

## NATIONAL PROTOCOLS

**Programme:** Antenatal haemoglobinopathy screening programme

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## Foreword

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The 2002 report 'Fair for all: Improving the Health of Ethnic Minority Groups and the Wider Community in Scotland'<sup>1</sup> and the subsequent guidance letter 'Fair for all: Working Together Towards Culturally Competent Services'<sup>2</sup> which was issued later that same year, highlighted the need for more work to be undertaken to meet the specific health needs of the differing ethnic minority communities emerging in Scotland. In response to this the National Resource Centre for Ethnic Minority Health (NRCEMH) was established.

In December 2004, NRCEMH published the outcome of the needs assessment in regard to antenatal and newborn screening policy for sickle cell disorders (SCD) and thalassaemia that it had conducted on behalf of the then Scottish Executive Health Department (SEHD)<sup>3</sup>. As part of the needs assessment process the group reviewed two Health Technology Assessment (HTA) on screening for haemoglobinopathies that had been published in 1999<sup>4</sup> and 2000<sup>5</sup>. The recommendations in this report also took account of advice from the National Screening Committee (NSC) Sickle Cell and Thalassaemia Screening Programme and current practice in Scotland, Wales and Northern Ireland.

CEL 31 (2008)<sup>6</sup> issued in July 2008 set out a number of changes to the pregnancy and newborn screening programmes, including the introduction of a standardised programme of screening for sickle cell disorders and thalassaemia in pregnancy and sickle cell disorders in newborn babies, with full implementation to be completed by March 2011. The pregnancy haemoglobinopathy screening programme will be based on the low prevalence screening model utilised in England<sup>7</sup>.

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<sup>1</sup> Scottish Executive Health Department (2002) Fair for all: Improving the Health of Ethnic Minority Groups and the wider community in Scotland. Scottish Executive. <http://www.sehd.scot.nhs.uk/publications/ffar/ffar1.pdf>

<sup>2</sup> Scottish Executive Health Department (2002) Fair for all: working together towards culturally competent services. NHS HDL(2002)51 [http://www.sehd.scot.nhs.uk/mels/HDL2002\\_51.pdf](http://www.sehd.scot.nhs.uk/mels/HDL2002_51.pdf)

<sup>3</sup> National Resource Centre for Ethnic Minority Health (2004) Screening for sickle cell disorder and thalassaemia in Scotland. Health Scotland, Glasgow. Dec 2004.

<sup>4</sup> Zeuner D. et al (1999) Antenatal and neonatal haemoglobinopathy screening in the UK: review and economic analysis. The Health Technology Assessment, vol 3, number 11. <http://www.hta.ac.uk/fullmono/mon311.pdf>

<sup>5</sup> Davies SC. et al (2000) Screening for sickle cell disease and thalassaemia; a systematic review with supplementary research. Health Technology Assessment 2000, vol 4, number 3. <http://www.hta.ac.uk/fullmono/mon403.pdf>

<sup>6</sup> Scottish Government Health Department (2008) Changes to the pregnancy and newborn screening programmes. NHS CEL 31(2008) [http://www.sehd.scot.nhs.uk/mels/CEL2008\\_31.pdf](http://www.sehd.scot.nhs.uk/mels/CEL2008_31.pdf)

<sup>7</sup> NHS Sickle Cell and Thalassaemia Screening Programme (2006). Standards for the Linked Antenatal and Newborn Programme. UK National Screening Committee. <http://sct.screening.nhs.uk/cms.php?folder=2493>

# Patient Pathway

## Pregnancy Screening Pathway for Sickle Cell and Thalassemia

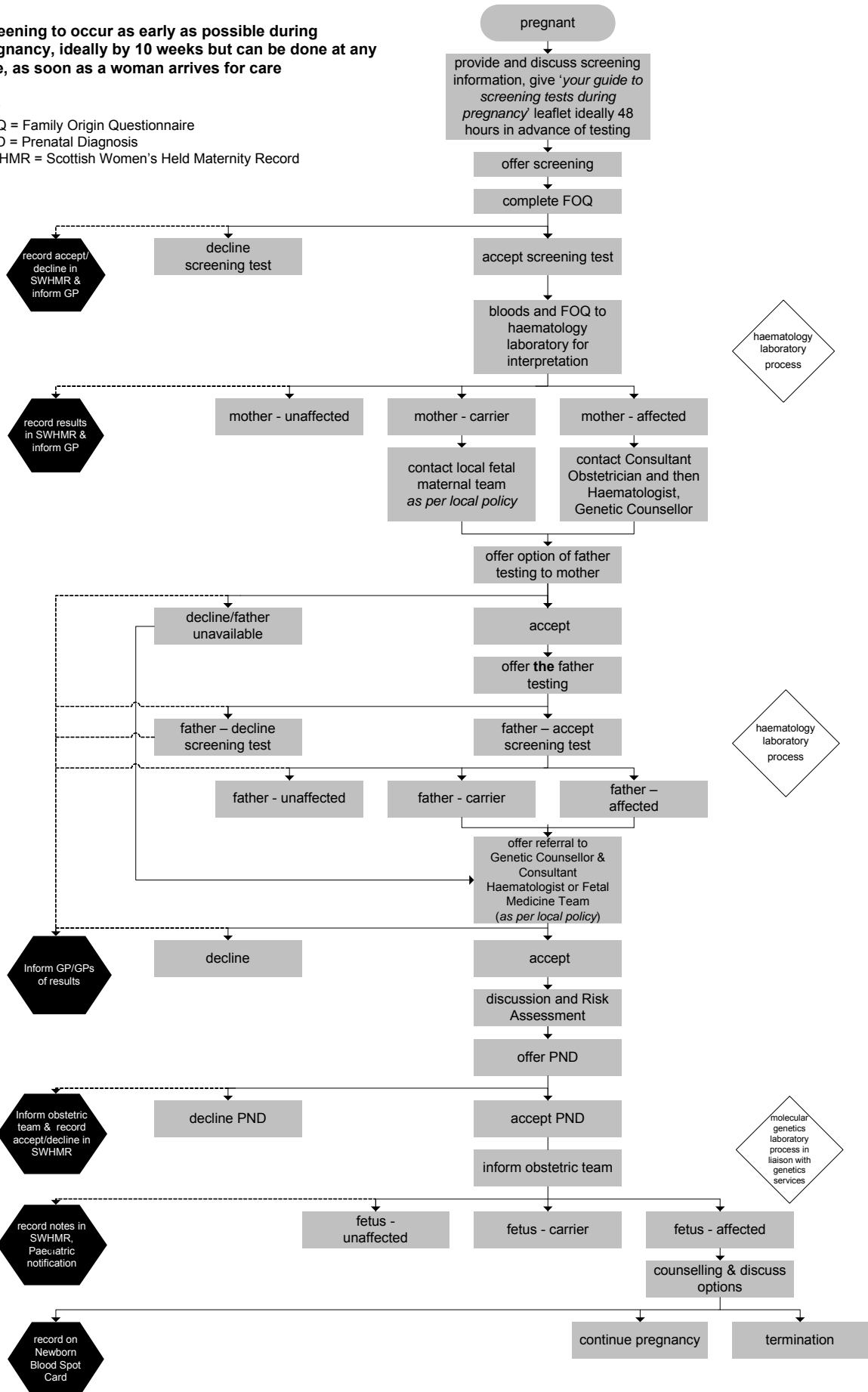
Screening to occur as early as possible during pregnancy, ideally by 10 weeks but can be done at any time, as soon as a woman arrives for care

Key  
 FOQ = Family Origin Questionnaire  
 PND = Prenatal Diagnosis  
 SWHMR = Scottish Women's Held Maternity Record

Midwife/GP

Healthcare Professional

Genetic Counsellor & Obstetric Team



# 1. Introduction

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This document contains standard national protocols for all healthcare professionals involved in the NHS Scotland screening programme for haemoglobinopathies in pregnancy. The programme aims to allow informed reproductive choice by identifying couples at risk of an affected pregnancy at an early gestation. 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.

