East Midlands Neonatal
Operational Delivery Network

NETWORK GUIDELINE

Guideline:	**Severe Combined Immune Deficiency (SCID) Newborn Screening Pathway for use on the Neonatal Unit (South Hub)**
Version:	**1**
Date:	**October 2021**
Review Date:	**October 2024**
Approval:	**EMNODN Clinical Governance Group**
Authors:	**Dr Ruth Radcliffe, Consultant Paediatrician**
Consultation:	**EMNODN Clinical Governance Group**
Distribution:	**Neonatal Units within EMNODN South Hub**
Risk Managed:	**Introduction of SCID screening as part of Newborn blood spot screening from September 2021. A guideline to manage abnormal results safely and promptly.**

This document is a guideline. Its interpretation and application remains the responsibility of the individual clinician, particularly in view of its applicability across the different Trusts in the East Midlands Neonatal Operational Delivery Network – South Hub. Please also consult any local policy/guideline document where appropriate and if in doubt contact a senior colleague.

Caution is advised when using guidelines after a review date.

REVIEW AND AMENDMENT LOG

Version	Type of Change	Date	Description of Change
1	New guideline	Sept 2021	-

1. Introduction and Who Guideline Applies To

This guideline is for use by Neonatal Unit 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 Women's & 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 (NBBS) programme.

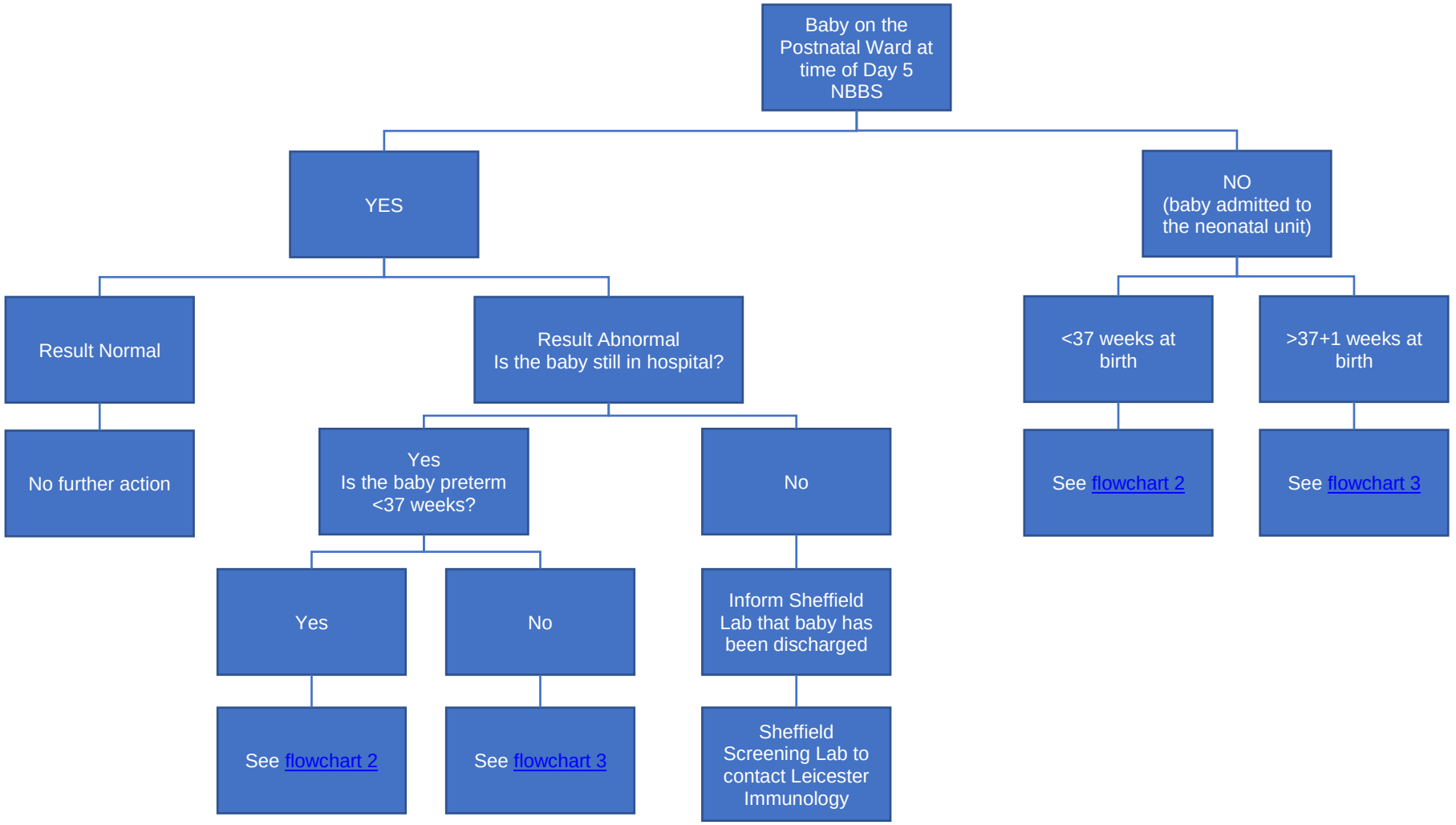
2. Rationale for Newborn Screening for SCID.

