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Drugs Health Technologies **Health Systems**

Policy Report

Toward a Future Pan-Canadian Coordinated Approach for Newborn Screening: A Report From the Advisory Panel

In Support of the National Strategy for Drugs for Rare Diseases
March 2025

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About the Advisory Panel Members

The advisory panel is composed of 2 co-chairs and 11 members who come from across Canada and represent dimensions of difference, including Indigenous Peoples and persons of various races, places of origin, religions, abilities, sexual orientations, and gender identities and expressions. The advisory panel brings together a range of expertise and experience, including health care providers (e.g., clinicians, program administrators, and researchers); persons with lived and living experience; and individuals with backgrounds in ethics, law, and/or health administration. The names, biographies, and conflict of interest declarations of the 13 members on the advisory panel are available on the Canada's Drug Agency website.

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Executive Summary

In March 2023, the Government of Canada announced investments to support the National Strategy for Drugs for Rare Diseases.[1] Canada's Drug Agency was asked to support key activities for this strategy under pillar 3 ("Collect and use evidence"), to help optimize access to drugs for rare diseases in Canada and to support decision-making.[2] As part of this work, Canada's Drug Agency convened an advisory panel to provide guidance on newborn screening to enhance the pan-Canadian coordination of newborn screening, including the consistency of conditions screened for in newborns across Canada.[3]

The Newborn Screening Advisory Panel comprised 2 co-chairs and 11 members with diverse expertise and perspectives from across Canada. The advisory panel built on prior Canadian newborn screening work and drew on their knowledge and experience to develop guidance and recommendations on key areas of newborn screening in Canada. This included a common set of guiding principles, exploring a potential process and criteria for adding conditions not currently screened or reassessing conditions that are already screened, and recommending a set of conditions for which newborn screening programs in Canada could screen.

The proposed guidance was publicly shared as a discussion paper for input.[4] The input was gathered through online consultations, focus group discussions, and key informant interviews, and subsequently reviewed by the advisory panel to further refine the proposed newborn screening guidance.

This final guidance provides recommendations on 7 topics related to newborn screening in Canada that are intended to consider short-term approaches to support existing programs, as well as the medium-term to longer-term developmental horizon for enhanced infrastructural opportunities for newborn screening. These topics are as follows:

- Guiding principles for newborn screening in Canada
  - The advisory panel recommends 6 guiding principles, which serve as a core set of values for the advisory panel's work and can guide future work related to newborn screening in Canada. The guiding principles are: the health rights of the newborn; equity; effectiveness, safety, and quality; transparency; collaboration; and sustainability. The advisory panel considered the health rights of the newborn to be an overarching principle.
- A future pan-Canadian newborn screening governance model
  - Newborn screening in Canada is within the scope of the provincial and territorial governments, as they provide health service delivery for their residents. As each province and territory governs over its own mandate, there is variation across jurisdictions in Canada in the governance of and use of advisory committees, the conditions screened and procedures to review them, the technologies used, legal frameworks and consent, and treatment and follow-up practices. Recognizing that some provinces and territories rely on the knowledge and infrastructure of other jurisdictions, including advisory committees that review and make decisions on adding or reassessing conditions, the advisory panel proposed an advisory coordinating body with 3 committees (a newborn screening advisory committee; an evidence review committee; and

a quality, standards, and education committee) as a governance structure to support a pan-Canadian approach for decision-makers in newborn screening. Having a centralized coordinating function for newborn screening guidance would enhance the standardization and uniformity of newborn screening policies, practices, and procedures across Canada and could improve equity in access and address differences in economies of scale among the jurisdictions.

- A need for processes for adding or reassessing conditions on the Recommended Pan-Canadian Newborn Screening List
  - Given the opportunities to enhance equitable access to newborn screening conditions in Canada, the advisory panel developed a high-level outline of a 4-step series of processes to inform the addition or reassessment of a condition to the Recommended Pan-Canadian Newborn Screening List to support better decision-making through standardization of review processes. The steps are: a process to nominate conditions for review; an evidence review process; a process to inform deliberation and the development of recommendations; and a process to inform communication and engagement with interested parties.
- Criteria for adding and reassessing conditions on the Recommended Pan-Canadian Newborn Screening List
  - The advisory panel developed the recommended criteria for adding a condition to the Recommended Pan-Canadian Newborn Screening List by modifying the Wilson and Jungner screening criteria[5] to adapt them to the newborn screening context in Canada. For reassessing a condition on the Recommended Pan-Canadian Newborn Screening List, the advisory panel modified the questions used by Australia's Newborn Bloodspot Screening Framework,[6] which covers similar domains to those in the Wilson and Jungner criteria.
- A recommended pan-Canadian list of conditions to screen for in newborns
  - The Recommended Pan-Canadian Newborn Screening List includes 25 conditions, and was built from the recommended list of conditions of a 2016 Intergovernmental Working Group.[7] The current list is intended to act as a foundation to foster discussion and decision-making leading to more consistent newborn screening across Canada. An additional 9 conditions were identified as requiring an evidence review to determine their eligibility for inclusion on the Recommended Pan-Canadian Newborn Screening List.
- Anticipating conditions that could be added to the Recommended Pan-Canadian Newborn Screening List in the future
  - With new and emerging health technologies, it becomes imperative to anticipate conditions that could become candidates for newborn screening. A list of potential candidate conditions to monitor was developed by the advisory panel through input from respondents who participated in engagement activities. Future work is required to develop a process for maintaining this emerging list.
- Other considerations for newborn screening at the pan-Canadian level

