NATIONAL PROTOCOLS

Programme: Newborn Bloodspot Screening Programme

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Foreword

Screening policy in Scotland is aligned with the rest of the UK and is determined by the Scottish Government Health and Social Care Directorates (SGHSC) on evidence based policy recommendations from the UK National Screening Committee (NSC). The NSC advises Ministers and the NHS in the four UK countries on all aspects of screening.

Screening programmes are designed to detect early signs of diseases or conditions in the population and then to provide a reliable method of referral for diagnostic testing and further treatment. Screening in itself is not indicative of the presence of disease, but in order for a screening programme to be considered for national designation, it must be acceptably accurate and designed to test for a disease where early detection and intervention would be of benefit to the patient.

The aim of the Newborn Blood Spot Screening Programme is to identify specific conditions, as soon after birth as possible and before the onset of recognisable clinical symptoms. By detecting these conditions early it is possible to treat and reduce their severity.

The Scottish Newborn Screening Laboratory (SNSL) is housed in the Queen Elizabeth University Hospital, Glasgow. It is nationally commissioned by National Services Division and is the sole newborn screening laboratory in Scotland.

The remit of the laboratory is:

- to screen all newborn babies in Scotland (currently around 60,000 per annum) for Phenylketonuria (PKU), Congenital Hypothyroidism (CHT), Cystic Fibrosis (CF), Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCADD), Sickle Cell Disorders (SCD), Maple Syrup Urine Disease (MSUD), glutaric aciduria type 1 (GA1), isovaleric acidaemia (IVA), and homocystinuria (HCU)
- to ensure the reporting of all results to the proper authorities and the prompt referral of all positive cases for diagnostic testing and treatment
- to provide data on the incidence of conditions as required
- to review new technology with a view to the incorporation of new tests/methods into the screening programme
- to undertake pilot studies and participate in research programmes related to newborn screening

The laboratory testing is highly automated with immunoassay analysers, a blood spot punching machine, high performance liquid chromatography (HPLC) and two tandem mass spectrometers all interfaced to a Laboratory Information Management System.

Contact details

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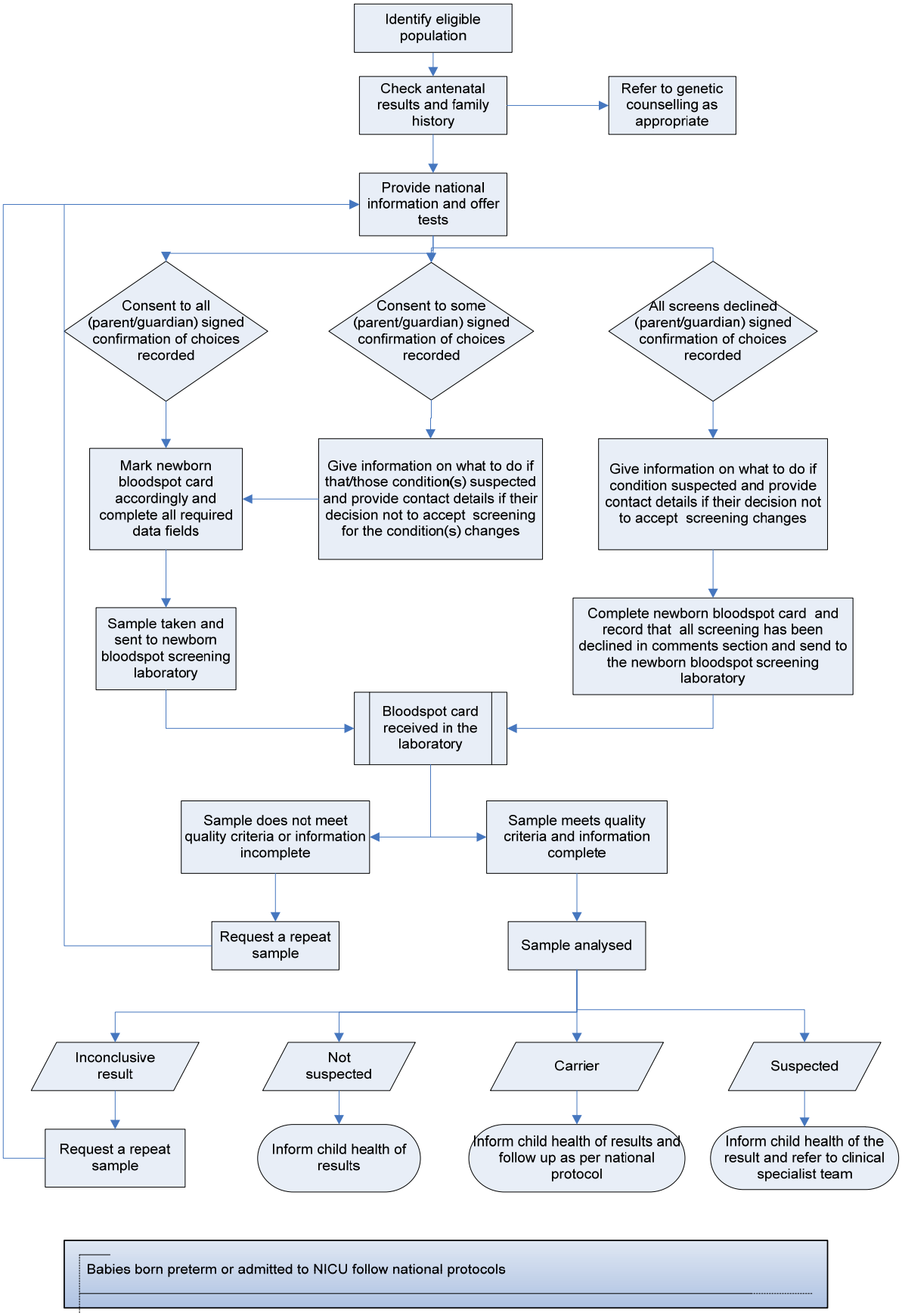
Key points

- The newborn screening pathway extends from a single entry point where parents are provided with information about newborn screening to one of two exit points:
    - Condition(s) not suspected – results recorded
    - Condition(s) suspected – clinical referral initiated
- Every baby born in Scotland is eligible for and routinely offered screening (approximately 60,000 per year)
- Includes tests for nine conditions:
    - Phenylketonuria (PKU)
    - Congenital Hypothyroidism (CHT)
    - Cystic Fibrosis (CF)
    - Sickle Cell Disorders (SCD)
    - Medium Chain Acyl CoA Dehydrogenase Deficiency (MCADD)
    - Maple Syrup Urine Disease (MSUD)
    - Glutaric Aciduria type 1 (GA1)
    - Isovaleric Acidaemia (IVA)
    - Homocystinuria (pyridoxine unresponsive) (HCU)
- The 6 Inherited metabolic disorders (PKU, MCADD, MSUD, GA1, IVA and HCU) are offered as a package so screening is either for all of the conditions or none of them
- Parents may decline any or all of the tests (the 6 IMD conditions count as one test) and must be informed that their baby remains eligible for screening within the Programme up to the age of 1 year.
- Written consent from a parent is required before the blood spot sample will be taken
- A newborn blood spot card must be completed for all babies, even if all tests are declined
- The blood spot sample should ideally be taken between 96-120 hours of life (4-5 completed days), day of birth is day 0, and sent on the day of sampling. In exceptional circumstances samples can be sent between day 4 and day 8.
- The time of birth and time the sample was taken have been added to the bloodspot cards issued in 2018 to allow the laboratory to confirm how many completed hours old the baby was at the time of the sample being taken to ensure all samples taken in the correct timescales.
- Sometimes it is necessary to take more than one blood spot sample for clinical reasons
- All newborn blood spot testing is carried out in the Scottish Newborn Screening Laboratory, Queen Elizabeth University Hospital Glasgow
- Every child up to one year of age who moves into an NHS Board and/or where no previous screening has been recorded is eligible for and should be offered relevant tests

Newborn bloodspot pathway



1. Introduction

This document contains standard national protocols for all healthcare professionals involved in the NHS Scotland newborn bloodspot screening programme. In order to ensure equity of service across Scotland, NHS Boards are required to ensure that the screening service provided locally adheres to these protocols. Standard operating procedures and local protocols are not included in the document; these need to reflect specific local arrangements and therefore need to be produced and maintained locally. Wherever possible this specification follows the English Newborn Bloodspot Screening Programme handbook with relevent aspects reproduced with kind permission by the programme centre.

Each NHS Board has a nominated Screening Coordinator, whose role is to lead and coordinate the screening programme locally. The Screening Coordinators work closely with colleagues across their NHS Board involved in the programme and represent their Board as a member of the NHS Board Screening Coordinators Group. The screening protocols for each disorder are designed to maximise sensitivity while seeking to reduce the number of false positive results generated and deliver an acceptable positive predictive value for the test overall (PPV%). In some cases improved specificity is achieved by the use of secondary testing as part of the screening protocol (total homocysteine in the case of HCU and C10 in the case of MCADD). In all cases, an analytical cut-off is set approximately 20% below the referral cut-off and those samples which exceed the analytical cut-off are re-tested in duplicate on the same day. If the mean of the three results exceeds the referral cut-off then the patient is referred, or in the case of MCADD and HCU, the C8:C10 ratio or total homocysteine is assessed respectively and the decision to refer is based upon these results.

1.1 Definition of screening

Screening is a process of identifying apparently healthy people who may be at increased risk of a disease or condition. They can then be offered information, further tests and appropriate treatment to reduce their risk and/or any complications arising from the disease or condition. For the small number of babies affected by the conditions screened for on the bloodspot card, early detection, referral and treatment can help to improve their health and prevent severe disability or even death.

1.2 Limitations of screening

Screening has important ethical differences from usual clinical practice, as the health service is targeting apparently healthy people, offering to help individuals to make better informed choices about their health. However, there are risks involved and it is important that people have realistic expectations of what a screening programme can deliver. Whilst screening has the potential to save lives or to improve the quality of lives through early diagnosis of serious conditions, it is not a fool-proof process. Screening can reduce the risk of developing a condition or its complications but it cannot offer a guarantee of protection. In any screening programme, there is a minimum of false positive results (wrongly identified as having the condition) and false negative results (wrongly reported as not having the condition). The UK NSC is increasingly presenting screening as risk reduction to emphasise this point.

1.2 What is newborn bloodspot screening

Newborn blood spot screening aims to identify babies who are at high risk of having certain serious but rare conditions before they develop symptoms. Screening is not the same as diagnosis; instead it identifies which babies need to go on to have diagnostic tests to determine whether or not they do have the condition. By detecting these conditions early it is possible to treat them and reduce their severity.

Newborn blood spot screening is offered to all babies in the UK. Ideally samples are taken between 96-120 hours of life (4-5 completed days), day of birth is day 0, and sent on the day of sampling. In exceptional circumstances samples can be sent between day 5 and day 8. A health professional pricks the baby's heel and collects a small amount of blood onto the newborn blood spot card (a special filter paper). The card is sent to the Scottish National newborn bloodspot screening laboratory.

2. Offer of Screening

Newborn blood spot screening is offered to all newborn babies up to one year of age. It is important that parents can make an informed choice about screening for their baby and are prepared for the blood sampling procedure. Parents should be offered screening for their baby at least 48 hours prior to taking the blood sample and provided with a copy of the national patient information leaflet, in order to allow them to the make an informed decision.

It is the responsibility of the NHS Board through the Screening Coordinator and the Director of Public Health, to ensure that robust systems are in place locally to confirm that every newborn baby or child up to the age of 1 year, resident in their NHS Board, is invited to participate in screening.

Midwives working in hospital or in the community are responsible for ensuring that testing is offered and national protocols are followed which includes, in Scotland, the legal requirement for written consent.

If the baby is still in hospital on the fifth day of life, it is the responsibility of the ward, Neonatal Intensive Care Unit (NICU), Special Care Baby Unit (SCBU), or the Surgical Unit staff to obtain the blood spot sample. See information in section 3.5 for additional screening arrangements for babies in Specialist Units.

2.1 Parental consent and refusal

Parents should have a pre-test discussion with the healthcare professional taking care of them and their baby regarding the newborn blood spot test. Discussions should include the purpose, processes and benefits of the test. Parents will be asked to complete a consent form stating that they have received sufficient information to understand the reasons for testing, the significance of the results and the possible consequences of not having tests performed. When obtaining consent for the newborn blood spot screening programme, you must ensure that parents understand they are consenting to the following:

- The sample being taken
- The sample being booked in and analysed in the newborn screening laboratory and used for quality assurance
- The laboratory sending the results to the child health record department
- The results being stored on the child health information system
- The potential identification of their baby as a “carrier” of SCD or CF
- A referral to specialist services if a result is positive
- The bloodspot card being stored for a minimum period by the laboratory to allow for retesting if required and then to be stored indefinitely unless permission for ongoing storage was declined
- Their baby’s anonymised data being used for research studies that help to improve the health of babies and their families in the UK, for example population studies, unless they specifically decline this.
- In rare circumstances , receipt of invitations from researchers who would like to use their baby’s blood spot card for named research

The form should be completed accepting or declining each individual test, storage of the card and the use of samples for anonymised research. This information should also be recorded on the bloodspot card in the comments section. The form should be countersigned by the healthcare professional taking the blood sample and filed in the maternity records. The midwife will also ascertain family contact details for the first month and establish the preferred method of communication, should it be necessary to repeat testing.

Occasionally parents decline testing of some or all of the conditions. In these circumstances the midwife must complete the blood spot card, in the usual manner, stating that the parents have

declined the offer of screening. Parents are given the option to take up screening at a later date and are provided with a copy of the information sheet **"When the blood spot screening test has not been undertaken**". The information sheet lists the possible signs and symptoms of the conditions that are screened for. This information is also given to the family's GP, so that the GP can also look out for these signs and symptoms.

2.2 Residual blood spots

After the blood spot cards are analysed they are stored for a minimum period by the laboratory. Where there is sufficient residual blood they may then be used in several different ways. These different secondary uses for the spots are explained below. Parents should be made aware of these possible uses.

- ***To check the screening result, or for other tests recommended by the baby's doctor***

If a baby becomes sick or dies unexpectedly, the laboratory and the baby's doctor may wish to retest the baby's newborn blood spots. This testing may help to answer parents' questions about the baby's illness or death.

- ***To improve the screening programme***

In order to check the quality of current laboratory analyses, or to explore the possibility of introducing new analyses, the stored blood samples may be re-analysed. This can involve re-analysing batches of blood spots of babies known to have particular conditions, as well as the blood spots of healthy babies. This use of the blood spots is crucial to the continuation of the newborn screening programme.

- ***For research to help improve the health of babies and their families in the UK***

Residual newborn blood spots may also be used for research where the samples have been anonymised and the research project meets high ethical standards. For example, such research could involve investigating possible links between sudden infant death syndrome and certain metabolic disorders. Access to the blood spot cards is controlled by a system of Caldicott guardians whose role it is to ensure high standards of confidentiality and security within the NHS

Parents are not asked to consent to the use of their babies' blood spots for this type of research - individual babies are not identified in publications of this research and parents will not be contacted.

