LRI Children's Hospital

Severe Combined Immune deficiency (SCID) Newborn Screening Pathway

Staff relevant to:	Children's Hospital staff managing babies referred for further Severe Combined Immune Deficiency (SCID) screening.
Team approval date:	May 2024
Version:	2
Revision due:	May 2027
Written by:	R Radcliffe
Trust Ref:	C48/2021

Contents

1. Introduction and Who Guideline applies to

This guideline is for use by Children's hospital staff managing babies referred from national blood spot screening with low TRECS (T cell receptor excision circles) requiring further assessment for SCID.

The UK National Screening Committee (UK NSC) has recommended that screening babies for severe combined immunodeficiency (SCID) should be evaluated in the NHS. Sheffield (our regional blood spot screening laboratory) is involved in this pilot, so as a Children's Hospital within that region managing children with SCID; we have developed a pathway to implement this programme.

The information gained from this evaluation will inform a final recommendation on whether screening for SCID should become part of the newborn blood spot screening programme.

Rationale for newborn screening for SCID.
Importance of early identification:

- Establish diagnosis and institute immediate lifesaving treatment to improve survival. In children identified before/at birth (because of family history), mortality is less than 10%. For those who are diagnosed through clinical presentation, mortality is around 60%.
- Avoid inefficient, costly and dangerous diagnostic journey.
- Provide families with genetic diagnosis and advice on reproductive risks.

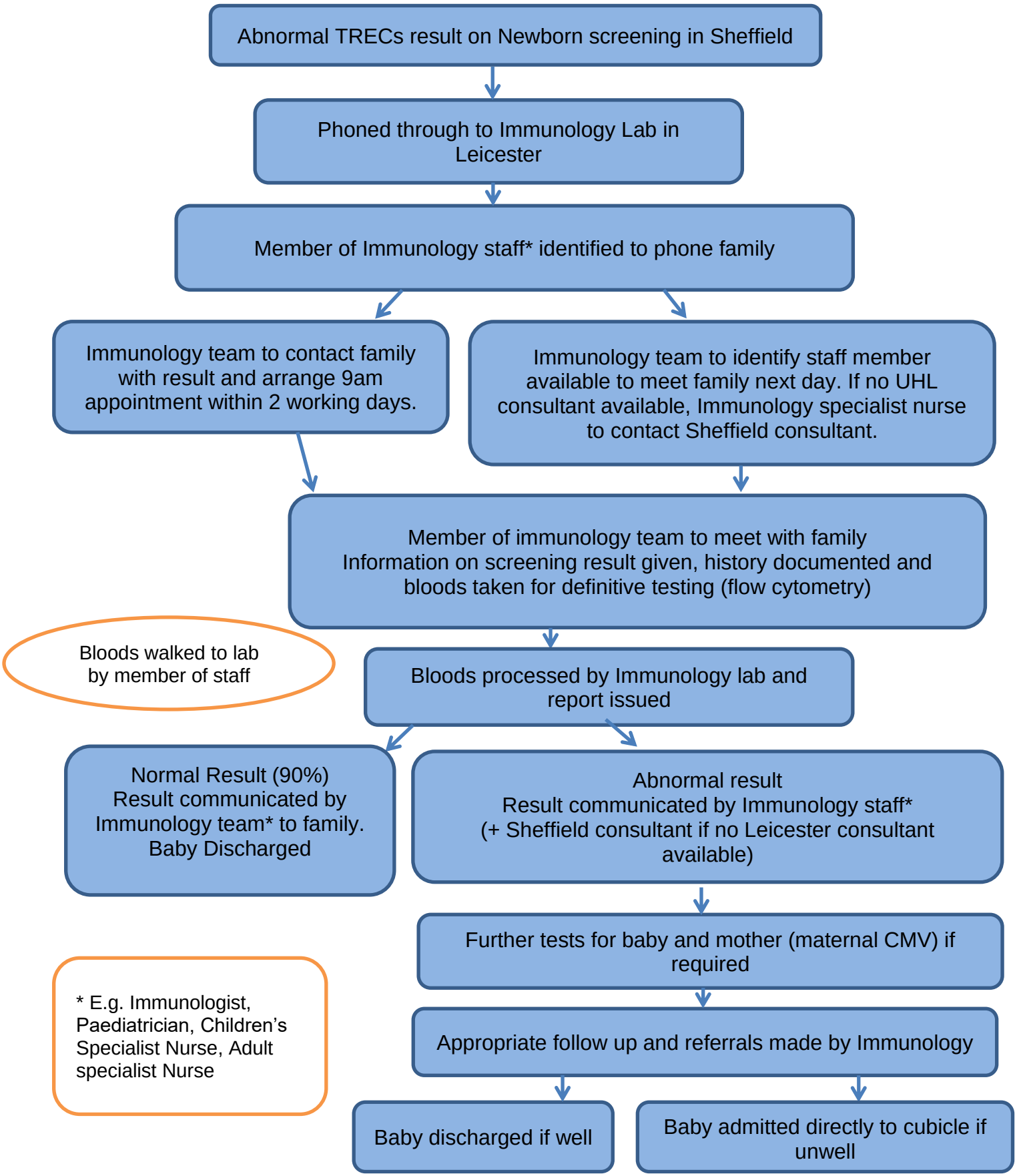
Related documents;