The haemoglobinopathies are a large group of inherited blood disorders which affect the haemoglobin (oxygen carrying) component of blood. They fall into two main groups – the haemoglobin variants (such as sickle cell disorders) which are associated with the production of abnormal forms of haemoglobin, and the Thalassaemias in which there is an abnormality in the amount of haemoglobin produced. Many haemoglobinopathies are of no clinical significance whereas others are associated with severe morbidity and mortality, most notably sickle cell disorders and beta thalassaemia major. Sickle cell disorders, caused by a haemoglobin variant, often result in severe life threatening clinical symptoms. Those with beta thalassaemia major require regular blood transfusions to maintain life.

Though no haemoglobinopathy is exclusive to any single ethnic group, the frequency of these disorders varies considerably in different ethnic groups. These disorders originated in areas of the world where malaria is, or was, endemic because their occurrence conferred a survival advantage to those living in such areas. Thus, though haemoglobinopathies may be encountered in northern Europe, they are mainly associated with populations whose ancestry originated in Africa, Asia or around the Mediterranean.

## 2. Offer of Screening

The aim of offering screening in pregnancy is to identify couples who are at risk of having an affected child and thereby offer them information on which to base reproductive choices. It is important that screening is offered early so that the results of the screening tests and any prenatal diagnosis (PND) are available sufficiently early for couples to be able to make timely informed choices. Screening for sickle cell disorders and thalassaemia should be offered to all women as early as possible in pregnancy, and ideally by 10 weeks. This is in order to offer the full range of reproductive choice, including the offer of termination of pregnancy, if chosen, especially for some groups such as those of Muslim faith; in a way that screening later does not. Screening should be discussed at whatever gestation the woman first presents as this may still be of clinical benefit. It is important that they are aware that this programme differs from the other pregnancy screening programmes, in that it is optimally a two stage screen. For the most accurate analysis of chance, testing of the father of the baby will be requested if the woman is confirmed as a carrier of or as having a haemoglobinopathy, however screening for that pregnancy using only the woman's result is also offered if the father does not wish/is not able to be screened, for whatever reason.

All pregnant women will be offered screening for thalassaemia based on a formal process of inspection of routine blood indices. Additionally Scotland will be following the low prevalence screening model for haemoglobinopathies utilised in England and offering women in high risk groups, or women whose partners are in high risk groups, screening for sickle cell disorders and other haemoglobin variants using a recommended Family Origin (Ancestry) Questionnaire (FOQ) to assess risk status (see appendix 1).

### Conditions to be screened for:

<p><b>(i) Significant maternal haemoglobinopathies</b> These should be detected by pregnancy screening and are important for maternal clinical care</p>	<p>Hb-SS Hb-SC Hb-SD<sup>Punjab</sup> Hb-SE Hb-SO<sup>Arab</sup> Hb-S/Lepore Hb-S/<math>\beta</math> thalassaemia <math>\beta</math> thalassaemia intermedia Hb H disease (<math>\beta</math> thalassaemia major would be clinically apparent)</p>
<p><b>(ii) Maternal conditions requiring partner testing</b></p>	
<p><b>a) Conditions in (i)</b></p>	
<p><b>b) Carrier states in mother</b></p>	<p><b>Potential significant disorders in the fetus</b></p>
<p>Hb-AS Hb-AC Hb-AD<sup>Punjab</sup> Hb-AE Hb-AO<sup>Arab</sup> Hb-A Lepore <math>\beta</math> thalassaemia trait  <math>\delta\beta</math>-thalassaemia trait <math>\alpha^0</math> thalassaemia trait HPFH</p>	<p>Hb-SS Hb-SC Hb-SD Punjab Hb-SE Hb-SOArab Hb-S/Lepore Hb-<math>\beta</math>/Lepore; Hb-S/<math>\beta</math> thalassaemia; Hb E/<math>\beta</math> thalassaemia; <math>\beta</math> thalassaemia major (except cases with silent or near silent maternal phenotype) Hb-S/<math>\delta\beta</math> thalassaemia Hb Bart's Hydrops Fetalis Hb - S/HPFH</p>
<p><b>c) Any compound heterozygote state including one or more of the above conditions</b></p>	
<p><b>d) Any homozygous state of the above conditions</b></p>	

## 2.1 Responsibilities

NHS Scotland is responsible for ensuring that all pregnant women known to the service are provided with clear information in an appropriate format to help them make an informed choice about whether to take up any offer of screening. It is important that the couple are aware that this programme differs from the other pregnancy screening programmes, in that it is optimally a two stage screen. For the most accurate analysis of chance, testing of the father of the baby will be requested if the woman is confirmed as a carrier of or having a haemoglobinopathy, however screening for that pregnancy using only the woman's result is also offered if the father does not wish/is not able to be screened, for whatever reason. Women should be offered advice regarding the advantages and implications of the screen appropriate for their gestation. If the offer of screening is accepted, women (and the fathers undergoing testing) should be made aware of the results of the screen as per NHS Quality Improvement Standards (NHSQIS) standards for similar tests.

NHS Scotland is also responsible for ensuring that all fathers who are offered screening are provided with clear information in an appropriate format to help them make an informed choice about whether to take up any offer of screening. If accepted, it is the maternity services responsibility to arrange for the sample to be taken (either in the maternity setting or arranging for this to be taken elsewhere such as the father's GP practice). Regardless of where the sample is taken it is the maternity services responsibility to coordinate the sample being taken and being received in the laboratory. Additionally maternity services should ensure that the sample is flagged as a 'father screen' being requested as part of the pregnancy screening programme for haemoglobinopathies. The results of the maternal and father sample should be combined to give a risk assessment for that pregnancy and for appropriate counselling to take place.

There are some responsibilities which rest with the woman herself including:

- the registration of pregnancy in time to access pregnancy screening and testing;
- making the decision whether to undergo screening and testing;
- provide accurate clinical information required for the accurate interpretation of the results;
- notifying the NHS if no result is provided within the agreed timeframe;
- attending appointments for onward care, where offered.

Similarly it is the fathers' responsibility to:

- decide whether to accept screening if offered;
- present for the sample to be taken;
- notify the NHS if no result is provided within the agreed timeframe;
- attend appointments for onward care, where offered.

The father's result should not be inserted in the maternity notes, however the result of the risk assessment for that pregnancy derived from the combined result of the woman and father and if accepted the PND, should be recorded in the relevant sections of Scottish Woman-Held Maternity Record (SWHMR) and hospital maternity systems.

A copy of the father's result, the outcome of any counselling regarding his results and if required details of any follow on appointments arranged for his onward care, should be issued to his GP.

Each NHS Board should have in place a *Multi-Disciplinary Clinical Steering Group* to oversee the clinical management, governance and quality of the NHS Boards pregnancy and newborn screening programmes.

