5 how are diseases added to NBS panels in the United States, in the United Kingdom, and in select EU countries?

> **Advocates should always be proactive, anticipate someone's questions, and leave the door open for someone to get back to you when they're ready to learn more.**

–Bob Wyborn
ADVOCATE IN AUSTRALIA

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The following information provides a brief overview of how conditions such as adrenoleukodystrophy (ALD) are added to newborn screening (NBS) panels in the United States, the United Kingdom, and in some European countries. Using the identified countries as examples, **the goal of this section is to give you a basic understanding of the required steps to add new diseases to a country's NBS panels and to obtain the necessary resources to finance implementation of the screening.** Once you have this understanding, you can start thinking about how to direct your advocacy efforts to advance ALD screening in your country or region.

This section may feel more technical and process-oriented than other components of this tool kit, mainly due to the need to refer to country-specific laws and regulations, but it includes relevant information for you to advocate more effectively. Each country-specific one-pager is divided into 3 areas of focus:

1. who are the **key stakeholders** that you will need to convince and who are the very final decision-makers that determine and decide whether to add a new disease to an NBS panel and to appropriate the specific expense for screening implementation
2. what is the **official process** and what are the required steps outlined in laws and regulations that will have to happen for authorities to effectively start screening for new diseases and for your goal to be considered and implemented;
3. what are the **criteria and evidence** that you will need to prove and present to have your request approved and to obtain a positive outcome

All this information can be a resource for you as you prepare for your engagements and give you a better overview of the data you might need to advocate effectively while navigating legal frameworks and conversing with stakeholders.

Don't forget, patient advocacy organizations can offer support as you begin your advocacy efforts in your specific state or country. Consider contacting an advocacy organization in your area. A list of resources including patient advocacy organizations can be found in section 7.

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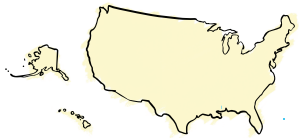

The United States

Key stakeholders

In the United States, newborn screening (NBS) programs are managed at a state level. **Key stakeholders include the state's Department of Public Health, the NBS advisory committee (if the state has one), and any institutional review boards that may be involved in deciding which diseases might be added to their NBS panel.** There are additional federal agencies and programs that help states to implement and expand NBS programs.

- The Centers for Disease Control and Prevention (CDC) helps to ensure the quality and accuracy of NBS tests
- The US National Institutes of Health (NIH) invests in the identification, diagnosis, and treatment of conditions that could be appropriate for NBS
- The Health Resources and Services Administration disburses Title V Maternal and Child Health Services Block Grants, which provide funding for screening, treatment, and follow-up care

Despite federal contributions, states finance their NBS operations by appropriating state funding and often by charging fees to state programs and/or commercial health insurers to cover the laboratory costs associated with NBS.

The official process

The process for getting a disorder included on a state's NBS program in the United States usually begins with an application to the federal **Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC).** This committee bases its decision on several factors, such as:

- The condition being nominated
- Evidence that supports the potential net benefit of screening
- Availability of effective treatments
- Ability of NBS programs to check for the condition

If the committee deems these conditions to be met, it can make a recommendation to the Department of Health and Human Services (HHS) to add the considered disorder to the list that makes up the Recommended Uniform Screening Panel.

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Criteria and evidence

To qualify for the Recommended Uniform Screening Panel (RUSP), the disease or condition must meet 3 criteria:

- Condition can be identified 24–48 hours after birth (before clinical symptoms are present)
- A specific and reasonable test is available for it
- There are measurable benefits for early detection, intervention, and treatment of the disease

Unfortunately, not all states are required to screen for all of the diseases included on the RUSP. Newborn screening (NBS) programs in the United States vary between states due to several factors, including:

- Laws of the state
- Financial costs of screening and funding sources
- Risk and frequency of the condition in the state
- Availability of treatments and follow-up for each condition

In some states, the state law requires that the state's NBS program align with the RUSP within a certain time period after the addition of a new disease. In others, final decisions as to which conditions are coded on each state's panel are made by the state's public health department or advisory panel.