Newborn Screening for Severe Combined Immune Deficiency (SCID) UHL Neonatal Guideline

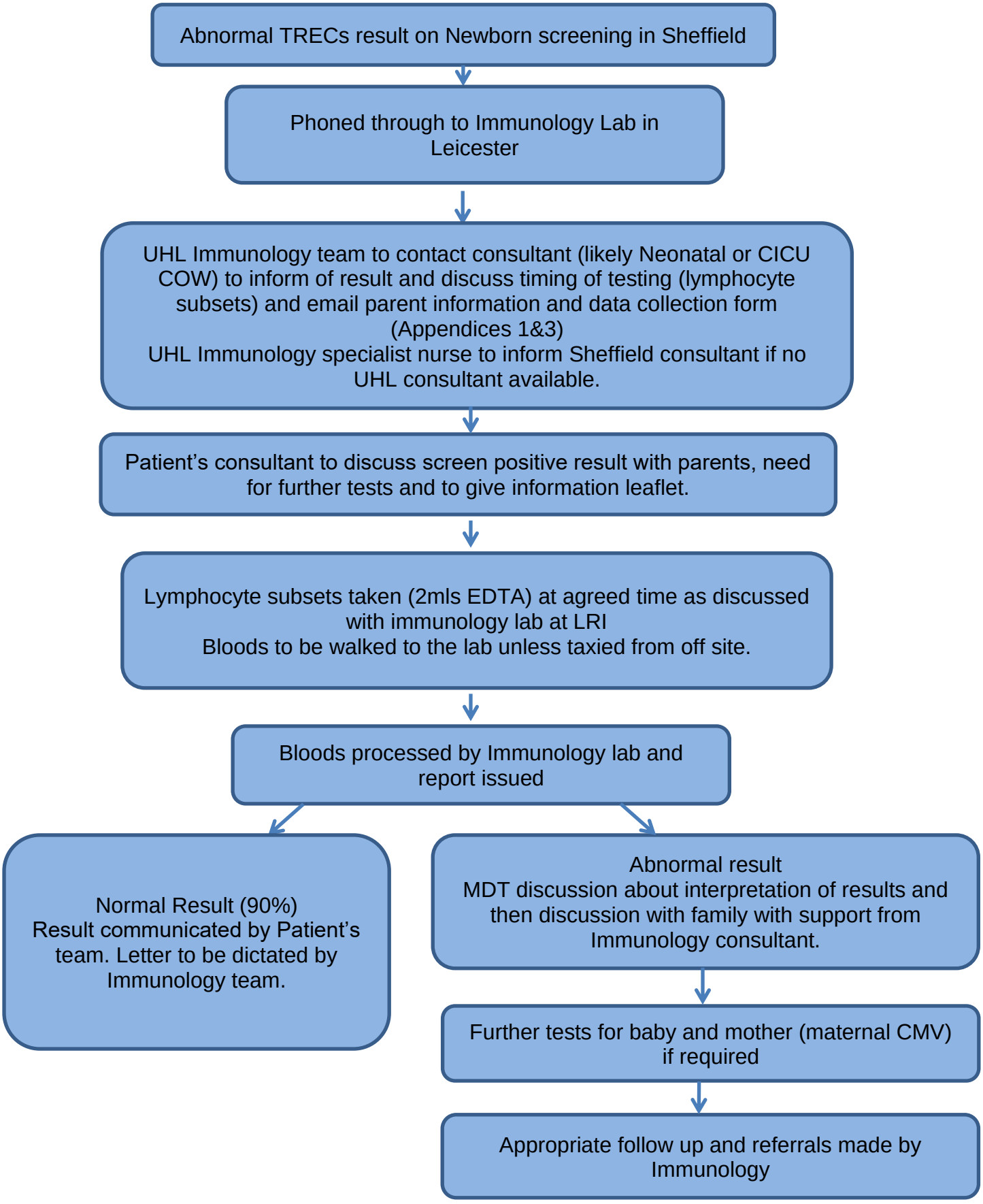
Newborn Blood Spot Screening For UHL and Community Midwives UHL Obstetric Guideline

