UK National Screening Committee

Newborn screening for Severe Combined Immunodeficiency (SCID)

November 2017

Aim

1. To ask, following the three month public consultation on screening for SCID, that the Chair of the UK National Screening Committee (UK NSC) approves the proposal for a practical evaluation of newborn screening for SCID to be undertaken in the NHS.

2. At the October 2017 meeting it was agreed that Chairs action would be taken on this issue and reported to the February 2018 UK NSC meeting if no major opposition to a practical evaluation of SCID came as a result of the consultation. This document was considered and approved by individual members of the UK NSC, the Chair of the Fetal, Maternal and Child Health Reference Group and the Director of Screening.

3. The aims of an evaluation would include:

    - define a cut off for screening and report on clinical outcomes which are achievable in the timeframe and realistic given the rarity of the condition
    - identify and undertake research priorities, for example to understand more about the impact of false positive results and the viability of alternatives to universal screening
    - clarify the logistics and costs of screening and outcomes monitoring as a basis on which to revisit the cost effectiveness evaluation
    - explore the possibility of international collaboration with ongoing pilots and research projects relating to SCID.

Current recommendation

4. The last UK NSC review on newborn screening SCID was published in 2013 and the current UK NSC recommendation is that systematic population screening for SCID is not recommended.

5. The previous review concluded that SCID was a promising candidate for a screening programme but further information on the following was needed:

    - the epidemiology of condition in the UK
    - the performance of the screening test in the UK
    - the management and outcomes of babies who are detected by screening but do not have SCID
    - the clinical and cost effectiveness of screening compared to current practice

Evidence Summary

6. The current review is comprised of two documents:

    - a set of systematic reviews which look at the evidence relating to three areas identified by the previous review; the incidence of SCID and its subtypes; the test accuracy of the TREC test populations studies of screening for SCID; and whether early hematopoietic stem cell transplantation (HSCT) leads to better outcomes compared with late HSCT in SCID patients
    - the results of a modelling exercise and cost effectiveness evaluation.

7. Both the systematic reviews and the cost-effectiveness evaluation were undertaken by the School of Health and Related Research, The University of Sheffield, in accordance with the triennial review process https://legacyscreening.phe.org.uk/scid.

8. The systematic reviews found:

    a. An estimated current UK incidence rate of 1 in 48,933 and that SCID is a severe condition which is invariably fatal if left untreated. **Criterion 1 met.**

b. There is a simple and safe test for screening for SCID, but due to the low positive predictive value of the TREC Assay and uncertainty about the number of false positives which may be identified in the UK through a screening programme, criterion 4 is only partially met. **Criterion 4 partially met.**

c. A suitable cut-off for a UK screening programme can be defined. The review suggested that a population study in the UK would provide a more precise cut off than the single, small, study included in the review. **Criterion 5 partially met.**

d. Whilst there are guidelines for the treatment of SCID, guidelines for the treatment of patients with low TREC count who do not have typical SCID are unclear. **Criterion 9 partially met.**

e. HSCT is an effective treatment for SCID. **Criterion 10 met.**

9. The cost effectiveness and modelling exercise found that:

- A PCR based screening strategy was estimated to cost £3.2 million / year and to have a high likelihood of being cost effective. Some uncertainties were identified such as the cost of the test.

- There are approximately 17 SCID cases in the UK each year 30% (5-6) of whom would be detected through cascade testing (i.e. would be found without the need for a screening programme)
- The main benefit of screening is to find and treat babies before they become infected. The model estimates that without screening eight babies would die from infections and with screening that would be reduced to around two. The babies found and treated before they become infected would have the same health outcomes as those currently identified through cascade testing
- earlier transplantation would not significantly alter long term outcomes in babies who are currently detected on the basis of symptoms and survive
- approximately 260 families would receive false positive results which would be confirmed by flow cytometry within two weeks
- approximately 26 cases of non SCID T cell lymphopenia of which seven would be likely to be asymptomatic at birth

Consultation

10. A three month consultation was hosted on the UK NSC website. Direct emails were sent to 20 individuals and organisations. **Annex A**

11. The review documents were accompanied by a two page SCID screening consultation information sheet which was produced by the Evidence Team. A one page summary of the June 2017 UK NSC recommendation that a practical evaluation of screening for SCID should be undertaken in the NHS was also published on the SCID recommendation webpage.

12. Stakeholders were invited to comment on the consultation documents and on the UK NSC's proposal for the practical evaluation of newborn screening to be undertaken in the NHS.

13. Responses were received from the following 11 stakeholders:

    - The Ataxia Telangiectasia Society
    - Professor Jim Bonham
    - Genetic Alliance UK
    - IPOPI - International Patient Organisation for Primary Immunodeficiencies
    - Primary Immunodeficiency UK (PID UK)
    - The Royal College of Midwives
    - The Royal College of Paediatrics and Child Health
    - Save Babies Through Screening Foundation UK (and on behalf of the UK Patient Advocates for Newborn Screening Group) PANS
    - Lesley Tetlow
    - UK Paediatric Bone Marrow Transplant Group
    - United Kingdom Primary Immunodeficiency Network

14. All respondents agreed that information needed to inform the introduction of introduction of screening could be gained from an evaluation in the NHS. However responses were divided on the function of the evaluation. For example, some respondents considered that an immediate recommendation to screen was appropriate and a pilot should only be undertaken as a lead in to screening. However others considered that further questions such as those highlighted in the consultation papers should be evaluated before a final recommendation on screening is made. One response suggested that further information

from NCARDRs would help inform the geographical areas in which a pilot might take place in the future.

Recommendation

15. The Committee is asked to approve the following proposal:

The Committee recommends that an evaluation of newborn screening for SCID using polymerase chain reaction (PCR) is undertaken in the NHS before a final recommendation is made.

Based on the 20 UK NSC criteria set to recommend a population screening programme, evidence was appraised against the following criteria:

	Criteria	Met / Not met
The condition		
1	The condition should be an important health problem as judged by its frequency and/or severity. The epidemiology, incidence, prevalence and natural history of the condition should be understood, including development from latent to declared disease and/or there should be robust evidence about the association between the risk or disease marker and serious or treatable disease.	Met ✓
The Test		
4	There should be a simple, safe, precise and validated screening test.	Partially met ✗
5	The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed.	Partially met ✗
The intervention		
9	There should be an effective intervention for patients identified through screening, with evidence that intervention at a pre-symptomatic phase leads to better outcomes for the screened individual compared with usual care. Evidence relating to wider benefits of screening, for example those relating to family members, should be taken into account where available. However, where there is no prospect of benefit for the individual screened then the screening programme should not be further considered.	Partially met ✗
10	There should be agreed evidence based policies covering which individuals should be offered interventions and the appropriate intervention to be offered.	Met ✓

Annex A

List of organisations\individuals contacted:

1. Dr Stuart Adams
2. ALD Life
3. Ataxia Telangiectasia Society
4. British Association of Perinatal Medicine
5. British Paediatric Allergy, Immunology and Infection Group
6. British Society for Immunology
7. CGD Society
8. Children Living with Inherited Metabolic Diseases
9. Faculty of Public Health
10. Professor Bobby Gaspar
11. Genetic Alliance UK
12. Dr Andrew Gennery
13. INGID - International Nursing Group for Immunodeficiencies
14. IPOPI - International Patient Organisation for Primary Immunodeficiencies
15. Primary Immunodeficiency UK
16. Royal College of Paediatrics and Child Health
17. Save Babies Through Screening Foundation UK
18. Lesley Tetlow
19. UK Primary Immune-deficiency Patient Support
20. UK Primary Immunodeficiency Network

UK National Screening Committee
Newborn screening for Severe Combined Immunodeficiency (SCID) – an evidence review

Consultation comments pro-forma

Name:	William Davis	**Email address:**	**xxxx xxxx**
Organisation (if appropriate):	Ataxia-Telangiectasia Society		
Role:	**Chief Executive**		

Do you consent to your name being published on the UK NSC website alongside your response?

Yes ☒ **No** ☐

Do you agree with the proposal to undertake a practical evaluation of newborn screening for SCID in the NHS?

Yes ☒ **No** ☐

Please explain why you agree or disagree with the proposal.

The A-T Society strongly that SCID screening would be beneficial for families living with the risk of a range of conditions, including ataxia-telangiectasia and would like to see screening implemented nationally straight away. We do not feel a strong case has been made for delaying implementation with a further study. However if gathering evidence in this way is the only way to move forward towards

implementation, we will support it.

On which consultation document are you commenting?

The systematic review ☐ The modelling and cost effectiveness evaluation ☒

Section and / or page number	Text or issue to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*
	Modelling and cost effectiveness evaluation	Given that the review seems to find that SCID meets the generally accepted criteria for an effective screening programme, we feel that the proposals for an evaluation study are overly cautious. If the study and evaluation lasts for 2 years, your figures suggest that 12 babies will die of SCID unnecessarily. Where does your study consider the impact of this on their families?
		There is also a potential benefit to families of children with non-SCID conditions, who are picked up early. Early diagnosis of ataxia-telangiectasia for example would enable more targeted and effective treatment of the frequent infections which contribute to the lung disease which is the major cause of death in A-T.
		We feel that the cost-effectiveness of the proposed implementation of screening is already demonstrated in the document and that there is no strong case for delaying implementation

Please return to the UK NSC Evidence Team at screening.evidence@nhs.net by **Saturday 4th November 2017**.