Importance of early identification:

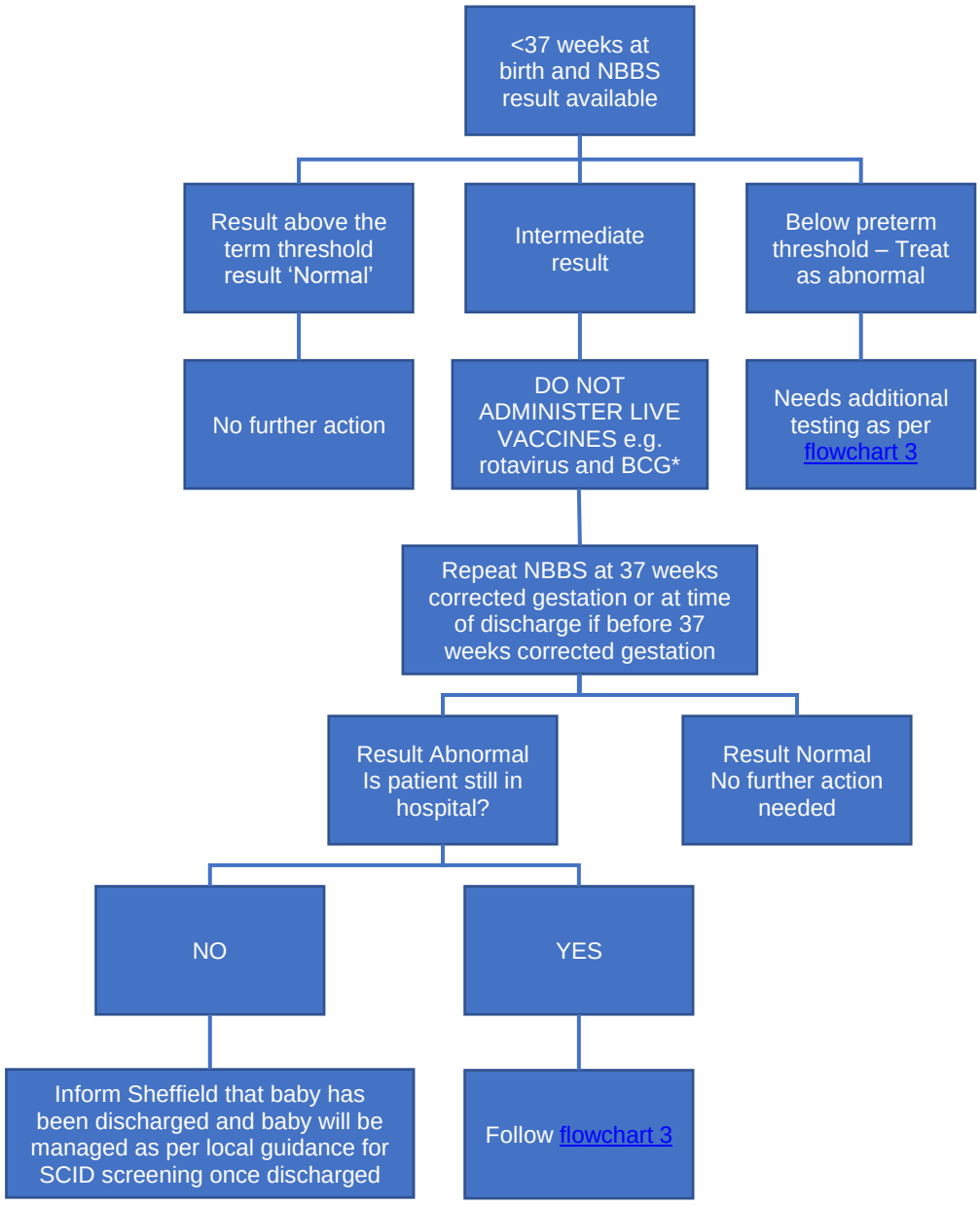
- Establish diagnosis and institute immediate lifesaving treatment to improve survival. In children identified before/at birth (because of family history), mortality is less than 10%. For those who are diagnosed through clinical presentation, mortality is around 60%.
- Avoid inefficient, costly and dangerous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