Severe Primary Immune Deficiency - Admission to Ward 27 Standard Operating Procedure UHL Childrens Hospital Guideline

Pathway for responding to abnormal TRECS result
(Patient in the community)



Pathway for responding to abnormal TRECS result
(Patient admitted to hospital)



2. Guideline Standards and Procedures

SCID includes a number of genetic disorders characterized by profound defects in both cellular immunity and specific antibody production, and is estimated to occur in 1/50,000 to 1/100,000 births. All SCID infants have absent or extremely low production of antigenically naïve T cells from their thymus. The combined defects of T cells, plus absent B and/or NK cells in some forms of SCID, severely compromise an infant's ability to resist infections, and lead to death in early life without treatment. Currently 30% of babies with SCID are identified via family history. The delay in finding the remaining 70%, means that they have been exposed to infection for longer before receiving treatment. This leads to poorer outcomes after Bone Marrow Transplant (BMT)

We expect 1-2 babies with abnormal results per month to assess in Leicester. Please refer to the flow chart on page 2 for details of the pathway.

The screening test will measure T cell receptor excision circles (TRECS). Those with numbers below the cut off will be referred for further tests (lymphocyte subsets by flow cytometry).

For centres with small paediatric immunology departments, the pathway developed includes adult specialist nurses meeting with the family and communicating normal results, in the unlikely event of no Paediatric Immunology staff being available. If no Leicester Immunology Consultant is available to discuss abnormal results, the consultant from Sheffield Children's hospital for Immunology and Infectious disease will be available to discuss via MS-Teams.

Please note that other than the specialist paediatrician and specialist nurse, other Immunology staff do not have Paediatric training. Therefore if no Paediatric Immunology staff are available then the Immunology staff will require support from Paediatrics to assess the baby, if they are concerned they are unwell.

2.1 Clinical Pathway

On notification of positive screen

- **If baby at home.** Organise an appointment on Children's day-care for the baby and their family within 2 working days. This should be at 9am and in a cubicle, if possible. Their extension number is 16317.
- Phone family and give SCID screening result following the checklist for immunology services. (Appendix 3, word document available in CSID folder on clinical immunology drive)This form will form part of the baby's hospital record.
- Send confirmation email following phone call using the text from appendix 1, with the details of the appointment added, using the uho-tr.immunology@nhs.net email. Ask for an email confirmation of receipt.
- **If baby is in hospital,** liaise with the local hospital/ treating consultant for review and management, (Newborn Screening for Severe Combined Immune Deficiency (SCID) UHL Neonatal Guideline).

- **If baby has since moved out of the Leicester catchment area**, agree with Sheffield screening lab which team (Sheffield screening lab or Leicester clinical Immunology team) will be responsible for ensuring appropriate testing and follow up.

