Genomic Screening of Newborns for Rare Congenital Disorders (Genomic Newborn Screening, gNBS)

The vision for gNBS was developed by the eight "Functies Zeldzame Ziekten" - "Fonctions Maladies Rares", the eight Centers for Human Genetics and the five Newborn Screening Centers, after a national consensus meeting on 8 January 2026.

Preamble

When introducing genomic analysis as part of neonatal screening, attention should not only focus on the list of genes and conditions but, more importantly, on the broader framework in which genomic newborn screening (gNBS) can be offered. gNBS should not be regarded as an isolated technological innovation but must be explicitly embedded within a coherent vision of genetic and genomic care throughout the entire life cycle. This vision should clearly define the role of prevention, preconception care, and prenatal diagnostics.

We aim to align with the global trend toward genomic screening at birth, while steering actions toward a carefully designed project for responsible implementation within public healthcare. A phased, nationally coordinated approach is necessary, in which gNBS is evaluated as part of a comprehensive pre-implementation project before structural implementation.

It is crucial that gNBS is societally supported. Implementation must be carefully considered to avoid a decline in participation rates for neonatal screening. It is essential to maintain trust among parents and society by communicating transparently about uncertainties, variable expressivity, incomplete penetrance, the probabilistic nature of genetic information and the limitations of any public health screening programme.

Readiness vs. Preparedness

1. Genomic analysis is a logical evolution in the context of neonatal screening. There are over 30 programs around the world, and there is no doubt that it is the future of NBS. The drivers are the desire to detect more conditions at birth and linked to this, the development of new therapies that make a significant difference for patients and their families when detected early. This approach is enabled by the availability of high-capacity DNA sequencing devices and increasingly sophisticated bioinformatics tools for interpreting genetic information.
2. The public health system is not ready to transition quickly to gNBS: a clear plan for potential implementation is needed, paying attention to the needs of future parents and healthcare providers. In addition, preventive strategies before birth, which are also part of the potential of genomic medicine, must be explicitly and structurally incorporated into the policy debate.

Gene List and Interpretation

3. It is important to create a national framework for compiling a list of screened conditions—and corresponding genes—and to update it regularly. The focus is on severe, treatable conditions (with an 'early onset,' meaning requiring early treatment), possibly supplemented with conditions that may manifest during childhood and for which increased vigilance can

reduce morbidity and mortality (‘actionable’). Gene list should be revised on a regular basis as flexibility is a major advantage of gNBS.

4. A thoughtful approach is proposed for interpreting genetic results to reduce false positive cases as much as possible. There are both scientific and technical limitations in interpreting genomic data. To avoid unnecessary anxiety and preventable follow-up, variable expression, reduced penetrance and genotype-phenotype correlations must be explicitly considered when selecting and interpreting results.
5. Emphasis should be placed on ensuring that all stakeholders clearly understand that gNBS is a screening tool, not a diagnostic test. The goal is not to identify all possible conditions, and a negative result does not exclude the presence of an early-onset disorder. Consequently, false negative results are an inherent and acceptable limitation of the screening approach.
6. No re-analysis will be performed on previous data, whether new genes or conditions are added to the list or not, nor to reclassify defects or at parents' requests.

Medical-Organizational Criteria

7. Clear guidelines must be established on who will contact and counsel parents before and after screening, and how follow-up should be organized for different conditions.
8. Access to corresponding treatments (for ‘treatable’ conditions) and tailored management and surveillance (for ‘actionable’ conditions) must be guaranteed.
9. Investment is needed in staff and facilities for counselling and genetic advice before and after sample collection.

Information and Consent as a Cornerstone

10. Large-scale and sustainable information campaigns on rare diseases and genetics for future parents, healthcare providers, and the public should be launched well before gNBS implementation. This communication should not be limited to gNBS. The distinction between screening and diagnostics, as well as the broader range of preventive services available before and during pregnancy, should be explicitly explained. Information must be centrally available for different target groups, and knowledge levels within these groups should be assessed.
11. Agreements must be made regarding the consent procedure.

gNBS as a Complement to NBS

12. Attention must remain on significantly expanding current neonatal screening: there is no reason to wait for gNBS implementation before adding new conditions that can be detected through biochemical or targeted genetic analyses.
13. It is necessary to examine which of the current population screening criteria may be difficult or only partially met with gNBS implementation, and whether criteria should be adapted or added so that gNBS can comply in the future.
14. gNBS will not replace biochemical screening; on the contrary, investment is needed in detecting more biological markers that can provide early indications of abnormalities and in functional tests to confirm the pathogenic nature of identified genetic variants. Bidirectional

data exchange must be established between genomic screening data and data obtained through conventional newborn screening methods, including biochemical and targeted genetic analyses, before classification of the screening as positive (and recall) or negative.

15. Leveraging conventional newborn screening centres is essential, as they already possess extensive expertise in population-based logistics, data management, and follow-up of positive screening cases. Ensuring strong complementarity between standard newborn screening and gNBS will be critical to achieving a sustainable and integrated screening model.

Data Storage and (Re)Use

16. For the newborn, only the genes and conditions included in the consensus list will be checked, but the question remains: will genomic information be stored or deleted, and will results be archived or destroyed?
17. It is important to clarify the legal and ethical context and adjust it if necessary.
    - Who owns the data?
    - Can parents request the data?
    - Will any information that could impact parental health be disclosed?
    - Can the child request the data at a later age?
    - What about non-reporting of certain findings?
    - What is the retention period for samples and raw genomic data?
    - Is the data destroyed, stored for a limited period, or retained long term?
    - Is secondary use for research permitted, and if so, under what conditions?

    The answers to these questions must be clearly and transparently established before implementation.
18. Consideration should be given to what structures need to be established for data management. In the context of a national plan for genomic medicine and gNBS, the creation of a national platform for genomic data sharing and variant interpretation while preserving patient privacy should be evaluated. This point should be discussed extensively with all stakeholders.

Broader Framework and Pre-Implementation Project

19. gNBS should fit within a much broader policy plan on genomic medicine. This includes rapid pre- and postnatal genomic diagnostics, use of individual genetic data for prevention, expansion of early detection of cancer and neurodegenerative diseases, solutions for genomic data storage, etc.
20. The implementation of genomic newborn screening cannot rely solely on a theoretical framework or small-scale pilot projects. A national project must be funded to test all the above aspects of genome-base screening and align gNBS implementation with Belgian healthcare systems.