The Multi-Disciplinary Steering Group should set out a comprehensive strategic plan for improving quality in accordance with the NHS Board's overall service developments; develop policies aimed at managing and reducing clinical risk and ensure inter-agency arrangements are in place to support women/couples through the screening and diagnostic pathways

The Multi-Disciplinary Steering Group also has a responsibility for:

- Contributing to the development and implementation of screening and diagnostic care pathways in line with national standards and policies;
- Ensuring that all care pathways are regularly reviewed and modified in line with the national programme's changing standards and policy;
- Ensuring arrangements are in place for the audit of the pregnancy and newborn haemoglobinopathy screening programmes and linking to an agreed quality assurance framework;
- Providing a supportive framework for women and their families who have higher risk of, or are found to have a pregnancy at higher chance of a significant haemoglobinopathy;
- Advising and supporting staff on antenatal screening and diagnostic issues;
- Communicating with primary care services;
- Ensuring an ongoing education and training programme is made available for staff offering screening and diagnostic testing to improve awareness and skills and reduce risk of serious untoward incidences;
- Providing an annual screening report which reflects the national minimum audit criteria for the haemoglobinopathy screening programmes.

## 2.2 Process

All pregnant women attending an antenatal booking clinic, or being seen in the community, should be given sufficient information on the screening tests available in time to seek more information and make a decision regarding whether to undergo testing. All women and their partners must be given the opportunity to discuss haemoglobinopathy screening options with an appropriately trained professional. Information on how the accuracy of the test can be affected if the pregnancy is the result of either egg or sperm donation should be conveyed sensitively, and if the woman chooses to divulge such information should be counselled appropriately on the clinical information available regarding screening.

All women should be offered haemoglobinopathy screening regardless of their gestation, acknowledging that those being screened later in pregnancy may have fewer management options available than those booking at an earlier gestation. Women, who wish to be counselled regarding chance on their result alone for whatever reason, should be informed that the sensitivity of the tests will be reduced because the father's information is not available. If the woman has been tested already, whether in a previous pregnancy or for some other reason, it is recommended by the NSC Sickle Cell and Thalassaemia Programme Centre that the woman need not be tested again in the same or a subsequent pregnancy provided that:

- The original result is unequivocal and well documented
- The red cell indices remain the same
- The patient identification has three or more matching data items

If a previous result is being used this fact must be recorded in the woman's notes for the current pregnancy. It should be noted that there have been recorded instances where the results do not match when the same person is tested on two different occasions. There could be many reasons for this, from labelling and laboratory errors, to deliberate swapping of identities and duplicate medical record numbers. For this reason there should be local protocols in place that should be followed depending on previous experience and prevalence of such problems. It may be decided to offer retesting in each pregnancy.

NHS Boards should identify a designated person who is responsible for ensuring that:

- Every eligible woman is given the opportunity to be screened;
- Both a primary and failsafe mechanism is in place to ensure that a result is received for all women screened;
- If the woman has a positive screening result partner testing is offered;

- If the woman is in agreement, the baby's father is given the opportunity to be screened as far as possible (paternity issues should be discussed with sensitivity);
- Both a primary and failsafe mechanism is in place to ensure that a result is received for all fathers screened regardless of whether the sample is taken within the maternity setting or elsewhere;
- Women/fathers have the opportunity to receive the results in writing with the offer of appropriate counselling and onward care into diagnostic pathways.

The host NHS Board of the antenatal clinic/community maternity service is responsible for the clinical governance of the service and for ensuring that:

- Every health professional involved in offering/performing a screening test is suitably qualified and trained;
- Every woman who presents for maternity care is offered screening for haemoglobinopathies;
- Every woman is sensitively made aware of the genetic nature of screening and for accurate results information regarding the biological parents of the fetus would be of relevance (for example if the pregnancy is a result of a donated egg or sperm). Additionally the woman should be made aware of the possibility that the test could reveal the paternity of the pregnancy;
- Every women will be made aware that unless declined they will be screened for thalassaemia through the red blood cell indices. Additionally, from the information provided in the FOQ, the chance of either the women or the father of the baby being a carrier for sickle cell and other haemoglobin variants will be assessed. Further testing will be offered on those assessed to be in the higher chance group;
- It will be made clear that screening will be offered to the partner (father of baby) of all carrier mothers (irrespective of family origin) for sickle cell, other haemoglobin variants and thalassaemia;
- Every woman who books for delivery at hospital or at home is offered screening appropriate to her gestation;
- Information on the offer made and any subsequent father testing offered (and whether or not it is accepted) is recorded in SWHMR or equivalent and relevant maternity systems;
- If screening is accepted the family origin of a woman and her partner should be determined using the FOQ and must be recorded appropriately in SWHMR/relevant maternity systems locally and in the laboratory records;
- Samples are easily identifiable from other haematological specimens for women, and linkage to partner (father) samples must be possible.

### 3. Consent for Screening

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Information should be made available, taking into account of the woman's physical, cultural, ethical educational and mental health needs, at least 48 hours in advance of the screening tests, unless precluded by late presentation.

Women and their partners should be provided with information about the implications of the screening tests. For haemoglobinopathy screening, this should include:

- implications of receiving high or low risk result;
- information on the false positive rates of the screening test;
- the techniques involved and risks that may be associated with any diagnostic tests and
- information about the conditions themselves.

Screening systems should be discussed as 'an option' rather than an inevitable aspect of routine maternity care.

Women and the baby's father, where applicable, must be given sufficient time to make decisions whenever options are presented.

Where maternal or paternal samples are being obtained, there should be information available about their storage and disposal. Should there be an interest in studying any excess material there should be a process for the woman/father to decline to give consent.

It is the responsibility of the health professional to ensure that the correct information is entered into all fields when completing a screening request card. A FOQ must be submitted with every laboratory request form, even if screening is declined (there is an appropriate field on the FOQ to record this).

If a woman declines a screening or diagnostic test, this should also be recorded in the notes by healthcare professional responsible for her care. A protocol should be in place to allow women who have opted out of screening or diagnostic testing to change their mind and still undergo gestationally appropriate screening or testing at a later date.

Supplementary information, including relevant informative/supportive websites or details of support organisations, should be offered to all women/fathers receiving a positive screening or diagnostic test result.

Professionals involved in screening for haemoglobinopathies should work collaboratively with primary care and appropriate agencies such as social services, voluntary sector support groups, religious bodies and bereavement services in order to provide a comprehensive support network that is centred on the woman's/father's needs and requests.

## 4. Screening for haemoglobinopathies in pregnancy

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### 4.1 Organisational requirements

#### 4.1.1 Laboratory organisation

There must be an agreed local written policy which adheres to national standards to define the purpose of laboratory based assessment of risk of a significant haemoglobinopathy.

The laboratory must be a member of the UK Genetic Testing Network (UK GTN) and comply with the quality criteria laid down by the UK GTN Steering Group.

Laboratories must be accredited by an appropriate body e.g. Clinical Pathology Accreditation (CPA) UK (Ltd), participate in an accredited external quality assessment scheme e.g. UK National External Quality Assessment Service (NEQAS), and be able to demonstrate satisfactory performance as defined by the criteria specified by the External Quality Assessment (EQA) organisers.

Unlike some other pregnancy screening programmes, there is no minimum specimen throughput specified, although where small numbers affect the timeliness of reporting, centralisation may be an option. Laboratories that detect few screen positive cases should link with centres of expertise that can provide diagnostic support for presumed positive cases.

Samples should be easily identifiable from other haematological specimens for women, and linkage to partner (father) samples must be possible.

There must be a senior member of the laboratory staff at medical consultant or clinical consultant level responsible for the DNA analytical service, with defined lines of accountability and authority for all laboratory aspects of the service.

The laboratory must have a standard operating procedure for the DNA work associated with the sickle cell and thalassaemia screening programme, describing the process of laboratory testing from initial receipt of the specimen until dispatching of the report.