- ***For research involving contacting parents asking them if they would like to take part***

There is a very small chance that in the future researchers may wish to contact parents or their children inviting them to take part in research through this screening programme. All research projects will have been approved by an ethics committee and be subject to peer review to ensure that the research is of high quality. In these circumstances, parents and/or their children will be informed about this research and allowed time to decide whether or not to accept such an invitation. Some parents may wish to indicate when the blood spots are collected that they do not want to receive any such invitations. If this is the case the blood spot card should be clearly marked ***'No research contact'.***

3. The newborn bloodspot screening sample

The following procedures for obtaining the blood spot sample are extracted from the Newborn Bloodspot sampling guidance. To take a newborn blood spot sample you will need:

- NHS Screening Programmes' patient information booklet
- an in-date bloodspot card
- baby's CHI number (use of a bar-coded label is recommended)
- blood spot card and glassine envelope

- personal child health record (PCHR) and maternity/professional record
- water for cleansing
- non-sterile protective gloves
- age-appropriate, preferably automated incision device
- sharps box
- cotton wool/gauze
- hypoallergenic spot plaster (if required)
- prepaid/stamped addressed envelope (first class)

- **Why blood spot quality matters**

Good quality blood spots are those where the circle is filled and evenly saturated by a single drop of blood that soaks through to the back of the blood spot card. They are vital to ensure that babies with rare but serious conditions are identified and treated early.

Poor quality blood spots could lead to false-negative or false-positive screening results – this means that babies with a condition might be missed or babies without a condition might be referred for further tests unnecessarily.

- **Avoidable repeats**

If poor quality blood spots are received, or the fields on the blood spot card are not completed fully and accurately, the screening laboratory will request an 'avoidable repeat' sample.
Avoidable repeat samples can cause anxiety for parents, distress to babies and delays in the screening process. This could lead to delayed identification and treatment of an affected baby. They are also a waste of healthcare resources.

The Scottish Newborn Screening Laboratory's (SNSL) follows a national, evidence-based consensus on blood spot quality, with standardised acceptance and rejection criteria. To ensure that an avoidable repeat sample is not requested, sample takers are advised to obtain four good quality blood spots and complete all fields on the card accurately.

It is vital that every section of the blood spot card is completed accurately. The information supplied is entered onto the SNSL Laboratory Information Management System (LIMS) and is used for:

- the identification of the infant – to ensure that the correct result is issued to the correct baby
- the determination of results – certain parameters have to be fulfilled before results are valid and issued
- ensuring the correct protocol is followed – different protocols are applied in particular tests

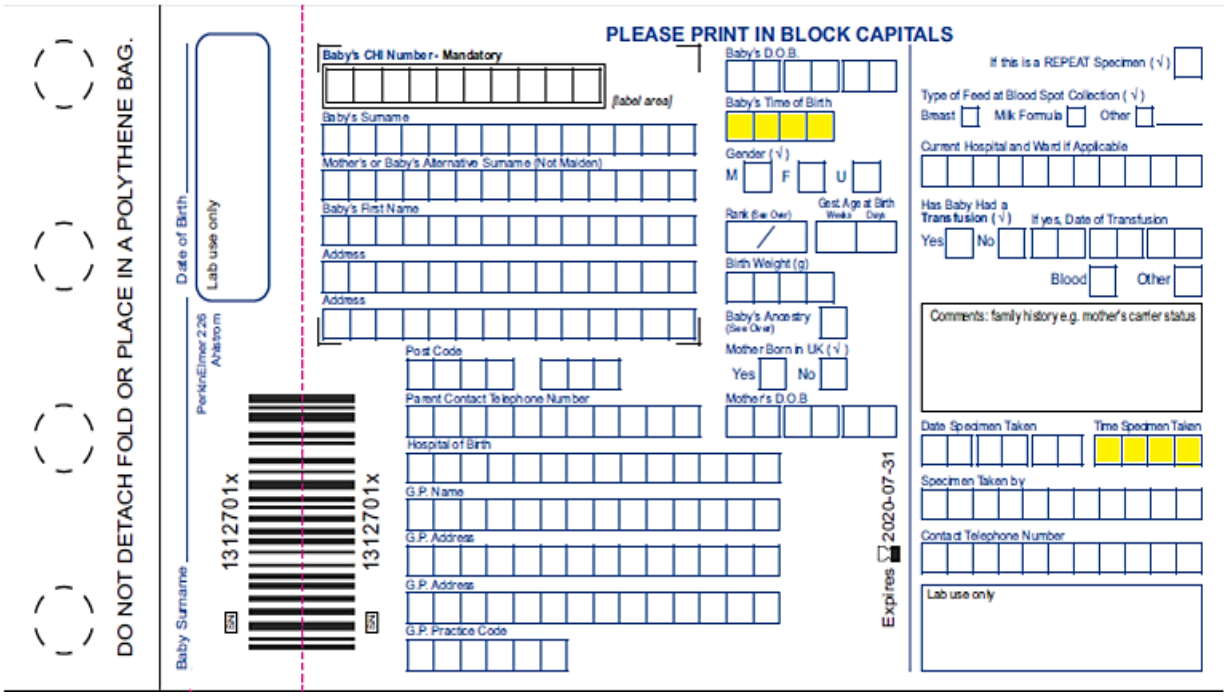
3.1 Completing the bloodspot card

Check the expiry date before completing the blood spot card. Expired cards should not be used, they should be returned to the SNSL. Complete the details **at the time of sampling**.

The middle section of the front of the card contains demographic details. It is best practice to use labels for this section if available. Always ensure that it is the baby's label and not mother's.

CHI number	The use of the CHI number is a **mandatory** requirement and should always be noted in full. Ensure the baby's CHI number is supplied and not the mothers.
Mother's or Baby's Alternative Surname	If more than one name is known please document both
Address	This is the home address of the baby at the time of birth
Post code	This should be in full

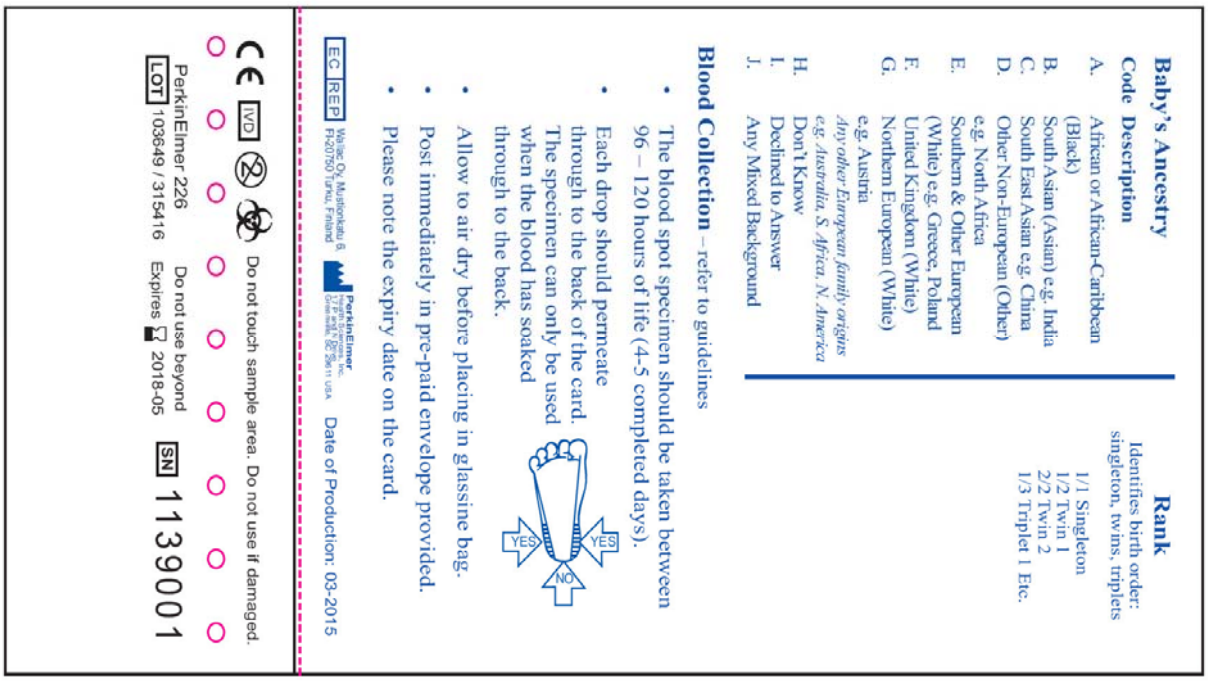
Parent contact telephone number	This is important as immediate contact with parents may be required
Hospital of birth	Name of hospital or if born before arrival then the hospital that the baby is delivered in. Home should be stated if not associated with a hospital
GP	General Practitioner with whom the baby will be registered
GP address	Name of surgery and address
Baby's DOB and time of birth	This must be accurate as the interpretation of results for some tests is dependent on the age of the child. If the sample is taken too early, i.e. before 4 completed days of age, this can invalidate the results
Gender	Tick box; M-Male F-Female U-Unknown or Uncertain
Rank	This is important to indicate whether baby is a twin etc as shown on the back of the card eg 1/1, 1/2. This will avoid the specimen being treated as a duplicate specimen of another baby
Gestation	This is the gestation that the baby was born at and is important for some of the tests. Mark in weeks and days
Baby's Ancestry	Choose from one of the family origin codes, as detailed on the back of the card
Mother born in the UK	This is used in relation to some epidemiological studies
Mothers DOB	Used as another link to the baby if details differ from those held by Child Health Information System



The right hand side of the front of the card is information used by the laboratory:

Type of feed	If more than one type applies tick both i.e. breast and bottle. 'Other' is for total parenteral nutrition (TPN) in cases of sick babies.
Current Hospital and ward if applicable	If the baby is still in hospital please supply the hospital and ward, this will allow child health to locate the baby if a repeat sample is needed.
Has baby had a transfusion	Date of transfusion must be included. Please also indicate if the transfusion was a blood transfusion or other product such as platelets or FFP. The interpretation of results will differ

	depending on whether blood or other products were given.
Comments	If sample taken on day 4 then how many completed hours old the baby was at the time of the sample being taken should be included here. This box should also be used to record any condition(s) where screening has been declined. This box should also be used to record 'No Storage' or 'No Research' if parents have requested this. This space should also be used to record any relevant antenatal screening results, parent(s) known carriers of haemoglobin variants/CF, Meconium Ileus, any family history relevent to the conditions screened for and reason for sample if not taken on day 5-8 (e.g. pre transfusion, preterm CHT)
Date and time Specimen Taken	***This is essential.*** The SNSL uses this to determine age of baby when sample was taken. Cards without this date will not be issued with a result until this has been established. The time the specimen has been taken must also be provided to allow the laboratory to confirm that the baby is over 96 hours old
Specimen Taken By	Name of healthcare professional
Contact Telephone Number of Health Professional	Will allow immediate contact in the event that the laboratory or clinical service needs to make direct contact with the healthcare professional
Lab use only	Must be left blank. This will be used for the laboratory's unique numbering system



The left hand side of the front of the card is for the specimen collection. The Baby's Surname and DOB must also be completed on this portion of the card as it shall be separated from the rest of the card and this is required for identification purposes in addition to the barcode included on both sections of the card.

The reverse side of the card describes the following:

Family origins – This information is important for SCD testing
Rank – This gives birth order in multiple pregnancies

3.2 Timing of the sample

Ideally samples are taken between 96-120 hours of life (4-5 completed days), day of birth is day 0, and sent on the day of sampling to the Scottish newborn screening laboratory. In exceptional circumstances samples can be sent between day 5 and day 8. Completing the time the sample was taken as well as the date is necessary to allow the laboratory to confirm that the baby was at least 96 hours old. Eligible 'movers in' should be offered screening as soon as possible.

Additional tests are offered to babies born preterm and babies at risk of blood transfusion and if required by a screening protocol to achieve a conclusive result. Babies who are premature, unwell, or have had blood transfusions should all have the newborn blood sample taken as usual and this information must be recorded on the blood spot card.

Records are kept of all tests including those declined. If all screens are declined a card should still be completed and sent to the laboratory indicating that all screening has been declined to ensure records are complete and the family is not contacted for a missed screen in error.

3.3 Taking the newborn bloodspot sample

Sample takers should check that consent for screening has been obtained and recorded. Recommend comfort measures for the baby. Ensure the baby is cuddled and in a secure position. Suggest that the baby is breast feeding. Clean the heel by washing thoroughly with plain water using cotton wool/gauze. The water should not be heated and the baby's foot should not be immersed. **Do not** use alcohol or alcohol wipes. Allow the heel to dry completely. Wash hands and apply gloves. Ensure the baby is warm and comfortable. Warming of the foot is not required.

Obtain the sample preferably using an age-appropriate automated incision device (manual lancets must **not** be used). An arched-shaped incision device is recommended. See diagram A and B for preferred puncture sites. Avoid posterior curvature of the heel. Allow the heel to hang down to assist blood flow.

Diagram A
For full and preterm infants
Skin puncture must be no deeper than 2mm

Diagram B
For infants who have had repeated heel punctures. An automated incision device with a penetrative depth of no more than 1mm is recommended.

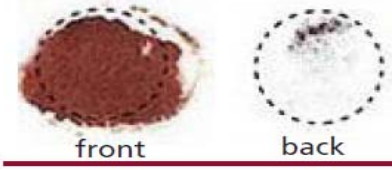
These sites are also suitable for infants up to a year of age.

Adapted from Jain and Rutter

The aim is to fill each circle on the blood spot card, using a **single** drop of blood for each circle. Puncture the heel – **wait** for the blood to flow and a hanging drop to form. Allow one spot of blood to **drop** onto each of the circles on the blood spot card. There is no need to discard the first drop.

- do not allow the heel to make contact with the card
- do not squeeze the foot in an attempt to increase blood flow
- allow the blood to fill the circle completely by natural flow, and seep through from front to back
- do not compress or apply pressure to the blood spots

	Correct	Reasoning
	A single, evenly saturated drop of blood that fills the circle completely and soaks through to the back of the blood spot card	Good quality blood spots are essential to obtain accurate screening results

	Incorrect	Reasoning
	Insufficient sample: small volume spots	Risk of false-negative result
 front back	Insufficient sample: blood not soaked through to back of blood spot card	Risk of false-negative result
	Inappropriate application of blood: multispotted	Risk of false-negative result
	Compressed sample	Significant risk of false-negative result
	Inappropriate application of blood: layered sample (for example, one spot of blood is layered directly on top of another) or blood applied to the front and the back of the blood spot card	Risk of false-positive result
	Contaminated sample	Risk of inaccurate result

Images courtesy of Wyn Griffiths, South East Thames Screening Laboratory and Roanna George, Wales Newborn Screening Laboratory

If the blood flow ceases the congealed blood should be wiped away firmly with cotton wool or gauze. Gently 'massage' the foot, avoid squeezing, and drop the blood onto the blood spot card. If the baby is not bleeding, perform a second puncture on a different part of the same foot or on the other foot. When sample collection is complete, wipe excess blood from the heel and apply gentle pressure to the wound with cotton wool or gauze. Apply a hypoallergenic spot plaster if required – remind parents to remove the plaster in a few hours.

Allow blood spots to air-dry away from direct sunlight or heat before placing in the glassine envelope – take care to avoid contamination. Despatch the blood spot card in the prepaid/stamped addressed envelope (first class) on the same day. Despatch should not be delayed in order to batch blood spot cards together for postage. If a post box is used, ensure it is one that is emptied daily (Monday to Saturday). No more than six blood spot cards should be placed in a single envelope as this will exceed the contracted postal weight and delay the delivery of specimens.

