

Sub-attachment A1

Newborn screening for Spinal Muscular Atrophy (SMA): information for parents

Dear Parents,

We are writing to you to ask you to give your permission for your child to take part in a Newborn Screening programme aimed at identifying patients with pre-symptomatic **Spinal Muscular Atrophy (SMA)**. This will identify individuals at a very early stage of the disease when there are still no clinical signs of the condition, allowing any treatment to begin as soon as possible.

What is newborn screening?

Newborn screening is a preventive procedure which is carried out all over the country. It is used for early diagnosis of some hereditary diseases for which treatment can be given to modify the affected child's state of health. Newborn screening is used for rare, genetic diseases that have an extremely varied incidence, and biochemical, molecular and clinical expression. The early diagnosis of these diseases is very important because it allows specific therapies and diets to be started quickly before there is any possibility of serious damage to the organism of the affected newborn child.

Why is newborn screening important?

Newborn screening is an important step in a procedure to identify soon after birth newborn babies affected by some congenital diseases so that specific treatment can be started as soon as possible. This treatment is carried out at highly specialised clinical centres of reference with specific drugs or special diets that allow the affected baby to develop normally and/or promotes a significant improvement in their health. **Being able to carry out this screening is, therefore, extremely important to prevent or limit the damage to the organism typical of these diseases, and to ensure a good quality of life to as many of the affected children as possible.** The Regional Reference Laboratory for Newborn Screening (LRRSN) of the V. Buzzi Children's Hospital (Ospedale dei Bambini V. Buzzi, Lombardy Regional Health Care Authority Fatebenefratelli-Sacco) in Milan is the regional laboratory where all the tests and samples from newborn babies born in Lombardy are sent, regardless of where the birth took place (public and private hospitals, private health institutes, etc.).

What happens during the newborn screening?

Between 48 and 72 hours after birth, a member of the screening team will take a few drops of blood from the baby's heel. The sample obtained is sent to the Regional Reference Laboratory for Newborn Screening (LRRSN) of the V. Buzzi Children's Hospital in Milan to be analysed. The sample is tested for all the pathologies covered by the Newborn Screening programme.

The samples are analysed soon after their arrival in the laboratory and the results are sent to the institute / hospital where the birth took place. If the results are **negative** (normal), the parents will not be contacted. In some cases, the sample obtained **may not provide sufficient material** to be tested or the **results are uncertain**; a second sample will then be required. If the results are "**not negative**", further tests are then carried out in the lab (biochemical and molecular tests); in this case, a member of the screening staff will contact you. Should the tests be **confirmed positive**, the regional centre of reference for the pathology in question will immediately be informed about the newborn baby's status, in order to:

- proceed with the diagnostic procedures (these are part of the clinical, lab and genetic consultancy procedures) until one of the hereditary conditions covered by the Newborn Screening programme has been identified or excluded;
- start targeted therapy where required.

A positive test result does not mean that the newborn child has the disease; it is only an **alarm signal** indicating that more specific diagnostic tests are needed. **Only a few of the newborn children called back after a positive test result go on to be actually diagnosed with the disease.** The nursing and medical staff of the institute where the baby is born will immediately provide the family with all the information related to these tests to explain what they mean.

Data management

In order to carry out the Newborn Screening Programme, and to allow a correct interpretation of the results, the newborn child's personal data (personal details, Health Service profile and case history) will be shared by the institutes involved in the Newborn Screening Programme network (the Punto Nascita office, the Regional Reference Laboratory for Newborn Screening and diagnostic service, Specialised Reference Clinics). Cases that test positive, for which a diagnosis is confirmed, will be registered on the National Rare Diseases Registry (RNMR) of the National Health Service through the Regional Rare Diseases Registry (ReLMaR), and the appropriate safety measures and procedures for the treatment of sensitive data will be taken according to the regulations in force.

Sample storage times

On completion of the Newborn Screening procedure, as a precaution, the blood sample will be stored for five years at the Regional Reference Laboratory for Newborn Screening; this 5-year period is considered necessary in order to carry out any required check-ups and to verify the state of health of the child. Following this, on receiving the required consent, the sample will be stored under an anonymised identification code for any epidemiological studies and/or research on the pathologies covered by the Newborn Screening Programme or on other pathologies destined to become part of the programme in the future.

What is SMA?

