# SUPPLEMENTAL DATA

## METHODS

Blood card samples were obtained at 36-72 hours of age. DNA was extracted and initially screened for the three most common German *CTNS* mutations as described (Fleige et al., submitted). All samples heterozygous for a *CTNS* mutation were submitted to next-generation sequencing of the *CTNS* exons for the 101 known, clinically relevant mutations as described (Fleige et al., submitted). In patients identified as having a homozygous or compound heterozygous mutation in the *CTNS* gene, the diagnosis was confirmed by determination of the leucocyte cystine level from 10 ml of EDTA blood within the first 14 days of life in a Metabolic Laboratory in Muenster. Mutation screening for SMA was previously described [1].

## FORMS

### Form 1: Parental information sheet

**Enclosure to the parent information of the regular Newborn Screening in Bavaria:**

**Pilot-Project for a Newborn-Screening for**
**Cystinosis and Spinal Muscular Dystrophy ***

In the course of a Pilot Project* parents have the opportunity to request a genetic screening free of charge on two additional severe rare diseases using the blood-probe of the regular newborn screening.

While the newborns seem healthy after birth the respective diseases can be diagnosed by means of molecular genetic investigations early on to start immediate medication in order to prevent progress of the disease.

In case you request the respective investigation(s) please fill in and sign the Declaration on Consent attached.

#### Description of the diseases:

##### Cystinosis

Frequency: ~ 1:100 000 to 1:200 000
Storage disease of the amino acid cystine.
Without treatment the disease results first of all in loss of appetite, vomiting and malnutrition and growth retardation followed by loss of kidney function with the need of kidney transplantation. Only early onset of medical treatment is able to prevent the course of disease.

##### Spinal Muscular Atrophy (SMA)

Frequency: ~1:10 000
Rapidly progressing degenerative of neurons in the spinal cord. Untreated the disease leads to increasing muscle weakness, muscle paralysis and often to difficulty in breathing/ impaired respiratory function. Severe manifestations of the disease take a lethal course within the first two years. Early onset of medical treatment is able to ease the course of the disease.

**Comment:**
The blood test and the respective data management are described in the Parent Information sheet (page 1 and page 3-5). Consent or revocation of the screening is only feasible for both diseases at a time. Data submission of the pilot project to the screening Center is done in accordance with your written consent of the newborns screening on congenital metabolic, hormonal diseases and Cystic Fibrosis.

*** Pilot project Information:**
The pilot project aims to evaluate whether it can be recommended to include the genetic screening for Cystinosis and Spinal Muscular Atrophy into the national wide performed newborn screening. The overall responsibility for the pilot project lies within the Cystinosis Foundation, located in Munich. The project was founded by the Cystinosis Foundation, as well as from the Dietmar Hopp Stiftung gGmbH, der Herzenssache e.V., den Sternstunden e.V. and the American Patient Support Group (CRF).

## Form 2: Consent

### Pilot project for a Genetic Screening on Cystinosis and Spinal Muscle Atrophy in Newborn

# Declaration on Consent

Name of child: _____

Name of mother: _____

Address: _____

**Phone number:** _____

We have been informed about the screening on Cystinosis and Spinal muscle Atrophy in Newborn. We also have been informed about the generation, evaluation and use of personal data and results and our right of refusal revocation.
We herewith agree to the implementation of the investigation(s) as well as to the submission of data to the screening center in charge until the results have been confirmed in accordance with our Declaration of Consent.
We herewith agree that in case of results requiring further clarification our contact data shall be submitted to a pediatric specialist and was hall be informed by him directly.

_____

Address, date — Signature of person having custody

_____

Address, date — Signature of physician in charge

Contact address: Laboratory Becker & Colleagues, phone: 089/544 654-0 or e-mail: kontakt@labor-becker.de

## TABLES

**Table S1. Principles proposed by Wilson and Jungner (1968) for the early detection of disease.**

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| 1. The condition sought should be an important health problem. |
| 2. There should be an accepted treatment for patients with recognized disease. |
| 3. Facilities for diagnosis and treatment should be available |
| 4. There should be a recognizable latent or early symptomatic stage |
| 5. There should be a suitable test or examination |
| 6. The test should be acceptable to the population. |
| 7. The natural history of the condition, including development from latent to declared disease, should be adequately understood. |
| 8. There should be an agreed policy on whom to treat as patients. |
| 9. The cost of case finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole |
| 10. Case finding should be a continuing process and not a "once and for all" project. |

## REFERENCE

[1] Czibere L, Burggraf S, Fleige T et al. High-throughput genetic newborn screening for spinal muscular atrophy by rapid nucleic acid extraction from dried blood spots and 384-well qPCR.Eur J Hum Genet 2019; Jul 30 (Epub ahead of print)