Taipei Institute of Pathology

Optional Neonatal Screening Programs Informed Consent Form

Dear Parents,

To detect, diagnose and intervene potential metabolic disorders early and to minimize the damages to your baby's physical and intelligent status caused by these disorders, the Health Promotion Administration currently specifies a neonatal screening program for 21 specific genetic disorders. The complete diagnosis and treatment process has been established, and part of the laboratory expenses (NTD$200) will be covered by the Health and Welfare Surcharge of Tobacco Products. For details, please refer to the "Screening of Neonatal congenital metabolic dysfunction diseases" in the "Children's Health Booklet."

Moreover, the screening center provides other optional screening items at your own expenses. We hereby invite you to participate and request for your consent to accept the following tests for your babies. For the detailed introductions about the disorders and the instructions of the tests, please refer to the education flyer.

These tests will not only increase the blood sample collection volume of your baby, but also help you discover the proper treatment if necessary. Through neonatal screening, early detection, early diagnosis and early intervention, the potential damages to the infants caused by these disorders could be minimized. The test results will be helpful as reference information for your future child-bearing and genetic counseling. The Ministry of Health and Welfare may decide whether or not to include these screening items as routine examinations in the future based on the test results.

Because the number of screening items have increased, the frequency of your baby's return for follow-ups has also increased. For highly suspicious cases, we will make definitive diagnoses and record them in the medical records in accordance with the regulations for the neonatal screening program – referral system. In this case, your baby's rights to take private insurance may be influenced. However, without your permission, your baby's samples collected during neonatal screening program will not be used for other purposes.

1. **Lysosomal Storage Disease (LSD):**

   LSD is composed of Pompe Disease, Fabry disease, Gaucher's disease ,Mucopolysaccharidoses (MPS) type 1 ,2 ,4A and 6 and CLN2 which can be detected using the related enzyme screening (for details, please refer to the education flyer). Currently, enzyme replacement therapy, a genetic engineering technology to produce enzymes that cannot be generated by the patients *in vivo*, is available for LSD treatment after early diagnosis. In addition, female carriers of Fabry disease are also symptomatic. *MPS 4A, MPS6 and CLN2 are new free pilot study for LSD screening since August 2020.

2. **Severe Combined Immunodeficiency (SCID):**

   SCID is a cellular immunity plus humoral immunity deficiency disease caused by T-lymphocyte dysfunctions. Patients with SCID usually fail to fight against viral and bacterial infections. The screening of SCID offers an opportunity of early diagnosis and early intervention for your baby. If you intend to allow your baby to receive such a test, please read the education flyer for SCID carefully to understand the purposes, methods and the importance of the disorder. Moreover, you should pay attention to the following terms:

   - The inoculation of Bacillus Calmette-Guérin (BCG) vaccine (a live attenuated vaccine) for infants with SCID may cause (BCG-induced) tubercle bacillus infection, and thus lead to sequelae or death. The incidence of SCID is at 1.4/100,000. For those neonates receiving SCID screening, it is recommended to receive the BCG vaccine after the test results are confirmed to be SCID-negative. According to the Centers for Disease Control, the recommended BCG vaccination should be scheduled at the age of 5 months of the neonate (the recommended vaccination period is between the

age 5-8 months).

- Currently, the probability of tubercle bacillus infection is 1-2/100,000. If a person without BCG vaccination is infected with the tubercle bacillus, the risks of tubercolous meningitis, sequelae and death are 40 times of those with BCG vaccination. Therefore, prior to the BCG vaccination, please prevent your baby from coming in contact with patients with tuberculosis if possible (*e.g.* prevent coughing relatives or friends from visiting or caring your baby, etc.).

3. Biotinidase Deficiency (BD):

The disorder can be classified as a profound deficiency or partial deficiency depending on the severity of the clinical presentations. Some clinical symptoms are irreversible, but some may be cured or prevented through oral intake of biotin. For detailed symptoms, please refer to the education flyer.

4. Adrenoleukodystrophy (ALD):

ALD is a genetic mutation disorder that results in the great amount accumulation of very long chain fatty acids (VLCFA) in the brain white matter and the adrenal cortex. The pathogenic gene of ALD is located in X chromosomes. The clinical presentations may vary due to different ages of onset. In addition to Lorenzo's Oil, bone marrow transplantation and gene therapy are also available at present (for details, please refer to the education flyer).

5. Spinal Muscular Atrophy (SMA):

SMA is an autosomal recessive inheritance disorder caused by genetic defects in SMN1 genes, it results in the degeneration of motor neurons in the anterior horn of the spinal cord, and thus leads to muscle weakness and atrophy. The incidence is estimated at 1/10,000. For the most severe sub-type, SMA1, the clinical manifestations are developed within 6 months after birth, including weak crying, weak milk sucking ability, difficulties in breathing and swallowing, four limbs and trunk severe weakness or floppiness. Most of the babies will die of respiratory failure before they reach 2 years old. The age of onset of SMA2 or SMA3 is in the infanthood or childhood, respectively. Currently, the treatment for SMA in clinical practice is mainly based on supportive therapies to ameliorate the occurrence of complications. By 2015/12/16, a total of 18 medications have been in the developmental pipelines for SMA treatment in the world, of which 7 medications are under clinical trial investigations. Through combined medical care, including the neonatal screening program and early diagnosis of SMA, the mortality rate as well as the morbidity rate of SMA can be significantly reduced.