UK National Screening Committee

UK National Screening Committee
Newborn screening for Severe Combined Immunodeficiency (SCID) – an evidence review

Consultation comments pro-forma

Name:	Jim Bonham	**Email address:**	**xxxx xxxx**
Organisation (if appropriate):	Sheffield Children's Hospital		
Role:	**Clinical Director**		
Do you consent to your name being published on the UK NSC website alongside your response? **Yes** ☒ **No** ☐			
Do you agree with the proposal to undertake a practical evaluation of newborn screening for SCID in the NHS? **Yes** ☒ **No** ☐			
Please explain why you agree or disagree with the proposal.			
Agree in essence although the lab costings may be a bit low. This probably does not affect the conclusions of the report very significantly,			

the lab costs in the first year may be around £1.50 per baby tested (see description below) in addition to the reagent cost for the assay which as the authors suggest may be around £3.00 per baby tested, the total £4.50 per baby tested still probably makes this a cost effective intervention depending upon the other factors such as the incidence and discount rate assumed.		
On which consultation document are you commenting? **The systematic review ☐** **The modelling and cost effectiveness evaluation ☒**		
Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*
P39	The laboratory costings to support SCID screening are rather low. The authors estimates are based upon 0.5 FTE Band 5 member of staff. While the actual staff needed would require further consultation, this is a new technique for screening labs, requiring new equipment and an additional punch with senior staff time input. A compromise might be 1 band 7 FT per lab – this, at mid-point would be 36,612 + 7,322 on costs = 43,934 or £571,147 for 13 labs vs the £166,000 quoted in the report. In addition the test will require LIMS update and interfacing of lab equipment, accurate costing would need to be established but taken together this may be £40k/lab or £520,000 (these would be one off costs with around £100k pa on-going maintenance). There would need tio be an EQA scheme established, perhaps £50k (again to be checked).	

	The cost of the UV cabinet + PCR workstation seems low, perhaps nearer £4k per lab (to be checked). An additional PC may also be needed, these are usually specified by the LIMS supplier and may be £1.5k per lab. Outside of the lab patients information sheets and pre-screening leaflets would need to be modified and CHIS systems updated. This is not costed in the report.	

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UK National Screening Committee
Newborn screening for Severe Combined Immunodeficiency (SCID) – an evidence review

Consultation comments pro-forma

Name:	Louise Coleman	**Email address:**	**xxxx xxxx**
Organisation (if appropriate):	Genetic Alliance UK Genetic Alliance UK is the national charity working to improve the lives of patients and families affected by all types of genetic conditions. We are an alliance of over 180 patient organisations. Our aim is to ensure that high quality services, information and support are provided to all who need them. We actively support research and innovation across the field of genetic medicine. Rare Disease UK is a multi-stakeholder campaign run by Genetic Alliance UK, working towards the delivery and implementation of a national strategy for rare diseases in the UK. The UK Strategy for Rare Diseases was published in November 2013. Pertinent to this consultation, the Strategy includes a commitment from all four Governments of the UK to: "Continue to work with the UK National Screening Committee to ensure that the potential role of screening in achieving earlier diagnosis is appropriately considered in the assessment of all potential new national screening programmes and proposed extensions to existing programmes." Commitment 9, The UK Strategy for Rare Diseases, November 2013. This commitment recognises the value that the rare disease community places on early diagnosis, not only for the benefits it can bring to an affected individual but because of the impact it can have on improving the quality of life for their whole family.		
Role:	**Policy Officer**		

Do you consent to your name being published on the UK NSC website alongside your response?

Yes ☒ No ☐

Do you agree with the proposal to undertake a practical evaluation of newborn screening for SCID in the NHS?

Yes ☒ No ☐

Please explain why you agree or disagree with the proposal.

Genetic Alliance UK enthusiastically welcomes the decision of the UK NSC to undertake a practical evaluation of newborn screening for SCID in the NHS. The evidence of the clinical and cost effectiveness of a screening programme is now overwhelming and any further delays would be unacceptable. We are however disappointed that the decision has been made to undertake a pilot rather than implementing a full national programme. The systematic review recognises that the UK NSC's criteria are all met: the test is sensitive and specific and the benefits of early diagnosis are clear, while the cost effectiveness evaluation found that even in the base case the screening programme had a 99% probability of being cost effective at the standard threshold.

Additionally, due to the rarity of the condition, any pilot would need to cover a substantial proportion of the country (a third or more of the English population) in order to pick up enough cases to make the necessary evaluations. The regions in which screening is carried out would need to be selected carefully so as to pick up enough cases of SCID and also be reflective of the UK population. Given the need for such a large scale prospective study in multiple regions of the UK it would be more reasonable and equitable to implement a national programme on a provisional basis. This would also have the advantage of allowing the necessary data to be collected more quickly, avoiding further delays. It will also be important to carefully define in advance the questions the evaluation study will need to address and the criteria that will need to be met for a full national programme to be rolled out, in order to avoid the situation of constantly shifting goalposts which has prevailed until now.

On which consultation document are you commenting?

The systematic review ☐ The modelling and cost effectiveness evaluation ☐

Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*

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UK National Screening Committee

UK National Screening Committee
Newborn screening for Severe Combined Immunodeficiency (SCID) – an evidence review

Consultation comments pro-forma

Name:	Johan Prévot	**Email address:**	xxxx xxxx
Organisation (if appropriate):	International Patient Organisation for Primary Immunodeficiencies (IPOPI)		
Role:	Executive Director		

Do you consent to your name being published on the UK NSC website alongside your response?

Yes ☒ **No** ☐

Do you agree with the proposal to undertake a practical evaluation of newborn screening for SCID in the NHS?

Yes ☒ **No** ☐

Please explain why you agree or disagree with the proposal.

IPOPI considers that newborn screening for SCID is a priority in all European countries and should, therefore, be implemented as part of the normal practice when children are born. SCID meets all the necessary requirements for diseases to be included in the screening

programmes for newborns, including the existence of a suitable test and cut off measures, the improvement of health outcomes for children diagnosed and treated before any infections appear and seems to be cost-economic. These reasons have led other countries, such as the United States of America (where 48 states out of 50 are currently screening and 92% of newborns have been screened for SCID last year), Taiwan, Israel, New Zealand and some provinces in Canada have it as a standard procedure. In Europe, Norway will be implementing it as of January 1st, 2018. Several other European countries are running pilot studies at national level (i.e. France, The Netherlands, Sweden, Iceland, Denmark). Spain and Italy also actively looking at implementation with the test already implemented in one or several regions (Catalunya, Tuscany). IPOPI feels that all the evidence collected by these experiences shows the urgent need to fully develop and implement a newborn screening programme in the United Kingdom, as a way of saving the lives of babies born with this devastating disease. IPOPI considers that the emergency situation in which babies with SCID are born, calls for the immediate implementation of the screening programme, as it was done in Israel or in the United States.

If the UK National Screening Committee feels the need to have a practical evaluation before SCID becomes part of the standard screening programme, IPOPI will support it but would encourage the persons involved in such evaluation to proceed diligently with the processing and analysis of the data, to avoid any unnecessary deaths of newborns, as it has been the case in another European country like Norway.

On which consultation document are you commenting?

The systematic review ☒ The modelling and cost effectiveness evaluation ☐

Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*
Key question 1 (incidence of SCID in the UK)	"*The current estimate of UK SCID incidence is 1 in 48,933. SCID is a severe condition, which, if left untreated, is invariably fatal. Although rare, the severity of the condition makes SCID an important health condition.*" (p 27)	IPOPI fully supports the qualification of SCID as a severe and, if untreated, fatal condition. We also believe that such characteristics make of it a paediatric emergency that should be addressed with no further delay and be included in a nation-wide screening programme to avoid the loss of children born with SCID.
	"*The current estimate of UK SCID incidence is 1 in 48,933. SCID is a severe condition, which, if left*	IPOPI urges the UK National Screening Committee to screen babies in the UK for SCID, as according to the number of

