LRI Children's Hospital

Haemoglobinopathy Transfusion in Paediatrics

Staff relevant to:	Paediatric haematology teams, paediatric medicine, paediatric intensive care
Team approval date:	January 2025
Version:	2 (Combined; Haemoglobinopathy Transfusion UHL Childrens Medical Guideline C21/2016 & Exchange Transfusion for Paediatric Sickle Cell Disease UHL Childrens Medical Guideline C20/2016) Automated Red Cell Exchange for Paediatric Sickle Cell Patients (C19/2023)
Revision due:	January 2028
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Trust Ref:	C6/2022

1. Introduction and Who Guideline applies to

This document aims to offer clinical guidance regarding red cell transfusions in paediatric patients with sickle cell disease and thalassaemia.

The guideline applies to all UHL staff involved in the care of children and young people with sickle cell disease and thalassaemia.

Cases need to be assessed individually and management tailored appropriately. If in doubt, please seek the opinion of the paediatric haemoglobinopathy team.

Contents

Guidelines are based on:

- Standards for the clinical care of children and adults with thalassaemia in the UK 3rd Edition 2016
- NHS Sickle Cell and Thalassaemia Screening Programme - Standards for the Care of Children with SCD 2009
- Sickle Cell Disease in Childhood: Standards and Recommendations for Clinical Care 3rd Edition 2019
- BSH Guidelines on red cell transfusion in sickle cell disease Part I: Principles and laboratory aspects & Part II: Indications for transfusion 2017
- 2021 Guidelines For The Management of Transfusion Dependent Thalassaemia (TDT) Thalassaemia International Federation 4th edition

Related documents:

Blood Transfusion UHL Policy B16/2003
Iron Chelation Therapy in Transfusional Iron Overload for Inherited Anaemias UHL Childrens Hospital Guideline E3/2019

2. Thalassaemia

2.1 General Principles

Transfusion-dependent thalassaemia describes an autosomal recessive condition characterised by absent or minimal B globin chains resulting in virtually no haemoglobin A production. After infancy, haemoglobin A is the major haemoglobin type found in red cells (typically over 90%) and so untreated its absence results in severe anaemia, failure to thrive, extramedullary haematopoiesis, bone marrow expansion and ultimately death.

Infants are monitored for these symptoms and signs on a monthly basis with the plan to initiate transfusion early to prevent the complications of anaemia and bone marrow expansion. Specific attention should be paid to:

- Worsening fatigue
- Poor feeding and impaired growth
- Developmental delay or regression
- Frequent infections
- Worsening splenomegaly
- Facial bone expansion

Other factors contributing to anaemia should be investigated such as iron deficiency, glucose 6-phosphate dehydrogenase deficiency and intercurrent infection.

2.2 Before starting transfusion

- Always discuss and document the indication for starting a red cell transfusion program.
- Potential complications of transfusion should also be discussed (use UHL blood transfusion consent sticker). The most frequent transfusion-related issue arising for patients with thalassaemia is secondary iron overload for which patients require chelation therapy.
- Ensure patients are immunised against hepatitis B.
- Check hepatitis B (Hep B surface Ag), hepatitis C (Hep C antibody) and HIV (HIV I & II antibody) serology prior to starting transfusion.

2.3 Aims of transfusion

- Maintain pre-transfusion Hb at 90-105g/dl, by transfusing red cells every 3-4 weeks.
- Transfuse ABO, Rhesus, Kell matched red cells which are as fresh as possible with a sample obtained within 72 hours of the transfusion.
- Timing of venepuncture and transfusion should aim to minimise disruption to the patient's life.
- Out of hours transfusion is offered at weekends when staffing permits during term time to avoid missing school but not during school holidays.
- The following table outlines the suggested transfusion volumes:

Hb <90g/l, transfuse 20ml/kg and bring back 1 week earlier

Hb 90-95g/l, transfuse 20ml/kg

Hb 95-105g/l, transfuse 15ml/kg

Hb 105-115g/l, transfuse 10ml/kg

Hb >115g/l, No transfusion - come back in 1 week

- The volume of red cells transfused should be capped at 3 units for children weighing over 50kg.
- To reduce donor exposure, where possible transfusion volumes should be rounded to whole units.