In the event of a postal strike or severe weather which may disrupt deliveries, staff should refer to their local NHS Board protocols and contingency plans to ensure the timely delivery of blood spot cards to the SNSL.

Record that the sample has been taken in the baby's personal child health record and in the maternity/professional record, complying with local protocols. If the baby is in hospital, record and notify the baby's screening status on discharge/transfer notifications.

3.4 Failsafe processes

NHS Board should implement failsafe measures that ensure that:

- all babies that are transferred have their screening status notified
- all eligible babies are identified and offered screening
- all babies whose parents accept screening are tested
- all samples arrive at the laboratory in a timely manner
- all positive babies receive timely treatment within national standard

Child Health Records Departments should also perform regular checks to identify babies that might have missed screening.

3.5 Special circumstances: babies born preterm or cared for in neonatal units

Babies admitted to neonatal units are likely to have multiple blood samples taken. Blood spot screening should be coordinated with other tests when possible. On admission/prior to blood transfusion, babies less than five days of age should have a single circle blood spot sample taken for routine SCD screening. This should be on a separate blood spot card marked 'Pre-transfusion'.

The pre-transfusion sample should be despatched to the newborn screening laboratory together with the routine day 4-5 day (96-120 hours) sample if the baby has received a blood transfusion in the interim. The pre-transfusion sample can be discarded appropriately if the baby has not received a blood transfusion. If the baby is transferred to another unit before the day 5 sample has been taken, ensure the pre-transfusion sample accompanies the baby.

The routine blood spot sample (four spots) should be taken between 96-120 hours of life (4-5 completed days) for all babies. For the purpose of screening, day of birth is day 0. *In exceptional circumstances the sample can be taken between day 5 and day 8.

When a baby has had a blood transfusion, either intrauterine or in the newborn period, an interval of at least three clear days is required between the transfusion and the routine blood spot sample for CF, CHT and the IMDs.

However, in the event of multiple blood transfusions, even if it has not been three clear days since the last transfusion, a routine blood spot sample should be sent by day 8 at the latest regardless. In this scenario, a repeat sample will be needed at least three clear days after the last transfusion. The date of the last blood transfusion before the blood spot must be recorded on the blood spot card and on discharge/transfer notifications. Inform parents of any outstanding screening tests, and record this in the PCHR and maternity/professional record.

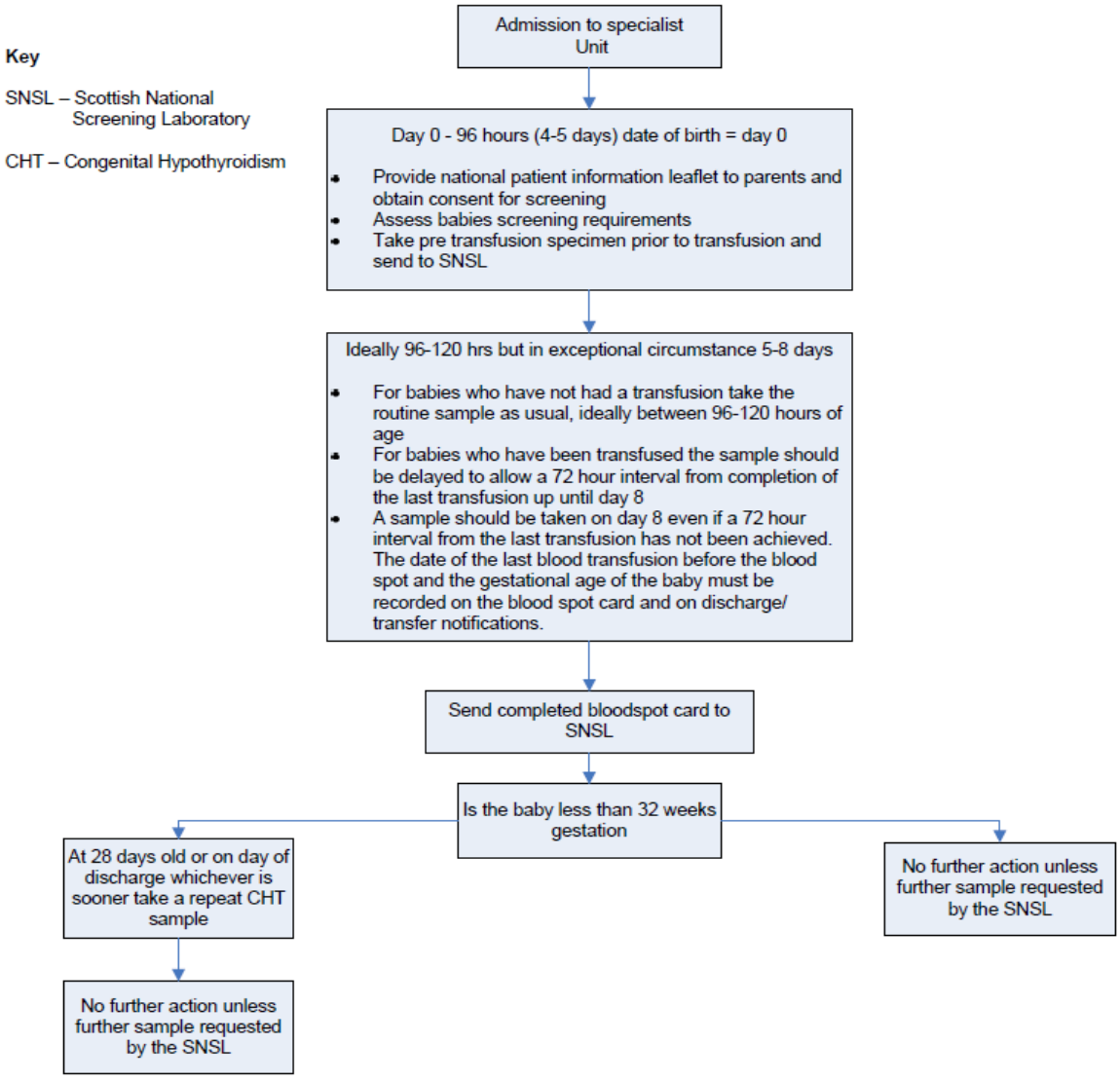
- **CHT screening for preterm infants**

Babies born at less than 32 weeks (less than or equal to 31 weeks + 6 days) require a second blood spot sample (two spots) to be taken, in addition to the day 5 sample. The explanation to be given to parents is that in babies born at less than 32 weeks of pregnancy, the routine test may not pick up congenital hypothyroidism. It is advised to have another test at either 28 days of age or immediately before the baby is discharged home, whichever comes first. Mark the card **'CHT preterm'**. Write the gestational age on the card.

If the baby is being discharged home before 28 days of age, write **'discharged home'** on the repeat sample. Record all blood spot samples taken in baby's hospital records, on transfer documentation, PCHR and on an auditable IT system.

- **Newborn Blood Spot Screening Pathway for Babies Admitted to Specialist Units**

Newborn bloodspot screening pathway for babies admitted to neonatal units



3.6 Biohazards

Screening is offered routinely to all babies whose mothers are known or suspected to be infected with HIV or Hepatitis B. The blood spot card should be identified as a Biohazard. The envelope in which the card is placed must not be marked as 'Biohazard' to avoid breach of confidentiality.

3.7 Ethylenediaminetetraacetic Acid

Ethylenediaminetetraacetic Acid (EDTA) is an anticoagulant used in some blood collection tubes. EDTA can interfere with the interpretation of testing and could lead to false negative results. Blood from EDTA tubes, citrate tubes or capillaries should never be used to fill blood spots as this will affect the measurement of Thyroid-Stimulating Hormone (TSH) for CHT and Immunoreactive Trypsinogen (IRT) for CF leading to false negative results.

3.8 Repeat samples

Repeat samples may be required from a few babies for a variety of reasons.

- There was insufficient blood available to perform all tests
- The blood spot card was damaged or did not reach the laboratory
- Layering or compression of the blood
- Equivocal or borderline test results – this means that the test result is not abnormal enough for the baby to be referred to a specialist but is not completely within normal ranges. There are several reasons why tests give an inconclusive result and often the repeat specimen provides a definitive result. If the repeat sample is also inconclusive then arrangements will be made for the baby to be assessed by a nominated clinical specialist
- There were insufficient details on the card to allow accurate analysis of the results
- The baby was too young when the specimen was collected (less than 72 hours old)
- The card was not dried properly prior to being posted
- The analysis was unsatisfactory due to specimen contamination or deterioration
- The specimen took more than 14 days to reach the laboratory and was therefore unsuitable for testing

These samples should be taken as soon as possible, or at the age directed by the screening laboratory. Informed consent must be taken and parents should be informed of the reason for the repeat. Tick the 'repeat sample' box on the blood spot card.

A one week interval between samples is recommended for borderline TSH results. Take a four spot sample and mark the card **'CHT borderline'**.

3.9 Storage of cards

After testing is complete, the blood spot card is stored in the laboratory for an initial period of 12 months so that if necessary, one or more of the tests can be repeated to check a particular result. The stored blood sample can also be used to test for other disorders which are not part of the standard screening programme. This may be useful if a child becomes ill and the doctor requests further tests. This is always discussed with the child's parents first.

If a parent does not want the blood spot card to be stored after the initial 12 month testing period then **"No card storage after 12 months"** should be marked in the **comments box** of the blood spot card.

Leftover blood spot specimens can also be used anonymously for other laboratory purposes such as comparing different screening methods and developing new tests. Occasionally it is necessary to use identifiable specimens in which case parent's permissions would always be sought.

If a parent does not want the stored blood spot card to be used for research then **"No research"** should be marked in the **comments box** of the blood spot card.

3.10 Families who are not resident with an NHS Board

In the case of travelling families or families who, for any reason, are not resident within a single NHS Board, the NHS Board where the child was born is responsible for offering screening and for following up results as necessary.

3.11 Babies transferring into area (up to 1 year of age)

For a child transferring into the NHS Board from within the UK, the Child Health/Screening Departments should check any available Health Visitor records received from the previous NHS Board of residence and document any results available for the child. If there are no records or results available, the previous NHS Board or health provider, if known, should be contacted to ascertain whether screening took place and if any written results are available. If a child has transferred in from abroad and has no verifiable documented screening results available in English screening should be offered for all conditions as detailed below.

If a child is under a year of age (up to but not including their first birthday) and has no documented results (or declines) for all five conditions screened for before the expansion of the programme, screening should be offered for all the untested conditions (including the four additional inherited metabolic diseases) **only** if the blood spot sample can be taken before they reach a year of age.

If for a child under a year of age, there are documented results (or declines) for all five conditions screened for in Scotland before the expansion of the programme (SCD, CF, CHT, PKU and MCADD), screening should **not** be offered for the four additional inherited metabolic diseases (MSUD, IVA, GA1 and HCU).

If parents accept screening and the blood spot sample is taken, the screening laboratory will perform all processes until screening has been completed for all the conditions – this includes processing initial samples received in the laboratory on or after the child's first birthday and requesting and processing repeat samples if required.

If parents decide not to accept the offer of screening, or the baby is over twelve months old, this should be recorded in clinical notes and on the child health system. Parents should be asked to seek medical advice and remind staff that their baby has not been tested if their baby has signs of chronic health problems such as developmental delay, chronic diarrhoea or repeated lower respiratory tract infections.

The screening test for CF is unreliable after a baby is 8 weeks old. Older babies with CF may have normal results and so this test will not be done in babies over 8 weeks of age. If a child has repeated chest infections or diarrhoea, medical advice should be sought and a test for cystic fibrosis may be arranged. This test is more complicated than the screening test and so it is not carried out on all babies.

NHS Boards should ensure that there is staff trained and responsible for taking the blood spots in infants that are no longer the responsibility of the midwifery unit. It may be easier to obtain a venous sample however this must be drawn into a plain syringe with no additives and then the blood should be applied directly to the card.

4. Scottish Newborn Screening Laboratory

Newborn screening should be provided using the nationally agreed screening protocols, these can be found within the newborn screening laboratory handbook. Specimens should be transported to

the laboratory in the usual way and kept in a dry environment at room temperature or 4°C before analysis; storage after analysis should follow agreed national guidelines.

4.1 Quality Assurance

There are three foundational aspects to maintaining quality in the clinical laboratory:

1. The need to participate in a recognised laboratory accreditation process that addresses: structure, process and outcome characteristics when providing a clinical laboratory service.

2. A requirement to use and participate in: real time performance monitoring using carefully designed internal quality control procedures with clearly defined batch acceptability criteria and trend analysis; participation in approved regular external quality assurance scheme arrangements with a clearly defined poor performer policy used to identify and address inadequate performance; when available, population data monitoring and analysis to identify and report performance and trend analysis using real patient data.

3. The need to record and report incidents using this as a learning tool to improve service provision.

Laboratories must establish appropriate quality and performance monitoring procedures; suitable levels are not always available commercially so there may be a need for in-house preparations to be used on each plate. The laboratory should participate in an approved external quality assurance scheme (e.g. UK National External Quality Assessment Scheme (UK NEQAS)), and demonstrate acceptable performance.

NSD, as commissioners of the SNSL, is responsible for the performance management of the service. The SNSL provides biannual reports to NSD and meets annually with NSD to discuss all aspects of the service including the monitoring of:

- clinical outcomes
- quality of service and achievement of targets
- activity and finance

The SNSL is represented on relevant governance groups to ensure ongoing and effective communication with representatives from NHS Boards and other partner organisations.

4.2 Child Health Records Departments

The SNSL reports blood spot screening results to the relevant NHS Board Child Health/Screening Department where a record is maintained of all babies resident in the area. Each Child Health/Screening Department has responsibility to:

- ensure every child known to be resident in the NHS Board has a blood spot result up to 1 year of age
- ensure results are recorded onto the Scottish Immunisation Recall System (SIRS)
- identify babies who do not have a screening result by 15 days of age
- ensure results are obtained and recorded for all pre-school children who transfer in to the NHS Board

4.3 Failsafe Arrangements

A range of failsafe arrangements are in place at various stages within the screening pathway. These are the responsibility of the relevant department and monitored and reported through local governance systems and processes.

- **Scottish Newborn Screening Laboratory**

Offer of screening - Requirement for a newborn blood spot card to be completed for all babies, regardless of whether the offer of screening has been declined.

Each quarter the Registrar General's Office provides the SNSL with data on a random selection of 10% of all births registered in Scotland. The SNSL compares this information with its own records to ensure that each baby has had a report issued. All anomalies are investigated and appropriate arrangements are made to follow up.

Referred cases - The SNSL notifies the nominated clinical specialist by telephone on the day the positive screening result is known and follows the referral up in writing. The clinical specialist is asked to provide written confirmation by way of a reply slip supplied with the referral letter that the child has been assessed. A system is in place within the SNSL to follow up any cases where written confirmation is not provided.

- **Child Health/Screening Departments**

Child Health/Screening Departments identify all babies who do not have a screening result by 15 days of age and issue a report to the relevant healthcare professional for appropriate action to be taken. In addition they notify the relevent health professional of any child moving into the area who has no documented results (or declines) for the screening programme in order for age appropriate screening to be offered.

4.4 Escalation Process for Adverse Incidents

Any screening programme has the potential for significant adverse incidents to occur at any stage in the screening process and for complaints/issues about the service to attract significant public, political and media attention. It is therefore important that robust risk management and audit systems are established to minimise the occurrence and impact of any adverse incidents and to facilitate continuous quality improvement. National agreed guidance on escalation procedures for the screening programmes should be followed.