2.2 First appointment

You should inform the family:

- of the SCID investigation result and explain about flow cytometry
- about the storage, use and analysis of their baby's data

You should take a blood sample for the SCID screening lymphocyte subset (2mls of EDTA) and walk the sample to the Immunology laboratory.

Please ensure all this information is recorded in the notes. Baby and family will wait on Daycare for the results.

2.3 Communicating results

If Flow cytometry normal

(See report, *Flow cytometry normal is defined as >=1,500 CD3/µl AND naïve T cell >=70%)

- See and reassure parents, discharge child.
- Provide discharge information.
- Confirm consent for follow-up.
- Give letter to parents (copying in their GP and Sheffield Screening lab*) using the SCID not found letter template for immunology services which includes advice about immunisations. A template letter is available on ICE 'SCID screening- normal result.

If flow cytometry <10% naive T cell

This indicates SCID/Leaky SCID/Omenn Syndrome. This result should be discussed with the family by a consultant. If no Immunology consultant available, please contact Sheffield Children's Hospital Immunology consultant via switchboard for remote consultation.

You should:

- Refer patient immediately to SCID transplant centre (Newcastle/GOSH)
- Obtain consent for genetic testing to identify the specific SCID type, and perform any further investigations recommended by transplant centre. See Appendix 2 for Genetics consent and referral forms.
- Determine maternal CMV IgG status on a fresh blood sample (ideally sample to be taken on daycare) to be able to advise about breast feeding – discontinue breast feeding until results available, milk can be expressed and stored to maintain supply until results available.
- Seek advice from SCID centre about starting co-trimoxazole, fluconazole, and immunoglobulin prophylaxis. Standard regime found in Appendix 5.

- If the baby is unwell they should be admitted to ward 27 (Severe Primary Immune Deficiency - Admission to Ward 27 Standard Operating Procedure UHL Childrens Hospital Guideline)
- If the baby appears unwell and cannot be reviewed by Dr Radcliffe, please contact the Paediatric COW via switchboard and ask for a Registrar to review the baby.
- If well the baby will be discharged whilst awaiting admission to transplant centre. Complete a discharge letter with appropriate clinical information. There is an ICE template letter 'SCID screening – SCID confirmed'. Copies should be sent to GP, Sheffield Screening lab* and a copy given to parents.
- Ward 27 should be informed of the patient for potential direct admission.

If Flow cytometry abnormal, but >10% naive T cells

This indicates non SCID T Cell Lymphopenia (TCL)** or secondary causes of TCL*** or idiopathic TCL.

This result should be discussed with the family by a consultant. If no Immunology consultant available, please contact Sheffield Children's Hospital Immunology consultant for remote consultation

You should:

- Follow-up with local paediatric immunology, according to clinical judgement, and refer to geneticist or other subspecialists depending on co-morbidities (for example, cardiologist, paediatric surgeon, community paediatrician)
- Consider if genetic testing is appropriate. See Appendix 2 for Genetics consent and referral forms.
- Dependent on level of T and other immune cell function, consider starting:
    - co-trimoxazole prophylaxis and anti-fungal prophylaxis
    - antibody replacement
- Make sure patient has all non-live vaccines in first 6 months unless immunoglobulin started
- Exclude live vaccines, for example BCG, rotavirus, MMR, VZV, if significant T cell lymphopaenia.
- Follow-up 6 weeks to 3 months depending on level of immune compromise and clinical scenario.
- Complete a discharge letter summarising the above clinical information. There is an ICE template letter 'SCID screening – Indeterminate result' Copies should be sent to GP, Sheffield screening lab* and a copy given to parents.
- If the baby appears unwell and cannot be reviewed by Dr Radcliffe, please contact the Paediatric COW via switchboard and ask for a Registrar to review the baby.

*Lynette Shakespeare, Sheffield Newborn Screening Laboratory, Sheffield Children's NHS Foundation Trust, Western Bank, Sheffield, S10 2TH.