Not all parents have received gene carrier tests at present. Therefore, a comprehensive neonatal screening program is helpful to achieve the early detection and early diagnosis, so the medical team can provide integrative care to the indicator earlier. This study aims to investigate whether or not the SMN1 copies in the neonatal screening program are helpful in detecting neonates with SMA earlier, and thus provide the proper clinical care to the patient through early diagnosis. Unfortunately, if your baby is confirmed to be a patient with SMA, your baby’s rights to take private insurance could be influenced. Ninety-five percent of SMA patients can be detected through this test. However, the test cannot detect the condition in approximately 5% of patients who have normal SMN1 copies but abnormal SMN1 functions. In addition, the clinical presentations may be milder in the patients with several copies of SMN2 genes. Only long-term follow-ups are capable of detecting the onset of SMA as early as possible.

For detailed symptoms, please refer to the education flyer.

6. Duchenne muscular dystrophy (DMD):

Duchenne muscular dystrophy (DMD) is an X-linked rare disease. DMD occurs as a result of mutations in the dystrophin gene. It leads to an absence of or defects in the protein dystrophin and is

manifested by progressive muscle degradation.

Typically the disorder is diagnosed only around 4-5 years of age. Duchenne patients are often wheelchair bound between the ages of seven and 13 years old. Eventually, increasing difficulty in breathing due to respiratory muscle dysfunction requires ventilation support, and cardiac dysfunction can lead to heart failure. The condition is universally fatal, and without intervention the mean age at death is around 19 years.

Although DMD is an X-linked recessive disease and females are typically asymptomatic carriers of mutations, some female carriers may manifest symptoms varying from mild muscle weakness to a more severe clinical course and are classified as manifesting or symptomatic carriers. The manifesting phenotype is based on inactivation of the normal X chromosome or on translocation between X chromosome and an autosome. Female carriers having elevated CK-MM concentrations due to muscle degeneration at birth may result as screen positive (depending on the cut-off used) in newborn screening for DMD. The incidence of DMD is 1 in 3000-6000 live male births worldwide.

Although no cure exists for the progressive muscle weakness of DMD, corticosteroid treatment improves muscle strength and function, and in combination with supportive medical care is associated with delayed loss of ambulation and markedly improved survival. In addition, novel molecular therapies are under development and therefore interest towards newborn screening is increasing.

For detailed symptoms, please refer to the education flyer.

If you agree to participate in this screening program, we will use your baby's blood sample originally collected for neonatal screening for this test. No additional sample collection or charges are needed. The abnormal test results are estimated to be one in 10,000 neonates. The infant with abnormal findings will be asked to return to the hospital for a definitive diagnosis. If the diagnosis is confirmed, the parents should consider allowing their babies to receive long-term follow-ups and initiate the related clinical assessments as early as possible for proper clinical interventions with the best timing.

If no abnormal neonatal screening findings are found, this does not indicate 100% negative results. The consultation with the pediatrician is still required if your baby displays any discomfort. If the values in the screening results are within high-normal range, you will be asked to bring your baby back for a re-test. This does not indicate that your baby is suffering from such disorder. For the most part, the high-normal value suggests a premature blood sample collection time or insufficient blood volume. All you have to do is to return to the hospital for the re-check of your baby. For details, please refer to the education flyer. If you are willing to participate in the screening program, please sign the following consent form and return the consent form to the nurse or pediatrician who is responsible for your baby's care.

The Taipei Institute of Pathology Website: http://www.tipn.org.tw TEL: (02) 85962065
(02)85962050 ext. 401-403

Taipei Institute of Pathology 台北病理中心

The Neonatal Screening Room Cares about Your Baby's Health

TEL: (02)85962050 ext. 401-403 Direct line: (02) 85962065
Website: https://www.tipn.org.tw (This slip is retained by the legal representative)

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Taipei Institute of Pathology

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Declaration of the legal representative:

I have read the associated information regarding the Neonatal Screening Pilot-Study Program carefully, and I have understood the objectives and methods of the program and the importance of the disease. All queries had been explained fully by the medical staff and thus, I have understood the above contents completely. I am selecting the following screening programs on my own free will:

☐Agree ☐Disagree to accept the optional screening for LSD (8 diseases)
☐Agree ☐Disagree to accept the optional screening for SCID
☐Agree ☐Disagree to accept the optional screening for BD
☐Agree ☐Disagree to accept the optional screening for ALD
☐Agree ☐Disagree to accept the optional screening for SMA
☐Agree ☐Disagree to accept the optional screening for DMD

Legal representative: (Signature) ID No. (ARC No.):

Please leave the correct corresponding phone number: __-_____ Cell Phone: _____

Date: yyyy mm dd This slip is retained by the delivery hospital.