- All blood should be given in line with UHL transfusion policy.

3. Sickle cell disease

3.1 General principles

The purpose of red cell transfusion in patients with sickle cell disease is to:

- Improve the oxygen carrying capacity by correcting anaemia.
- Prevent or reverse complications of sickle cell disease due to vaso-occlusion or haemolysis.

Anaemia alone in an otherwise well child with sickle cell disease is not an indication for transfusion unless the haemoglobin falls by greater than 20g/l below the steady state haemoglobin, in which case these patients should be assessed and the need for transfusion discussed with the haematologist.

Indications for acute transfusion include:

- Acute aplastic anaemia due to:
  - aplasia from Parvovirus B19 infection
  - acute splenic or hepatic sequestration
- Acute chest syndrome – early top up may avoid need for exchange transfusion.
- Stroke or acute neurological deficit – exchange transfusion is usually necessary to reduce the Hb S to less than 30% with a target Hb of 100-110g/l.
- Multi-organ failure.
- Preparation for surgery – preoperative transfusion is recommended for patients with haemoglobin SS and haemoglobin SC undergoing medium risk surgery (e.g. abdominal, tonsillectomy, orthopaedic) and patients with sickle cell of all genotypes requiring high risk surgery (e.g. cardiovascular, brain).

Regular long-term transfusion consists of repeated red cell transfusions to keep the Hb S less than 30% over time. It is indicated for:

- Primary and secondary stroke prevention.
- Recurrent acute chest syndrome or painful episodes not prevented by hydroxycarbamide.
- Progressive organ failure.

3.2 Before starting transfusions

Transfusion can be a life-saving therapy for acute complications and reduce the risk of chronic progressive organ damage from ischaemic stroke but any decision to use transfusion therapy has to be weighed up against the potential risks and these should be discussed with the patient/family and documented in the notes.

Patients with sickle cell disease receiving red cell transfusion are at particular risk of:

- Alloimmunisation resulting in red cell antibody formation. This can lead to a higher risk of delayed haemolytic reaction and make it more challenging to get appropriately cross-matched red cells.
- Hyperhaemolysis where there is bystander red cell destruction in the absence of antibody development. Management is individualised but should include avoiding further transfusion if possible. In severe cases early use of intravenous

immunoglobulin and methylprednisolone is recommended as well as supportive care with recombinant erythropoietin, intravenous iron and B12/folate supplementation. With certain clinical criteria, ecluzimab is commissioned for use in hyperhaemolysis but its use would need to be decided by a Consultant Haematologist.

- Increasing blood viscosity with an increase in overall haemoglobin in addition to Hb S containing cells.
- Secondary iron overload from chronic transfusion.

Before starting transfusions:

- Always discuss and document the indication for starting a red cell transfusion program.
- Potential complications of transfusion should also be discussed (use UHL blood transfusion consent sticker). The most frequent transfusion-related issue arising for patients with thalassaemia is secondary iron overload for which patients require chelation therapy.
- All new patients should have a transfusion history taken and extended red cell phenotyping performed in addition to red cell grouping and antibody screen.
- Blood bank must be informed that the patient has sickle cell disease and requires sickle negative blood.
- Ensure patients are immunised against hepatitis B.
- Check hepatitis B, hepatitis C and HIV serology prior to starting transfusion.

3.3 Aims of transfusion

- For all children and young people with sickle cell disease receiving red cell transfusion, the following investigations should be checked before and after:
    - Hb, reticulocytes, WCC, platelets, HCT, Hb S%, U&E, LFT, bone
- Red cells for transfusion should be sickle negative, ABO compatible, Rh and Kell matched.
- There are two types of red cell transfusion and the choice of transfusion method should be decided by clinical judgement of each individual case, taking consideration of indication to transfuse, minimising hyperviscosity and alloimmunisation risk as well as venous access:

3.3.1 Top-up transfusions

- The aim is to increase the haemoglobin level to baseline with sickle-negative red cells so improving the oxygen carrying capacity and reducing haemolysis and vaso-occlusion.
- **It is important to not raise the haemoglobin above baseline as this can result in hyperviscosity.**
- Red cells should ideally be less than 10 days old for a top-up transfusion.