At that point, disease advocacy organizations, affected families, physicians, and biopharmaceutical companies are able to lobby each state individually to include the diseases in their state panel and to appropriate funding for screening implementation. To accelerate this process, there are a variety of steps individuals and advocacy groups can take:

Thanks to the efforts of advocates across the country, on February 16, 2016, adrenoleukodystrophy was added to the RUSP, the federal list of genetic diseases recommended for state NBS programs.

ORGANIZE

Establishing a larger organization of local groups can help raise awareness among the public as well as in the state legislature, especially if there is no presence at the national level.

PETITION

Address the ACHDNC directly. Even if they reject a new test, going through the process can raise awareness and deliver valuable support for future inclusion.

FUNDRAISE

Identify sources that are available, both federal and commercial. Getting funding from patient advocacy groups, drug companies, and governmental agencies for test development can speed the adoption of new tests while streamlining the process

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United Kingdom

Key stakeholders

In the UK, **policy recommendations on screening programs are made on a countrywide level by the UK National Screening Committee (NSC).** The UK NSC was established to move screening policy away from a localized approach, with the aim to have all of the devolved constituent countries (Scotland, Wales, England, and Northern Ireland) follow the UK NSC's advice. The UK NSC meets privately 3 times a year, and its members include individuals with several different areas of expertise, such as health economics, pediatrics, laboratory services, and epidemiology, with cancer and public health being the most represented areas of expertise. The UK NSC does not involve rare disease patients in their work or review process; stakeholders may, however, be included in the evidence review process of an application by providing comments to the final review reports.

The official process

In the UK, the process to add a disease to the newborn screening (NBS) panel could either be **automatic**, ie, prompted by a regular review of current recommendations by the UK NSC committee itself, or through the **submission of a proposal** either to:

1. suggest a modification to an existing screening program
2. request an early update for a topic
3. propose a new topic that has not been previously reviewed by the UK NSC

The UK NSC conducts an annual call for new topics, starting in the first week of September and lasting for 3 months. Any individual or organization can submit a topic for consideration as long as they meet the UK NSC's application requirements. Indeed, each proposal will need to be submitted using the templated submission form to be found within the UK NSC website.

Using the submission form, the applicant will need to **explain** why the topic is within the remit of the UK NSC, **summarize and provide necessary justifications** as to why the criteria for adding a disease to the panel have been met, and also **provide up to 10 references** to support the application. All provided information should be based on referenced evidence published in peer-reviewed journals and be, ultimately, aimed at demonstrating that if a baby should be diagnosed with a condition through the NBS program, it would be able to access an effective intervention, be able to largely prevent or avoid the harm of the condition, with clear and extensive evidence that intervention at a presymptomatic phase would lead to better outcomes for the screened individual compared with usual care.

Criteria and evidence

The UK NSC criteria for appraising the viability, effectiveness, and appropriateness of a screening program are based on the criteria developed by **Wilson and Jungner** in the mid-1960s and relate to the **condition**, the **test**, the **treatment**, the **screening program**, and relevant implementation criteria.

The UK NSC will review the submitted application using an evidence review process. In particular, UK NSC will only consider evidence published in peer-reviewed journals and mostly, if not exclusively, literature or papers referencing UK-specific data. So far, only three types of evidence have been regarded as sufficiently strong to use as the basis for making recommendations: systematic reviews, randomized controlled trials, and population-based studies.

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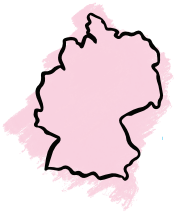

Germany

Key stakeholders

The decision to include a new disease in the newborn screening (NBS) program and into the reimbursement catalogue of the statutory health insurances lies with the **Federal Joint Committee (G-BA), the Institute for Quality and Efficiency in Health Care (IQWIG)**, and, ultimately, with the **Ministry of Health**. The official process starts with a **member of the G-BA plenary petitioning** for the assessment of a new "screening" method. The G-BA plenary comprises 13 members, from statutory health insurers and healthcare providers to impartial participants. In particular, except for the impartial participants, the members of the G-BA plenary are part of the following organizations: the Umbrella Organization of Statutory Health Insurers (**GKV-Spitzenverband**), the Association of Statutory Health Insurance Physicians (**Kassenärztliche Bundesvereinigung**, KBV), the Association of Statutory Health Insurance Dentists (**Kassenzahnärztliche Bundesvereinigung**, KZBV), and the German Hospital Association (**Deutsche Krankenhausgesellschaft**, DKG). Patient advocacy organizations are nonvoting members and only have the right to petition and co-consultation.

