-Time genotyping PCR, accounting for 80.6% of pathogenic variants in the Northern European Caucasian population. If one pathogenic variant is found further screening is undertaken using Elucigene™ CF-EU2v1 ARMS methodology (see below).

Service offered:

- ***CFTR* pathogenic variant analysis is carried out using the Elucigene ™ CF-EU2v1 ARMS kit*, unless undergoing newborn screening.**
- The variants screened (see below) account for approximately 90% of all *CFTR* pathogenic variants in the Northern European Caucasian population.
- The most common pathogenic variant is p.Phe508del accounting for approximately 75% of pathogenic variants in the Northern European Caucasian population.
- Further analyses are available for:
  - **Intron 8 PolyT analysis:** is included in the CF-EU2v1 kit and is reported where clinically appropriate
  - **Linked *CFTR* intragenic markers:** These are used in families where a pathogenic variant remains unidentified and in CF prenatal analysis.
- **In cases where CF is diagnosed or suspected and only one pathogenic variant has been identified using the CF-EU2 screen,** further *CFTR* analysis by gene sequencing and MLPA is available. The cost of this testing must be met by the Trust of the referring clinician.

Referrals should be accompanied by sufficient detailed information regarding either:

- The clinical investigations carried out in cases where CF is diagnosed or suspected, including any results from biochemical investigations such as sweat tests.
- Family history including details of the *CFTR* pathogenic variant carried by family members (and where tested) including their exact relationship.

Information document No.23 Version 12
Active date of this version: 30/03/2019
DETAILS CORRECT AT DATE OF PRINTING ONLY.
Approved by: Catherine Delmege

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

NHS North Bristol NHS Trust

Cystic Fibrosis (CF)

Contact details:
Bristol Genetics Laboratory
Pathology Sciences
Southmead Hospital
Bristol, BS10 5NB
Enquiries : 0117 414 6174
FAX: 0117 414 6168
Email address:
nbn-tr.geneticsenquiries@nhs.net

Head of department:
Rachel Butler FRCPath

Consultant Lead for Molecular Genetics:
Maggie Williams FRCPath

Service Lead:
Catherine Delmege
Email:
Catherine.Delmege@nbt.nhs.uk

Sample Required:

Adult: 5mls blood in EDTA
Paediatric: at least 1ml EDTA (preferably >2ml)

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 DNA 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.

In cases of **infertility referrals** details of sperm count (azoospermia / oligospermia) and whether the patient is known to have CBAVD. Referrals are not accepted directly from GPs. Please provide details of the referring infertility consultant who will receive the report and billing address.

- A **'BGL request form for infertility referrals'** (Lab Information Form 16) is required to be completed for these cases (please contact the laboratory).
- Where the patient is not of Northern European ancestry, details of the family origin would be required to ensure the appropriate pathogenic variants had been excluded, e.g. in Asian patients.

Target reporting in calendar days

	TAT
Routine CF analysis	42 days
Echogenic bowel referrals	14 days
Prenatal samples	3 days
Fertility referrals	42 days
Carrier testing	42 days

Please contact the laboratory for up to date prices.

- **Quality Assurance**
- BGL participates in the GenQA schemes for CF and CF bloodspot analysis for this service.

***Pathogenic variants tested for in Elucigene ™ CF-EU2 v1 ARMS kit**

p.Phe508del	p.Gly551Asp	p.Gly542*
c.489+1G>T	p.Arg553*	c.1585-1G>A
p.Trp1282*	p.Asn1303Lys	c.3717+10kbC>T
p.Arg117His	p.Arg334Trp	p.Ala455Glu
c.3528delC	c.948delT	p.Ile507del
p.Arg347Pro	p.Ser1251Asn	p.Glu60*
c.2988+1G>A	c.1766+1G>A	c.579+1G>T
p.Gly85Glu	c.2052delA	p.Arg560Thr
p.Asp1152His	p.Pro67Leu	c.1679+1.6kbA>G
c.262_263delTT	c.313delA	p.Leu671*
p.Arg117Cys	c.2215delG	p.Tyr122*
p.Trp846*	c.2657+5G>A	p.Gln890*
p.Leu206Trp	c. 3140-26A>G	p.Arg1066Cys
p.Tyr1092*	p.Arg347His	p.Met1101Lys
p.Arg1158*	p.Arg1162*	p.Tyr515*
p.Val520Phe	c.3773dupT	p.Ser549Arg
p.Ser549Asn	c.54-5940_273+1025del21kb	

Information document No.23 Version 11
Active date of this version: 21/01/2019
DETAILS CORRECT AT DATE OF PRINTING ONLY.
Approved by: Catherine Delmege