The methodology for ascribing levels of risk should be consistent with local clinical and non clinical governance systems and processes. It is recognised that the assessment of impact and likelihood of risk can be subjective and is based upon the knowledge and expertise of those involved. Evidence and statistics, where they exist, should be used to inform decisions.

5. The Conditions

5.1 Phenylketonuria (PKU)

PKU is an autosomal recessive genetic condition. If a person has only one copy of the altered gene that causes PKU, they are a healthy carrier of the condition. Either parent can be a carrier of the condition without knowing. When both parents are carriers they may both pass on the altered gene that causes PKU to their children. If both parents are carriers, they have a one in four chance, with each and every pregnancy, of having a baby with PKU. People with PKU are unable to break down phenylalanine, an amino acid present in many foods. This is because the liver does not have enough of an enzyme called phenylalanine hydroxylase (PAH). This enzyme is needed to convert phenylalanine into tyrosine, which is essential for normal brain development after birth. People with PKU accumulate too much phenylalanine in the body and not enough tyrosine. The level of phenylalanine in the blood is higher than normal so a blood test can show whether or not someone is likely to have PKU. The most serious form of PKU is sometimes called 'classical' PKU. If classical PKU is left untreated it almost always leads to severe mental disability as well as seizures. People with untreated classical PKU are usually unable to talk, read or write and need help to look after themselves throughout their life.

A baby with untreated PKU doesn't usually show any signs of the condition for the first few months. By the time they are 6-12 months they show delayed mental development. By the time they are two years old they show serious and permanent mental disability [2]. Around a fifth of babies with PKU detected by newborn screening in the UK have the milder form of the condition. Milder forms of PKU are called hyperphenylalaninaemia (HPA), previously referred to as 'benign' PKU. Someone with untreated mild PKU might have 'slight to moderate' mental disability, depending partly on how much phenylalanine they have in their blood.

A very small number of people who are found to have raised levels of phenylalanine do not have a primary defect in the enzyme PAH, but in its cofactor, biopterin. Biopterin is also needed in order for the liver to break down phenylalanine. People with these rare biopterin defects have problems additional to PKU and are treated differently. An increased blood phenylalanine is not specific for PKU. In addition to disorders of PAH deficiency, increased phenylalanine detected via newborn screening at 5-8 days may occur in several other situations; in some cases the phenylalanine increase may also be associated with an increase in tyrosine. In these latter cases PKU is not suspected (although not impossible if there are two co-existing disorders) and these babies with an associated increase in tyrosine require different investigation and management, and urgent referral to an appropriate specialist clinician. It has been well established that an elevated phenylalanine and tyrosine on newborn screening is a feature of galactosaemia and for this reason it is important to consider galactosaemia as part of the differential diagnosis of a raised phenylalanine. The incidence of galactosaemia in the UK is approximately 1 in 40,000 births.

5.1.1 Incidence of PKU

In the UK and Europe there is an overall incidence of 1 in 10,000 live births. PKU is highest amongst white Caucasians, and is less prevalent in populations with Sub-Saharan African and South Asian ancestry. There are around 800,000 babies born in the UK each year, and in 2010-11 100 babies had a positive result for PKU following newborn blood spot screening. The likelihood of having PKU is related to your ethnic origin. PKU is twice as common in Ireland, where there is around 1 baby born with PKU in every 4,500 births, compared to 1 in every 200,000 in Finland. By contrast, PKU is very uncommon amongst certain groups, including African-Americans and Ashkenazi Jews.

Early diagnosis of a baby with PKU through screening can also alert the parents to their risk of having other affected children. When an infant is diagnosed with PKU, it is recommended that any future baby should be tested 48-72 hours after birth for PKU, rather than waiting until they are five days old.

5.1.2 Treatment of PKU

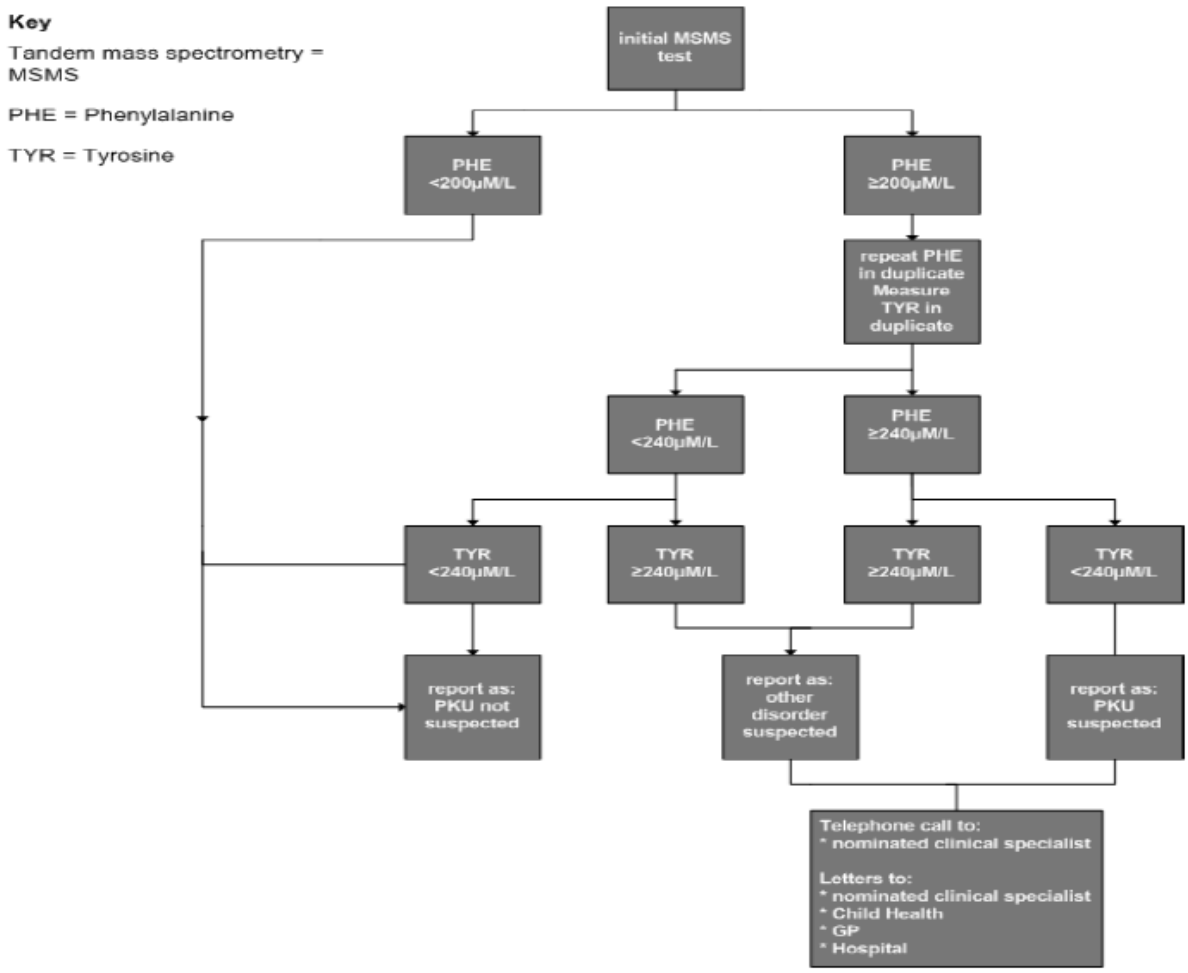
If started early, treatment for PKU is very effective. It involves a special diet. Patients cannot eat foods that contain a lot of phenylalanine, which means they have to be very careful about how much protein they eat. Because people need protein to stay healthy and children need it to grow, they need a special dietary supplement, containing all the other essential amino acids except phenylalanine, and extra minerals and vitamins. They need, and can manage, a very small amount of phenylalanine in low protein foods. Their blood is tested regularly to check their levels of phenylalanine. For the best treatment, a person with PKU needs help from a team of experienced health professionals, including doctors, nurses and dieticians.

There are several reports demonstrating the effectiveness of treatment for PKU. In the UK the aim is to start dietary treatment before 14 days to minimize the risk to the baby's development. In the past, patients with PKU stopped taking their special diet as teenagers but, increasingly, research points to the fact that the adult brain remains sensitive to high levels of phenylalanine. The recommendation is now to maintain the diet for life. This has major social and financial implications.

It is possible for mothers to breast feed their babies with PKU so long as they balance the amount of breast milk with the baby's special dietary supplement. This may require mothers to express and discard their breast milk initially, until their baby's phenylalanine levels are within target levels.

Women who have PKU and stopped the special diet when they became adults are at risk of having babies with physical and mental disabilities. This is due to the mother's high phenylalanine levels affecting the baby in utero and not because the baby has PKU. The evidence shows this can be prevented through strict control of the mother's phenylalanine levels; the mother must maintain the special diet before conception and throughout her pregnancy. For this reason it is especially important for women with PKU and HPA to remain in contact with PKU services to ensure the diet is undertaken prior to conception and throughout pregnancy.

5.1.3 Newborn Screening Laboratory pathway for PKU



5.1.4 Clinical pathway when PKU is suspected

- **Referral**

The screening laboratory informs the Consultant Paediatrician in Inherited Metabolic Disorders of all babies in whom 'PKU is suspected' (phenylalanine > 240 micromol/l; Tyrosine normal) by telephone on the day that the result has been reported by the lab. This is followed by written confirmation. The Consultant then contacts the relevant PKU Specialist or Nominated Team depending on NHS Board that day to arrange for the family to be contacted.

The specialist/team will contact the GP, midwife and/or health visitor, by telephone, as necessary. This should be backed up with written information. The PKU specialist or nominated team will then contact the family and arrange an appointment for baby and family to be seen on the same or the next day (if this is a Friday and it is not possible for the family to be seen on Friday or Saturday,

then the family should not be informed until Monday).

- **First face to face review**

Wherever possible, this appointment should be face-to-face with at last one member of the PKU specialist or nominated team. In rare circumstances, geography and/or weather may make this impossible. In these circumstances, the positive screening result may be given by a local Health Professional, supported by the PKU Specialist or Nominated Team by telephone or telemedicine.

This appointment should include an explanation of the condition including introduction to inheritance, an Introduction to dietary management, including infant feeding by breast or bottle, and instruction in how to make up special phenylalanine-free feeds (if clinically required before diagnosis confirmed). If required, initial supplies of special feeds will be provided by the PKU team, and the family will be advised to contact their GP to prescribe further supplies of these specialist feeds. The baby should have a full clinical examination and have a blood test taken for plasma amino acids and bloodspots for pterins and DHPR

There should also be an introduction to home blood test monitoring, which may include demonstration of heel prick method to parents. The family should be provided with the IMD Scotland PKU Parents Pack. This includes the 'PKU is suspected' leaflet, contact details for the PKU Specialist and/or Nominated Team, information about PKU and its management and information about parent support groups. A written report from the first appointment should be sent to the GP, Midwife and Health Visitor. Confirmation of the appointment (and diagnosis, when available) should be sent to the Scottish Newborn Screening Laboratory.

Results of the diagnostic tests (plasma phenylalanine concentration) should be available on the same day or the next day and communicated to the parents by the PKU Specialist or Nominated Team as soon as they are available (usually by telephone). Diet should be commenced at the first appointment if clinically necessary prior to diagnostic results being available, otherwise it must be commenced before day 14 of life

- **Ongoing**

A follow up appointment will usually be within 10 working days of the first appointment for babies who have been started on dietary treatment. For babies diagnosed with hyperphenylalaninaemia, not requiring dietary treatment, the timing of this appointment will be decided by the Consultant Paediatrician. If the family have not been seen initially by a PKU Specialist Team, they should be offered a review by a PKU Specialist Team within 10 working days of the initial positive screening result. This could be in a local IMD Scotland Network Clinic or at Royal Hospital for Sick Children Glasgow or Edinburgh.

Follow-up management should include a review of the condition and inheritance (supported by written information), information on dietary management, blood monitoring requirements, growth and developmental and general health, and support information – including contact details of parent support organisations.

A specialist nurse should be available if possible to provide advice and support. As appropriate, the parents should be taught how to perform the heel prick on their baby (if required for the condition). The specialist dietician may make contact with the local dieticians as appropriate.

5.2 Congenital hypothyroidism (CHT)

CHT is a condition where, for one of several reasons, the thyroid gland doesn't work when a baby is born and fails to make the thyroid hormone called thyroxine. Problems with the gland itself are

called primary CHT. This can be caused by the complete absence of the thyroid gland (called agenesis) or the lack of normal development of the gland, which means it is situated in the wrong place (called ectopic thyroid). Another cause of primary hypothyroidism is when the gland is of normal size and position but there is a problem with production of thyroxine (called dyshormonogenesis).

Alternatively, hypothyroidism can be caused by defects earlier in the chemical pathway that regulates the production of thyroxine. The thyroid gland doesn't work in people who have very low levels of thyroid-stimulating hormone (TSH) (also called thyrotropin), produced by the pituitary gland. This is called secondary hypothyroidism. Cases of secondary hypothyroidism are not detected by newborn screening.

The thyroid gland usually starts working in the unborn fetus from about 20 weeks gestation. The mother's own thyroid doesn't provide enough thyroxine to maintain sufficiently high levels in the fetus. In very severe cases of CHT babies are born with, or quickly develop, the following symptoms: a very low hair-line, a protruding tongue, cold skin, an umbilical hernia, jaundice, feeding difficulties, constipation, and generally sluggish behaviour. However, only very few babies will have all of these symptoms and primary CHT is rarely diagnosed by clinical means in the newborn period.

Some babies are initially hypothyroid but it resolves on its own later in childhood. This is called transient hypothyroidism and may be caused by exposure to iodine in antiseptics soon after birth or by maternal antibodies. It is very rare in full term babies. There may also be other reasons why a baby initially has insufficient thyroxine after birth but these are not yet well understood.

Preterm infants are at risk of hypothyroxinaemia (having a low level of thyroxine) due to several factors, including immaturity of thyroid function, the effects of acute illness and/or the use of iodine-containing compounds in imaging and surgery. There is no evidence that preterm infants are at increased risk of CHT when compared with term infants.

The current TSH-based screening test may not detect those preterm infants who do have CHT, especially those born between 23 and 27 weeks gestation, because they show a delayed rise in TSH levels after birth, mainly due to immaturity of the hypothalamic-pituitary axis. All babies born at less than 32 weeks (less than or equal to 31 weeks + 6 days) should be offered a preterm repeat test at 28 days of age or discharge home, whichever is the sooner. This policy means that babies eligible for a CHT preterm repeat test should complete their newborn blood spot tests before they are discharged home from hospital.

5.2.1 Incidence of CHT

Several papers in the literature quote an incidence of about 1 in 3,000 babies; similar rates of CHT are reported in the US and Europe. Several US programs have reported a higher incidence in the Asian, Native American and Hispanic populations and a lower incidence in the American Black population.

CHT is also reported to be higher in infants born to older women and in infants born preterm. Nearly all screening programmes report an increased female prevalence, approaching a 2:1 female to male ratio. CHT is not usually an inherited condition (with the possible exception of dyshormonogenesis). In 90% of cases CHT seems to happen completely by chance. One in ten cases is thought to be inherited.