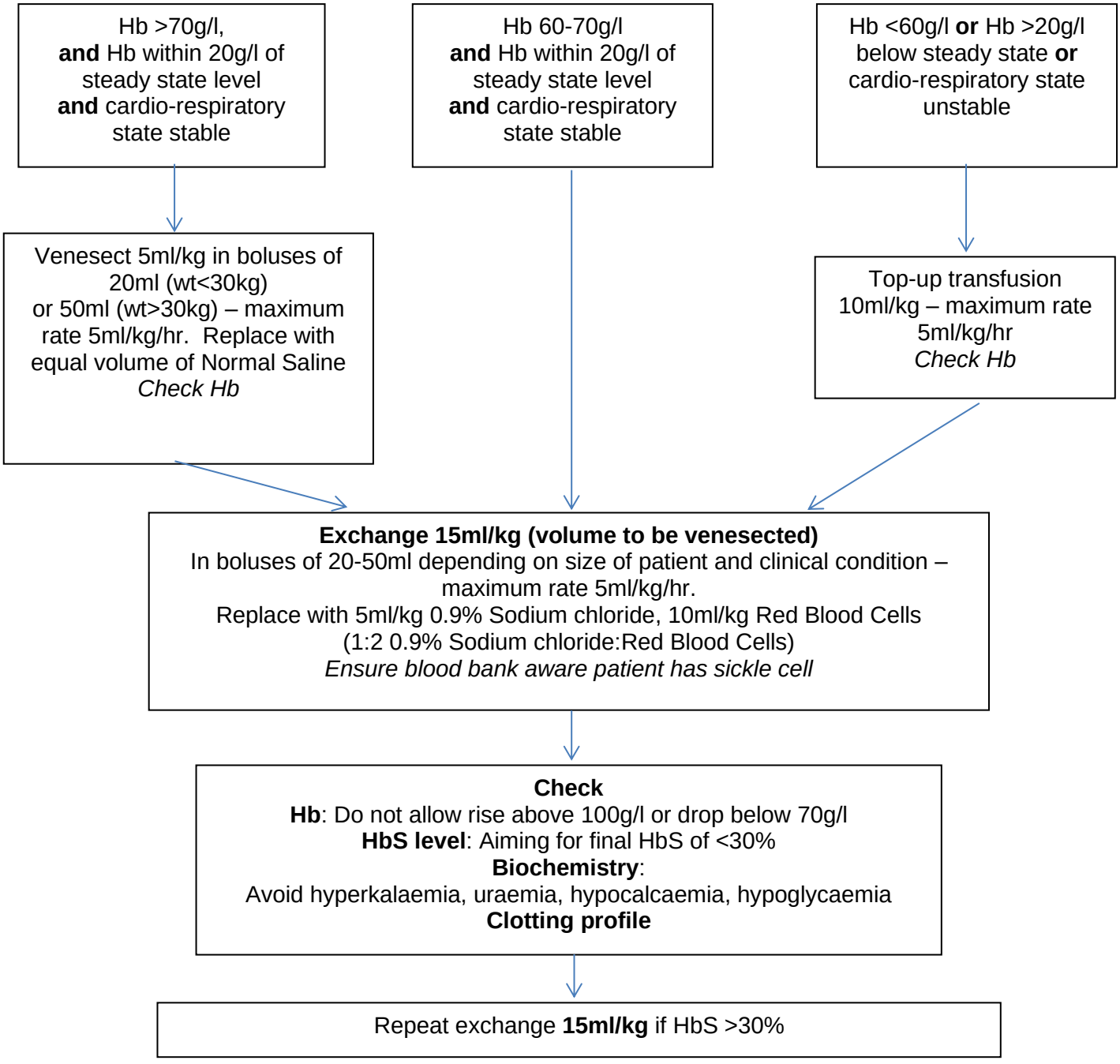
$$\text{The volume to transfuse in ml} = (\text{desired Hb} - \text{actual Hb}) \times \text{weight} \times 0.4$$

In patients with sickle cell disease not on regular transfusions, the post-transfusion haemoglobin should not exceed 100g/L, particularly if Hb S% is greater than 30%.