Spinal Muscular Atrophy is a rare neuromuscular disease. Its clinical characteristics involve progressive muscle paralysis caused by the loss of control of voluntary muscle movement. The patient's intellectual development is normal. SMA is classified in 4 types according to the seriousness of the symptoms and the patient's age at their presentation.

- SMA 1 (around 50-60% of patients): the most severe form of the disease, presenting in the first six months of life. Life expectancy is less than 2 years. The cause of death is usually respiratory failure due to weakness of the intercostal muscles.
- SMA 2 (around 30% of patients): of intermediate severity with presentation of symptoms before 18 months of age. Affected children will never be able to walk without assistance. Although there is little reduction in life expectancy, quality of life is quite poor because movement is extremely limited. Furthermore, patients nearly always experience serious sclerosis that requires corrective surgery.
- SMA 3: symptoms appear after 18 months of age and there is wide variability in the disease course. Patients may or may not lose their ability to walk. Life expectancy is normal, and quality of life is compromised according to the extent to which movement is limited.
- SMA 4: the mildest form of the disease presenting in adulthood (20-60 years of age) and with slow disease progression.

The cause of SMA is the absence or mutation of the *SMN1* gene. *SMN1* is responsible for the production of a protein that is essential for motorneuron survival. Motorneurons are the cells that send the signals to our muscles that allow us to move, breathe and swallow.

Spinal Muscular Atrophy usually involves a single member of the family, and is, therefore, an autosomal recessive genetic defect. This means that while neither of the child's parents will have the disease, they are both healthy carriers of the genetic defect that causes the condition. The condition is only revealed if they both pass it on to their children. It is estimated that one child in every 6-8,000 newborns are affected by SMA. Healthy carriers account for around 2-3% of the population.

What therapies are currently available to treat SMA?

Until very recently, treatment of SMA was limited to supportive measures to prolong patient survival that had little positive impact on their quality of life. SMA was, therefore, considered an incurable and, in the case of SMA1 and SMA2, extremely serious condition. In recent years, various promising treatment approaches have been developed and approved, and these can be prescribed in Italy. Currently available scientific data show a clear improvement in treated patients, although therapies are not to be considered completely curative. However, it is now clear that the earlier treatment is started, the greater the recovery of muscle strength. It is, therefore, extremely important that SMA be diagnosed as soon as possible in order to reverse muscle weakness and improve patient quality of life. Some preliminary data indicate that if patients with a probable diagnosis of the more severe forms of SMA (types 1 or 2) receive treatment before any symptoms appear, their motor development almost matches that of children who are not affected by the disease.

INFORMED CONSENT FORM: NEWBORN SCREENING FOR SPINAL MUSCULAR ATROPHY

I / We, the undersigned,

as parent(s) / legal guardian(s) of the child _____

born _____ in _____

having read the relative information document, give my / our consent for my / our child to participate in the Newborn Screening Programme for **Spinal Muscular Atrophy** using the card already received for the compulsory Newborn Screening Programme and the compulsory Extended Newborn Screening Programme according to the information received.

I / We also declare that:

- I / we have had time to consider what the decision to allow my / our child to participate in the Newborn Screening Programme for Spinal Muscular Atrophy involves;
- I / we have received a copy of the Informed Consent Form;
- I / we give my / our consent to my / our child taking part in the Newborn Screening Programme for Spinal Muscular Atrophy:

Yes No

- I / we wish to be informed of the results of the analyses carried out for my / our child should these be clinically relevant:

Yes No

- I / we give our consent to my / our family doctor / pediatrician being informed of the

participation of my / our child in this Newborn Screening Programme and being provided with the results of the same should they be clinically relevant:

Yes No

- I / we request that the sample be stored under an anonymized identification code for any epidemiological analyses and/or research on the pathologies covered by the Newborn Screening Programme or on other pathologies destined to become part of the programme in the future;

Yes No

- Finally, I / we undertake to inform you immediately of any change in my / our decision relating to the declarations made above.

Name(s) of parent(s) (CAPITAL LETTERS): _____

Signature of parent 1: _____ Date: _____

Signature of parent 2: _____ Date: _____

Name of legal guardian (if applicable) (CAPITAL LETTERS): _____

Signature of legal guardian: _____ Date: _____

Name of witness (should the participant / parent / guardian be unable to sign in person)

(CAPITAL LETTERS): _____

Signature of witness: _____ Date: _____

Name of doctor responsible for the Informed Consent Agreement (CAPITAL LETTERS):

_____ Date: _____