DEPARTMENT OF PAEDIATRICS

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www.paediatrics.ox.ac.uk

Population-based New-Born Screening of Spinal Muscular Atrophy to evaluate the uptake and feasibility in the UK context
(NBS for SMA)

Participant Information Booklet

Dear Parents,

We would like to invite you to consider taking part in our research study on newborn genetic screening for spinal muscular atrophy (SMA). Taking part is voluntary; it is entirely up to you to decide whether this is something you would like to do.

To help you decide, we have prepared this information sheet which explains why we want to do this research study and, most importantly, what taking part would involve for you and your newborn baby.

Please take your time to read the information. If you have any questions, or would like to know any more about the study, please do not hesitate to ask our research midwife who has approached you about the study. You can also contact the study team by phone or email; their contact details are at the end of this booklet. Please talk about it with your partner, family or friends, if that would help you.

Why have I been chosen for this study?

All babies that are born in the Thames Valley, are eligible to take part in this study which tests for a condition called Spinal Muscular Atrophy (SMA). This is a rare disorder, and so the vast majority of babies who are tested will not have the condition, but for those that do, early diagnosis and treatment are critical.

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The standard newborn screening programme

In the first week of life, all newborns are checked for treatable metabolic and hormonal disorders as part of their standard newborn screening tests. For these tests, a few drops of blood from a newborn's heel, are collected onto specimen collection paper (the Guthrie card), normally within a week of birth. We are offering your baby another screening test as part of a research project which would be performed on surplus bloods spots collected on the Guthrie card. The research study is being carried out by staff at the four Hospital Trusts in the Thames Valley, and blood spots will be screened at the NHS Oxford Regional Genetics Laboratory. This test aims **to identify newborns who will develop Spinal Muscular Atrophy (SMA).** SMA is not currently screened for as part of the newborn screening programme. This screening test can be done on the blood spot that is already being taken as part of the standard newborn screening programme. This means **no extra blood samples will be needed**.

Why are we interested in newborn screening for spinal muscular atrophy and why we are asking you to take part in this study?

Spinal muscular atrophy (SMA) is a rare, but treatable, genetic disease affecting approximately 1 in 10,000 births, and it typically presents in infancy and early childhood. SMA is caused when part of the gene is found to be missing (deletions) or disrupted (mutations). The gene is called survival motor neuron 1 (*SMN1*), which is important to maintain motor neurons (nerve cells). SMA progressively, and irreversibly, destroys the nerve cells in the brain and spinal cord, that control movement. SMA also leads to muscle weakness.

The conditions can begin within the first 3 months of a child's life. In children with the most common and severe type of SMA, 95% of all motor neurons can be lost before the age of 6 months. Most children with this type of SMA, if untreated, will not survive beyond 2 years of age without permanent ventilator support. Many children who survive will not be able to sit or walk independently.

A challenging aspect of treating SMA is that the diagnosis is often only made once the child has serious clinical symptoms, such as movement problems, by which point many motor nerves will have been lost. There are now some new treatments for SMA that are being assessed by the National Institute for Health and Care Excellence (NICE). The treatments have

been shown to benefit children with certain types of SMA who are treated at an early stage. The treatments have been approved by UK regulatory bodies, and can be given on the NHS.

Our newborn screening study aims to make it possible to detect SMA within days of birth, before symptoms develop, so that any affected newborn can receive diagnosis and treatment at the earliest possible opportunity. We hope that the findings from this study will help the National Screening Committee decide whether SMA screening should be included in the UK newborn screening programme. To do this, we would like to involve as many mothers as possible who receive their maternity care in the Thames Valley. We are inviting women who are more than 18 weeks pregnant, or have given birth in the last 28 days, to be part of this study with their newborn babies.

What do I need to do if I decide to take part in this study?

If you would like to take part in this study and to have this additional screening test for SMA performed on your baby's routine blood sample, we will ask you to sign a consent form. We will ask you to provide us with the following information:

- your name, contact details and NHS number
- your expected date of delivery
- whether your pregnancy/birth is single or multiple (and if you are having twins or triplets, which baby/babies you give your consent for)

The study team will securely store this information in their database. No-one outside the study team will have access to this information.

This research will use leftover blood from your baby's newborn blood spot (Guthrie card) taken in the first 5 days after birth. No additional blood samples will be required. If you decide to take part, a spare bloodspot from your baby's card will be collected from the NHS Screening Laboratory at the John Radcliffe Hospital, which carries out all of the newborn and antenatal screening tests in the Thames Valley. This sample will undergo DNA extraction and be tested for SMA at the NHS Oxford Regional Genetics Laboratories at the Churchill Hospital. The SMA test is a genetic test, or DNA test. The sample and data will be securely stored for 12 months and any left over sample will be securely destroyed once the genetic analysis is complete.

Although DNA can never be completely anonymous because it is unique to each person, we will de-identify your baby's sample by giving it a unique code. This will help keep you and your baby's personal information confidential. The anonymised sample will only be used by authorised researchers at the NHS Oxford Regional Genetics Laboratory at the Churchill Hospital, based at the Oxford University Hospitals NHS Foundation Trust. The sample will not leave this laboratory.

What tests will be performed on by newborn's sample?

The bloodspot from the Guthrie card will be collected by the NHS Oxford Regional Genetics Laboratories, and submitted for genetic testing. DNA will be extracted from the sample and run on a sensitive assay called qPCR, which will allow us to detect the presence of the affected gene in SMA, called *SMN1*. This test is being used in many countries, and has been validated for use in the UK.