3.3.2 Exchange transfusions

- The aim is to remove the patient's sickle cells and replace with donor sickle-negative red cells so that the Hb S% is rapidly reduced to less than 30%, whilst maintaining a steady state blood volume throughout the procedure.
- This is the optimal emergency management in acute sickle cell complications such as acute stroke, acute chest syndrome, fulminant hepatic failure, splenic or hepatic sequestration and fulminant priapism unresponsive to other therapies.
- This can be done via a manual or automated process.
    - **In UHL elective regular automated red cell exchange is available for selected children and young people in paediatrics. These patients are offered regular automated red cell exchange based on their sickle cell related complications, venous access and compliance/adherence to the exchange process. Each of these patients is discussed in the regional EMSTN Haemoglobinopathy MDT before commencing the exchange program.**
    - **Emergency automated red cell exchange is not readily available for children and young people at UHL but suitability of each case requiring this intervention as an emergency is reviewed at the time and a decision made on relevant staffing and availability to use the apheresis machine on ward 27 at the time.** For young people aged 16 years old and over, these patients can also receive the exchange transfusion process through the adult haematology and apheresis team, but at the same time will remain under the medical and nursing care of the paediatric team.
    - For patients aged 15 years old and under, if automated red cell exchange is not available manual exchange should be undertaken, preferably in the paediatric intensive care with close working between haematology, intensivists and blood bank.
- Pre- manual exchange checklist:
    - Obtain informed consent from parents before starting procedure explaining the purpose and risks.
    - Red cells should ideally be less than 7 days old for an exchange transfusion.
    - Initially start with 15ml/kg, provided Hb 60-70g/l and within 20g of steady state. Usually a second 15ml/kg exchange is required.
    - Each red cell unit should be used within 4 hours of commencing transfusion.

Manual Exchange Transfusion Protocol for Paediatric Sickle Cell Disease



3.3.3 Manual exchange procedure

Two large bore access lines are required (peripheral venous, central venous or arterial for venesection only) for simultaneous venesection/infusion.

Single access may be used in the discontinuous technique with alternating withdrawal of blood and infusion. This should be reserved for patients where it is difficult to gain 2 access lines.

Blood is exchanged in aliquots according to the patient's weight and clinical condition – provided the patient is cardiovascularly stable, aliquots of 20mls should be used in patients <30kg or 50mls in those >30kg.

Each aliquot for removal of blood should not exceed 5% of the child's circulating volume (80mls/kg). Take care in children <5kg.

For an isovolaemic exchange, a total of 15ml/kg of patient's blood is to be exchanged with 5ml/kg of 0.9% Sodium Chloride and 10ml/kg red blood cells
(1:2 0.9% Sodium Chloride: Red Blood Cells).

Start by venesecting the patient's blood from cannula A as aliquot 1 (OUT) and then infuse the 0.9% Sodium Chloride then red blood cells sequentially (discontinuous) or concurrently (continuous) into cannula B as aliquot 1 (IN) according to table below. Use infusion rates of no more than 100-150mls/hr or maximum of 5ml/kg/hr.
Do this in turns until the exchange is completed.

	OUT (cannula A)	IN (cannula B)
Aliquot 1	20ml	20ml 0.9% Sodium chloride
Aliquot 2	20ml	20ml Red Blood Cells
Aliquot 3	20ml	20ml Red Blood Cells
Aliquot 4	20ml	20ml Normal Saline
Aliquot 5	20ml	20ml Red Blood Cells
Aliquot 6	20ml etc	20ml Red Blood Cells etc
Continue until Total IN = Total OUT	15ml/kg	15ml/kg

Examples:

Child 1, weight=30kg, Hb 80g/l

1. Initially venesect 5ml/kg = 150ml, replace with 0.9% Sodium chloride
2. Venesect 15ml/kg = 450ml, replace with 150ml 0.9% Sodium chloride and 300ml red blood cells (1:2 0.9% Sodium chloride: Red Blood Cells)

Child 2, weight=20kg, Hb 65g/l

1. Venesect 15ml/kg = 300ml, replace with 100ml 0.9% Sodium chloride and 200ml Red Blood Cells (1:2 0.9% Sodium chloride: Red Blood Cells)

Monitor blood pressure, pulse, oxygen saturations every 15 minutes and temperature hourly throughout the procedure.