Flow Chart 1: All babies still in hospital for NBBS

(Babies already discharged will be managed as per the Leicester Children's Hospital Guideline for SCID screening or local guideline as appropriate)



Flowchart 2: Specific guidance for those babies born preterm <37 weeks

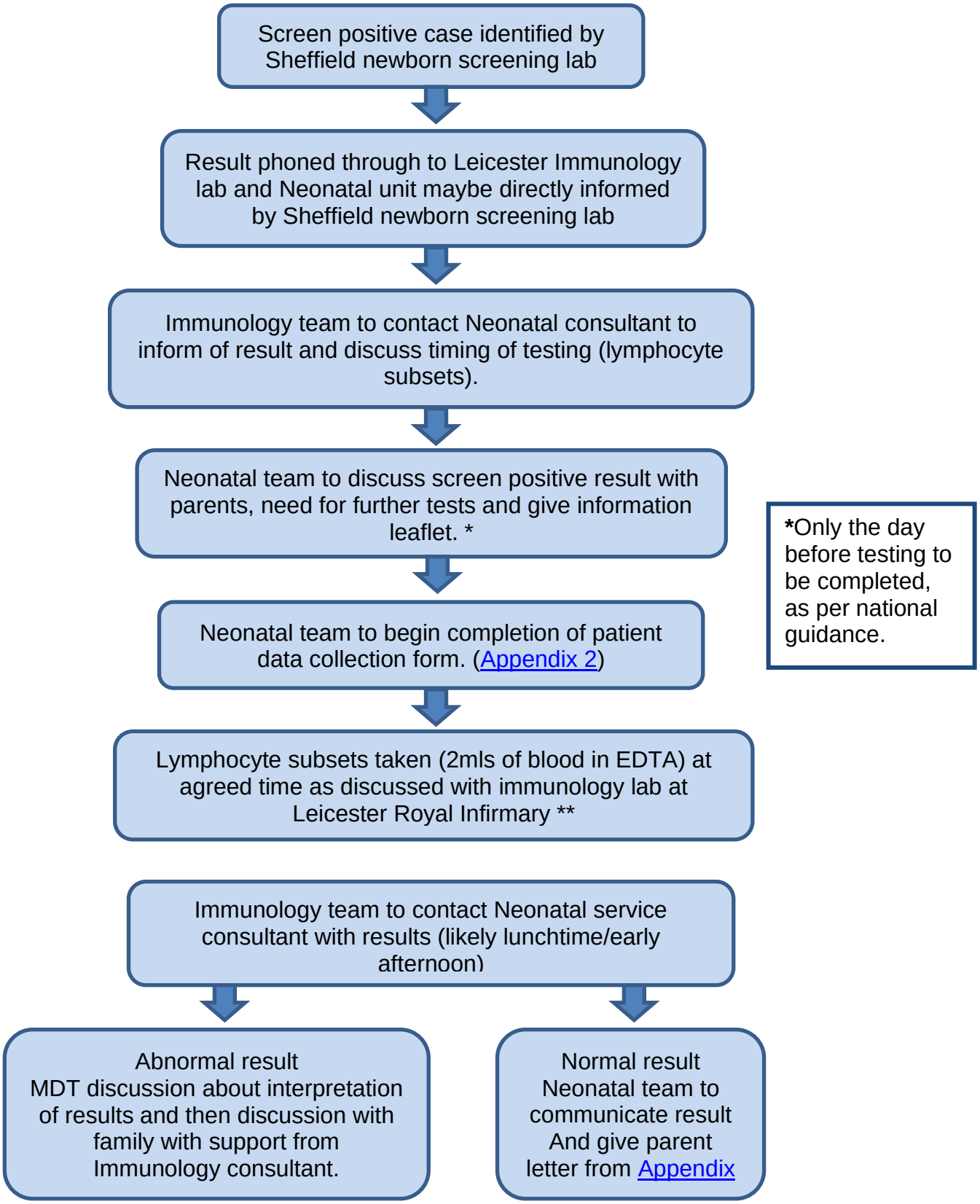


**Also observe for serious/ frequent infections and if concern contact immunology: paedsimmunology@uhl-tr.nhs.uk*

IMPORTANT

If a baby has initial intermediate or an abnormal result but then subsequently has flow cytometry, which is normal, this baby can be then treated as normal. Catch up vaccination as appropriate and discharge information containing details of testing should be documented. The family will need a copy of the discharge letter to access community vaccination as the result of the NBBS will remain as the initial report and so details of the subsequent testing must be available to other practitioners. Examples of parent letter are in Appendix 3 of this guideline.