	untreated, is invariably fatal. Although rare, the severity of the condition makes SCID an important health condition." (p.27)	births in England and Wales in 2016 (based on the data provided by the Office for National Statistics, 14 babies could have been identified, diagnosed and treated on time for their disease.
Key question 2 (TREC test accuracy)	"*There is clear evidence of the high sensitivity of the NBS TREC assay in detecting SCID cases. […] However, even when low TREC cut-off values are used, the test identifies neonates with other TCLs.*" (p. 39)	Finding through a TREC test for SCID other TCLs should not deter from the implementation of the test for SCID. These other diseases identified as a result of the TREC analysis are serious as well and require of further follow-up to prevent any complications in babies' health. Identification of babies with other TCLs is already happening in other countries where SCID newborn screening is a reality and lessons could be learnt from their experience to adapt it to the UK scenario.
	"In addition, false positive results are found in preterm babies." (p.39)	False positive results should not prevent the implementation of SCID screening, as the number of lives that could be saved in the UK per year would outweigh the uncertainty caused until a confirmatory test is done by the false positive result.
Key question 3 (early vs late HSCT treatment)	"*Early transplant is consistently shown to improve survival and other long-term outcomes. The evidence base is growing steadily, and is consistent. These findings support a need to diagnose SCID at as early age as possible, and before patients become symptomatic and develop infections.*"	IPOPI considers that this sentence is key when considering whether to introduce SCID on the panel of diseases children born in the UK should be screened for. As the systematic review states: the sooner the transplant is made, the greater is the survival rate and long-term outcomes; transplant is only an option when a confirmed diagnosis has been made and this, in turn, is only possible if screening is introduced in a systematic way at national level. A recent article has been published in the Journal of Allergy and Clinical Immunology (Volume 139, number 5, page 1713) with data from a Swedish study stating that: "*The implementation of an NBS program might help to reduce the number of in-hospital care days and outpatient clinic visits and thus lead to a decrease in health care costs. With NBS*

		programs children with SCID are diagnosed at birth and the life-saving HSCT can be provided much earlier in the pre-infectious period. […]. It is concluded that early HSCT of children with SCID substantially reduced health care costs, number of in-hospital care days, and visits to the outpatient clinic. It is furthermore concluded that for children with SCID undergoing HSCT in Sweden, the cost of drugs is not a major cost issue."
	Studies of gene therapy (p 62/63)	Gene therapy is a relatively new field and the European Medicines Agency only in 2016 approved the first gene therapy for ADA-SCID in Europe. As more patients benefit from the therapy in the coming years, it will become a more standard therapy. Just on October 23rd, 2017 the National Institute for Health and Care Excellence (NICE) has given approval for a gene therapy for treating ADA-SCID, Strimvelis. As it has been recently acknowledged by **xxxx xxxx**
On which consultation document are you commenting? **The systematic review ☐** **The modelling and cost effectiveness evaluation ☒**		
Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows*

P4-5	Screening for SCID as part of the NHS Newborn Blood Spot Screening Programme is predicted to prevent early mortality in affected infants. For the UK as a whole and with complete uptake of screening, it is estimated that 17 (14, 22) newborns with SCID may be detected annually, leading to a reduction in 5 mortality of 6.4 (4.0, 9.7) newborns per year and a total gain of 184 (118, 274) discounted quality adjusted life years (QALY).	IPOPI supports the statement that SCID newborn screening prevents early mortality of children affected by this life-threatening disease.
P 5	Many of these newborns may be expected to show symptoms or be otherwise diagnosed in the absence of screening. However it is estimated that 7 (2, 16) newborns might be identified by screening that would otherwise be healthy at birth. There is currently no evidence to suggest that early diagnosis can benefit these children and no relevant UK evidence on incidence.	IPOPI considers that the few children with other diseases that will be identified through the screening can actually benefit from an early diagnosis. Maybe not in medical terms, but the reassurance to the families that their children has a disease that can be diagnosed will help coping with the disease itself from a mental perspective, avoiding them to have to go through the diagnostic ordeal that some families need to face.
Overall document		IPOPI considers that the modelling performed takes into account important aspects of the therapy, such as the health economics overview, the costs of screening and the costs of HSCT. These are important aspects that need to be included in the appraisal of the screening test, but we consider that there is a lack of reference to the human part of what this test would mean if implemented across the country. Besides the obvious life-saving benefit of the test, the human component should also include the reduction in suffering for these children who were diagnosed with SCID and will endure recurrent life-threatening infections until it is too late to save them because the treatments provided did not target the underlying cause: a defective immune system. The human

		component should also take into consideration that children and their families will spend most of their time in hospital being denied a normal life that all children deserve. But this is not only IPOPI's position. Recently, on the occasion of NICE approval of Strimvelis, [redacted] the centre for health te XXXX XXXX This is the human component that we call upon the UK National Screening Committee to include in its considerations as a key factor speaking in favour for the introduction of SCID in the panel of diseases children should be screened for at birth in the UK.

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UK National Screening Committee
Newborn screening for Severe Combined Immunodeficiency (SCID) – an evidence review

Consultation comments pro-forma

Name:	Dr Susan Walsh	**Email address:**	**xxxx xxxx**
Organisation (if appropriate):	Primary Immunodeficiency UK (PID UK)		
Role:	Director		

Do you consent to your name being published on the UK NSC website alongside your response?

Yes X ☐ No ☐

Do you agree with the proposal to undertake a practical evaluation of newborn screening for SCID in the NHS?

Yes X ☐ No ☐ but see comment below

Please explain why you agree or disagree with the proposal.

Comment: PID UK is very disappointed that a full national screening programme has not been recommended at this stage given that the criteria for implementing a newborn screening programme for SCID have been met as attested by the conclusions in the systematic review and economic analyses produced by UKNSC.

However we support and welcome the recommendation to proceed with an evaluation study as the next 'best step' with the following caveats:

1. **That the proposed evaluation study is of a sufficient scale in order to pick up enough cases to make the necessary evaluations.** This is essential due to the low incidence of SCID.
2. **That the regions chosen in the study are reflective of the ethnic composition of the UK population.** This will help ensure that accurate data is obtained.
3. **That the necessary resources to carry out such a study will be made available by UKNSC.** This is essential for its success and implementation.
4. **That the exact timelines of the evaluation study are defined at its outset.** We suggest that a reasonable amount of time would be 1 year with 2 years as a maximum. An evaluation study should not be used as an opportunity to further delay implementation of a full screening programme, the evidence for which is already compelling.
5. **That the questions that the evaluation programme seeks to address are reached by expert consensus and are clearly set out in an open and transparent framework.** This will help ensure that the 'goalposts' are not changed further down the line. Clarity is needed on when enough evidence, is enough.
6. **That an interim analysis based on specific criteria is carried out at a defined time point during the evaluation study.** If certain criteria are met then we need to be assured that a full national screening programme will be implemented as quickly as possible.

On which consultation document are you commenting?

The systematic review ☐ X **The modelling and cost effectiveness evaluation ☐ X**

Section and / or page number	Text or issue to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*
Systematic review	Overall comment	The review is comprehensive and states that the key criteria for screening have been met. As such this document fully supports the implementation of a newborn screening programme for SCID. PID UK therefore does not understand why UKNSC are seeking to address other questions.
		A screening programme would allow early diagnostic and the start of care and treatment for ALL families, not just those for whom a prior devastating experience had made them alert to the risk in future children.

	Impact of UK NSC decision on families who have lost their child to SCID	There is bewilderment, frustration and anger among bereaved families that newborn screening for SCID has not yet been fully implemented in the UK. Bereaved families know that there is a solution ready so that other families do not have to go through the agony of seeing their child's health deteriorate in terrible circumstances and the pain of bereavement **(see below).** They are also at a loss to understand why the UK is lagging behind other countries in implementing SCID NBS (**see below)** especially when cures for the condition are proven and available.
	Public support for SCID screening	Screening for SCID has public backing. A petition, 'Stop the unnecessary deaths of babies. Include SCID in the UK new-born screening programme' set up by a mum whose child died due to SCID not being picked up early enough has received over 25,000 signatures. **xxxx xxxx**
Page 6	1. Importance of early diagnosis and curative intervention for affected children and families.	The document does not address the parent/carer perspective of the importance of an early diagnosis of SCID. We have therefore included testimonies from bereaved parents who lost their child because their SCID wasn't picked up early enough. These stories exemplify the diagnostic odyssey that parents can go through to get a diagnosis of SCID (at cost to the NHS and emotional and financial toll on parents), the importance of early intervention and the horror and anguish of losing a child when this could have been avoided through a screening test. **1. xxxx xxxx** story told by **xxxx xxxx** 'Our family has been personally affected by SCID. Our baby xxxx xxxx was born with X-linked SCID, xxxx xxxx died on xxxx xxxx at xxxx xxxx, just 10 days before xxxx xxxx This is our sad story, please let me share it with you to give you an insight into why it is so important that this curable condition is detected at birth. xxxx xxxx, our xxxx xxxx, was born on xxxx xxxx. xxxx xxxxwas a huge baby weighing xxxx xxxx. xxxx xxxxwas very strong, alert and engaging. xxxx xxxxhad xxxx xxxxroutine heel prick test done when xxxx xxxxwas xxxx xxxxand the results came back negative. xxxx xxxx appeared very healthy, we had no concerns. xxxx xxxxfed well, gained weight and thrived. We already had a xxxx xxxxcalled xxxx xxxx, who was xxxx xxxxyears of age. xxxx xxxx had been well and healthy, we had no idea that I was a carrier of X-Linked SCID. The first few months of family life were great. We did normal everyday things. I took xxxx xxxxto