The official process

Contrary to what other countries do with respect to extension of the NBS programs, the G-BA does not assess a disease to be included in the screening catalogue, but considers a new screening as **a new "method" or "examination."** In particular, in accordance with §135 of the 5th Book of the German Social Code (SGB V), the G-BA is mandated to assess the **therapeutic benefit, medical necessity, and cost effectiveness** of new examinations and/or treatment methods. Based on the result of this review, the G-BA decides whether a new examination for the early detection of illnesses should be eligible for reimbursement by the statutory health insurance. Considering that the official process starts with a petition from G-BA, it needs to be stressed that patient advocacy groups and healthcare providers may suggest to the G-BA a disease for inclusion in the NBS catalogue by **submitting a proposal.**

After an initial consultation, the G-BA mandates the **IQWIG to conduct an assessment**, which, apart from the relevant scientific and economic analysis, will also include input from several stakeholder groups, including the commission for gene diagnostics at the Robert-Koch-Institute. Indeed, medical societies and patient advocacy groups may provide their own opinion by completing a **questionnaire**, which will be taken into account by the IQWIG when it drafts its final assessment report. Based on the final IQWIG report, the G-BA will hold an expert hearing and could recommend the reimbursement of the screening procedure by the federal health insurances. Unless the Minister of Health objects to the G-BA's recommendation, the recommendation enters into force 1 day after the Ministry's publication in the Federal Gazette.

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France

Key stakeholders

As a result of the administration's endorsement of a public action on newborn screening (NBS), starting in 2018, the French NBS program was completely reorganized. As part of this new organization, the Minister of Health announced the establishment of a **National Steering Committee, chaired by the Director General of Health**, whose role would include "to propose to the Minister of Health any change in the list of detected diseases." The National Steering Committee would include representatives from the following agencies: the Directorate General of Health (DGS), the Directorate General for the Provision of Care (DGOS), the Superior Health Authority (HAS), the Agency for Biomedicine (ABM), the National Agency for the Security of Medicines and Health Products (ANSM), the National Agency for Public Health (ANSP), ARS, CNAMTS, CCNE, CRDN, SFSP, the French Pediatric Society (SFP), and the French NBS Society (SFDN).

The official process

The current process to add a disease to the NBS panel requires that the National Steering Committee propose modifications of the list of diseases **directly to the Minister of Health, who will change the list of diseases by issuing a binding order, an "arrêté."**

It is important to highlight that the National Screening Committee's proposal shall be made only after the occurrence of a **mandatory screening assessment by HAS**, with the collaboration of the ABM if required.

Several questions, however, remain unanswered. Who triggers the HAS assessment? What is the division of roles among the HAS, the ABM, and the National Screening Committee? What is the timeline of the procedure and the information required?

The HAS previously affirmed that it will assess the value of including approximately 30 diseases, as it is assessing the feasibility of extending the NBS panel to metabolic diseases using the mass tandem spectrometry technique.

Considering the multitude of organizations represented within the National Screening Committee and the fact that the proposal will need to come from the Committee itself, it is clear that patient associations and/or scientific societies will be critical for raising awareness and highlighting community and scientific consensus regarding the importance to add a specific disease to the NBS program.

Criteria and evidence

The criteria that are considered for the French NBS Program are those that lay the foundation for the majority of NBS programs. Indeed, according to the **Wilson-Jungner criteria**, the disease must be **serious**, have an **effective treatment**, and be detectable at a presymptomatic stage via a **simple, reproducible, and reliable test**. Notwithstanding, there is still a need to obtain clarity on the specific criteria utilized by the HAS in its preliminary assessment and by the National Steering Committee in deciding whether to submit a proposal.