**Non SCID T Cell Lymphopenia includes Nijmegen breakage syndrome, Noonan, CHARGE, Schimke immuno-osseous dysplasia, Down syndrome (trisomy 21), CLOVES, Ataxia telangiectasia, Jacobsen, Tar, DiGeorge, Cytogenetic abnormality, ECC, Cartilage hair hypoplasia, Rac2 defect, Kabuki, Fryns syndrome, Renpenning, Dock8

***Secondary causes of TCL includes congenital heart disease (apart from DiGeorge syndrome), Gastrointestinal malformations such as intestinal lymphangiectasia and hydrops, neonatal leukaemia and HIV

2.4 BCG

A SCID screen positive result will be reported to the BCG teams, to ensure that these babies are not administered BCG until further testing has been completed. Local BCG teams should contact the Immunology department on paedsimmunology@uhl-tr.nhs.uk to confirm if an eligible child can receive BCG.

3. Education and Training

Departmental training provided.

E learning for health package:

https://portal.e-lfh.org.uk/Component/Details/717669

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Data submitted to UKHSA	Nationally by UKHSA	R Radcliffe	Case by Case	UKHSA to report
Local monitoring of cases: Seen within 2 working days Results communicated same day Results communicated by appropriate member of staff Outcome (Normal/SCID/other abnormal)	Diary exercise monitoring each case.	R Radcliffe	Duration of pilot	Regional Paediatric Immunology meeting

5. Supporting References

https://phescreening.blog.gov.uk/2019/10/29/scid-update-bloodspot-screening/

Neonatal Screening for Severe Combined Immunodeficiency (SCID) Puck, J, Curr Opin Pediatr. 2011 Dec; 23(6): 667–673.

Neonatal diagnosis of severe combined immunodeficiency leads to significantly improved survival outcome: the case for newborn screening; Lucinda Brown, Jinhua Xu-Bayford, Zoe Allwood, Mary Slatter, Andrew Cant, E. Graham Davies, Paul Veys, Andrew R. Gennery, H. Bobby Gaspar. **Blood (2011)** 117 (11): 3243–3246.

SCID screening evaluation: templates for immunology services and teams – original documents available to download here: https://www.gov.uk/government/publications/scid-screening-evaluation-templates-for-immunology-services-and-teams

Clinical pathway for babies who screen positive for SCID – national pathway: https://www.gov.uk/government/publications/clinical-pathway-for-babies-who-screen-positive-for-scid/clinical-pathway-for-babies-who-screen-positive-for-scid

6. Key Words

Blood spot, Flow cytometry, TRECS, T Cells

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) Dr Ruth Radcliffe Consultant Paediatrician	**Executive Lead** Chief Nurse
Details of Changes made during review: **April 2024;** Hyperlinks added Format updated	

Appendix 1 - SCID screening evaluation: higher chance information for parents

Please cut and paste and insert details of patient, appointment and healthcare professional

Dear Parent/Carer of **(insert name of baby)**

Congratulations on the birth of your baby.

As discussed, your baby needs an extra test to check for SCID or another related condition following their newborn screening heel prick.

It does not mean your baby definitely has SCID or another condition, but it does mean that they have a higher chance of having SCID.

If your baby was born before 37 weeks

If your baby was born before 37 weeks, they are more likely to have a newborn screening result that needs following-up. However, they are not more likely to have SCID.

What will happen at your appointment

During your baby's appointment you will see a specialist team who will carry out a diagnostic test (blood test) to check your baby's immune system.

This test will confirm if your baby:

- does not have SCID or another condition, and can be discharged
- has another condition affecting the immune system
- has SCID

In most cases, you will get the results the same day although further tests may be needed. You will have time to ask any questions.

Please be aware that the appointment can take all day.

SCID

SCID is the name given to a group of rare inherited conditions which cause major problems with the immune system. Babies with SCID are at higher risk of infection because their immune system does not work properly.

SCID screening: helping you decide if you want this for your baby has more information about screening for SCID. Great Ormond Street Hospital for Children has more information about SCID.

Treatment

If your baby is confirmed as having SCID, the team will explain any treatment that your baby may need.

Treatment for SCID is far more likely to be successful if started early and screening makes this possible.