		toddler groups and we went and visited family and friends and showed off our new smiling, happy baby to everyone. A few months later it was Christmas. We shared a happy first Christmas together with Ge xxxx xxxxorge, we were very happy, we opened presents and enjoyed the day feeling blessed that we had xxxx xxxx Had we known it was to be xxxx xxxx first and last Christmas we would have been absolutely horrified. Once xxxx xxxxreached xxxx xxxx months of age, at the beginning of xxxx xxxx, things took a dramatic turn for the worse. I can only describe what happened over the course of the next xxxx xxxxas utterly nightmarish. xxxx xxxxdeveloped a cough and cold that xxxx xxxxjust could not get over. This developed into a chest infection. Despite going to our GP and having antibiotics prescribed xxxx xxxxdid not get better. xxxx xxxxbegan to develop breathing difficulties. This was very frightening and often xxxx xxxx would become worse at night. During the whole of xxxx xxxx and xxxx xxxx and half way through xxxx xxxx we were back and forth from the GP, to the out of hours "Grab a Doc" service and multiple visits to Accident and Emergency. In total we visited A&E xxxx xxxxtimes during those xxxx xxxx, we visited the "Grab a doc" out of hours service xxxx xxxxand our GP xxxx xxxxand also saw our health visitor. xxxx xxxxwas hospitalised on xxxx xxxx occasions at our local hospital, xxxx xxxx . Consultants were baffled; they couldn't understand why xxxx xxxxwas repeatedly ill and having lengthy stays on the ward. The xxxx xxxx and xxxx xxxx xxxx xxxx xxxx xxxxwas put down to xxxx xxxxand the xxxx xxxx was put down to xxxx xxxx, but on the xxxx xxxx they really didn't know what was wrong. They thought xxxx xxxx may have whooping cough or Cystic Fibrosis so xxxx xxxxwas tested for these conditions but both came back negative. During these xxxx xxxxof toing and froing and sitting for hours upon hours in A&E waiting room and in Grab a Doc centres and GP waiting rooms etc we were, unbeknown to us, exposing xxxx xxxxto even more germs and viruses. xxxx xxxx began to rapidly lose weight. xxxx xxxxhad been a good weight at birth and had been on the xxxx xxxx, which is just as well, as by the time xxxx xxxxwas finally diagnosed at xxxx xxxxhe was on the xxxx xxxxand weighed less than xxxx xxxx did when xxxx xxxx was xxxx xxxx. Now during these xxxx xxxx of consultants trying to reach a diagnosis xxxx xxxx was growing weaker and I could see that xxxx xxxx was wasting away. I had asked a consultant if xxxx xxxx was

		dying and xxxx xxxx laughed off my concern and said “Children lose weight when they are ill”. I began to be afraid of the hospital discharging xxxx xxxx home because xxxx xxxx would become unwell within a few days of being home and I found the worry unbearable. I felt as though xxxx xxxx was being pumped with IV antibiotics, xxxx xxxxwould perk up and then we would be discharged and then a few days later the nightmare would continue. xxxx xxxx would struggle to breath and we would be back at A&E again. Even on our xxxx xxxxthe plan had been to get xxxx xxxxwell and send xxxx xxxxback home while we wait for an xxxx xxxx for the xxxx xxxx. They had also referred xxxx xxxx as xxxx xxxx to xxxx xxxx, although the xxxx xxxx was being pursued as a sideline. There was no sense of emergency and I was worried xxxx xxxx didn’t have time to wait. I took it upon myself to contact xxxx xxxx and xxxx xxxx and asked if they had received the referral letters. I found out after calling them that xxxx xxxx had received the referral letters. So I faxed the letters over myself and rang to confirm receipt. Once xxxx xxxx had the letter they acted on it and asked for xxxx xxxx xxxx xxxxto be taken and couriered to them. The next day we were transferred to xxxx xxxxwhere we received the most shocking and devastating news, xxxx xxxx was diagnosed with SCID. I felt my world crash around me! I had thought something was wrong but I had no idea how serious it was! It was so shocking I had a panic attack and had to leave the ward to get some air. Now during all of this xxxx xxxxwas still working xxxx xxxx and our xxxx xxxxwas being passed from pillar to post while I was on the hospital ward or at A&E and sometimes xxxx xxxx , our xxxx xxxx had to come with us when we had to rush xxxx xxxx to the Grab a Doc centre in the middle of the night. This put a huge strain and worry on the whole family. The uncertainty of it all was very stressful. Once xxxx xxxx received a diagnosis even though it was terrible we knew that at least xxxx xxxxwould now receive the care and treatment xxxx xxxxdesperately needed and the diagnosis also confirmed to us that we were not going crazy, xxxx xxxx really did have something wrong with him. By the time we got xxxx xxxx diagnosed xxxx xxxx was ravaged with infections. xxxx xxxx had xxxx xxxx which can be fatal in SCID patients, xxxx xxxx had xxxx xxxx and xxxx xxxx also had to cope with a horrible common tummy bug called “Rotavirus” which in people with a functioning immune system would just be a 24hr sickness bug but with xxxx xxxx as xxxx xxxx body couldn’t fight it xxxx xxxx would have to contend with it until xxxx xxxx had xxxx xxxx transplant. xxxx xxxx was malnourished due to these illnesses. xxxx xxxx lung was also partially collapsed upon arrival to xxxx xxxx. I had been breastfeeding xxxx xxxx and unknown to myself my milk contained cytomegalovirus (CMV), which would be harmful to a SCID baby so I had to cease

		breastfeeding. Over the next xxxx xxxx xxxx xxxx was an xxxx xxxx at xxxx xxxx xxxx xxxx got over the xxxx xxxx and was given gut rest and nourished back to better health. We were discharged home to live in isolation while a donor could be found on the register. A 10/10 match was found but the donor lived in xxxx xxxx and it would take time to organise. We went home. I was scared to go home and after just xxxx xxxx became unwell again. xxxx xxxx began to spike temperatures and slept for much longer than normal. xxxx xxxx also started to cover xxxx xxxx eyes and vomit. xxxx xxxx was not xxxx xxxx, xxxx xxxx had no energy. We went back to xxxx xxxx they took xxxx xxxx and found markers for infection and so we were transferred back to xxxx xxxx. Over the next few days xxxx xxxx leg started to tremor. At first this was put down to malnutrition but it soon became clear and to our horror that it was neurological. The tremors became more pronounced. They thought xxxx xxxx could possibly have a virus on the brain. We had no time to wait for xxxx xxxx xxxx match as xxxx xxxxneeded an immune system as soon as possible. So a cord was used instead that was an xxxx xxxx. xxxx xxxx was too unwell for chemotherapy conditioning which is the usual procedure prior to transplant. xxxx xxxx began to have seizures. Ironically the BMT had engrafted well but the virus was attacking xxxx xxxx brain. We then received the most horrific news ever that xxxx xxxx was now profoundly brain damaged. We felt defeated, I felt as though the fight was over, we were absolutely devastated. A few weeks later xxxx xxxx died as the virus had attacked xxxx xxxx brain stem. xxxx xxxx died from encephalitis. The suffering xxxx xxxx went through was indescribable, xxxx xxxx fitted to death in our arms and to think that this could have all been prevented from early screening and diagnosis makes me feel physically sick and very angry. SCID babies need to be identified at birth. SCID babies look completely normal unlike other genetic conditions there are no physical signs or markers. Doctors cannot identify it, this means that there are huge delays in getting these children diagnosed and by the time they are diagnosed they are in no fit state to survive a transplant. It seems crazy that there are 2 specialist centre in the UK geared up to treat SCID (GOSH & Newcastle) but no diagnostic test is in place to give these babies a chance at life. The need for a screening programme I feel sure that xxxx xxxx would be alive today had xxxx xxxx been identified as having SCID when xxxx xxxx was born. xxxx xxxxwas so healthy the first few months of life we would have had time for

		xxxx xxxx to receive a 10/10 match and we could have kept xxxx xxxx well by keeping xxxx xxxx isolated and away from infection. Losing a child never leaves you The psychological impact of this tragedy has been immense. xxxx xxxx was xxxx xxxx when xxxx xxxx died and is still confused by what happened. The whole family have been shocked and emotionally upset, we have literally been to hell and back. Losing a child never leaves you. I would like to think that this could be prevented from happening to other families in the future. There are currently two conditions rarer than SCID that are on the heel prick test and SCID is the only condition that is curable if found at birth with a 95 percent survival rate. It is also more cost effective to screen for it than not to and would cost just £2.50 per child. We need to get this condition onto the screening programme to save lives and prevent suffering to the patients themselves and their families. If all SCID babies die before the age of 1 without treatment then xxxx xxxx didn't stand a fighting chance having been diagnosed at xxxx xxxx . xxxx xxxxbattled bravely and smiled throughout xxxx xxxx ordeal. If SCID is put onto the new born screening programme I would feel happy that such a great positive can come out of this awful tragedy. We were fortunate to go on to have xxxx xxxx xxxx xxxx after xxxx xxxx died. I was able to have screening when I was pregnant to determine if xxxx xxxx was well or not. Luckily xxxx xxxx was not affected. xxxx xxxx was one of the fortunate babies to have been able to receive a diagnosis. How many babies die from pneumonia and other infections when really SCID is the underlying course? No family should have to endure what we have had to go through. All we ask is that you read our story and help to get this test implemented immediately.' 2. xxxx xxxx is told by xxxx xxxx. 'I would like to share our story with you about our baby xxxx xxxx , who we tragically lost in xxxx xxxx as xxxx xxxx had Severe Combined Immunodeficiency (SCID). xxxx xxxx was born a healthy baby on the xxxx xxxx, weighing in xxxx xxxx. xxxx xxxx was xxxx xxxx overdue and so I had to be induced to have xxxx xxxx . Now I know why our poor xxxx xxxx didn't want to come out sooner.