There must be a documented risk management policy for the laboratory aspects of the DNA service. This should describe the steps in the testing protocol where mistakes could occur and the procedures that have been implemented to minimise the risk of mistakes occurring.

The laboratory must agree to collect a minimum dataset of information for monitoring purposes. The laboratory must participate in audit of the screening service at local and national level and provide an annual report, or the necessary data for the preparation of an annual report.

At least 95% of pregnancy screening reports must be issued to an appropriate healthcare professional within 3 working days of receipt of the specimen.

In the absence of universal or standardised maternity information systems, the laboratory information management system will be used as a repository of national aggregated data on the screening programme.

#### 4.1.2 Screening for haemoglobin variants

As recommended by the NSC Sickle Cell and Thalassaemia Programme Centre the low prevalence testing algorithm (appendix 2) should be utilised. It should be noted that some women may not be tested if the ethnic group is incorrectly stated on the Family Origin Questionnaire or hidden and the following conditions will be missed using the proposed algorithm:

- 'silent' or 'near silent'  $\beta$ thalassaemia trait
- $\beta$ thalassaemia obscured by B12/folate deficiency or liver disease
- possibly some  $\beta$  thalassaemias obscured by severe iron deficiency anaemia
- $\alpha^0$ thalassaemia occurring outside the defined at risk ethnic groups
- dominant haemoglobinopathies in the partner when the woman is Hb AA, but these are very rare and should be suggested by the family history
- any significant haemoglobin silent on HPLC or IEF
- Hb S, C, D<sup>Punjab</sup>, E, O<sup>Arab</sup> in the North-European ethnic group.

Samples and forms should be given a number and the details on the form entered into the screening database. The assigned number should be used to link sample, patient details and analytical results and appear on the final report.

The request form must contain fields which conform to the minimum dataset including:

- Patient identifying details (name, date of birth, Community Health Index (CHI) number)
- Hospital attended or other referral source.
- The date the sample was taken.
- Information on the pregnancy needed to interpret the screening results including a completed FOQ.

Routine measurement of blood indices includes measurements of MCH and MCV. MCH should be used to screen for the risk of thalassaemia. These measurements are usually reported for all routine blood counts.

The following techniques can be used in screening for haemoglobin variants:-

- high performance liquid chromatography (HPLC)
- isoelectric focusing (IEF)
- cellulose acetate electrophoresis (CAE) at alkaline pH (8.2-8.6)
- capillary electrophoresis (CE).

Abnormal results should be confirmed by a different technique to the original and which is appropriate for the likely variant:

Sickle solubility testing can be used as confirmation of an initial screen suggesting the presence of sickle haemoglobin. Examination of the blood film can be very useful if any abnormality is detected.

Initial method	Confirmatory Method
HPLC	CAE/IEF/CE
IEF	CAE/HPLC/CE
CAE	acid agar electrophoresis/HPLC/IEF
CE	HPLC/IEF

#### Other supporting investigations:

##### Hb A2 measurement:

Microcolumn chromatography or high performance liquid chromatography is acceptable.

Electrophoresis with elution is acceptable but only in a laboratory performing the technique regularly. **IEF and scanning densitometry are not acceptable.**

No confirmatory test is necessary if the Hb A2 is raised and the red cell indices are typical of  $\beta$ thalassaemia trait.

### **Hb F measurement:**

HPLC or two minute alkali denaturation is acceptable. Kleihauer test is not appropriate for measurement but is useful to confirm the identity of the variant.

#### **4.1.3 Laboratory analysis, interpretation and reporting of pregnancy screening results**

NHS Scotland has agreed to follow the low prevalence standard operating procedures included in the Sick Cell and Thalassaemia Handbook for Laboratories issued by the NSC Sick Cell and Thalassaemia programme centre. For full details of the techniques for the measurement and analysis of samples and the interpretation and reporting of pregnancy screening results please refer to the Laboratory Handbook. Copies have been issued to all screening laboratories in Scotland in hard copy. Further copies can be downloaded using the following link:

<http://sct.screening.nhs.uk/cms.php?folder=2493>

#### **4.1.4 Partner testing**

Partner testing is done by the same haematological testing strategy as for maternal phenotype testing. If the partner has a haemoglobinopathy that can interact with the maternal phenotype as depicted in Appendix 4, then the couple should be counselled. If the parents so choose, fresh blood samples sent to a DNA referral laboratory with appropriate consent for molecular analysis in preparation for prenatal diagnosis.

If the partner is unavailable for testing or his haemoglobinopathy status is unknown, then counselling based on the woman's result alone should be provided. The NHS Scotland haemoglobinopathies screening programme supports the woman being offered prenatal diagnosis in this situation if she requests it. Prenatal diagnosis for some genotypes of sickle cell disorders can be undertaken without the partner's DNA. Similarly, prenatal diagnosis for  $\beta$ thalassaemia can be undertaken without the partner's DNA, although the diagnosis will not be able to be given with as high a degree of certainty if the partner's mutation is not known.

## **4.2 Training and Education**

All those directly involved in the provision of pregnancy screening information or services should have an induction to the programme and must undertake regular updating in line with continuing professional development guidance for their profession.

Additional training for more specific aspects of the programme such as specialist counselling for 'couples at higher chance' of an affected pregnancy is required.

## **4.3 Laboratory reports**

The results should be reported using the recommended formats stated in the Sick Cell and Thalassaemia Handbook for Laboratories. The report issued from the laboratory must contain information which conforms to the minimum data set which includes:

- The patient (name, date of birth, CHI number)
- Hospital or other referral source
- The date the sample was taken as this can be essential if a person has had a recent blood transfusion
- The information used to determine these results
- Analytical fact must be separated from interpretative opinion. Factual results should be given first followed by a clear conclusion, which may include recommendations. If there is likely to be a delay in producing a final result, consideration should be given to issuing an interim result which may be sufficient for the clinician to move forwards with the woman's clinical care.
- The blood count should always be reviewed as it may be the only indication of  $\alpha$ thalassaemia. The red cell distribution width (RDW) may flag up a complicating situation.

The blood film should be available and is especially important if the RDW is abnormal. It can sometimes provide essential information, for instance to detect a transfused homozygous sickle cell anaemia (Hb SS) person who can otherwise appear like a sickle cell carrier (Hb A + Hb S) in other analytical procedures. If the blood film is inconsistent with the other analytical data it may indicate a specimen mix up and examination of the blood film can therefore reduce errors.

- If information from the blood count is used in coming to a conclusion about the significance of the analytical data (as in probable  $\alpha$ thalassaemia) then those aspects of the blood count used (such as RBC, MCH, MCV) must be included in the haemoglobinopathy report.
- If the sickle solubility test is positive and at that point it is the only test result available, it should only be reported as an 'Interim' report. The final report with information from the blood film, HPLC and/or electrophoresis and any other appropriate tests should follow as soon as possible.
- Since it improves clarity, the conclusion should always be given both in full text and in standard abbreviation form in parentheses. For example: Sickle Cell Carrier (Hb AS) or Homozygous Sickle Cell Anaemia (Hb SS). The convention recommended is for the Hb initials to be reported in the order of greatest to least percentage.
- If no further action is required it should state that partner testing is not indicated.
- The report should also comment that the interpretation of the results is only correct provided the relevant information is correct.

Computer generated reports conforming to the agreed minimum dataset should be issued by each laboratory. Over 95% of results should be available within 3 working days of receipt of the sample by the laboratory.

All reports should be communicated to the referrer and on receipt; the details on the report should be checked. If any information is inaccurate, the laboratory should be contacted as soon as possible with the correct information before the woman is notified. The laboratory should recalculate the risk result and issue an amended report.

