Title	CF Diagnosis & Newborn Screening
Version	2.0

1. Background

- Newborn screening for Cystic Fibrosis in West Midlands commenced November 2006 and is part of the Guthrie test (Heel Prick) carried out on all new-born babies on the 5th day of life.
- Babies presenting with meconium ileus are tested at presentation.

2. Process

- Results are available within 2 weeks.
- Blood is tested for IRT (immune-reactive trypsin) and if positive for CF gene mutations.
- Extended or repeat testing may be required.
- Results will be phoned though to the CF Team by the West Midlands Regional CF Laboratory. at the Birmingham Children's Hospital.
- Screening may reveal zero, one or two CFTR variants. All positive results require clinical assessment and further investigation prior to making a diagnosis of cystic fibrosis.

3. Management of Positive Screening

The CF Team will:

- Agree a home visit date from the Specialist Screening nurse in Birmingham
- Confirm a hospital appointment for the child & family that will take place within 24hrs of the home visit, avoiding a Friday
- The hospital appointment will involve the CF Multi-Disciplinary Team
- Arrange a sweat test either on the day of the hospital appointment of shortly afterwards
- Arrange blood test for CF genetic testing

4. Sweat Testing

- All children with a positive CF NBS should have a sweat test performed as soon as possible (can be deferred if child weighs <3000g).
- Performed by experienced nurses/technicians using the Macroduct Method.
- If there is insufficient sweat test the test will be repeated.
- Concentration of sweat chloride is measured.
- Interpretation of sweat chloride level:
  > 60mmol/l supports the diagnosis of CF
  30 – 60 mmol/l is suggestive but not diagnostic of CF
  < 30mmol/l = a low probability of CF

5. Genotyping and Genetics Referral

- All children with a positive CF NBS (even if 2 CFTR variants have been identified) should have bloods sent for CF genetics. The initial analysis will screen for the commonest 39 CFTR variants (used to confirm findings of CF NBS). Next generation sequencing can be requested to find CFTR variants not identified by CF NBS.
- Carrier testing is not routinely carried out.
- After diagnosis the family will be offered referral to the Regional Genetics Service, to receive counselling and advice regarding the genetic implications to the rest of the family.

6. MDT Initial Roles & Actions

6.1 Babies with 2 CF mutations

The Consultant will:
Give a basic review of screening results, Cystic Fibrosis & answer questions
Take history & full examination
Measure length, weight and head circumference
If the child is unwell take appropriate action
Arrange stool sample collection for faecal elastase
Provide pancreatic Enzymes if pancreatic insufficiency suspected
Prescribe vitamins, sodium chloride and antibiotics to start within 2 weeks of diagnosis.

The CF Nurse Specialist will:
Provide contact numbers
Provide a CF trust parents pack
Arrange FU appointment/home visit

The Other CF MD Team members
Will arrange to see the child and family over the following 2 weeks

6.2 Babies with 0 or 1 CF mutations

Consultant assessment and further investigations arranged
All require urgent sweat test & next generation sequencing to identify CFTR variants not on the 39 variant panel included in CF NBS
Diagnosis of CF cannot be confirmed without results of the above
No treatment started unless indicated
CF Nurse support as required

7. Outcome

Based on results of the sweat test and the genetic analysis, babies with a positive CF NBS can be identifed as:

1) **Confirmed CF**
   Sweat chloride ≥60mmol/L
   OR
   Sweat chloride >30 and x2 CF-causing mutations
2) **CF Screen Positive Inconclusive Diagnosis (CFSPID)**
   Sweat chloride: <30mmol/L and two CFTR mutations at least one of which has unclear phenotypic consequences.
   OR
   Sweat chloride: 30–59mmol/L and one or zero CF-causing mutations.
3) **CF carrier**
   Sweat chloride: <30mmol/L and one CFTR mutations.

4) All CF related disorders excluded.
Sweat chloride: <30mmol/L and zero CFTR mutations.

If there is doubt about the likely clinical effect of a CFTR variant, see the CFTR2 website (https://cftr2.org/).

8) Late presentation of CF

Late presentation of CF may occur:

1. In older children and adults born prior to CF screening that started in the W Mids in November 2006, and
2. With rare false negative screening

Refer to separate guideline Section A Guideline 1.3 “Late-presentation of CF” for further details.