Keep strict fluid balance chart throughout procedure as these unwell patients may require additional maintenance fluids.

Repeat bloods post exchange:

- Ensure Hb is >70g/l and <100g/l.
- Beware of hyperkalaemia/hypocalcaemia/hypoglycaemia.
- Ensure normal clotting.
- The total Hb S% should be <30% and a 30ml/kg exchange is usually required to achieve this.
- In a stable child following a 30ml/kg exchange, leave a 4-6-hour break if further exchange is required. Very unwell children may require continuous exchange.

For those on regular exchange programmes, a single 15ml/kg exchange is usually adequate.

3.4 Regular top up transfusion program

Some patients with sickle cell disease will be on a regular chronic top up transfusion program. In this situation **once the pre-transfusion Hb S% is less than 30%,** these patients can be transfused to higher target transfusion haemoglobin level, but this should be individualised to each patients.

Below is a guide for transfusion volume requirement in patients chronically transfused and Hb S% <30%. Where possible the volume should be round into red cell units to minimise excess donor exposure.

Hb <95-100g/l, transfuse 10ml/kg

Hb 90-94g/l, transfuse 12ml/kg

Hb <90g/l, transfuse 15ml/kg

3.4.1 Managing top-up transfusion appointments

- Most patients will attend ward 27 day care at a pre-arranged time for pre transfusion sampling (FBC, G+S, U+Es, LFTs, ferritin,Hb S% for patients with sickle cell disease).
- This will be requested by the day care nurses/haemoglobinopathy specialist nurse.
- This should be done to minimise absence from school but no later than 4.30pm.
- 'All-in-one' transfusions are pre-arranged with the haematology team and are for exceptional circumstances only.
- For day time transfusions patients should arrive on ward 27 day care no later than 11am (ideally 9-10am unless agreed with the ward nurses).
- Patients will be admitted to the ward, weight and observations recorded and reviewed by clinician if there are any concerns.

- The transfusion will be prescribed by the junior doctor according to the transfusion algorithm and transfused at a rate of 5ml/kg/hr.
- Prompt cannulation will be performed by appropriately trained nursing staff / junior doctor, with no more than 3 attempts per person.
- Patients arriving later than 12pm (regular transfusion) and 11am for 'all in one' will be rescheduled.
- Evening transfusion sessions in emergency only.
- An accurate electronic transfusion record will be recorded for each patient with documentation of transfusion date and volume by the haematology CNS/ day care nurses.
- Transfusion administration, monitoring and management of transfusion reactions should be according to trust guidelines.

3.5 Regular automated red cell exchange program

With exchange transfusion the aim is to remove the patient's sickle cells and replace with donor sickle-negative red cells so that the Hb S% is rapidly reduced to less than 30%, whilst maintaining a steady state blood volume throughout the procedure.

3.5.1 Before exchange transfusion

- Written consent before starting red cell exchange program then verbal consent at each transfusion.
- A decision made by the paediatric haemoglobinopathy team regarding desired Hb S%, haematocrit, frequency of transfusions and run time.
- Patients with haemoglobin of 60g/L or below will require a top up transfusion pre-exchange transfusion.
- Most patients will attend ward 27 day care at a pre-arranged time for pre transfusion sampling (FBC, G+S, U+Es, LFTs, ferritin, calcium, bone profile, magnesium and Hb S% for patients with sickle cell disease).