All women who are identified as having a lower chance of a pregnancy affected by a significant haemoglobinopathy should have the opportunity to receive the result in writing and for the report to be filed in SWHMR and hospital maternity systems.

For those women who are identified as having a higher chance, the results should be given priority and faxed, telephoned or securely emailed to the referrer depending on prior arrangement between referrer and screening laboratory. This also applies to the results of fathers who are offered and agree to screening. There should be a robust system in place to ensure that any results arriving at the referral source can be identified immediately on their receipt. This will usually involve a phone call from the laboratory to the referrer indicating that a written report is on its way. Fax or email systems should be in a secure location and only accessible to the relevant staff.

Women/fathers who have undergone screening should have previously indicated how they would like to receive any higher chance result and had their preference documented in SWHMR and/or hospital maternity systems.

The result should be communicated to the patient within 3 working days of it being received and an opportunity to attend for a diagnostic appointment given within a further 2 working days.

Copies of all reports should be provided to the General Practitioner (GP) and to the original referral source if that differs from the unit where antenatal care is being provided.

All reports should be retained in electronic format by each laboratory. It should be possible for information and results relating to individual pregnancies held on the laboratories' screening database to be accessed by telephone enquiry from an identifiable and verifiable source.

All laboratory documentation should be retained for appropriate periods of time and then disposed of as specified in the laboratory Standard Operating Procedure.

#### **4.4 Failsafe**

All results should be sent by the haematology laboratory to the referral source unless indicated otherwise.

There should be a local system in place to ensure that a result has been received for every woman/father who has been screened.

If no result has been received within the timeframe agreed with the haematology laboratory, the laboratory should be contacted and should provide a report as soon as possible. If no sample or request was received at the laboratory a repeat sample should be taken and sent to the laboratory as soon as possible.

#### **4.5 The Diagnostic Process**

##### **4.5.1 Organisation**

It is the responsibility of each NHS Board to ensure that there is a diagnostic pathway for all women/couples identified as having a pregnancy affected by a significant haemoglobinopathy. Women/couples should be counselled by medical and midwifery staff who have specific and recent experience in the diagnostic tests available.

The decision whether to have a diagnostic test should be the woman's choice. Women should be given time to make that choice even if it involves further appointments. Written information about the diagnostic tests, their techniques and associated risks should be made available at the time the woman is informed that there was a higher chance of a significant haemoglobinopathy from the screening tests. Further information about the conditions themselves with local figures about techniques and number of tests performed by operators (but not necessarily about local miscarriage rates – see Royal College of Obstetricians and Gynaecologists (RCOG) guideline - should be available at the time of the diagnostic appointment. The option to have a diagnostic test should not be dependent on the intention to terminate, if a significant haemoglobinopathy is identified, but information about the techniques and processes involved in termination should be available if requested.

The invasive tests of chorionic villus sampling (CVS) and amniocentesis should be conducted according to the standards laid down in the RCOG guideline: Amniocentesis and Chorionic Villus sampling, Greentop Guideline No 8 2010<sup>8</sup>. The auditable standards of this guideline should be monitored locally but also be available for national audit subject to the NHS Board's policy on confidentiality.

##### **4.5.2 Diagnostic results**

It must be emphasised that the screening programme for haemoglobinopathies in pregnancy is designed to identify most carriers for sickle cell disorders, thalassaemia and related disorders. The screening programme will not identify every couple at risk for every haemoglobinopathy.

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<sup>8</sup> Available for download at <http://www.rcog.org.uk/files/rcog-corp/GT8Amniocentesis0111.pdf>

## 5. Evaluation of the antenatal haemoglobinopathy programme

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Audit and monitoring of the screening programme should be performance managed at all health service levels (national and local).

All screening programmes are expected to have the appropriate tools to support the minimum criteria for the audit process. This must include clerical support, information technology (IT) equipment/software and networks that link with appropriate data collection systems within the NHS Board.

All abnormal findings subsequently proved to be normal should be kept on a database for the purposes of quality control; confirmed diagnosis should be recorded on/in the:

- i. NHS Board's clinical information system
- ii. Woman's maternity hand held notes (SWHMR)
- iii. Woman's hospital notes

A high standard of cytogenetic and perinatal pathology with feedback to the laboratory departments are an essential element for a screening service.

### 5.1 Quality control

Laboratory services must be able to provide (as a minimum) from the proportion of the pregnant population that had screening,

- Detection rate (DR):
- Screen positive rate (SPR)

Each NHS Board should aim to regularly carry out an exploratory survey of user views and experiences.

## 6. Adverse Incidents

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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 patient and participating NHS Boards. NSD's Pregnancy and Newborn Screening Programme Escalation Procedures<sup>9</sup> should be consulted.

An adverse incident can be any of the following:

### ***Administrative***

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

### ***Laboratory***

- Assay errors
- Interpretation errors
- Failure to analyse sample

### ***Clinical***

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

## 6.1 Procedure

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

Local clinical governance procedures may vary from one NHS Board to another but commonly involve an initial period of local investigation and establishment of extent of the 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 NHS Board management decide not to invoke this.

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

NSD will notify 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.

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<sup>9</sup> The Pregnancy and Newborn Screening Programme Escalation Procedure can be found here: <http://www.pnsd.scot.nhs.uk/wp-content//Pregnancy-and-Newborn-Screening-Programme-Escalation-Procedures-Final-v1.0.pdf>

## 7. Confidentiality

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Professional staff involved in the screening programme should 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 should be on a strict need to know basis. Everyone in the organisation should be aware of their responsibilities with respect to patient confidentiality and the organisation should 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.

## Screening for Haemoglobinopathies Family Origin Questionnaire (FOQ)



Hospital Name .....  
 CHI No. ....  
 Estimated Delivery Date .....  
 Surname .....  
 Forename .....  
 Date of Birth .....  
 Address 1 .....  
 Address 2 .....  
 Postcode .....

Screening test declined

This form must be attached securely to the haematology laboratory request form with the antenatal blood samples. A second copy of the form should be added to the patient's maternity record. (A third copy can be added to the hospital records if applicable). The completion of this form is an ESSENTIAL part of the screening process.

### What are your family origins?

Please tick all boxes in ALL sections that apply to the woman and the baby's father