		Myself and James's dad, xxxx xxxx, were so relieved when xxxx xxxx arrived safe and well. We both have xxxx xxxx xxxx xxxx and xxxx xxxx just completed our family. Everything was fine until xxxx xxxx developed a bit of a cold at xxxx xxxx. I took xxxx xxxxto our GP who checked xxxx xxxx over and said it was just a cold and indeed xxxx xxxx did improve over the next few days, although xxxx xxxx weight was starting to drop off a bit and I was recommended by my Health Visitor to change xxxx xxxx milk formula to see if that helped. At xxxx xxxx had his xxxx xxxxweek check-up with the GP and then saw the nurse for xxxx xxxx first lot of immunisations. As soon as I got xxxx xxxxhome xxxx xxxx started coughing. I remember thinking it was strange and thought it must be a reaction to the immunisations. The cough got worse and I was so concerned that I rang the out of hours 111 service on the xxxx xxxx for advice. As xxxx xxxx was so little they advised me to take xxxx xxxx to see the out of hour's doctor at our local hospital, which we did and the doctor said xxxx xxxx had a temperature and cough probably as a result of the immunisations and to just give xxxx xxxx some Calpol. However xxxx xxxx didn't get any better over the following days and so I took xxxx xxxx back to our GP. The GP didn't like the sound of xxxx xxxx cough and agreed that xxxx xxxx weight was still dropping off and sent us to the xxxx xxxx at our xxxx xxxx. xxxx xxxx was kept in for xxxx xxxx as xxxx xxxx required oxygen and IV antibiotics as they said xxxx xxxx had pneumonia. We were discharged home but xxxx xxxx just didn't improve. I took xxxx xxxx back to my GP xxxx xxxx times within the next xxxx xxxx weeks as I was concerned that xxxx xxxx wasn't showing any signs of improvement and in fact was getting worse. My GP prescribed oral antibiotics and said it would take a while for xxxx xxxx to get over a serious chest infection. But when I took xxxx xxxx to the GP for the xxxx xxxx time I was extremely concerned as xxxx xxxx wouldn't even feed and xxxx xxxx looked terrible. My GP said xxxx xxxx had thrush in xxxx xxxx mouth probably from all the antibiotics and as I expressed concern that xxxx xxxx was breathing very fast. xxxx xxxx sent us back to the xxxx xxxx. When we arrived at the Hospital the doctor came round and said they were really busy but that xxxx xxxx looked ok and they would put xxxx xxxx on a monitor and get to xxxx xxxx as soon as they could. The nurse put xxxx xxxx on a monitor and was shocked to see that xxxx xxxx sats were at xxxx xxxx %. All of a sudden doctors and nurse came running into the room and it turned out that xxxx xxxx was having some sort of vacant seizure and xxxx xxxx almost stopped breathing. Doctors were concerned xxxx xxxx may have meningitis so they performed a lumbar puncture which came back ok. xxxx xxxx was admitted onto the xxxx xxxx and underwent a range of tests, including loads

		of blood tests, xxxx xxxx lumbar punctures, an EEG, MRI scan of xxxx xxxx brain and CFS monitoring and the doctors were telling us that xxxx xxxx was still suffering from Pneumonia and that now xxxx xxxx has epilepsy. We were devastated that xxxx xxxx had epilepsy and I wondered how we would ever cope at home if xxxx xxxx kept having seizures. Little did I know then about the nightmare that was about too unfold. xxxx xxxx deteriorated every day xxxx xxxx was in hospital over the xxxx xxxx and despite myself and xxxx xxxx expressing our frustration and concern with the doctors there, they were adamant that xxxx xxxx just had a chest infection and epilepsy. After being in there for xxxx xxxx xxxx xxxx was in an awful way. xxxx xxxx required increasing amounts of oxygen, couldn't tolerate feed even through xxxx xxxx NG tube so was just on fluids and xxxx xxxx just laid there completely lifeless. It was only when xxxx xxxx eventually had an echocardiogram which was very abnormal that the doctors said they didn't know what was going on and that xxxx xxxx needed to be ventilated and transferred to xxxx xxxx or xxxx xxxx. xxxx xxxx were the only one to have a bed on PICU and so xxxx xxxx was transferred by the xxxx xxxx team that day. The doctors repeated all of the tests that xxxx xxxx had had done in xxxx xxxx and carried out further tests that were recommended by xxxx xxxx. After xxxx xxxx at xxxx xxxx the doctors told us that they thought xxxx xxxx had SCID and xxxx xxxx would need to be transferred to xxxx xxxx for urgent specialist care. xxxx xxxx was then moved again by the xxxx xxxx team to xxxx xxxx on the xxxx xxxx. The doctors at xxxx xxxx were amazing but were extremely concerned about how poorly xxxx xxxx was and told us that xxxx xxxx may not survive as his body was being destroyed by the cytomegalovirus (CMV) virus. xxxx xxxx had to be put on an oscillator ventilator as xxxx xxxx was struggling on the conventional ventilator and this was a massive step backwards. We also found out from the xxxx xxxx at xxxx xxxx that xxxx xxxx had CMV retinitis which had been present for at least xxxx xxxx and that it had caused so much damage to xxxx xxxx eyes that xxxx xxxx would be blind. This was yet another blow and we were distraught at the thought that this had been missed at our xxxx xxxx. xxxx xxxx was on a ventilator for xxxx xxxx but with intensive treatment did eventually come off the ventilator and after a short time on CPAP was able to breathe all by xxxx xxxx. xxxx xxxx was extremely weak and couldn't move but we were so relieved to finally be able to hold xxxx xxxx. xxxx xxxx had lost so much weight that xxxx xxxx had dropped right off the centile chart. The doctors from xxxx xxxx were brilliant and they told us that they felt xxxx xxxx only chance was to have a stem cell transplant, but that xxxx xxxx was too weak to have a full bone marrow transplant with Chemotherapy so they would use cells from xxxx xxxx who was only a half match, but with regular

		immunoglobulins this would be xxxx xxxx best chance. xxxx xxxx donated xxxx xxxx T-cells to xxxx xxxx on the xxxx xxxx. We were told it could take up to six months for the cells to engraft and xxxx xxxx would be tested regularly to check for engraftment. xxxx xxxx perked up a lot while on the ward in xxxx xxxx. xxxx xxxx even managed to feed through a bottle, only requiring xxxx xxxx medication down xxxx xxxx nasogastric tube (NG tube). xxxx xxxx gained a little strength in xxxx xxxx arms with regular physiotherapy and started to gain a little weight. We were transferred back to xxxx xxxx xxxx xxxx on the xxxx xxxx to try and establish a relationship with the doctors there as they would be the first point of call if xxxx xxxx got poorly. We were not happy about this as we feel they let xxxx xxxx down immensely and as a result xxxx xxxx got so poorly with lasting consequences. After only being at the xxxx xxxx for xxxx xxxx xxxx xxxx got very sick and again couldn't tolerate any feed. xxxx xxxx eyes then started to go yellow and after much pushing and complaining at the lack of care yet again from the doctors there, xxxx xxxx was transferred back to xxxx xxxx by ambulance for review by the xxxx xxxx. They discovered that xxxx xxxx had gallstones and a stone was blocking xxxx xxxx bile duct. xxxx xxxx was going to be considered for surgery at xxxx xxxx, but thankfully the stone dislodged and xxxx xxxx returned to a normal colour and managed to start feeding again. After xxxx xxxx we were able to be discharged home as we refused to go back to xxxx xxxx. However, xxxx xxxx at home had got chickenpox so we were unable to expose xxxx xxxx to them. So we did a house swap with xxxx xxxx xxxx xxxx who stayed with xxxx xxxx and we then stayed at xxxx xxxx with xxxx xxxx while xxxx xxxx got over the chicken pox. xxxx xxxx we were finally able to move back home and be a family again, albeit a very different family. Because xxxx xxxx still had no immune system xxxx xxxx couldn't be exposed to anyone who was poorly, even with a simple cold, and we had to limit the number of people xxxx xxxx could be around and had to be very strict with hand washing and cleanliness. After a couple of weeks at home where xxxx xxxx seemed to be doing well, xxxx xxxx started to have seizures again. They were different to the last ones and after another hospital admission xxxx xxxx diagnosed xxxx xxxx with infantile spasms as a result of all the scaring on xxxx xxxx brain which the CMV virus caused. They gave us yet more devastating news that infantile spasms were very difficult to control and meant that xxxx xxxx would be severely disabled if xxxx xxxx even survived. Going home with yet more bad news was horrendous and so hard to comprehend. However we