5.2.2 Treatment of CHT

The aim of treatment is to normalise thyroid function as rapidly as possible to improve IQ. Babies with primary hypothyroidism are treated with thyroxine, given as either a suspension or in the form of crushed tablets, mixed in a small quantity (less than 5 ml) of milk / water, by mouth. If babies are treated early they will grow normally and reach normal height. The delay in mental development

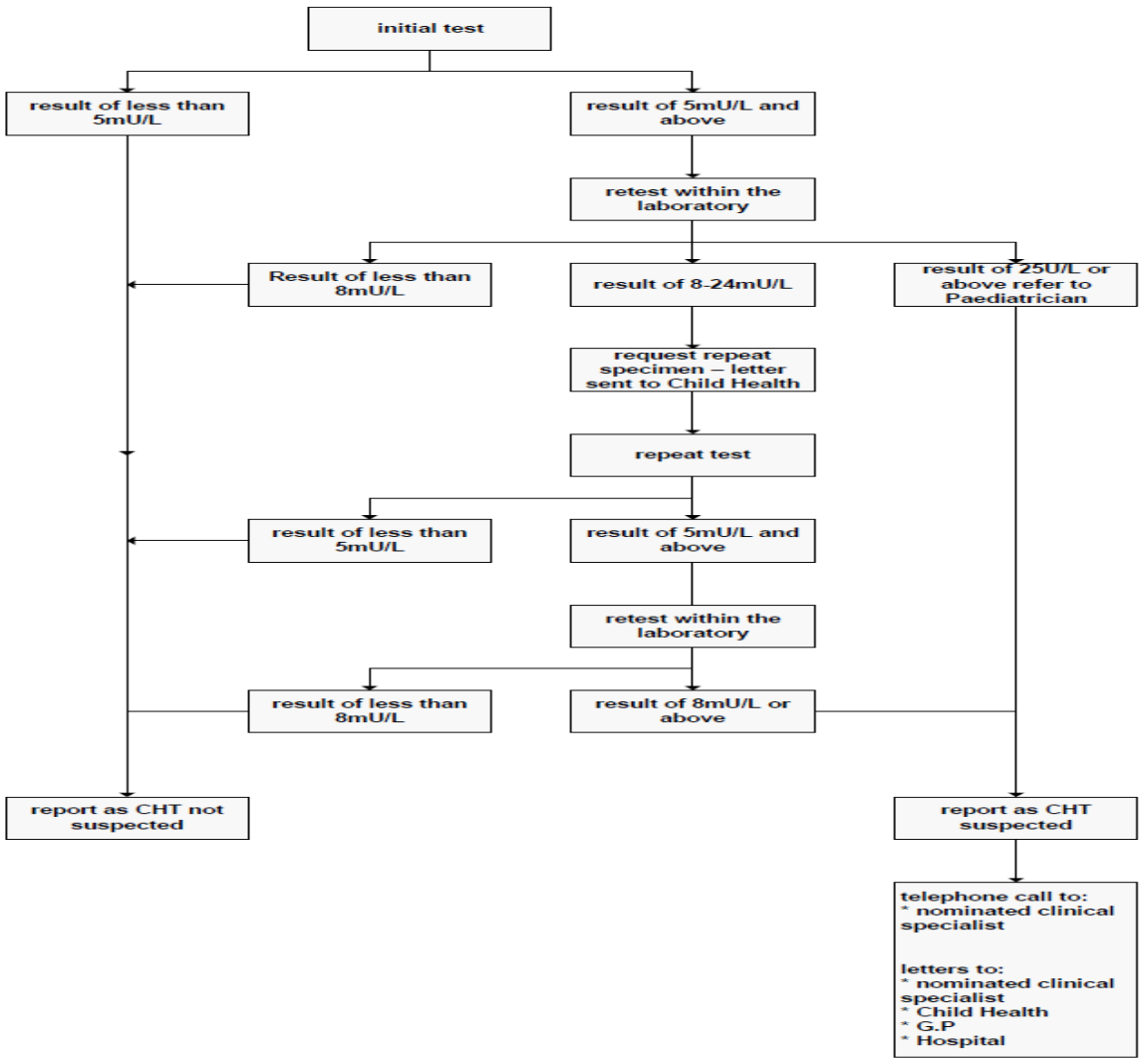
can also be largely corrected. The later treatment is started, the more the baby's development is affected by the condition. Whilst it is known that newborn screening can prevent severe disability in babies with CHT, it is not known whether treatment for babies with CHT can reverse any effects of hypothyroidism caused before the baby was born. It is thought these effects will only be small.

Whilst it is understood that screening for CHT is highly effective in preventing severe mental disability in children, it is difficult to calculate exactly how accurate screening for CHT is. A positive screening result does not mean that the baby definitely has the condition and a negative result does not necessarily mean that they will never have the condition. There are a number of reasons for this:

- Transient hypothyroidism: Some children do have hypothyroidism, but it is the transient form. Some research suggests that up to 50% of children who have CHT get better on their own later in childhood. These children are usually sick preterm babies. Transient hypothyroidism is very rare in full term babies.

- Later onset of hypothyroidism: Other babies don't develop hypothyroidism until they are a few weeks old. This means that they are not picked up by the newborn blood spot test (sample taken on day 5).

5.2.3 Newborn Screening Laboratory Pathway for CHT



5.2.4 Clinical pathway when CHT is suspected

On detecting a borderline result a second blood spot sample is to be taken as close to (but no sooner than) 7 days after the initial sample. If CHT is suspected or the result remains 'borderline' on the second sample, the baby will be followed up as detailed below.

- **Referral**

The screening laboratory informs the paediatric endocrine team) and/or to a clearly identified lead paediatrician with a special interest in CHT or experience of managing these patients depending on NHS Board, that day or the next working day. There must be access to the full range of diagnostic investigations recommended.

The specialist/team will contact the GP, midwife and/or health visitor, by telephone, as necessary. This should be backed up with written information. The CHT specialist or nominated team will then contact the family and arrange an appointment for baby and family to be seen on the same or the next day (if this is a Friday and it is not possible for the family to be seen on Friday or Saturday, then the family should not be informed until Monday).

- **First face to face review**

This appointment should include investigations to confirm diagnosis, an explanation of the condition, an introduction to medication and clinical monitoring, the specialist team's contact details, and provision of available written information including the 'condition is suspected' leaflet if not already given.

The report of the first review should be communicated via letter to the GP, with a copy to midwife, HV and screening laboratory.

- **Ongoing**

Follow-up management should include a review of the condition (supported by written information) and medication, information on blood monitoring requirements, growth and developmental and general health, and support information – including contact details of parent support organisations.

5.3 Sickle Cell Disease (SCD)

SCD is the name given to a group of inherited genetic blood conditions that affect the haemoglobin in red blood cells. They are autosomal recessive conditions, so inheritance of an affected gene from both parents results in a disorder whilst inheritance of one abnormal gene results in a healthy carrier.

SCD is a condition that affects the normal oxygen-carrying capacity of red blood cells. When the cells are de-oxygenated and under stress, in sickle cell conditions, they can change from round flexible disc-like cells to elongated sickle or crescent-moon shapes. The effect of these changes is that the cells do not pass freely through small capillaries and form clusters, which block the blood vessels. This blockage prevents oxygenation of the tissues in the affected areas resulting in tissue hypoxia and consequent pain (known as sickle cell crisis pain). Other symptoms of SCD can include severe anaemia, susceptibility to infections, early cerebrovascular accidents and damage to major organs. SCD is a lifelong condition that can be diagnosed from a simple blood test, before the baby becomes ill.

The most serious type of SCD is sickle cell anaemia (Hb SS); other forms of SCD include Hb SC and Hb S beta thalassaemia. There are also some rarer forms. Babies with SCD who are not identified through screening usually begin to show symptoms in their first year. The first time they become ill can be fatal. Babies with Hb SC, rather than Hb SS, are usually less severely affected. The severity and pattern of disease within each condition, as well as between individual patients, varies in an unpredictable way.

Despite improvements in life expectancy, SCD remains a cause of significant morbidity – even in developed countries. The objective of the newborn screening programme is to detect babies at risk of SCD so they can enter the healthcare system as early as possible. Screening aims to identify the following specified conditions: Hb SS, Hb S beta thalassaemia (beta+, beta0 and Lepore), Hb S/HPFH, Hb SC, Hb SDPunjab, Hb SE and Hb SOArab. Other clinically significant haemoglobinopathies likely to be detected as 'by-products' of newborn screening include beta thalassaemia major, Hb E beta thalassaemia, beta thalassaemia intermedia and Hb H disease. It has been shown that early treatment improves the health of babies with SCD and can prevent death.

Early diagnosis of a baby with SCD, or identification as a carrier of SCD can also alert the parents to their risk of having other affected children. Newborn screening for SCD can also identify babies with combinations of gene variants that do not cause illness. This may have psychological effects on families, who may not fully understand the result and worry that their child may become ill. This has resource implications, because the health service needs to provide education and counselling for families with these results.

An area of concern in newborn screening for SCD relates to the possibility of SCD babies being missed because of a blood transfusion prior to a blood spot sample being taken. These babies do not have a valid sickle cell screen result. Taking one blood spot prior to transfusion is recommended, however if this is missed DNA testing of transfused babies should be offered.

5.3.1 Incidence of SCD

Haemoglobinopathies are common in people whose family origins are in malarial parts of the world. In the UK, haemoglobinopathies are seen particularly among minority ethnic groups from Africa, the Caribbean, the Mediterranean, South East Asia, the Middle East, and the Far East [39], but can be found (less frequently) in all ethnic groups. Approximately 1000 haemoglobin gene variants have been identified worldwide. As well as identifying babies with SCD the screening procedure also identifies babies who are healthy carriers of the sickle gene variants.

If a baby is found to be a healthy carrier this result is reported to the parents and counselling is offered. Sometimes another blood test is requested to confirm the result. This carrier result needs to be carefully explained so that parents understand what it means and recorded in the personal child health record (PCHR). Carrier status information should be provided to GPs.

5.3.2 Treatment of SCD

Treatment for SCD includes taking penicillin and receiving effective vaccines to reduce the risk from serious infections, especially while the child is under five when the risk is highest. Educating patients and parent/carers on how to identify and treat symptoms as early as possible has been shown to be important in ensuring quick treatment for serious complications caused by SCD. Some adults and older children with SCD can also be treated with hydroxyurea, which reduces the frequency and severity of sickle cell crises. Regular transcranial doppler ultrasonography and appropriate treatment reduces the risk of stroke.

Bone marrow transplantation offers the only chance of a cure for children with SCD depending on the type of disorder, but this relies on there being a compatible donor. The procedure itself is very risky as it involves suppressing the immune system and can cause death.

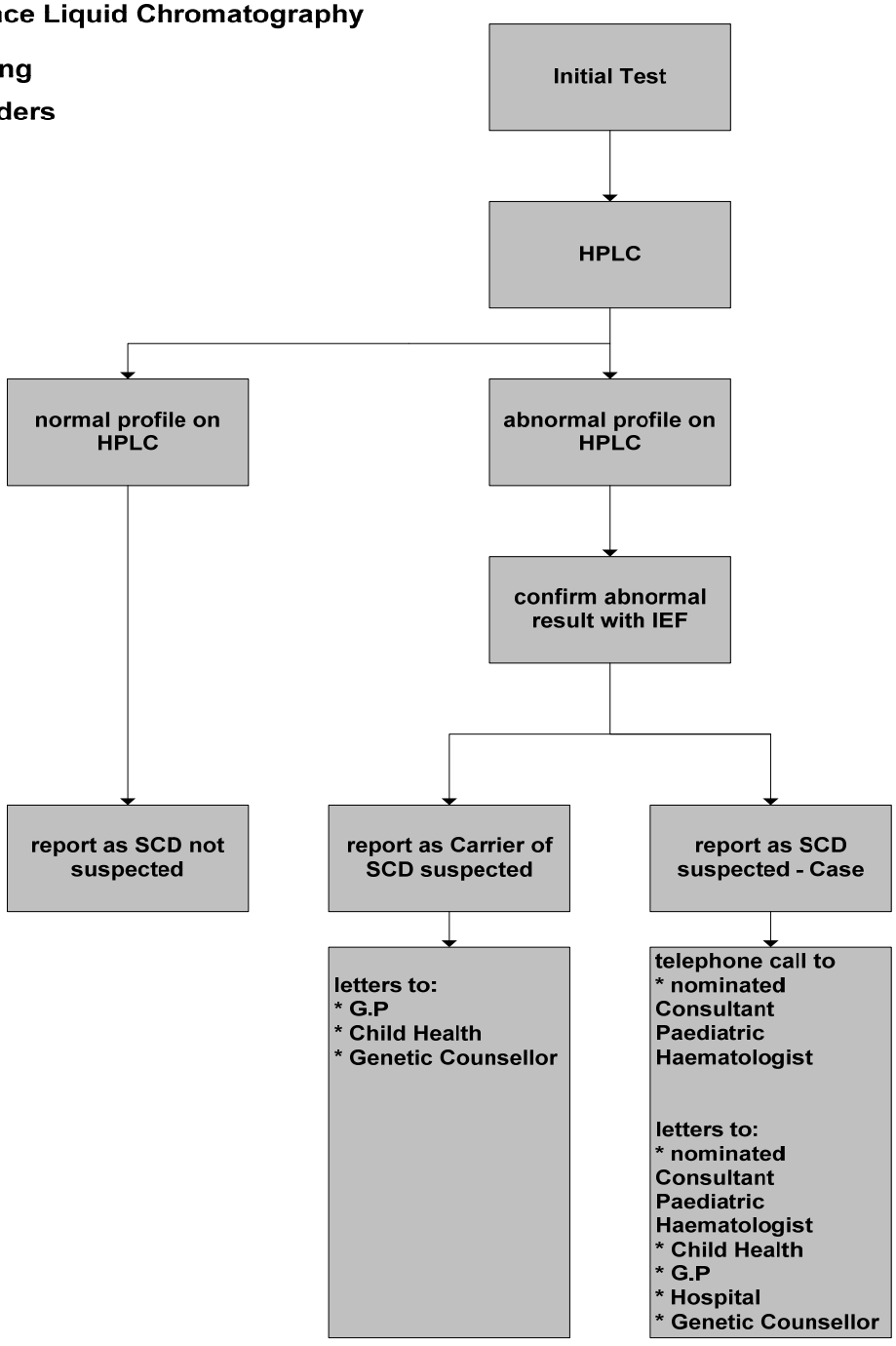
5.3.3 Newborn Screening Laboratory Pathway for SCD

Key

HPLC = High Performance Liquid Chromatography

IEF = Isoelectric Focusing

SCD = Sickle Cell Disorders



5.3.4 Clinical pathway when SCD is suspected

- **Referral**

The screening laboratory should send the results as a matter of urgency to the designated healthcare professional/team for that NHS Board, and confirmation of receipt should be documented. Parents should be informed by personal contact. Copies of all reports should be sent to the GP and HV.

The designated health professional is responsible for:

- Informing parents of the results and arranging clinical follow-up of infants with SCD
- Informing parents of the results and arranging clinical follow-up of infants with other potentially clinically significant conditions
- Ensuring that infants are not lost to clinical follow-up before registration in a clinic
- Providing information and counselling for the parents of infants who are carriers or have other benign conditions detected
- Arranging a repeat as indicated by the laboratory

- **First face to face review**

This appointment should include investigations to confirm diagnosis, an explanation of the condition including an introduction to inheritance, an introduction to medication management and monitoring (if clinically required), the specialist team's contact details, provision of available written information including the appropriate condition is suspected leaflet, and a check to ensure that the infant has received their pneumococcal conjugate vaccine (by 8 weeks of age).