	Woman	Baby's father
<b>A. AFRICAN OR AFRICAN CARIBBEAN (BLACK)</b>		
1/ Caribbean Islands	<input type="checkbox"/>	<input type="checkbox"/>
2/ Africa (excluding North Africa)	<input type="checkbox"/>	<input type="checkbox"/>
3/ Any other African or African-Caribbean family origins (please write in...)	<input type="checkbox"/>	<input type="checkbox"/>
<b>B. SOUTH ASIAN (ASIAN)</b>		
1/ India or African-Indian	<input type="checkbox"/>	<input type="checkbox"/>
2/ Pakistan	<input type="checkbox"/>	<input type="checkbox"/>
3/ Bangladesh	<input type="checkbox"/>	<input type="checkbox"/>
<b>C. SOUTH EAST ASIAN (ASIAN)</b>		
1/ China including Hong Kong, Taiwan, Singapore	<input type="checkbox"/> #	<input type="checkbox"/> #
2/ Thailand, Indonesia, Burma	<input type="checkbox"/> #	<input type="checkbox"/> #
3/ Malaysia, Vietnam, Philippines, Cambodia, Laos	<input type="checkbox"/> #	<input type="checkbox"/> #
4/ Any other Asian family origins (eg Caribbean-Asian) (please write in...)	<input type="checkbox"/>	<input type="checkbox"/>
<b>D. OTHER NON-EUROPEAN (OTHER)</b>		
1/ North Africa, South America etc	<input type="checkbox"/>	<input type="checkbox"/>
2/ Middle East (Saudi Arabia, Iran etc)	<input type="checkbox"/>	<input type="checkbox"/>
3/ Any other Non-European family origins (please write in...)	<input type="checkbox"/>	<input type="checkbox"/>
<b>E. SOUTHERN &amp; OTHER EUROPEAN (WHITE)</b>		
1/ Sardinia	<input type="checkbox"/> #	<input type="checkbox"/> #
2/ Greece, Turkey, Cyprus	<input type="checkbox"/> #	<input type="checkbox"/> #
3/ Italy, Portugal, Spain	<input type="checkbox"/>	<input type="checkbox"/>
4/ Any other Mediterranean country	<input type="checkbox"/>	<input type="checkbox"/>
5/ Albania, Czech Republic, Poland, Romania, Russia etc	<input type="checkbox"/>	<input type="checkbox"/>
<b>F* UNITED KINGDOM (WHITE) refer to guidance at the back</b>		
1/ England, Scotland, N Ireland, Wales	<input type="checkbox"/>	<input type="checkbox"/>
<b>G* NORTHERN EUROPEAN (WHITE) refer to guidance at the back</b>		
1/ Austria, Belgium, Ireland, France, Germany, Netherlands	<input type="checkbox"/>	<input type="checkbox"/>
2/ Scandinavia, Switzerland etc	<input type="checkbox"/>	<input type="checkbox"/>
3/ Any other European family origins, refer to chart (eg Australia, N America, S Africa) (please write in...)	<input type="checkbox"/>	<input type="checkbox"/>
*Hb Variant Screening Requested by F and/or G (ie request from low risk group)	<input type="checkbox"/>	<input type="checkbox"/>
# Higher risk for alpha zero thalassaemia		
<b>H. DON'T KNOW (incl. pregnancies with donor egg/sperm)</b>	<input type="checkbox"/>	<input type="checkbox"/>
<b>I. DECLINED TO ANSWER</b>	<input type="checkbox"/>	<input type="checkbox"/>
<b>J. ESTIMATED DELIVERY DATE (please write in if not above)</b>	<input type="text"/>	<input type="text"/>
<b>K. GESTATION AT TIME OF TEST</b>	<input type="text"/>	<input type="text"/>

OFFER haemoglobin variant screening to all women if they or their baby's father have answers in a shaded box

Signed \_\_\_\_\_ Print Name \_\_\_\_\_  
 Job Title \_\_\_\_\_ Contact Tel No \_\_\_\_\_ Date \_\_\_\_\_  
 (By Health Care Professional completing the form)

# Guidance for Health Care Professionals

## Screening and Diagnostic Uses of the Family Origin Questionnaire

The Family Origin Questionnaire (FOQ) is principally used as a tool to identify women who are at highest risk of being a carrier or having a baby with a haemoglobin variant or disorder.

The FOQ is also used as a tool by laboratory staff to help with the interpretation of results, particularly in the interpretation of results indicating possible alpha or beta thalassaemia. The family origin is also relevant in the interpretation of red blood cell indices and essential for accurate prenatal diagnosis. More information about its use can found in the laboratory handbook <http://sct.screening.nhs.uk/publications>

Therefore you need to ask for the family origins of both the woman **AND** the baby's father going back at least 2 generations (or more if possible).

## Women with Sickle Cell Disease

Screening will also identify women with sickle cell disease, who should be considered "high risk" requiring specialist care during pregnancy from an Obstetrician and Haematologist, and who should be booked for a hospital delivery.

## "Low risk" Family Origins

People with family origins from the countries listed below are considered at low risk for haemoglobin variants.

### United Kingdom (White)

England, Scotland, Northern Ireland, Wales.

### Northern European (White)

Austria, Belgium, Denmark, Greenland, Iceland, Ireland (Eire), Finland, France, Germany, Luxembourg, Netherlands, Norway, Sweden, Switzerland.

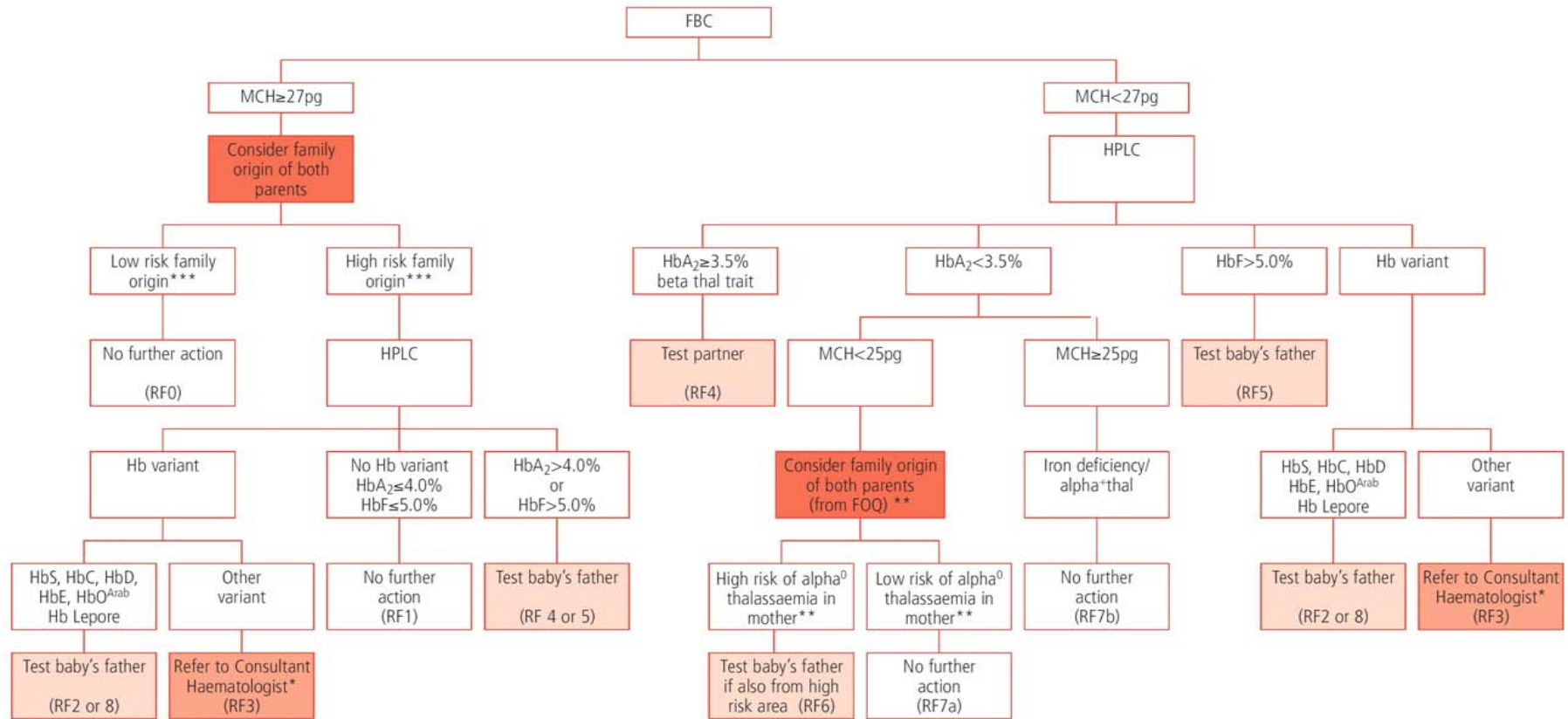
Some populations of the following countries have Northern European origin (countries listed above) and are also at low risk for haemoglobin variants :

### Northern European Origin (White)

Australia, North America (USA, Canada), South Africa, New Zealand.