What will happen if my baby's screening result is normal (negative for SMA)?

You will be contacted and told your baby's screening result is normal. Your contact details will be held until the end of the study when they will be deleted from our database.

What happens if my baby's screening result is positive for SMA?

If your baby is found to be screen-positive for SMA, you will be contacted by phone about the result as soon as it is available. You will be invited to attend the John Radcliffe Hospital in Oxford to meet with the SMA specialist doctor and clinical team within 48 hours, or as soon as it is practically possible for you.

The diagnostic investigations and any treatment that is required would be provided through the NHS and are not part of this research study. NICE may monitor care if one of the new treatments is provided. We have described below what would happen next if your baby is found to be screen-positive for SMA:

Your baby's screening result would be discussed with you during this visit, which will be with Professor Laurent Servais, the Chief Investigator of this study or, another Paediatric SMA specialist consultant. At this visit, an additional blood sample of approx. 5 mL (equivalent to about 1 teaspoon) would be taken from your baby for diagnostic testing. This blood sample would be analysed at the West Midlands Regional Genetics Laboratory, based at the Birmingham Women's and Children's NHS Foundation Trust.

If the diagnostic test confirms your baby has SMA then you and your newborn would be referred to a specialist paediatric neuromuscular consultant to discuss the best treatment options. This may include new treatments such as Nusinersen, which is administered on a regular basis, or the gene therapy product, Zolgensma, which is administered once only. Both of these treatments are currently being assessed by NICE. **The study team would also ask for consent to store your contact details in case there is a need to communicate with you in the future, but your child would not be involved in further research without your consent.**

What should I consider?

In 95% of people who have SMA, the same part of the gene is found to be missing (deletion). The genetic screening test for SMA allows us to detect this common deletion. In 5% of people with SMA, there is a rarer genetic deletion that cannot be found by the screening test. If your child has the rare deletion we may not detect it by screening.

The genetic tests used in this screening study will only detect whether your newborn will develop SMA. They will not provide any information about the likelihood that your baby will pass on SMA to their children.

What will happen to my, and my baby's, data, and will our taking part in the study be kept confidential?

The data that we obtain from you and your baby will be kept strictly confidential.

The data protection regulation requires that we tell you how we will process information about you and your baby and what the legal basis for processing is. We will be processing your data for research in the public interest. The University of Oxford is the sponsor for this

study, based in the United Kingdom, and is the data controller for the SMA NBS study, therefore is responsible for making sure all personal information from you and your baby is managed appropriately.

The SMA NBS study team, as researchers, will use information collected from you and your newborn to undertake the study, but will only use the minimum personally-identifiable information needed to do so. The information you provide to us about yourself and your newborn, and the genetic information about SMA from your newborn's blood test, will be assigned a unique study code for our study database. Access to the database will also be protected by password and via a secure, encrypted connection. No data from you, or your newborn collected for this study, will leave the University of Oxford or the Oxford University Hospitals NHS Trust. Responsible members of the University of Oxford and the relevant NHS Trust, may be given access to data for monitoring and/or audit of studies to ensure that the research is complying with applicable regulations. We will keep identifiable information about you for 12 months after the study has finished. This excludes any research documents with personal information, such as consent forms, which will be held securely at the University of Oxford for 3 years after the end of the study.

The data protection regulation provides you with control over your personal data and how it is used. However, when you agree to your information being used in research, some of those rights may be limited. You can find out more about how we use your data by contacting the study team who will be happy to answer your questions. Our contact details are at the end of this information booklet.

Further information about your rights with respect to your personal data is available at https://compliance.web.ox.ac.uk/individual-rights.

What will happen to the results of this study?

Although the results of this study may be presented to companies, and at conferences and/or used in manuscripts, abstracts, press releases, and any other publication, neither you nor your newborn will be identifiable from any report or publication placed in the public domain.

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What if I decide to withdraw from the study?

You are free to withdraw at any time. You do not have to provide a reason, and this will not affect your or your baby's medical care. If you would like to withdraw from the study, please contact the study team using the contact details at the end of this Information booklet.

If you decide to withdraw after your newborn's dried blood spot sample has been taken, but not yet processed, the study sample will be destroyed and recorded as 'taken but not processed' for the study purposes.

If you decide to withdraw during the sample processing, in the rare event of a screen positive result we would still notify the SMA consultant/clinical care team at the site from which you were recruited.

What if there is a problem?

If you have any concerns about the study that you would like to discuss, or wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact the study team, or you may contact the University of Oxford Research Governance, Ethics & Assurance team (RGEA) office on 01865 616480, or the head of RGEA at ctrg@admin.ox.ac.uk.

The University of Oxford, as Sponsor for this study, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study.

Who is organising and funding the study?

The study is being conducted at the University of Oxford, Paediatrics Department, by Prof. Laurent Servais alongside the Nuffield Department of Women's and Reproductive Health led by Prof. Manu Vatish. The study has been funded by Novartis Gene Therapies, Roche Products Ltd., and the Oxford Biomedical Research Centre.
Other than direct costs, including Midwives salaries, none of the recruitment sites are receiving additional payment for their participation in this study.

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Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given favourable opinion by Research Ethics Committee.

Contact us

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Thank you for reading this information, and thank you for considering taking part.