		weren't prepared to give up and with a change of medication the seizures stopped and with regular physiotherapy and lots of hard work xxxx xxxx proved xxxx xxxx was a fighter once again and gained some head control and even managed to play with xxxx xxxx toys on xxxx xxxx play mat. xxxx xxxx started smiling which was amazing and I actually thought we were going to win this fight. We had regular clinic visits to xxxx xxxx where they checked for engraftment, but unfortunately it seemed that the transplant hadn't worked as there was no sign of any T-cells. In xxxx xxxx we started talking about arranging for xxxx xxxx to have a full BMT with chemo in the xxxx xxxx, xxxx xxxx post last transplant as xxxx xxxx had made such good improvement. But unfortunately just before xxxx xxxx xxxx xxxx started having seizures again and they were constant and very damaging to xxxx xxxx. xxxx xxxx was stressful and sad and it was so hard watching xxxx xxxx constantly have seizures. The way xxxx xxxx would cry out and the fear in xxxx xxxx little eyes was horrendous. After another admission to xxxx xxxx in xxxx xxxx where xxxx xxxx had lots more tests, the doctors told us that the CMV virus had once again taken over xxxx xxxx body and that because of the infantile spasms xxxx xxxx would be so severely disabled that they would not be able to do a BMT for xxxx xxxx as xxxx xxxx just wouldn't survive it. After long and distressing discussions with the doctors, we had to agree to take xxxx xxxx home with palliative care. We were lucky to have the help of the xxxx xxxx at xxxx xxxx and the nurses were lovely, helping me to keep xxxx xxxx as comfortable as possible at home. xxxx xxxx died xxxx xxxx weeks later in my arms on the xxxx xxxx, xxxx xxxx days before his xxxx xxxx birthday. **Our famly is broken** We are absolutely heartbroken. I can't believe we have lost xxxx xxxx when we just thought xxxx xxxx had a chest infection. xxxx xxxx xxxx xxxx have been hugely affected by the amount of time we have been so far away from home in hospital and now to have lost xxxx xxxx after all xxxx xxxx went through. Our family is broken. **The need for SCID screening** We have since learnt that SCID can be tested for as part of the newborn screening programme and that it is currently being done in many states across the USA and in other countries too. To learn that the UK does not include SCID as part of the new-born screening programme is incomprehensible and frankly disgusting. And after finding out that this test would only cost £2.50, I am horrified that we have lost xxxx xxxx for such a tiny cost of a simple test. SCID is a life threatening condition and there is a test which can diagnose it at birth and if diagnosed early and treated, has a 95% survival rate. In fact I understand that if SCID was included in the new-born screening programme that it would be

		the only condition which could be diagnosed by the heel prick test that can be cured. I am horrified that my baby's life wasn't even worth £2.50 to this country. I wonder how many tests could have been carried out on babies across the UK for the cost of all of xxxx xxxx treatment when xxxx xxxx was so poorly. It seems ironic that it cost us more to park our car at our local hospital when we went to have xxxx xxxx then it does to perform a life-saving test. This test should have been available for our xxxx xxxx. xxxx xxxx should still be here with me. But xxxx xxxx not and I have to try and live with that every day. I sincerely hope that the screening committee takes some responsibility and finally does what they should have done years ago and include SCID in the newborn screening programme. With all the unrest and horrible diseases in the world which can't be cured and take so many lives, we have the opportunity to save the lives of innocent babies; why would you not take it. xxxx xxxx certainly wishes we did much earlier. The image of my baby's still cold body will haunt me forever. Putting xxxx xxxx precious little body into a casket on the day of xxxx xxxx funeral, knowing I will never see xxxx xxxx again. I can't even begin to describe how that feels. I hope no other baby is made to suffer the way that xxxx xxxx did. We cannot let this carry on. Losing xxxx xxxx has broken my heart and ruined mine and my family's lives.' 3. xxxx xxxx **is told by** xxxx xxxx**.** 'My xxxx xxxx, xxxx xxxx, died in xxxx xxxx, xxxx xxxx. xxxx xxxx died from B Cell Lymphoma driven by the Epstein Barr Virus as a direct result of, what could only be described at the time, as 'leaky SCID'. xxxx xxxx had been poorly almost since birth. Within 24 hours xxxx xxxx developed a rash all over xxxx xxxx body and would sweat profusely when xxxx xxxx tried to feed. xxxx xxxx also started with a cough when xxxx xxxx was approximately xxxx xxxx weeks old. At xxxx xxxx months of age xxxx xxxx was admitted to xxxx xxxx with what was later diagnosed as Cytomegalovirus. Within those first xxxx xxxx of xxxx xxxx life xxxx xxxx was admitted to hospital xxxx xxxx times, each time for at least xxxx xxxx and it was then that a primary immunodeficiency was suspected. Unfortunately, due to there only being 2 centres in the UK with specialised paediatric knowledge of PID, xxxx xxxx was treated by a xxxx xxxx at xxxx xxxx and it wasn't until she contracted chickenpox aged xxxx xxxx which then set off a chain of tragic events leading to xxxx xxxx developing B Cell Lymphoma. xxxx xxxx was admitted to xxxx xxxx on xxxx xxxx, was diagnosed with Lymphoma on xxxx xxxx and admitted to xxxx xxxx on xxxx xxxx. In xxxx xxxx notes from the xxxx xxxx, xxxx xxxx xxxx xxxx

		wrote ‘so much to do, so little time’. xxxx xxxx recognised that xxxx xxxx had a very severe form of immunodeficiency and that xxxx xxxx should be under the care of either xxxx xxxx or xxxx xxxx, however by that time xxxx xxxx was too sick to be moved. All of xxxx xxxx notes were sent by taxi to xxxx xxxx and were reviewed by xxxx xxxx whose professional opinion was that xxxx xxxx had a ‘leaky SCID’ which should have treated by a bone marrow transplant (BMT) at birth. A BMT was carried out at the beginning of xxxx xxxx, however xxxx xxxx was too poorly and xxxx xxxx never recovered. It is my strong belief that if newborn SCID screening had been in place when xxxx xxxx was born then it would have been detected that xxxx xxxx had a complex immunodeficiency and xxxx xxxx would have received timely and appropriate treatment, possibly resulting in saving xxxx xxxx life. Obviously for me the most important outcome that this screening could have had for my family is that my xxxx xxxx could have been alive today, thus avoiding xxxx xxxx suffering and also the devastating effects that grief have had on xxxx xxxx xxxx xxxx and I and also xxxx xxxx. For the NHS and the government though, screening at birth (hopefully picking up immunodeficiencies early) would have saved hundreds of thousands of pounds and valuable resources both human and material. It does not make any financial sense to me why this newborn screening would not be implemented and it certainly does not make any humanitarian sense for it not to be implemented.’
	2. Impact of late diagnosis of ADA-SCID on child and family.	Parent testimonies from families affected by ADA-SCID provided to PID UK through a survey: 1. ‘My xxxx xxxx who xxxx xxxx xxxx xxxx, got sick around xxxx xxxx months old. xxxx xxxx had been diagnosed with ada-scid when xxxx xxxx was xxxx xxxx months old. xxxx xxxx had a bacteria called pneumococcus and that bacteria shut down both xxxx xxxx kidneys but sometime in xxxx xxxx life xxxx xxxx will need a kidney transplant.’ 2. xxxx xxxx wasn't diagnosed until xxxx xxxx was xxxx xxxx years old and by then xxxx xxxx had suffered a lot through infections/pneumonia and other complications. This has had an impact on xxxx xxxx future health and treating xxxx xxxx by the usual means of BMT was not possible initially and was still not the preferred option later on. ‘ 3.’ xxxx xxxx struggled at school due to time off for weekly infections and other appointments. xxxx xxxx ended up repeating xxxx xxxx last year of primary school to catch up. Due to xxxx xxxx ADA not being picked up early enough xxxx xxxx has been left with life-long lung issues and serious kidney problems, as well as the issue SCIDs bring. Emotionally, especially as getting older xxxx

		xxxx struggled with what had to happen to xxxx xxxx.' 4. 'Exposed my xxxx xxxx to a life of serious risk. As stated my xxxx xxxx weakened state meant staying in a laminar flow room. We wore gowns over aprons, hairnet/hat, covers on shoes and had to scrub. My xxxx xxxx had to be in a head box for 100% oxygen then induced coma and ventilated for xxxx xxxx weeks. I was told to prepare for my xxxx xxxx death!. Drains were needed for burst air sacs by the ventilator followed by suction for mucus. A permanent line put in chest for meds and to take blood. Fluid retention from ventilator. Around xxxx xxxx weeks the last thing to try was nitric gas which after xxxx xxxx hours xxxx xxxx oxygen levels altered. Eventually coming of the ventilator, still xxxx xxxx needed to be treated for pneumonia. xxxx xxxx weeks of no touching between mother and xxxx xxxx, trying to avoid xxxx xxxx hands near my face.' 5. 'Massive impact on all my families lives. Financial issues'. 6. 'My wife almost has a total breakdown due to the strain and worry. I almost lost my job due to the time needed to support my wife and to be present in hospital with xxxx xxxx.' 7. 'Husband and I both had to stop work. Huge impact on our xxxx xxxx who was xxxx xxxx at the time. Living in isolation and often in separate rooms.'
Page 6	Screening programmes outside of the UK. In the USA	48 states in the USA are now screening for SCID. 92% of all newborns in the US are receiving SCID screening. Source: Immune Deficiency Foundation https://primaryimmune.org/idf-advocacy-center/idf-scid-newborn-screening-campaign/
	Use of NBS for SCID, outside of the USA	Canada, Israel, Qatar, Taiwan, the Netherlands, Sweden, Norway and New Zealand now have screening programmes. Pilot studies are underway in Germany, France, Italy, Spain, Iran, Saudi Arabia, Brazil and Japan.
	Comment	The information above indicates how far the UK is lagging behind the rest of the world!
Page 6	Use of NBS for SCID	The government is pledged to improve the diagnosis of rare conditions through Rare Disease Strategy Implementation plans. Implementation of a full screening programme for SCID would be a concrete demonstration of that commitment.
Page 8	Key question 1	The review provides solid data that criterion 1 is met (page 27). We agree that SCID should be treated as 'an important health condition'. Indeed it is treated as a paediatric emergency because it is a fatal condition if not detected early enough as our patient stories above indicate. Early detection through a NBS screening programme that has been demonstrated to be able to pick up all SCID cases would ensure curative options can be offered to affected children.
Page 10	Detecting children with DiGeorge (22q11 deletion syndrome) by	McDonald-McGinn et al., 2015 report that '*early diagnosis, preferably prenatally or neonatally could improve outcomes, thus stressing the importance of universal screening'*. Nat Rev Dis Primers. 2015 Nov 19;1:15071. doi: 10.1038/nrdp.2015.71.This emphasises that the detection of these