The report of the first review should be communicated via letter to the GP, with a copy to midwife, HV and screening laboratory.

Diagnostic testing should be undertaken before 8 weeks of age. Parental samples (where required) should also be tested at the same time. Samples for diagnostic testing for SCD should be sent to a specialist laboratory, which has expertise in haemoglobinopathy analysis in the newborn period.

- **Ongoing**

Follow-up management should include a review of the condition and inheritance (supported by written information), information on medication management, blood monitoring requirements (if required), growth and developmental and general health, and support information – including contact details of parent support organisations.

A specialist health professional should be available if possible to provide advice and support

5.4 Cystic Fibrosis (CF)

CF is an autosomal recessive genetic condition. If a person has only one copy of the gene with a CF-causing alteration, they are a healthy carrier of the condition. Either parent can be a carrier of the condition without knowing. When both parents are carriers of a CF-causing alteration they may both pass the alteration to their child and they have a one in four chance with each and every pregnancy of having a baby with CF. In CF there is a problem transporting chloride across cell membranes. This affects certain organs in the body, particularly the pancreas and lungs; the thick secretions in these organs cause digestive problems and chest infections. The abnormal transport of chloride in sweat glands leads to an increased level of chloride in the sweat of children with CF. This is the basis of the ‘sweat test’, often used to investigate suspected cases. There are now other ways of diagnosing CF, including looking for alterations (mutations) in the CF gene. This gene is called the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Alterations to this gene can cause CF. While some alterations usually cause severe symptoms, others are more often associated with milder forms of CF.

CF can affect the baby before birth. Fifteen per cent of affected babies are born with blocked intestines, a condition called meconium ileus. About 70% of screen positive babies with CF show some symptoms by the time they have a diagnostic sweat test. These can include problems

absorbing food, as well as breathing difficulties. Eventually all patients with CF develop long-term chest infections. Now most people with CF can expect to live into early adulthood (25 years).

Screening does not identify all of the 15% of babies with CF who have meconium ileus. These babies will need treatment at birth for this condition and will therefore be diagnosed. An initial analysis of the blood spots is used to identify babies at higher risk of having CF; this test is called an immunoreactive trypsinogen (IRT) test. These babies will then have DNA testing on the same sample to look for CF-causing alterations.

Some babies will require a second blood spot sample to be taken between day 21 and day 28 (day of birth is day 0) in order to confirm a CF screening result. Parents should be told of the reasons for the repeat sample (that their baby's CF result is 'borderline'). This need for a second sample may cause anxiety whilst they await the results. It is recommended that this second sample is taken ideally as near to day 21 as possible so that parents get a conclusive screening result as soon as possible to reduce their anxiety.

Using DNA analysis as part of CF screening inadvertently identifies a small number of CF carriers, babies who carry one identified alteration on the CFTR gene and who are healthy. It can be difficult to distinguish between babies who are healthy carriers (i.e. those with only one alteration), and babies who have CF (i.e. those who have a second, unidentified alteration). Not all alterations can be tested for as there are over 1,200 identified alterations. Furthermore, not all these alterations affect a baby's health. This uncertainty means some babies will need further tests and others may need to be followed up.

There are implications for siblings and other family members who might also carry the altered gene for CF. Other family members, including the parents, will be offered genetic counselling and testing. If both parents are carriers of a CF-causing alteration, for each subsequent baby, there is a one in four chance that the baby will have CF.

5.4.1 Incidence of CF

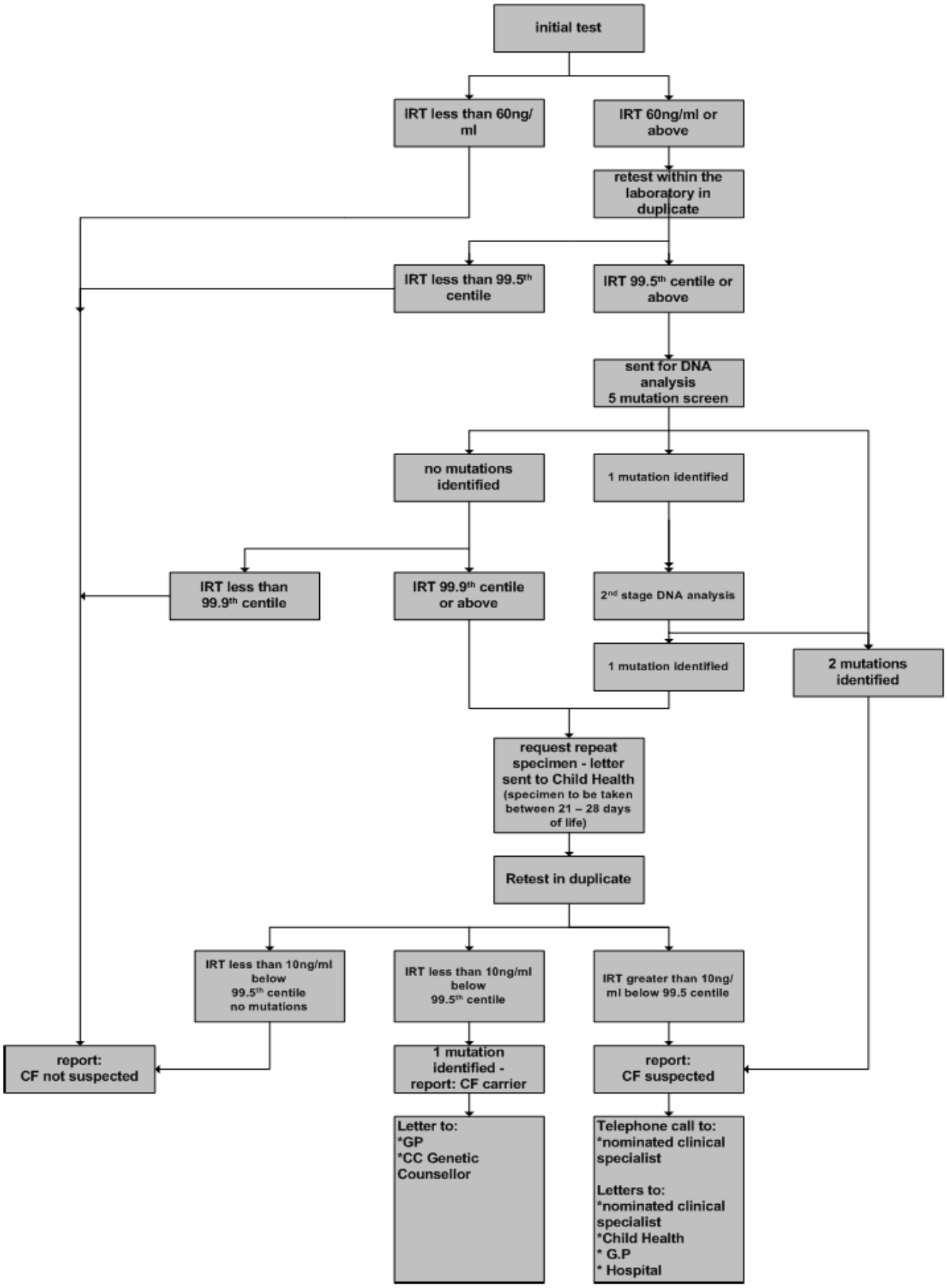
About 1 in 2,500 babies born in the UK has CF. There are around 800,000 babies born in the UK each year. CF is caused by a large number of different alterations in the CFTR gene (over 1,200 are known). The most common in the UK is called Delta F508. Whilst most of the common alterations in the CFTR gene are known to cause CF (referred to from now on as 'CF-causing alterations'), other alterations do not cause CF, and others are not yet well understood.

5.4.2 Treatment of CF

Babies with CF are treated vigorously as soon as they are first diagnosed. Treatment of children with CF aims to do two things: improve nutrition by providing supplements containing enzymes to help digestion; and reduce chest infections with frequent physiotherapy and either occasional or continuous antibiotics. Treatment can slow down the effects of the disease, but cannot stop it progressing. With treatment, half of those with CF now live to be over 30 years old with therapies improving this all the time. The research evidence is inconclusive but several studies suggest that children who are diagnosed following newborn screening might be healthier than those diagnosed later.

Newborn screening for CF may also reduce any delays in diagnosis, reducing anxiety and uncertainty about why the child is ill, however, a confirmed diagnosis following newborn screening can also take time and cause parents anxiety. Early diagnosis of a baby with CF through screening can also alert the parents to their risk of having other affected children. Longer-term benefits of screening are hard to assess, as improved treatments make living with CF better than in the past (whether or not a person is diagnosed through screening).

5.4.3 Newborn Screening Laboratory Pathway for CF



5.4.4 Clinical pathway when CF is suspected

A **second blood spot sample** may be required if the laboratory detects either one mutation on DNA analysis or a raised IRT on the first sample. The sample should be collected on day 21. If CF is suspected on the second sample, the baby will be followed up as detailed below.

- **Referral**

The screening laboratory informs the designated healthcare professional/team for that NHS Board of a 'CF is suspected' screening result in any of the following situations:

  - Two detected CFTR mutations
  - One mutation and a second sample high IRT
  - High IRT concentration in two blood samples taken approximately 3 weeks apart

The HP/team refers to the designated clinician for CF and arranges an appointment for the family to be seen within five days following receipt of a positive screening result. Families should not be informed on a Friday, Saturday or Sunday unless there is sufficient primary care support. The HP/team must make contact with the family's GP to co-ordinate first family contact, and obtain a telephone number for the family.

The family will be given the 'CF is suspected' leaflet, contact details for the support team and details of the time and location of an appointment with the paediatric specialist team.

- **First face to face review**

This appointment should include investigations to confirm diagnosis, an explanation of the condition including an introduction to inheritance, an introduction to medication management, contact with a specialist dietician (if clinically required), and monitoring (if clinically required), the specialist team's contact details, provision of available written information including the appropriate condition is suspected leaflet.

- **Ongoing**

Follow-up management should include a review of the condition and inheritance (supported by written information), information on medication management, growth and developmental and general health, and support information – including contact details of parent support organisations.

A specialist health professional should be available if possible to provide advice and support

5.5 Medium-chain acyl-CoA dehydrogenase deficiency (MCADD)

MCADD is an autosomal recessive genetic condition. If a person has only one copy of the gene with an MCADD-causing alteration, they are a healthy carrier of the condition. Either parent can be a carrier of the condition without knowing. When both parents are carriers of an MCADD-causing alteration they may both pass the alteration to their child and they have a one in four chance with each and every pregnancy of having a baby with MCADD. It is a rare inherited disorder where the body cannot metabolise (break down) fat properly. Most infants are asymptomatic at birth, and most cases present before 2 years of age (mean age 13 months), but in rare cases they may not appear until adulthood. Current estimates of mortality after the first few days are about 5 to 7% over the first 6 years, unless both early diagnosis and appropriate management are in place.

MCADD can cause drowsiness, lack of energy and diarrhoea, and there is a risk of complications such as seizures, breathing difficulties and even coma or sudden death. The episodes are usually

precipitated by metabolic stress such as inter-current infections, particularly gastroenteritis which may appear to be quite mild.

Among those who experience acute episodes the risk of death is estimated to be 25%, and up to 30% of survivors have significant long term morbidity including fits, learning and behavioural difficulties and other neurological deficits.

During long periods between eating, the body breaks down its fat stores to produce energy. Fats are broken down into fatty acids, which are then broken down into shorter and shorter lengths. At each step, energy is released. People with MCADD cannot break down fatty acids properly, because they lack one of the enzymes needed. This leads to a build-up of medium-chain fats, which can become toxic. Because they cannot get energy from fat, they must rely on glucose for their energy.

Screening aims to identify infants with MCADD and prevent onset of symptoms by early dietary management to reduce adverse outcomes of intellectual disability and death. Early diagnosis of a baby with MCADD through screening can also alert the parents to their risk of having other affected children. When an infant is diagnosed with MCADD, it is recommended to screen any siblings for the condition as it is possible to find undiagnosed siblings. It is also recommended that any future baby should be tested 24 to 48 hours after birth for MCADD (a routine blood spot sample should still be taken on day 5).

5.5.1 Incidence of MCADD

MCADD is the most common inherited disorder of mitochondrial fatty acids oxidation. Around one in 10,000 babies born in the UK has MCADD. There are around 800,000 babies born in the UK each year. The incidence is highest in the northern European population. A review of the ethnicity of 1.1 million newborns in the UK did not find a single case of MCADD among babies of Black/Asian ethnic origin who were screened at birth.

Around one in 80 healthy people is a carrier of MCADD, and will not have any symptoms. However, if both parents are MCADD carriers, there is a one in four chance of their child being born with MCADD.

One concern is that a proportion of screen positive babies will never experience any ill-effects and there is no way of predicting which babies these will be. Thus, all babies identified as having MCADD by newborn screening must be treated as at risk. Fortunately, the treatment is not onerous or expensive, but the need to carefully monitor inter-current illnesses for the first few years of life is bound to provoke parental anxiety.

5.5.2 Treatment of MCADD

Once diagnosed, MCADD is usually quite straightforward to manage and children can lead healthy, normal lives. It is managed by eating regular meals and having frequent glucose drinks if the child falls ill, so that their blood glucose level does not fall. Whenever patients are at risk, the emergency (illness or crisis) regimen should be started early. When started early, treatment appears to be remarkably effective, reducing mortality and morbidity at specialist centres to near zero.