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Italy

Key stakeholders

The National Agency for Regional Health Services **(AGENAS)**, the Higher Health Institute "**Istituto Superiore di Sanità (ISS)**," the newborn screening (NBS) Center of Coordination established within the ISS "**Centro di coordinamento per lo screening neonatale presso l'Istituto Superiore di Sanità**," the sector-specific **scientific societies**, and the **Ministry of Health** will all play a role in adding a new disease to the Italian NBS panel. The need for overall scientific and political consensus is therefore specifically important in Italy considering how the Ministry of Health will need to collaborate and consult with several institutions before the final decision is made to add a disease to the national NBS panel.

The official process

The official decision-making process to add a disease onto the Italian NBS panel is detailed in the Italian NBS legislation, also called "**Taverna law**" (L.167/2016), as recently amended by the 2018 budget law.

The process requires the Ministry of Health, in collaboration with the ISS, AGENAS, the regions, and the autonomous provinces of Trento and Bolzano **to review the current list** of screened pathologies **every 2 years** on the **basis of ongoing progress of scientific evidence** in the relevant diagnostic and therapeutic fields for hereditary genetic diseases. The Ministry's decision will also depend on **mandatory consultations** with relevant scientific societies, and, based on a systematic interpretation of the law, on the results **of health technology assessment evaluation** to be carried out by AGENAS.

Even if the decision-making process has been recently detailed in legislation, some doubts remain with respect to the relevant "application" process. The Ministry may update the list of screening pathologies based on informal requests coming from patient associations and/or scientific societies and brought forward by the NBS Center of Coordination.

Criteria and evidence

In order to be potentially successful, all relevant requests should be able to demonstrate the fulfillment of the following criteria: (i) **severity of the illness**, (ii) existence of an **efficient laboratory test** selected on the grounds of its diagnostic accuracy in differentiating potentially affected subjects from the normal population, and (iii) availability of an **effective treatment** able to substantially modify the natural history of the illness, if adopted early. These criteria have been used to compile the current list of approximately 45 diseases that are included into the extended NBS program, together with (iv) the comparison with the recommendations provided within the "Guidelines for the extended neonatal screening and for diagnostical confirmation" published by the Italian NBS scientific society, and (v) comparison with international experiences.

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The Netherlands

Key stakeholders

The stakeholders who will ultimately make the decision of adding a new disease to the newborn screening (NBS) panel in the Netherlands are the **Health Council of the Netherlands (Gezondheidsraad)**, the **National Institute for Public Health and Environment (RIVM)**, and the **Minister of Health, Welfare, and Sports**. It is interesting to note that, in the Netherlands, public health falls within the responsibility of the State Secretary.

The official process

The process starts with an **advisement by the Health Council** of the Netherlands (Gezondheidsraad) to expand the NBS panel. The advice coming from the Health Council automatically prompts the National Institute for Public Health and Environment (RIVM) to start a so-called **feasibility study** to see whether the expansion of the NBS panel may be needed or is otherwise feasible.

Based on the results of the RIVM study, the Minister of Health makes a preliminary decision. The Minister may either **opt for a phased implementation** or directly **make a final decision**. As it relates to the phased implementation, it is usually based on phased pilot projects, including various validation tests managed by an academic research team. The phased implementation is supervised by the RIVM. Based on the results of the pilot, the minister will make a final decision on the addition of the disease to the NBS panel, including the timing of the addition.

Criteria and evidence

The Gezondheidsraad's advice and final recommendation to extend the NBS panel is based on the following 5 criteria: (i) **improved scientific knowledge**; (ii) the screening should be aimed at **preventing irreparable damage** to the child and/or achieving significant health benefits for the child; (iii) the screening should be able to permit the **shortening of the diagnostic process**; (iv) the screening should be aimed at **facilitating reproductive choices** for parents; and (v) the screening should help to **alleviate** the **burden** of disease in society.

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