	SCID screening	children should be viewed in a positive way. Furthermore a UK consensus of care document on 22q11 deletion syndrome is available http://www.maxappeal.org.uk/knowledge/consensus_document and care for affected children is covered by the NHS contract service specification B04/S (HSS)/b for severe immunodeficiency and related disorders service (children).
Page 10	Detecting children with Ataxia telangiectasia	Note that medical guidelines for AT are available at https://www.ataxia.org.uk/clinical-guidelines and that the UK has Specialist Ataxia clinics to care for AT affected children https://www.ataxia.org.uk/Pages/News/Category/ataxia-centres.
	Detection of non-SCID T cell lymphopenia	We understand that the TREC test may pick up non-SCID T cell lymphopenia. This should be seen as an opportunity to understand the incidence and prognosis of T cell lymphopenia in the newborn population. Such information would add valuable data for the PHE NCARDRS initiative https://www.gov.uk/guidance/the-national-congenital-anomaly-and-rare-disease-registration-service-ncardrs. Although there is doubt over the guidelines for the treatment of non SCID TCL, detection would provide an opportunity to intervene in a child's care where possible. It would also drive the development of guidelines by the clinical community. Centres in the USA are already using this an opportunity to drive research.
Page 24	Section 4.1.3. Incidence of SCID	It is only through a large-scale, well-planned evaluation study that the true incidence of SCID will be determined in the UK.
Page 34/36	TREC test cut off and specificity	The review confirms that a suitable cut off for the TREC test can be defined and that the test has high specificity for detecting SCID.
Page 36	Number of false positives	We agree that it is only through a population wide pilot screening programme will a more accurate picture of the rate of false positives be obtained. Please see comment above on detection of non-SCID TCL.
Page 58	Key question 3 Efficacy of early vs late treatment using HSCT	The review confirms that early HSCT for SCID substantially improves outcomes for affected children. It also confirms that there are established guidelines for the treatment of SCID {see ESID EBMT HSCT GUIDELINES 2017} and the NHS has specialist commissioned services for SCID HSCT.
Page 62	Other curative treatment options: Gene therapy for SCID	The recent decision by NICE on Strimvelis confirms gene therapy offers an alternative curative therapy for ADA-SCID when an HSCT is not considered a viable option. Successful clinical trials for ADA-SCID have also been conducted at GOSH. See also publications by Kohn and Gaspar; J Clin Immunol. 2017 May;37(4):351-356. doi:

		10.1007/s10875-017-0373-y. Epub 2017 Feb 14. Ferrua and Aiuti; Hum Gene Ther. 2017 Nov;28(11):972-981. doi: 10.1089/hum.2017.175. Gene therapy clinical trials for X-SCID are also on going at GOSH with good success rates. See also the publication by Ravin et al., Sci Transl Med. 2016 Apr 20;8(335):335ra57. doi: 10.1126/scitranslmed.aad8856.
		This evidence confirms that SCID is a condition for which there are two curative options available. So the necessary criteria 9 and 10 have been met.
Economic review	Overall comment	There is bias around the emphasis of the cost analysis: NOT taken into account are the 'opportunity lost' costs i.e. cost of NOT identifying babies with SCID at birth – diagnostic odyssey, cost of ER/referrals to get diagnosis, impact of children's deaths on family, an holistic view of societal gain. **Please read the patient testimonies given above.**
	Page 3 treatment of SCID by gene therapy	NICE have recently recommended the use of STRIMVELIS, a gene therapy treatment for ADA-SCID, be made available on the NHS. This approval, along with the highly successful clinical trials carried at GOSH, indicates that gene therapy is an accepted form of curative treatment for SCID when a haematopoietic stem cell transplant (HSCT) is not possible.
	Page 14: incidence rate in UK affecting economics	It is only through a large-scale, well-planned evaluation study that the true incidence of SCID will be determined in the UK.
	Page 14: point 5 productivity costs	The impact of SCID is on the whole family and much broader than loss of earnings for caring: see patient testimony.
	Page 24: Babies identified by screening rather than family history	The document acknowledges results from a 5-year UK study showing approximately 30% of babies with SCID are identified as a result of family history. The economics analysis suggests that this figure has to rise to over 40% before the QALY threshold rises above £20,000**.** It seems that this issue has been effectively answered without having to undertake an evaluation study.
	Page 28 treatments options for ADA-SCID	See comment on NICE recommendation of Strimvelis
	Page 30, 31 Quality of life of SCID patients	A recent paper by Hamid et al., 2017 https://www.ncbi.nlm.nih.gov/pubmed/28209722# reports that the current approach of low-toxicity myeloablative regimens for transplanting patients have better B-lymphocyte/myeloid chimerism and are free from immunoglobulin replacement therapy. IL2RG/JAK3 SCID survivors free from immunoglobulin replacement have normal QoL.
	Page 38 Costs of	The price of the screening test is being reduced to £2.50 per infant screened, and the modelling of screening shows that probability of SCID screening being cost effective at a QALY threshold of

	screening	£20,000 is 96%. There is therefore little doubt based on this modelling that SCID screening is cost-effective.
	Page 41 Costs of late diagnosis versus early	The figures quoted speak for themselves: £128k for an early-diagnosed child with SCID and £231K for care for late diagnosis. Whilst compelling these figures do not tell the full story of the costs associated with the impact of a late diagnosis on the wider family unit. These include the financial burden of care in terms of lost earnings, necessary changes needed to the home in caring for an affected child, costs of travel to hospital and clinics through the diagnostic odyssey, over night stays near hospital when a child is severely ill as well as the emotional toll on parents, relationships and wider family. **Please read the testimonies given above from affected families.**
	Page 39 - 42. Evidence or questions omitted by the review that might contribute to the recommendation	There is bias in the analysis. Considerable emphasis is placed on the psychological effect of screening on parents with babies identified as false positives and non-SCID conditions, but there is no mention or analysis of psychological effect on parents who have lost a child with SCID and the huge impact this has. **Please read the testimonies given above from affected families.** The death of a child is a traumatic life-changing event for any parent to have to deal with. The loss of a child for a condition for which there is a simple test available and that would enable an early curative intervention to be given is even harder to live with. The cost and psychological impact of bereavement on affected parents such as funeral expenses; impact on mental health, relationships, need for counseling etc MUST be taken into account. We ask the panel to read the following document 'How to calculate the economic impact of grief' by Professor Van der Berg, Professor of Economics, University of Bristol http://theconversation.com/how-to-calculate-the-economic-impact-of-grief-68936 We urge the panel to redress the balance in the analysis with regard to the above.
	Page 57 Scenario analysis – impact of discount rate	We suggest that a lower discounting rate of 1.5% be used. This would make the probability even greater and there is an argument that this lower discount rate should be used given that the intervention has a substantial and sustained positive outcome.

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UK National Screening Committee
Newborn screening for Severe Combined Immunodeficiency (SCID) – an evidence review

Consultation comments pro-forma

Name:	Mervi Jokinen	**Email address:**	xxxx xxxx
Organisation (if appropriate):	The Royal College of Midwives		
Role:	**Professional Adviser**		
Do you consent to your name being published on the UK NSC website alongside your response? **Yes x☐ No ☐**			
Do you agree with the proposal to undertake a practical evaluation of newborn screening for SCID in the NHS? **Yes x☐ No ☐**			
Please explain why you agree or disagree with the proposal.			
RCM believes the review of the evidence has been thorough. This combined with the assessment of cost-effectiveness of a proposed			

screening programme clearly raises further questions that have not been answered adequately by the current available evidence. The decision to further evaluate those issues/questions before recommending a systematic population screening is valid. The need to review is underpinned by NSC criterion 1 being met as well as criterion 5 and 10. The practical evaluation will hopefully provide NSC with information that either supports full implementation of the screening programme or not in the future.