If tests show that your baby has SCID, a bone marrow transplant can restore the body's defence against infections.

Some types of SCID respond to gene therapy. This involves replacing an unhealthy gene in your baby's body with a healthy one.

Following treatment, babies may need long-term medication.

Support for your family

We understand this screening result is unexpected and may be upsetting for you and your family.

Please remember that your baby's screening result does not mean your baby definitely has SCID.

You can discuss any concerns with the SCID team at your hospital appointment. Everything will be done to support your family and make sure you get to know test results as soon as possible.

If your baby has SCID, please remember that the condition has been found very early because of newborn screening and that this will help to give your baby the best possible start in life.

Further information

Occasionally, your baby may need to stay in hospital overnight. We suggest that you bring an overnight bag for you and your baby.

If your baby becomes unwell before this appointment, please take your baby to your local Accident and Emergency department (also known as emergency department or casualty).

Appointment details

Date: **(detail to be added by clinician at time of or after discussion with parents)**

Time: **(detail to be added by clinician at time of or after discussion with parents)**

Location: **Children's Day Care Unit (Ward 28), Windsor Building Level 4, Leicester Royal Infirmary, Infirmary Square, Leicester LE1 5WW –access to car park including multi-storey car park via Havelock Street**

Contact details:

Children's Day Care Unit, Tel 0116 258 6317 / 0116 258 6922

You will be seen by a member of the Leicester Immunology team. Telephone 0116 2586702 (8.30am to 4.30pm)

Travel

Information about travelling to the Leicester Royal Infirmary can be found on this web page

https://www.leicestershospitals.nhs.uk/patients/getting-to-hospital/leicester-royal-infirmary/

Nearest train station: **Leicester:** 10 – 15 minute walk to hospital via Waterloo/Tigers Way and Nelson Mandela Park;
Taxis usually available from Leicester Station

Public transport links:

UHL Hospital Hopper operates between Leicester General, Royal and Glenfield Hospitals every 30 minutes from 6.30am – 6pm – stops outside railway station and Leicester Royal Infirmary, Aylestone Road.

There are numerous bus services into and out of Leicester city centre

Yours Sincerely

(Insert name and job title)
On behalf of
Leicester Clinical Immunology team

The generic text is also available in Arabic, Bengali, Hindi, Polish, Somali and Urdu here:
https://www.gov.uk/government/publications/scid-screening-evaluation-templates-for-immunology-services-and-teams

Appendix 2: Genetic testing primary immune deficiency

Genetic testing for Primary Immune deficiency is now performed by the Whole Genome Sequencing technique, and consent should be taken by someone who has undergone training. Links to the record of discussion form and request forms can be found on the following webpage.

https://www.eastgenomics.nhs.uk/for-healthcare-professionals/genomic-tests/rare-and-inherited-diseases/genome-sequencing/

Test required – R15 – Primary Immune Deficiency
Clinical Information – SCID suspected on flow cytometry post screening, and T/B/NK phenotype
Mark as urgent.
Send 2-5mls EDTA, samples can be returned to the Immunology lab for sending on.

Appendix 3: Information for a child screened positive

Information for a child screened positive for Severe combined immunodeficiency (SCID)

Name						Date of Birth	DD/MM/YY					
NHS No.												
Hospital No.												
Address												
Birth Location		Gestation		(w)+ (d)		Weight (g)						
Mother's name and DoB				Siblings								
Father's name and DoB												
Screening result	Date	DD/MM/YY		Received by								
Family informed	Date	DD/MM/YY		By whom								
Diagnosis	DD/MM/YY	Age				Weight (g)						
GP details				Information sent Y/N DD/MM/YY		Initials						
Health Visitor details				Information sent Y/N DD/MM/YY		Initials						
Consanguinity Y/N	Maternal Immunosuppression Y/N			Ethnic group								
Relevant clinical information												
Interpreter required	Yes	No		Language								

Parental Communication check list for newly diagnosed children with Severe combined immunodeficiency (SCID)