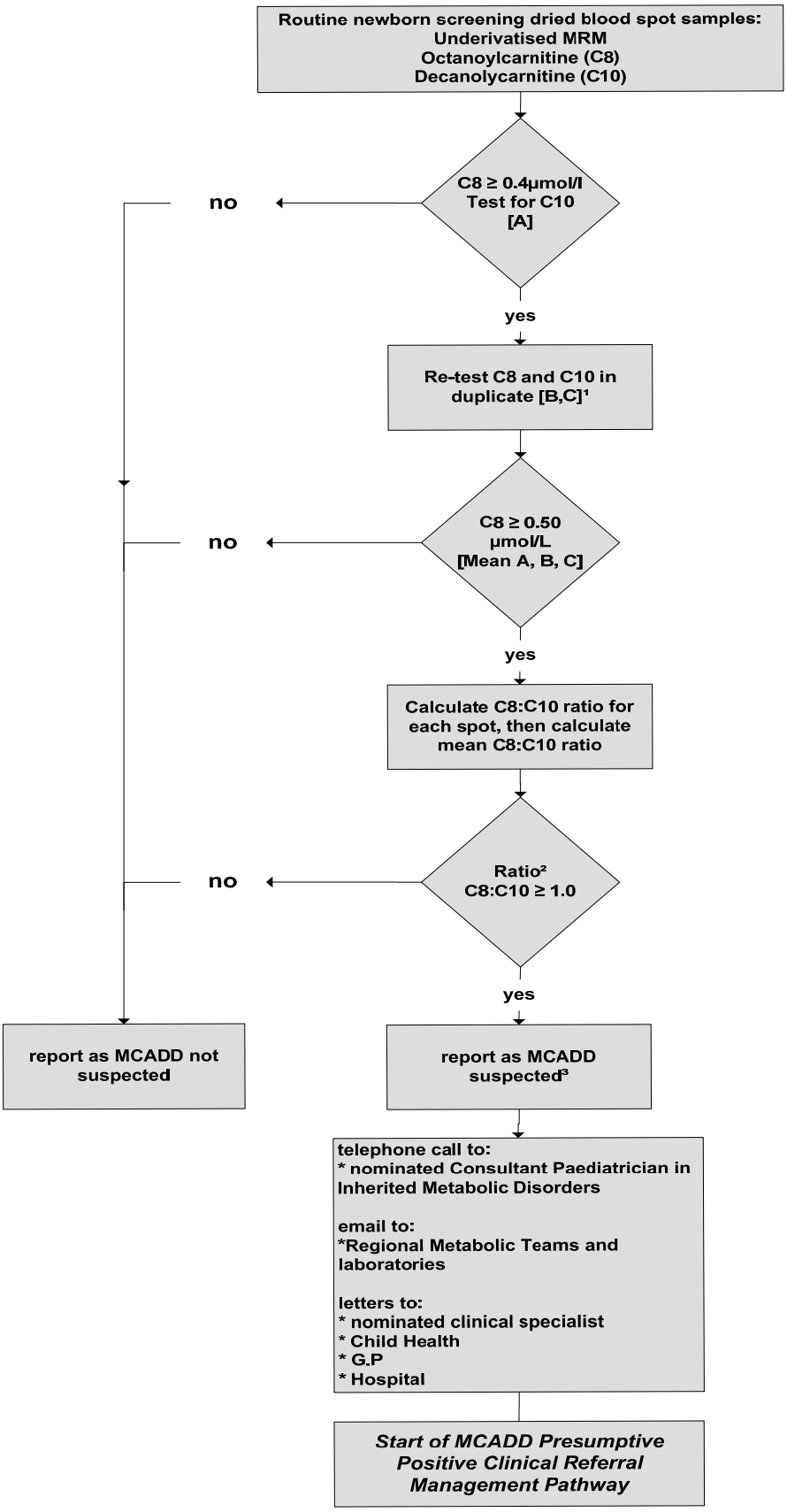
However, if MCADD is not identified and treated early, children may fall into repeated comas with complications including breathing problems, seizures, brain damage or sudden death. In the published literature, reported deaths after the diagnosis of MCADD have been rare and have mainly occurred in children diagnosed late or in whom early signs were unrecognised and / or intervention was delayed. MCADD is a lifelong condition that will always need careful dietary management during periods of fasting or fever.

5.5.3 Newborn Screening Laboratory Pathway for MCADD

[1] If insufficient blood to retest but raised initial C8 (≥ 0.40) treat as MCADD suspected.

[2] Refer to methodology for calculating C8:C10 ratio.

[3] Recommended to provide clinician with full **acylcarnitine scan** (on elute and/or derivatised) as soon as possible.



5.5.4 Clinical pathway when MCADD is suspected

- **Referral**

The SNSL will urgently contact the IMD consultant of any positive screening result on the same day as the positive result has been reported by the laboratory. The IMD consultant will then notify the appropriate designated local IMD contact/team to arrange for the family to be contacted and given an appointment to be seen the next working day. *(Parents should NOT be informed of a positive result if an appointment cannot be given for the same or next day e.g. parents should not be informed on a Friday unless an appointment is for that day or the Saturday. In this case contact should be deferred until after the weekend to the next working day).* The GP/Health Visiting and midwifery teams will be informed as soon as practicable.

- **First face to face review**

This will be directed by the IMD consultant. This should include investigations to confirm diagnosis, an explanation of the condition including an introduction to inheritance, an introduction to medication management and monitoring (if clinically required), the specialist team's contact details, provision of available written information including the appropriate condition is suspected leaflet.

- **Ongoing**

Follow-up management should include a review of the condition and inheritance (supported by written information), if deemed appropriate sibling testing will be considered. Information on ongoing dietary management, growth and developmental and general health, and support information – including contact details of parent support organisations should be provided as appropriate.

5.6 Maple Syrup Urine Disease (MSUD)

Maple syrup urine disease (MSUD) is an autosomal recessive disorder caused by a deficiency of the branched chain alpha keto acid dehydrogenase complex which consists of four subunits, E1α, E1ß, E2 and E3. The resulting metabolic block leads to an increased concentration of the branched chain amino acids leucine, valine, isoleucine and alloisoleucine and their corresponding keto acids. These compounds accumulate in tissues resulting in a life threatening metabolic decompensation in some affected individuals and are elevated in the blood and urine. The name of the condition derives from the sweet smelling urine sometimes produced by affected individuals which some have likened to the smell of maple syrup.

The classic form of the disorder presents shortly after birth, often in the first two weeks of life. Vomiting or difficulty feeding are often early symptoms accompanied by lethargy and progressive neurological deterioration. Intermediate and intermittent forms of the condition are also described. Patients with the intermediate form may present with developmental delay although the characteristic elevation of branched chain amino acids is still present. The intermittent form of the disease may only manifest at times of stress or infection and branched chain amino acids may not be continuously elevated. Rarer thiamine-responsive disease has been described together with the E_3 variant which also affects the pyruvate dehydrogenase complex resulting in marked lactic acidosis.

It is likely that newborn screening will detect patients with the classic condition but may not detect individuals with intermediate or intermittent forms which have a spectrum of clinical and biochemical severity.

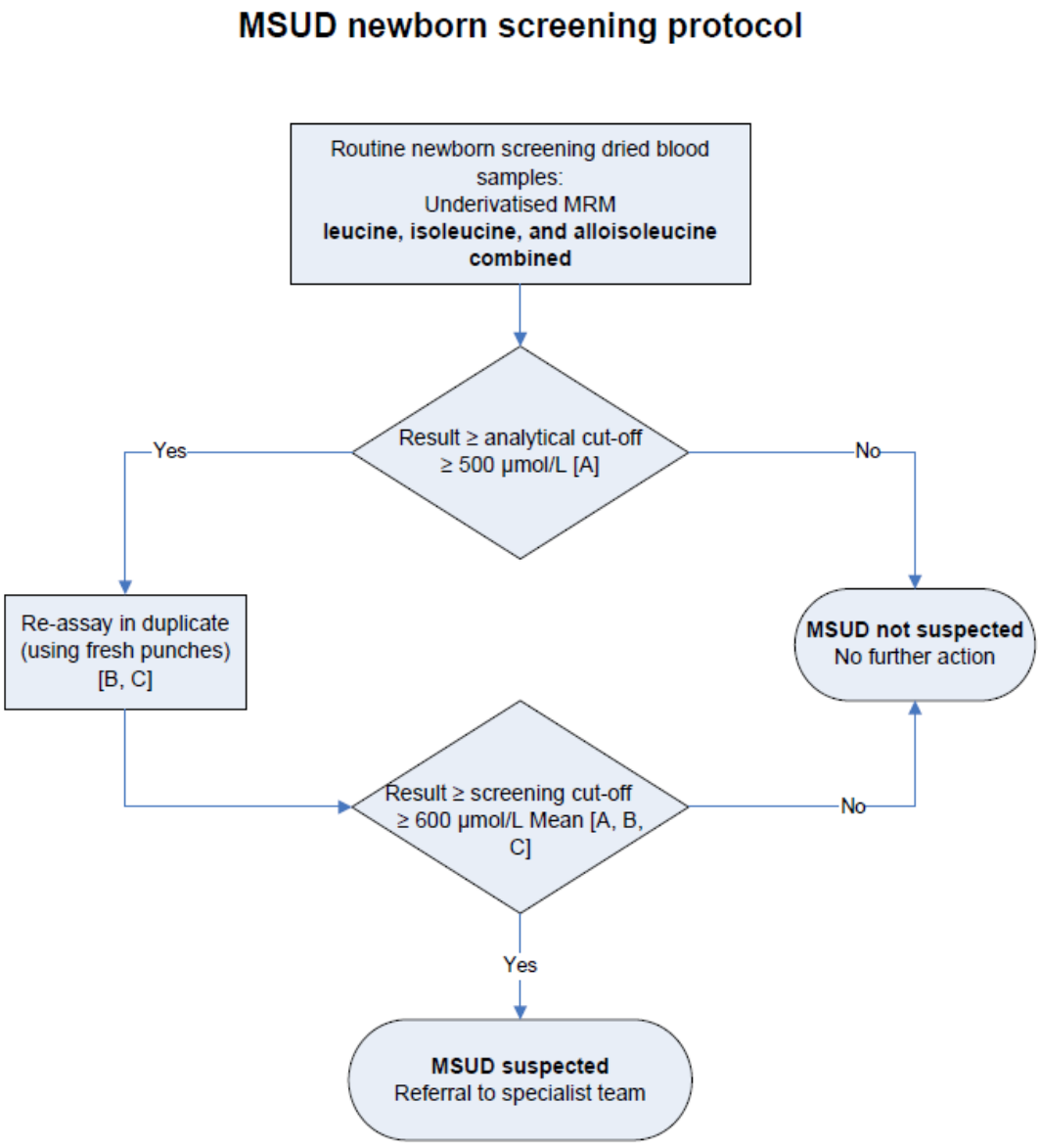
5.6.1 Incidence

MSUD occurs in approximately 1 in 200,000 live births.

5.6.2 Treatment

Treatment aims to control the levels of branched chain amino acid (leucine, isoleucine and valine) because high levels are harmful to the body. If patients become severely unwell, they may need dialysis on an intensive care unit. This is sometimes needed in newborn babies but it is seldom needed in older children. Life-long management is required to stay healthy. This involves a special diet, low in branched chain amino acids, and regular monitoring.

5.6.3 Newborn Screening Laboratory Pathway for MSUD



5.6.4 Clinical pathway when MSUD is suspected

- **Referral**

The SNSL will urgently contact the on call Metabolic Paediatrician and team with any positive screening result on the same day as the positive result has been reported by the laboratory. The metabolic team will contact the family immediately and arrange for the admission, assessment and interim management of the baby and for diagnostic testing to be carried out. This would include arranging an ambulance if required. The metabolic team will also inform the GP, Health Visiting and midwifery teams as soon as possible.

- **First review within 24 hours of screening result**

This will be carried out by the metabolic team. This will include investigations to confirm diagnosis, an explanation of the condition including an introduction to inheritance, an introduction to dietary management and monitoring, the specialist team's contact details and provision of written information

- **Ongoing**

Follow-up management should include a review of the condition and inheritance (supported by written information), if deemed appropriate sibling testing should be considered. Information on ongoing dietary management, growth and developmental and general health, and support information – including contact details of parent support organisations should be provided as appropriate.

5.7 Homocystinuria (HCU)

The most common cause of homocystinuria (HCU) is a defect in the enzyme cystathionine β synthase (CBS); this is referred to as “classical” homocystinuria. Classical homocystinuria is associated with a number of clinical and pathological abnormalities. Infants are usually normal at birth and without screening the diagnosis is not usually made until the first 2–3 years of life. Myopia followed by dislocation of the lens, osteoporosis, thinning and lengthening of the long bones, learning disabilities and thromboembolism affecting large and small arteries and veins are the commonest clinical features. Without treatment, 25% of patients will die before the age of 30, usually as a result of arterial thromboembolism. There is a great deal of clinical heterogeneity, with some patients displaying all clinical symptoms whilst others display very few or none. The concentration of plasma total homocysteine can be measured to assess the clinical severity of disease and can be monitored to determine the response to treatment.

People with homocystinuria can be sub-divided into two important biochemical phenotypes:

- Pyridoxine responsive (screen undetectable)
- Pyridoxine unresponsive (screen detectable)

In the UK approximately 50% of people with classical homocystinuria are classified as pyridoxine responsive; these people usually have milder symptoms and disease progression is slower and slowed further by oral pyridoxine (Vitamin B6) supplementation. They are very unlikely to be detected by newborn screening.

Screening for homocystinuria is based on quantitation of methionine in dried blood spots. Confirmatory testing for classical homocystinuria is done by measuring plasma amino acids and total homocysteine.

5.7.1 Incidence

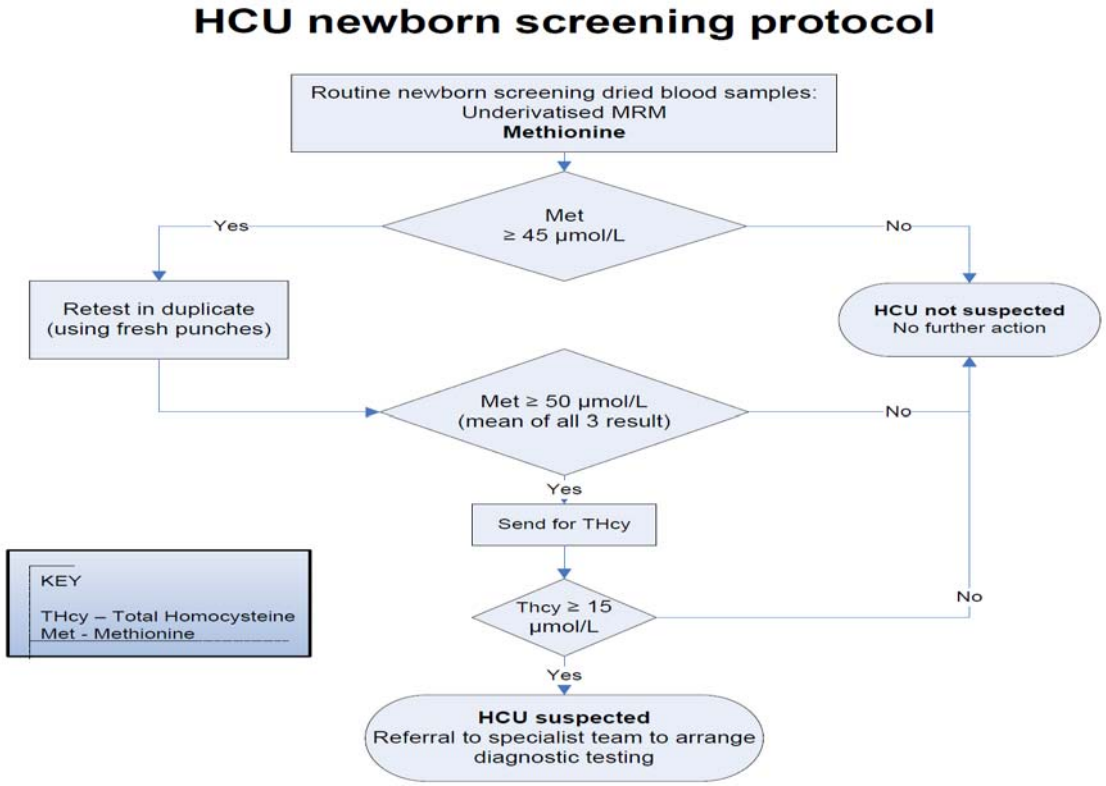
The overall incidence in the UK is reported to be around 1 in 100,000 live births. The mode of inheritance of classical homocystinuria is autosomal recessive.

5.7.2 Treatment

The mainstay of the treatment of homocystinuria in children is a carefully controlled semi-synthetic diet restricted in methionine. Some children may respond to treatment with pyridoxine. Some may also need folic acid, vitamin B12 and/or betaine.

Learning disability and physical problems can be prevented if treatment is started promptly and continued life-long.