On which consultation document are you commenting?

The systematic review ☐ **The modelling and cost effectiveness evaluation** ☐

Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*

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UK National Screening Committee
Newborn screening for Severe Combined Immunodeficiency (SCID) – an evidence review

Consultation comments pro-forma

Name:	Comments provided on behalf of the following: Dr Martin Ward Platt (Clinical Lead, National Congenital Anomaly and Rare Disease Registration Service)	**Email address:**	xxxx xxxx
Organisation (if appropriate):	Royal College of Paediatrics and Child Health		
Role:	**NA**		
Do you consent to your name being published on the UK NSC website alongside your response? **Yes** ☒ **No** ☐			
On which document are you commenting? **The systematic review** ☒ **The modelling and cost effectiveness evaluation** ☐			

Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*
Systematic review - general	General	While we have no specific comments on any parts of the documents, we agree with the NSC's arguments for not pursuing the option of developing a screening programme at this time. As NCARDRs develops it should be possible to build up an accurate national picture of SCID epidemiology in the UK which will feed into any future debate on the merits of developing a screening programme and may point to geographical areas in which it might be appropriate to pilot any proposed programme. The further development, and potentially diminishing costs, of candidate screening technologies will probably affect the health economic argument over the next few years.

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UK National Screening Committee
Newborn screening for Severe Combined Immunodeficiency (SCID) – an evidence review

Consultation comments pro-forma

Name:	Pat Roberts (Mrs)	**Email address:**	xxxx xxxx
Organisation (if appropriate):	Save Babies Through Screening Foundation UK (and on behalf of the UK Patient Advocates for Newborn Screening Group) PANS.		
Role:	**Executive Director**		

Do you consent to your name being published on the UK NSC website alongside your response?

Yes x☐ No ☐

Do you agree with the proposal to undertake a practical evaluation of newborn screening for SCID in the NHS?

Yes x☐ No ☐

Please explain why you agree or disagree with the proposal.

Yes we do support the practical evaluation however please see our request for further clarity as at point 2 below.

On which consultation document are you commenting? **The systematic review x☐** **The modelling and cost effectiveness evaluation x☐**		
Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*
General Response	Consultation	1. We acknowledge that there are other stakeholders clinical, scientific and patient organisations who will respond to this consultation and who have a more detailed knowledge of SCID, research, treatments that our members. Also they are better placed to advise how a practical evaluation study might be structured, timescales etc. I have therefore left it to those stakeholders to drive into the detail of the document and I have tried to reflect higher level points from the report that are of key importance to our PANS Group members..
Systematic Review	General	2. We are encouraged that the evidence review is supportive of NBS for SCID and at a reasonable cost and that very key criteria has been met. Also we are generally supportive of the recommendation to undertake a practical evaluation study in the NHS. However, in light of evaluation studies for disorders previously accepted onto the UK NBS programme, the terminology is not absolutely clear to us. Is this evaluation study in essence a pilot study i.e. to gather the perceived uncertain parts of the evidence by practical application of screening in some laboratories prior to national implementation or is something else e.g. research? Can we not just call it a pilot study? Any clarification would be appreciated. We recognise that there may be a need for additional information prior to national roll out, however would not wish for any study to be unnecessarily protracted. Children are dying of this terrible disorder now. From a patient organisation perspective we would value National Roll out of NBS for SCID at the very earliest opportunity.

Modelling and cost effectiveness evaluation	General	3. Challenges on false positive results. As always this is an important issue to address and is data that should come from the practical application of a screening programme for any pilot or evaluation study. However considerable emphasis is given to the impact on parents of false positive results. However, as with all other disorders that are considered by the UK NSC, absolutely no focus is given to the psychological effect on parents who have lost a child with SCID and the longer term impact this might have.
	2 Review of Economic Analysis	4. Socio and Economic Burdens on Parents: The paper compares the costs of treatment and management of non screened detected patients with the cost of screening, management and treatment of screened detected SCID patients. We are pleased to see that some wider economic costs have been included in this evaluation as opposed to only medical costs.
		5.There is an issue on the number of babies who would be identified through screening rather than through family history. This is one of the key questions being asked as part of the proposed evaluation. We understand that data has been already provided from a UK study covering 5 years in the UK and this appears adequate for any economic analysis. We would therefore question the need to undertake further evaluation.

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UK National Screening Committee
Newborn screening for Severe Combined Immunodeficiency (SCID) – an evidence review

Consultation comments pro-forma

Name:	Lesley Tetlow	**Email address:**	xxxx xxxx
Organisation (if appropriate):	Central Manchester University Hospitals		
Role:	**Consultant Paediatric Biochemist/ Director of Newborn Screening**		
Do you consent to your name being published on the UK NSC website alongside your response? **Yes ✓**			
Do you agree with the proposal to undertake a practical evaluation of newborn screening for SCID in the NHS? **Yes ✓**			
Please explain why you agree or disagree with the proposal.			
The systematic review has answered key questions regarding the incidence of SCID (as far as possible in the absence of published UK studies), the accuracy of the TREC test and the impact of early HSCT on improving outcomes. The case for implementation of SCID			

screening based on the additional evidence provided is strong. Further information required by the NSC on the impact of identifying non-SCID conditions (and practical testing of protocols for the care and treatment of babies identified with these conditions) and detailed costings of the screening pathway can only be obtained by undertaking a practical evaluation of newborn screening for SCID in the UK. This therefore is the only way in which the committee can fill the gaps in the evidence, allowing a final decision to be reached.

On which consultation document are you commenting?

The systematic review ✓ modelling exercise and cost effectiveness evaluation ✓

Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*
p9 (Discussion) Systematic review	UK SCID incidence	An estimate of UK incidence has been obtained based on 4 year data from 2 studies. Further evidence on the number of "false positives" (babies with low numbers of white cells for reasons other than SCID) can be obtained via the proposed practical evaluation.
p11 (Discussion) Systematic review	Defining TREC cut-offs	It is important to define a suitable UK cut-off and test it using the proposed technology from Perkin Elmer in UK Screening Labs. Only by doing this will the NSC have a clear idea of the numbers of false positives likely to be identified if implementation is approved.
p39 (section 3.8) cost effectiveness evaluation	Costs of screening and confirmatory testing	Consultation is required with UK Newborn Screening Labs via UKNSLN. In addition to the staff costs associated with the analysis, senior staff time will be required to manage the service and to undertake clinical reporting and quality control. There will also need to be changes to the Screening IT system. It may be preferable to fund labs on the basis of a sum per baby screened (as for all other more recently implemented programmes).

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UK National Screening Committee
Newborn screening for Severe Combined Immunodeficiency (SCID) – an evidence review

Consultation comments pro-forma

Name:	Professor Persis Amrolia	**Email address:**	xxxx xxxx
Organisation (if appropriate):	UK Paediatric Bone Marrow Transplant Group		
Role:	**Chair**		
Do you consent to your name being published on the UK NSC website alongside your response? **Yes X** **No** ☐			
Do you agree with the proposal to undertake a practical evaluation of newborn screening for SCID in the NHS? **Yes X** **No** ☐			
Please explain why you agree or disagree with the proposal.			

There is compelling evidence from US screening programmes that newborn screening is highly effective in diagnosing SCID. Equally, there is strong evidence that making a diagnosis in the neonatal period in siblings of affected probands prevents the development of infectious complications through early implementation of prophylaxis and improves stem cell transplant outcomes because patients come to transplant with reduced comorbidity (Brown et al Blood 2011). Therefore implementation of neonatal screening for SCID is likely to improve clinical outcomes for affected children and the UK Paediatric BMT Group strongly support the proposal to perform a limited practical evaluation of this approach as a step towards universal screening

On which consultation document are you commenting?

The systematic review X **The modelling and cost effectiveness evaluation** ☐

Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*

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UK National Screening Committee
Newborn screening for Severe Combined Immunodeficiency (SCID) – an evidence review

Consultation comments pro-forma

Name:	Tomaz Garcez	**Email address:**	xxxx xxxx
Organisation (if appropriate):	United Kingdom Primary Immunodeficiency Network		
Role:	**Chair**		
Do you consent to your name being published on the UK NSC website alongside your response? **Yes** ☒ **No** ☐			
Do you agree with the proposal to undertake a practical evaluation of newborn screening for SCID in the NHS? **Yes** ☒ **No** ☐			

Please explain why you agree or disagree with the proposal.
UKPIN is broadly supportive of an evaluation study in the NHS as this will enable screening to take place, but would support a national programme straight away.
On which consultation document are you commenting? **The systematic review ☒ The modelling and cost effectiveness evaluation ☐**

Section and / or page number	**Text or issue to which comments relate**	**Comment** *Please use a new row for each comment and add extra rows as required.*
General		Thorough and well performed review
Page 9	Key question 1	Agree SCID meets criteria and is an important health condition
Page 11	Key question 2	A suitable cut off can be defined but the review highlights that a population wide pilot screening programme would give a clearer indication of the rate of false positives. This should therefore be considered
Page 13	Key question 3	HSCT is effective for the treatment of SCID and early treatment improves prognosis. Strongly supporting screening. The matter of non-typical SCID low TRECs is being defined and should not deter a screening programme

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