Name of child:			
Name of person communicating result:	Sign Print		
Profession of person communicating result:	Consultant ☐ Nurse ☐ GP ☐ HV ☐ Other_____		
Method of communication:	Home visit ☐ Telephone ☐ Other_____		
Location of baby at contact	Home ☐ Hospital ☐		
RECOMMENDED DURING INITIAL COMMUNICATION OF POSITIVE NBS RESULT			
		Date	Initial
Introduction	Who you are and where you're from (if two parents present, speak to both) General enquiry regarding the babies health	DD/MM/YY	
Check correct baby	Name DoB DD/MM/YY	DD/MM/YY	
Reason for visit / call	Remind parents baby had 'heel prick' when 5 days old	DD/MM/YY	
	One of the results has come back suggesting one of the conditions is **suspected**	DD/MM/YY	
	Name of the condition	DD/MM/YY	
	Not diagnostic, a screening test	DD/MM/YY	
	Need more tests to confirm the result	DD/MM/YY	
Initial information	SCID is the name given to a group of rare, inherited disorders that cause major abnormalities of the immune system.	DD/MM/YY	
	There are many different types of SCID, each with different genetic causes.	DD/MM/YY	
	The immune system abnormalities in SCID lead to greatly increased risks of infection and other complications that are life-threatening.	DD/MM/YY	

	Not caused by anything the parents did before or during pregnancy	DD/MM/YY	
	Reassure parents that it is safe to wait until they are seen by clinical team	DD/MM/YY	
	Advise parents to write down any questions they think of so they can ask these at their clinic appointment	DD/MM/YY	
	Ask for email address to send information sources and appointment details	DD/MM/YY	
	Give contact name and number of member of clinical team	DD/MM/YY	
	Give UKHSA 'suspected' leaflet	DD/MM/YY	
	Discuss suitable websites if appropriate	DD/MM/YY	
Afterwards	Send email with appointment details, contact information and information source(s) www.piduk.org	DD/MM/YY	
Optional information (If confident and qualified to discuss *and* if parents are interested in hearing more)	In all infants affected by SCID, specialised white blood cells, known as lymphocytes, are missing or not functioning properly. The three main types of lymphocytes that can be affected are called T-cells, B-cells and natural killer ('NK') cells.	DD/MM/YY	
	In infants affected by SCID, a genetic mistake results in the absence or malfunction of a protein that is necessary for normal development and/or function of the immune system. Many different genes can be affected, each causing a different type of SCID.	DD/MM/YY	
	The first signs of SCID usually occur within the first three to six months	DD/MM/YY	
	1 in every 35,000 babies in the UK will be born with the condition each year.	DD/MM/YY	

Comments		DD/MM/YY	

Appendix 4: New Newborn blood spot screening result: SCID not suspected

Dear parent/carer,

I am glad to say that the result of your baby's recent blood test for SCID showed that it was highly unlikely that your baby has the condition.

It is never possible to be 100% certain, but we know of no baby in the world who has had a normal test result and then been found to have SCID.

Although we have ruled out this severe immune deficiency in your child this does not rule out other less severe problems with the immune system. If you have any concerns about an infection or the health of your child, you should contact your GP, health visitor or:

- visit www.nhs.uk
- call NHS 111 for general health advice and information

Your child should now start the childhood immunisation progamme which includes the live rotavirus vaccine, and if eligible, the BCG vaccination.

Please check with your health visitor, who will be able to tell you if your baby is eligible for the BCG vaccine.

Yours

[signed by immunologist]

(Please send a copy to the family GP, with a note for the GP to pass onto the health visitor)

(Health visitor – please send a copy to the local CHIS)

Appendix 5:Standard Prophylaxis for SCID babies.

All to be discussed with Transplant Centre, and likely to be initiated by them.

PO Co-trimoxazole 30mg/kg once daily, starting once baby is 2 weeks old and physiological jaundice has resolved

PO Fluconazole 6mg/kg OD twice weekly for <44 week gestational age, 6mg/kg OD from 45 weeks gestational age

Immunoglobulin Replacement Therapy – as soon as possible / convenient

Aciclovir – not routine