## Appendix 2

Testing algorithm for laboratory screening in LOW PREVALENCE areas (RF = Report Format)



\* Refer analytical results to consultant for an opinion on the need for a clinical referral. Possible role of website/telephone advice

\*\* High risk if any ethnic/family origins in China (including Hong Kong), Taiwan, Thailand, Cambodia, Laos, Vietnam, Burma, Malaysia, Singapore, Indonesia, Philippines, Cyprus, Greece, Sardinia, Turkey, or if ethnic/family origin uncertain/unknown.  
Reconsider low risk couples if fetal anaemia/hydrops seen on ultrasound scanning or if family history of hydrops fetalis

\*\*\* Low risk or high risk as determined by the family origin questionnaire. **Note - If partner is in high risk ethnic group, test the mother's sample regardless of her family origins.**

## Appendix 3

Table of parental carrier state combinations that give rise to the risk of a fetus with significant sickle cell disease of  $\beta$ thalassaemia

(Table base on the work of Prof. B. Modell)

		Mother									
Carrier of		Hb S	$\beta$ thal	$\delta\beta$ thal	Hb Lepore	Hb E	Hb O <sup>Arab</sup>	Hb C	Hb D <sup>Punjab</sup>	HPFH	Not a carrier
Father	Hb S										
	$\beta$ thal										
	$\delta\beta$ thal										
	Hb Lepore										
	Hb E										
	Hb O <sup>Arab</sup>										
	Hb C										
	Hb D <sup>Punjab</sup>										
	HPFH										
	Not a carrier										

	Serious risk - refer couple for counselling - prenatal diagnosis to be offered
	Less serious risk - refer couple for counselling - further investigation may be required
	No risk

## Abbreviations

BSH	British Society of Haematology
CEL	Chief Executive Letter
CHI	Community Health Index
CI	Confidence Interval
CPA UK (Ltd)	Clinical Pathology Accreditation United Kingdom Limited
CPD	Continuous Professional Development
DR	Detection Rate
EDD	Estimated Date of Delivery
EU	European Union
FOQ	Family Origin (Ancestry) Questionnaire
GMC	General Medical Council
GP	General Practitioner
HBO	Haemoglobin variant
HDL	Health Department Letter
HIE	Higher Institute of Education
HPC	Health Professional Council
HTA	Health Technology Assessment
IT	Information Technology
KPI	Key Performance Indicator
MoM	Multiples of the Median
NHS QIS	National Health Service Quality Improvement Scotland
NICE	National Institute for Clinical Excellence
NMC	Nursing and Midwifery Council
NSD	National Services Division
NSS	National Services Scotland
PND	Prenatal Diagnosis
QC	Quality Control
QF PCR	Quantitative Fluorescent-Polymerase Chain Reaction
RCOG	Royal College of Obstetricians and Gynaecologists
SGHD	Scottish Government Health Directorates
SPR	Screen Positive Rate
SWHMR	Scottish Woman Held Maternity Record
UK GTN	UK Genetic Testing Network
UK NEQAS	United Kingdom National External Quality Assessment Service
UK NSC	United Kingdom, National Screening Committee

## Glossary

Affected pregnancies	Pregnancies in which the fetus has the target condition.
Alpha thalassaemia major (haemoglobin Barts hydrops fetalis)	A severe anaemia that affects the fetus. No normal fetal haemoglobin is produced and this leads to stillbirth or neonatal death.
Amniocentesis	An invasive procedure undertaken from about 15 completed weeks (15+0) onwards to obtain a sample of amniotic fluid surrounding the fetus. A needle is passed through the mother's abdomen into the uterus, under continuous ultrasound guidance, and a sample of fluid is withdrawn. The fluid, and cells within it, can be tested for certain conditions such as Down's syndrome and other chromosomal and inherited disorders. Out of 100 women who have this test from 15 weeks it is likely that one will miscarry as a direct consequence of the procedure.
Amniotic fluid	The fluid surrounding the fetus in the uterus, which protects it during pregnancy and labour. It contains substances and cells from the fetus, which can be removed by amniocentesis and examined.
Anomaly	An aberration or change often used related to a gene that may or may not result in a disease or condition.
Antenatal	The period from conception to birth.
Autosomal inheritance	Mode of inheritance that is independent of the sex chromosomes. It can be dominant or recessive.
Autosome	A chromosome not involved in sex determination. The human genome consists of 46 chromosomes – 22 pairs of autosomes and one pair of sex chromosomes (the X and Y chromosomes).
Beta thalassaemia major	A severe anaemia caused by inheritance of two beta thalassaemia genes, resulting in a lack of normal haemoglobin production. Treatment by regular monthly blood transfusions and drugs to remove excess iron leads to long-term survival. Some affected children can be 'cured' by bone marrow transplantation.
Carrier	An individual who carries a single altered gene for a condition where two altered genes are required for an individual to be affected. The carrier can pass on the gene to their offspring, who may be affected if they also inherit an altered gene from their other parent. A carrier is a heterozygote for the gene carried.
Carrier testing	Testing to find out if a person who does not show symptoms of a condition nevertheless 'carries' a copy of an altered gene which could be passed to his or her children.
Chorionic villus sampling (CVS)	An invasive procedure performed under ultrasound guidance after 10 completed weeks of pregnancy to obtain a sample of placental tissue, which is taken through either the cervix or the abdomen. The range of chromosomal and genetic conditions that can be detected is similar to those for amniocentesis except that Neural Tube Defects cannot be diagnosed. For every 100 women who have this test from the 11th week in pregnancy one or two will miscarry.

Chromosome anomaly	A change in the number or arrangement of the normal 23 pairs of chromosomes.
Confirmed result	The results of initial screening tests are not usually 100% certain, and are often called presumptive results. The results of screening tests are NOT confirmed results. They are often confirmed later, with further diagnostic tests
Congenital	Present at or shortly after birth.
Coverage	This is the proportion of people in the eligible group who actually undergo the screening.
Cut-off level	Screening tests divide people into a group at lower risk of the condition being screened for, and a group at higher risk who are then offered further investigations. Cut off level is a point defined by the programme used to distinguish higher and lower risk.
Detection rate	Proportion of affected individuals, or carriers who may have a genetic reproductive risk, with positive screening results
Diagnostic test	Refers to the analytical process involved in obtaining a result. For example the diagnostic test on an amniocentesis sample (invasive procedure) is the karyotype or PCR.
Disability (WHO definition)	Consequence of impairment in terms of functional performance (i.e. disturbance at the level of the person)
Disorder	Several words are used to describe illnesses. They are sometimes called diseases, disorders or conditions.
Dominant inheritance	Every cell contains two copies of each gene. If only one of these copies is altered and one is not, but the person is affected by a characteristic or disorder caused that alteration, the alteration is dominant. A characteristic or disorder caused by a dominant gene alteration only requires one of the genes to be altered for the person to be affected.
Effectiveness	The extent to which intervention results in the desired outcomes under everyday conditions.
Embryo	A fertilised ovum (egg) in the early stage of development. In humans the term is reserved for the first eight weeks of development.
Epidemiology	The study of the distribution of and influences on health-related states and events in populations and the control of health problems, the study of epidemic disease.
False-negative result	Screening tests divide people into lower and higher risk groups. Some people with a negative screening test result do actually have the condition being screened for. These people are said to have a 'false-negative' result.
False-positive result	Screening tests divide people into lower and higher risk groups. Some people with a positive screening test result do not actually have the condition being screened for. These people are said to have a 'false-positive' result.
Family history	History of a condition in at least one of the following family members: parent, sibling, grandparent, great-grandparent, aunt, uncle, nephew, niece or cousin or child.
Family origins	A term used to describe a person's ancestry
Fetus	In humans, the unborn child after the end of the eighth week of pregnancy to the moment of birth.
Genetic counselling	Information and support provided by an appropriately