3.5.2 Pre-transfusion assessment

- Check all above blood tests completed within the last 48 hours
- Baseline observations stable
- Height and weight
- Check appropriate venous access
- Check general health – if any general concerns discuss with appropriate consultant prior to starting procedure

Set up Terumo Spectra Optia for red cell exchange procedure and further discussion with consultant if depletion or depletion/exchange procedure is required.

3.5.3 Process during procedure

- Monitor patient observations 5 minutes after the start of the exchange transfusion then after 5 minutes of commencing each unit of blood and more frequently if patient becomes unstable
- Document run times and machine values alongside observations with each unit of blood

3.5.4 Potential complications

- Managing citrate toxicity

a) Pause the system
b) Notify medical team of patient's condition

c) Options of treatment include slowing down inlet flow rate, reducing AC infusion rate. If symptoms still not alleviated, pause procedure, check calcium level and consider calcium replacement:

Hypocalcaemia guideline: Calcium Disorders UHL Childrens Hospital Guideline Ref C6/2019

- Vasovagal episodes

a) Pause the procedure
b) Lower the head of the patient and raise their feet
c) Restart once patient blood pressure is stable and consider reducing inlet flow rate to slow down procedure
d) If hypotensive, administer intravenous fluid bolus of 0.9% sodium chloride 10ml/kg and discuss with medical team to avoid hypervolemia
e) Consider monitoring the patient's observations more frequently

- Blood transfusion reaction

a) Manage transfusion related reactions as per UHL blood transfusion policy: Blood Transfusion UHL Policy

3.5.5 Post procedure

- End procedure without rinse back as this is not recommended in paediatric red cell exchange due to this procedure giving sickle cells back to the patient
- Record final run values on procedure flow chart
- Monitor patient's observations 15 minutes and 30 minutes after end of procedure.
- Recheck FBC and HbS %
- If patients well and observations stable after thirty minutes then flush port and lock with Heparin 100units/ml in total 4mls and remove access lines
- Ensure patient has follow up appointment for next blood tests and exchange transfusion

4. Monitoring for patients on chronic red cell transfusion

- All patients should have the following regular assessments at each transfusion visit and these will be documented in their electronic transfusion spreadsheet:
    - Weight
    - Pre-transfusion haemoglobin
    - Renal function
    - Liver function
    - Ferritin
    - Volume red cells transfused
- Iron chelation therapy will be reviewed every 3 months.
- Patients with secondary iron overload/on chelation therapy will undergo regular ferriscan liver and cardiac T2* MRI to assess for iron loading in the heart and liver.
- Patients on iron chelation therapy will undergo annual audiology and ophthalmology surveillance.
- Viral serology for hepatitis B (Hep B surface Ag), hepatitis C (Hep C core antibody) and HIV (HIV I & II antibody) will be checked every 12 months as well as anti-Hepatitis B surface antibody.
- Other relevant investigations related to endocrine, bone, cardiac and liver systems will be reviewed and requested at the time of annual review.

5. Education and Training

Regular teaching provided on ward 27, in paediatric emergency department, paediatric specialist trainees regional training days and nursing training days.

6. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Transfusion spreadsheets	3 monthly clinical review of patient and spreadsheets	Dr Kaljit Bhuller	3 monthly	Seen by haemoglobinopathy team

7. Supporting References

1) Sickle cell disease in childhood – standards and recommendations for clinical care 3rd edition November 2019

2) Standards for the clinical care of children and adults with thalassaemia in the UK 3rd Edition 2016

3) BSH Guidelines on red cell transfusion in sickle cell disease Part I: Principles and laboratory aspects & Part II: Indications for transfusion 2017

4) 2021 Guidelines For The Management of Transfusion Dependent Thalassaemia (TDT) Thalassaemia International Federation 4th edition

8. Key Words

Sickle Cell, Anaemia, Thalassaemia, Haemoglobinopathy, Transfusion, Exchange Transfusion

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The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) Kaljit Bhuller, Consultant in Paediatric & TYA Haematologist	**Executive Lead** Chief Nurse
Details of Changes made during review: Combined previous guidance C19/2023 Include automated red cell exchange transfusion process in this guideline Addition of Rachael Coulson, Haemoglobinopathy Specialist Nurse to author list	