5.7.3 Newborn Screening Laboratory Pathway for HCU



5.7.4 Clinical pathway when HCU is suspected

- **Referral**

The SNSL will urgently contact the on call Metabolic Paediatrician and team with any positive screening result on the same day as the positive result has been reported by the laboratory. The metabolic team will contact the family immediately and arrange for the baby and family to be seen on the same or the following day. The metabolic team will also inform the GP, Health Visiting and midwifery teams as soon as possible.

- **First review within 24 hours of screening result**

This will be carried out by the metabolic team. This will include investigations to confirm diagnosis, an explanation of the condition including an introduction to inheritance, an introduction to dietary management and monitoring, the specialist team's contact details and provision of written information.

- **Ongoing**

Follow-up management should include a review of the condition and inheritance (supported by written information), if deemed appropriate sibling testing should be considered. Information on ongoing dietary management, growth and developmental and general health, and support information – including contact details of parent support organisations should be provided as appropriate.

5.8 Isovaleric Acidaemia (IVA)

Isovaleric acidaemia (IVA) is caused by a deficiency in isovaleryl-CoA dehydrogenase (IVD), involved in the catabolism of the amino acid leucine.

Loss of function of the enzyme leads to the toxic build-up of metabolites including isovaleric acid and its glycine and carnitine derivatives. Over 25 mutations in the IVD gene have been associated with disease, a number of which lead to complete lack of the enzyme.

Although a firm phenotype/genotype correlation has not been identified, recent research suggests that the 932C>T mutation in the IVD gene may be associated with a milder phenotype. The disease has a spectrum of clinical phenotypes which might include acute neonatal presentations, acute presentations at a later age and chronic intermittent presentations.

The acute neonatal presentation is characteristically in the first two weeks after birth. Infants are initially well, then develop vomiting and lethargy, progressing to coma. Patients may also present with similar symptoms at a later age, usually precipitated by an infection. Other patients present with chronic symptoms – failure to thrive and/or developmental delay, usually within the first year. Newborn screening has identified individuals with partial as well as complete IVD deficiency.

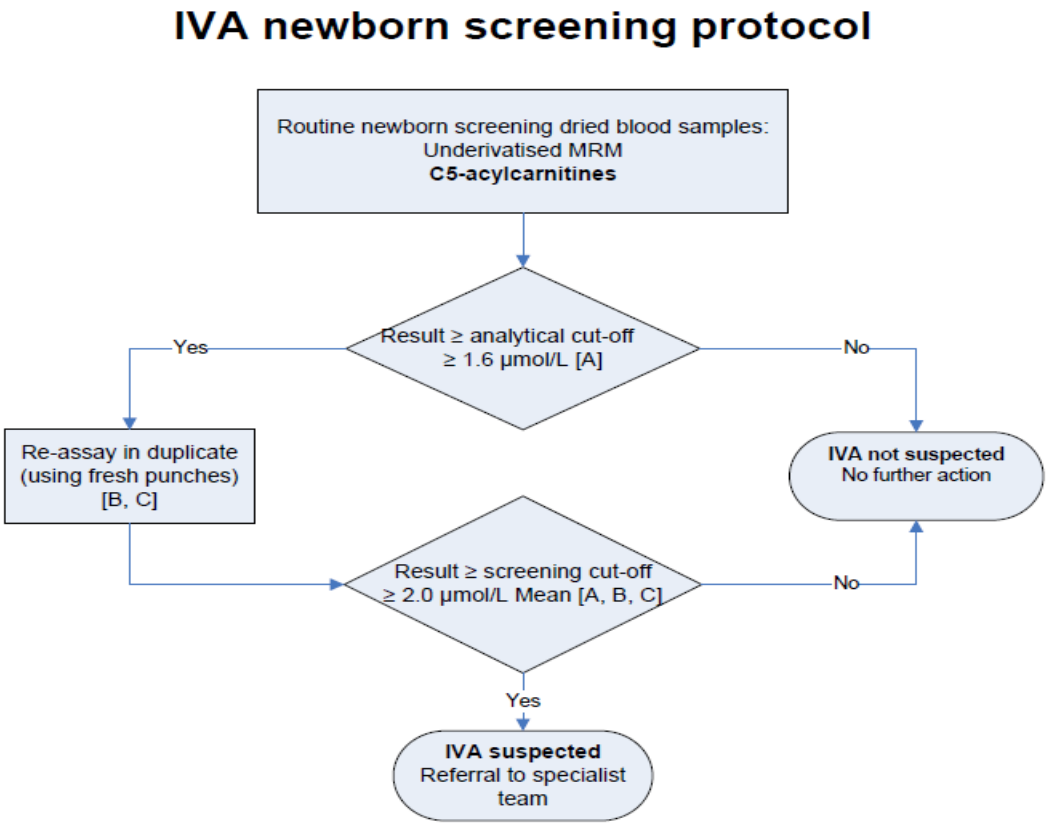
5.8.1 Incidence

It is an autosomal recessive disease, with an estimated incidence of around 1 in 100,000 with higher incidence in some locations and ethnic groups.

5.8.2 Treatment

Treatment may include a low protein diet and medicines (carnitine and glycine). The diet reduces the formation of harmful chemicals and the medicines help the body to get rid of them. Children with IVA are at risk of 'metabolic decompensation with viral illnesses'. Families will be provided with an emergency plan to be used, under the guidance of the metabolic team, during times of illness. Rarely, this may require hospital admission for intravenous fluids.

5.8.3 Newborn Screening Laboratory Pathway for IVA



5.8.4 Clinical pathway when IVA is suspected

- **Referral**

The SNSL will urgently contact the on call Metabolic Paediatrician and team with any positive screening result on the same day as the positive result has been reported by the laboratory. The metabolic team will contact the family immediately and arrange for the baby and family to be seen on the same day. The metabolic team will also inform the GP, Health Visiting and midwifery teams as soon as possible.

- **First review within 24 hours of screening result**

This will be carried out by the metabolic team. This will include investigations to confirm diagnosis, an explanation of the condition including an introduction to inheritance, an introduction to dietary management and monitoring, the specialist team's contact details and provision of written information.

- **Ongoing**

Follow-up management should include a review of the condition and inheritance (supported by written information), if deemed appropriate sibling testing should be considered. Information on ongoing dietary management, growth and developmental and general health, and support information – including contact details of parent support organisations should be provided as appropriate.

5.8 Glutaric Aciduria type 1 (GA1)

Glutaric aciduria type 1 (GA1) is an autosomal recessive condition caused by a deficiency of the enzyme glutaryl-CoA dehydrogenase (GCDH). GCDH is involved in the dehydration and subsequent decarboxylation of glutaryl-CoA, which is an intermediate in the breakdown of the amino acids lysine, hydroxylysine and tryptophan. Defective catabolism causes the toxic accumulation of glutaric acid, 3-hydroxyglutaric acid, glutaconic acid, and glutaryl carnitine. Over 150 disease causing mutations have been identified; of these the R402W mutation is the most prevalent among Caucasians. Most mutations, including the R402W mutation, are associated with undetectable GCDH activity and excretion of high amounts of glutaric acid. However, mutations that lead to varying levels of residual GCDH activity and low excretion of glutaric acid have also been reported. Consequently, patients with GA1 can be divided into two biochemically defined subgroups based on the levels of glutaric acid present in the urine: low excretors are those with less than 100 mmol/mol creatinine and high excretors are more than 100 mmol/mol creatinine. Although these subgroups are clinically similar, confirmatory testing in low excretors requires more complex follow-up, with either determination of GCDH enzyme activity or by mutation analysis of the GCDH gene.

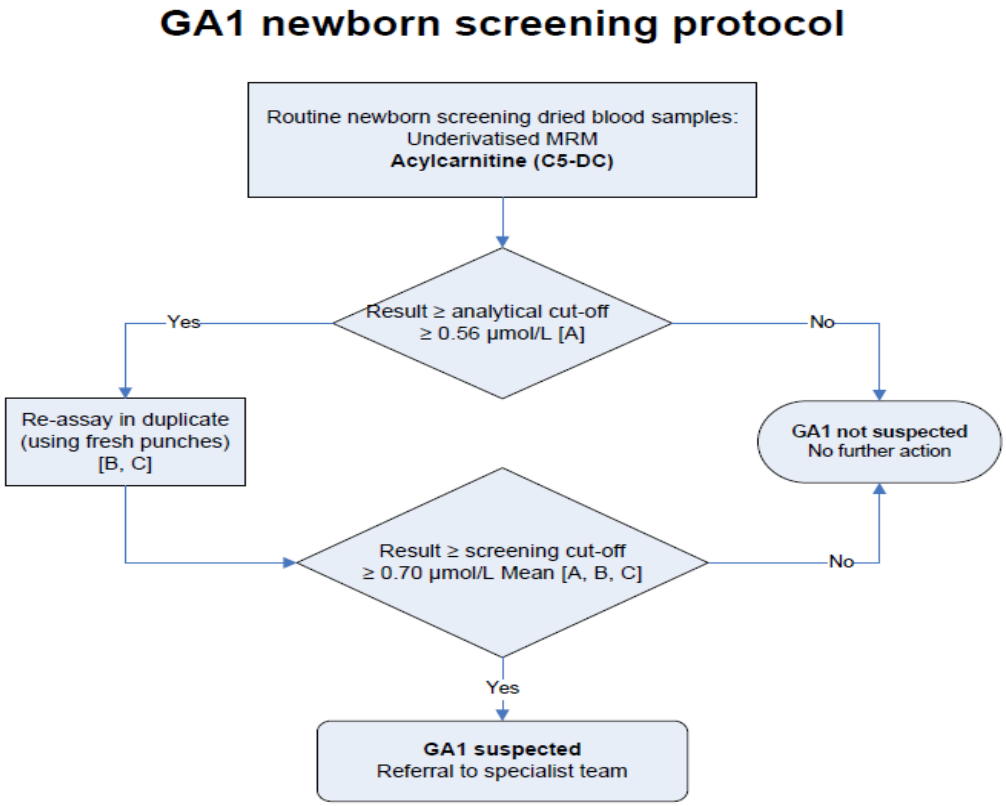
5.9.1 Incidence

The estimated incidence in the UK is around 1 in 100,000 live births.

5.9.2 Treatment

It is important to make an early diagnosis and begin treatment before brain damage has occurred. Treatment involves a lysine-restricted diet along with a medicine (carnitine). An emergency regimen is used when the patient has an illness to prevent a metabolic decompensation. This emergency regimen involves giving glucose (sugar) either by mouth (at home) or into the veins (in hospital).

5.9.3 Newborn Screening Laboratory Pathway for GA1



5.9.4 Clinical pathway when GA1 is suspected

- **Referral**

The SNSL will urgently contact the on call Metabolic Paediatrician and team with any positive screening result on the same day as the positive result has been reported by the laboratory. The metabolic team will contact the family immediately and arrange for the baby and family to be seen on the same day. The metabolic team will also inform the GP, Health Visiting and midwifery teams as soon as possible.

- **First review within 24 hours of screening result**

This will be carried out by the metabolic team. This will include investigations to confirm diagnosis, an explanation of the condition including an introduction to inheritance, an introduction to dietary management and monitoring, the specialist team's contact details and provision of written information.

- **Ongoing**

Follow-up management should include a review of the condition and inheritance (supported by written information), if deemed appropriate sibling testing should be considered. Information on ongoing dietary management, growth and developmental and general health, and support information – including contact details of parent support organisations should be provided as appropriate.

6. Adverse Incidents

As with any screening programme, there is potential for significant adverse incidents. All adverse incidents should be managed appropriately to minimise the risks to, and effects on the woman and participating Boards.

An adverse incident can be any of the following:

Administrative

- Failsafe procedures not instigated
- Woman/requesting midwife/ GP not notified of result

Laboratory

- Assay errors
- Interpretation errors

Clinical

- Misdiagnosis
- Long waiting times through the pathway from positive screening test to confirmed diagnosis

6.1 Procedure

Any healthcare professional involved in the NHS Scotland newborn bloodspot screening programme who becomes aware of a suspected problem should follow agreed local Board clinical governance procedures.

Local clinical governance procedures may vary from one Board to another but commonly involve an initial period of local investigation and establishment of extent of problem followed by external independent peer review when appropriate.

In all cases associated with the screening programme, there will be a thorough investigation and National Services Division (NSD) will be notified early in the process – at the time of internal investigation. In view of the sensitivities of national screening programmes and the public interest in them, NSD may require an external peer review even if local Board management decide not to invoke this.

If necessary NSD and the Board will meet to discuss and agree what action, if any, is required.

NSD will notify the Scottish Government Health Directorates (SGHD) and decide if action is needed in other NHS Board areas.

Note:
These protocols are to be used in addition to, and do not replace, the Boards' Clinical / Adverse Incident Reporting Procedures.

7. Confidentiality

Professional staff involved in the screening programme will comply with the provisions of the Caldicott Report. In particular, patient-identifiable information will only be used in clearly defined and monitored circumstances, only when absolutely necessary and should entail the use of the minimum necessary patient-identifiable information.

Access to patient identifiable information will be on a strict need to know basis, everyone in the organisation will be aware of their responsibilities with respect to patient confidentiality and the organisation will ensure that its use of patient-identifiable information is lawful.

National Services Scotland (ISD and NSD) does not require aggregated information returns on the performance of the screening programme to include patient-identifiable information; information on clinical activity for national data sets and monitoring must be submitted in anonymised format.

Appendix 1 – Consent for Newborn Blood Spot Screening

Consent for Newborn Blood Spot Screening for Congenital Hypothyroidism (CHT), Cystic Fibrosis (CF), Sickle Cell Disorders (SCD) and 6 Inherited Metabolic Disorders (IMDs) ***[Phenylketonuria (PKU), Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCADD), Maple Syrup Urine Disease (MSUD,*** **Homocystinuria (HCU),** ***Isovaleric Acidaemia (IVA) and Glutaric aciduria type 1 (GA1)]***

I have received and read the national patient information leaflet and have had an opportunity to discuss the tests I am being offered with a health professional. I understand the reasons for the tests and the consequences of the results. I also understand the significance of not having these tests performed. I am aware that my decision whether or not to have these tests will not affect the quality of care delivered by healthcare professionals.

Baby's Name……. Date of birth …/…/…

CHI Number……

☐ **I wish** ☐ **I do not wish** my baby to be tested for Congenital Hypothyroidism

☐ **I wish** ☐ **I do not wish** my baby to be tested for Cystic Fibrosis

☐ **I wish** ☐ **I do not wish** my baby to be tested for Sickle Cell Disorders

☐ **I wish** ☐ **I do not wish** my baby to be tested for the 6 IMDs

I understand that the Newborn Blood Spot Screening Programme needs to obtain my permission to store the newborn blood spot card beyond the initial 12 month testing period and to use any of the blood spots left over after testing is complete for anonymised research, such as the development of new screening tests. If any research was proposed in which the researcher would be able to identify me or my baby, a member of staff from the Newborn Bloodspot Screening Programme would always contact me again to seek my approval.

☐ **I agree** ☐ **I do not agree** for the storage of my baby's blood spot sample beyond the initial 12 month testing period.

☐ **I agree** ☐ **I do not agree** to the use of any leftover blood spots for anonymised research.

Signature:…… (Parent/Guardian) Date …/…/…

Signature:……(Witness: Healthcare professional)

Print:……

Designation: ……. Date …/…/…