Genetic counsellor	trained health professional, to individuals who have known conditions in their families or who are concerned about the future possibility of genetically inherited conditions. A health professional with specialised training in genetics and counselling who can provide information and support for individuals or families with concerns about a genetic disorder that may run in the family.
Genetic disorders	Conditions that result from alterations in an individual's genetic makeup. They may be the consequences of alterations in single genes, or in whole chromosomes, parts of which may be lost, duplicated, misplaced or replaced; or may result from the interaction of multiple genes and external factors such as the environment.
Genetic testing	Examination of an individual's genetic material to identify alterations that may cause a disorder.
Genetics	1. The study of the structure and function of genes. 2. The genetic features which occur in individuals, families and populations.
Gestational age	The duration of an ongoing or completed pregnancy, measured from the first day of the last menstrual period (usually about two weeks longer than that measured from conception). Gestational age is usually measured in completed weeks.
Haemoglobin	The main protein in red blood cells, which carries oxygen from the lungs to the tissues. It consists of four protein subunits called globin chains, each carrying one molecule of haem, which binds and releases oxygen. Haem is red, and this is why blood is red. There are several types of human haemoglobin. Adults have mainly haemoglobin A, which consists of two alpha and two beta globin chains (a <sub>2</sub> b <sub>2</sub> ), and fetuses have mainly haemoglobin F, which consists of two alpha and two gamma globin chains (a <sub>2</sub> g <sub>2</sub> ).
Haemoglobin disorders	Mild or serious disorders that can occur in people who have inherited two haemoglobin gene variants. The most common haemoglobin disorders are sickle cell disorders and thalassaemia disorders, also called haemoglobinopathies.
Impairment (WHO definition)	Dysfunction resulting from pathological changes in a system.
Incidence	The number of new instances of a specific condition occurring during a certain period in a specified population.
Inheritance	The passing of familial characteristics from one generation to the next.
Inherited	Having a hereditary characteristic; there are many inherited characteristics, including eye colour, hair colour and health disorders.
Invasive procedure	Invasive procedure - is a method used to obtain a sample, usually to aid diagnosis e.g. amniocentesis and chronic villi sampling are invasive procedures.
Invited group	Those to whom a screening test is offered.
In vitro fertilisation (IVF)	The process whereby an egg is fertilised with sperm in the test tube and then transplanted into a woman's uterus.
Karyotype	A photomicrograph of an individual's chromosomes arranged in a standard format showing the number, size, and shape of each chromosome type; used to correlate

	chromosomal anomalies with the characteristics of specific diseases. Karyotyping is often used for prenatal diagnosis of conditions such as Down's syndrome.
Marker	An identifiable physical location on a chromosome whose inheritance can be monitored. Markers can be expressed regions of DNA (genes) or some segment of DNA with no known coding function but whose pattern of inheritance can be determined.
Miscarriage	Loss of a fetus before the 24th week of pregnancy.
Morbidity	The extent of being affected by a disease or condition. In epidemiology, the morbidity rate is the prevalence of a disease within a particular number of the population.
Morbidity rate	In epidemiology, the prevalence of a disease within a population, usually expressed as cases per 100,000.
Mortality/mortality rate	The incidence of death in a population in a given period.
Non-invasive	A procedure that does not require incision into the body or the removal of tissue.
Placenta	The structure that provides the fetus with nourishment during development. It is attached to the wall of the uterus and connects to the fetus through the umbilical cord.
Prevalence	The proportion of people in a population who have a given disease or attribute.
Prevalence rate	The number of people with the condition or attribute, divided by the population at risk.
Prognosis	Predicted course and outcome of a disorder, based on all the knowledge related to a specific case, eg, age, sex, the course of the disorder in other patients.
Quality assurance	A system for monitoring and maintaining high standards in every aspect of a screening programme.
Recessive	Every cell contains two copies of each gene. Each gene contains the information to produce a particular gene product, such as a protein. If a gene is altered, it may no longer code for the gene product. Where an individual has one altered gene copy, the cell will only produce half the usual gene product and may also produce half of the altered gene product. If this does not result in any disorder for the individual, the alteration is described as being 'recessive' to the unaltered copy of the gene. An individual with this genetic constitution is said to be a 'carrier' of a recessive gene alteration. For a recessive gene alteration to result in a particular characteristic or disorder, both copies of the genes must be altered.
Risk	Risk is usually taken to mean the chance of an event happening. It can be expressed in a number of ways.
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.
Screening programme	The whole system of activities needed to deliver high quality screening. It ranges from identifying and informing those to be offered screening through to the treatment and follow up of those found to have abnormality, and support for those who develop disease despite screening.
Screening test	A test or inquiry used on people who do not have or have not recognised the signs or symptoms of the condition

	being tested for. It divides people into low and higher risk groups.
Sensitivity	This is a measure of test performance. High sensitivity means that the test 'catches' as many people with the condition as possible. It is measured as the proportion of those with the condition, who have a positive test result. It is the same as the detection rate.
Sickle cell anaemia (SS)	A sickle cell disorder caused by inheritance of two genes for haemoglobin S, which often results in significant health problems and requires treatment. Some affected children can be 'cured' by bone marrow transplantation.
Sickle cell disorders	A group of inherited disorders that are characterised by sickling of red blood cells when there is a shortage of oxygen. The most common sickle cell disorders are sickle cell anaemia (SS), haemoglobin SC disorder, and haemoglobin S/beta thalassaemia. Sickle cell disorders can cause episodes of acute pain (crisis), anaemia, increased risk of infections, and chest problems. They can be life-threatening, particularly for young children.
Specificity	This is a measure of test performance. High specificity means the test has as few false positives as possible. It is measured as the proportion of those without the condition, who have a negative test result.
Surveillance	Ongoing observation of the health of individuals or populations.
Syndrome	Combination of symptoms and signs grouped together to form a disorder.
Termination of pregnancy	The medical expulsion or extraction from the uterus of a fetus in the first, second or third trimester of pregnancy.
Thalassaemia major	A group of inherited conditions caused by a reduction in the amount of haemoglobin produced. People with a thalassaemia condition have various degrees of severe anaemia.
Thalassaemia carrier (also called thalassaemia trait)	The presence of one thalassaemia gene and one normal haemoglobin gene in an individual. This causes the red cells to be small and individuals may have very mild anaemia, but this does not usually cause any problems.
True-negative result	Screening tests divide people into low and higher risk groups. Most of the people with a negative screening test result do not have the condition being screened for. These people are said to have a 'true-negative' result.
True-positive result	Screening tests divide people into low and higher risk groups. Some people with a positive screening test result do have the condition being screened for. These people are said to have a 'true-positive' result.
Twins	May be genetically identical (monozygous) when they arise from a single fertilised egg or non-identical (dizygous) when they arise from two separate eggs.
Uptake	Is the proportion of people, who when offered a test, take it up.
Variant	A change for example in a gene or protein. For example, a variant in a haemoglobin gene resulting in a variant in the haemoglobin the body produces thus causing a sickle cell disease.