Flowchart 3: SCID screening pathway for abnormal screening result



** Samples from hospitals outside LRI will need to be taxied to the immunology lab and arrive before 12pm.

Address: Immunology Department, Hearing Services Building Level 1, Leicester Royal Infirmary, LE1 5WW

3. 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)

On current modelling, we expect 1-2 babies with abnormal results per month to assess in the region. Please refer to the Flowchart 3 for details of the pathway.

The screening test will measure T cell Receptor Excision Circles (TRECs).

This screening test is likely to pick up a higher proportion of false positive TREC screens in the premature population. Therefore an additional pathway has been added for babies born at <37 weeks gestation whose samples are taken in hospital. Please see flow charts 2 and 3.

If the second sample screens positive with low TRECs, or in the case of a term baby, the flow charts illustrate the process. Those with numbers below the cut off will be referred for further tests (lymphocyte subsets by flow cytometry). **2mls of blood in EDTA** will be required. This should be a free-flowing venous sample. If sampling is an issue, a smaller sample may be adequate, please discuss with the lab.

Only about 10% of those identified by TREC screening with have a severe lymphopaenia with a diagnosis such as SCID.

In the event of a Paediatric Immunology consultant not being available in Leicester to discuss results, an agreement has been made with Sheffield Children's Hospital that their Immunology/ID consultant of the week will provide remote support, including video consultation with the family if required.

In the event of a moderate (but not diagnostic of SCID) lymphopaenia, a plan for monitoring and follow up will be made on a case-by-case basis with the immunology team. In the event of a SCID diagnosis, an individual management plan will be made for the baby with the BMT centre (GOSH/Newcastle), this will include appropriate antimicrobial prophylaxis, infection prevention requirements and timeframe for transfer. The Paediatric Immunology teams in GOSH and Newcastle are available 24/7 for advice.

Appropriate information will be given to clinical staff to equip them in communicating with the families.

4. Education and Training

E- Learning package available on e-LFH platform

5. Parent Information

Parent information leaflets are available via the PHE website.

6. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Data submitted to PHE	Nationally by PHE	R Radcliffe	Case by Case	PHE 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

7. 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.

8. Key Words

Blood spot, Flow cytometry, TRECS, T Cells

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 now
We are going to 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 can ask any questions you want about this process.

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 with the medical team. 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.
Yours Sincerely

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

This 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.

Although this translated information is not specific for babies still in hospital at the time of screening so does not exactly mirror that included above but does describe the process.

Appendix 2: Information for a child screened positive for Severe Combined Immunodeficiency (SCID)

Name						*Date of Birth*						
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*			*Received by*								
Family informed	*Date*			*By whom*								
Diagnosis		*Age*				*Weight (g)*						
GP details				*Information sent Y/N*		*Initials*						
Health Visitor details				*Information sent Y/N*		*Initials*						
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*		
Check correct baby	*Name* *DoB* *DD/MM/YY*		
Reason for visit / call	*Remind parents baby had 'heel prick' when 5 days old*		
	*One of the results has come back suggesting one of the conditions is **suspected***		
	Name of the condition		
	Not diagnostic, a screening test		
	Need more tests to confirm the result		
Initial information	*SCID is the name given to a group of rare, inherited disorders that cause major abnormalities of the immune system.*		
	There are many different types of SCID, each with different genetic causes.		
	The immune system abnormalities in SCID lead to greatly increased risks of infection and other complications that are life-threatening.		

	Not caused by anything the parents did before or during pregnancy		
	Reassure parents that it is safe to wait until they are seen by clinical team		
	Advise parents to write down any questions they think of so they can ask these at their clinic appointment		
	Ask for email address to send information sources and appointment details		
	Give contact name and number of member of clinical team		
	Give PHE 'suspected' leaflet		
	Discuss suitable websites if appropriate		
Afterwards	*Send email with appointment details, contact information and information source(s) www.piduk.org*		
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.*		
	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.		
	The first signs of SCID usually occur within the first three to six months		
	1 in every 35,000 babies in the UK will be born with the condition each year.		
Comments			

Appendix 3: 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 programme 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.

SCID evaluation research

An evaluation is taking place which will help determine whether screening for SCID works in practice as part of the NHS Newborn Blood Spot (NBS) Screening Programme in England.

Researchers working on behalf of Public Health England (PHE) may contact you to ask your opinion about screening for SCID and your experiences. This will help us to improve our programme.

If you told the researcher you didn't want to be contacted, this will already have been recorded.

If you change your mind at any time, please contact the PHE Screening national helpdesk phescreening.blog.gov.uk/helpdesk

If you decide not to take part in this research, it will in no way affect how you or your family are treated in the future.

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)