- During the development of this guidance, several topics were identified that bear on newborn screening in Canada and will require further exploration as part of future work. These additional considerations include: other types of newborn screening, including screening to identify potential conditions beyond the newborn stage; genomic sequencing; laboratory infrastructure; data sharing, privacy, and quality metrics; and educational materials.

The Advisory Panel's Recommendations

The advisory panel developed short-term (1 to 2 years) and medium-term to long-term (3 or more years) nonbinding recommendations to support the implementation of this guidance report. With the exception of the first 2 short-term recommendations, which were identified as a priority for implementation, the recommendations are not ranked.

Short-Term Recommendations (1 to 2 Years)

- Adopt the guiding principles to support a pan-Canadian approach to newborn screening in Canada.
- Develop and implement a pan-Canadian governance model for guidance for newborn screening by working with and building from existing organizations. This could be explored by piloting a secretariat support function for guidance for newborn screening programs across Canada by working in collaboration with a pan-Canadian health organization, such as Canada's Drug Agency, to evaluate and learn.
- Adopt the proposed criteria and processes for adding and reassessing a condition for the Recommended Pan-Canadian Newborn Screening List. This would include developing transparent deliberative processes to support recommendations for adding or reassessing a condition.
- Pilot the proposed processes for adding a condition by conducting an evidence review on a candidate condition and developing recommendations. This would provide learnings for coordination among interested parties and explore the development of a secretariat support function.
- Adopt the Recommended Pan-Canadian Newborn Screening List as a starting foundation to foster discussion and decision-making, leading to more consistent newborn screening across Canada.
- Leverage existing processes within pan-Canadian health organizational capacity to develop a process for horizon scanning to anticipate candidate conditions for newborn screening in Canada.
- Work with experts to develop pan-Canadian case definitions for primary newborn screening conditions to facilitate a common language and understanding across newborn screening programs.
- Explore and establish opportunities to engage with and educate the public about newborn screening, in collaboration with other organizations.
- Assess the need for and feasibility of a pan-Canadian data repository and a centralized resource and laboratory reference centre to provide Canadian-specific data and information to support newborn screening programs and laboratories.

Medium-Term to Long-Term Recommendations (3 Years or More)

- Further develop the proposed pan-Canadian newborn screening governance model to enhance coordination for newborn screening in Canada by establishing and convening expert committees, such as a newborn screening advisory committee; an expert review committee; and a quality, standards, and education committee.
- Establish and apply a nomination process for adding or reassessing conditions for the Recommended Pan-Canadian Newborn Screening List.

- Develop a process for reassessing conditions on the Recommended Pan-Canadian Newborn Screening List and prioritize conditions for reassessment.
- Evaluate and refine the criteria for adding and reassessing conditions on the pan-Canadian newborn screening list.
- Continue to build on the horizon scanning service to anticipate and expand the list of emerging conditions and technology trends in newborn screening, such as genomic sequencing.
- Establish the groundwork for a pan-Canadian data repository by convening interested parties and decision-makers to work toward purpose; participation; and data governance, protection, and sharing. These activities should be done in collaboration with national Indigenous health organizations and organizations representing underserved communities.

Setting the Context

Through its National Strategy for Drugs for Rare Diseases, the Government of Canada is supporting a range of activities to increase access to, and affordability of, promising and effective drugs for rare diseases. The national strategy aims to take action across 4 broad pillars, as follows:

1. to seek national consistency in coverage for drugs for rare diseases
2. to support patient outcomes and sustainability
3. to collect and use evidence
4. to invest in innovation.[2]

As part of this work, funding has been provided toward activities that support the advancement of screening and diagnosis of rare diseases.

The early identification of rare diseases through screening is an important means for enabling timely and appropriate access to treatments and interventions for patients. A key opportunity for early identification of rare diseases is through newborn screening. Newborn screening has existed across Canada since the 1960s, beginning with the screening for phenylketonuria.[8] As new conditions were identified and new therapies emerged, newborn screening programs across the provinces and territories expanded to include screening for additional diseases. With an estimated 60 new transformative cell and gene therapies anticipated over the next 10 years,[9] newborn screening is a critical component to support the early identification of rare disease in newborns[10] and facilitate access to timely and effective treatment.

Canada's Drug Agency is a leader in providing evidence-informed solutions, advice, and recommendations to best support health systems across Canada. It is supporting the National Strategy for Drugs for Rare Diseases through activities related to pillar 3 and is working to improve the collection and use of evidence to help optimize access to drugs for rare diseases in Canada. These activities include building on existing work and developing pan-Canadian guidance to support newborn screening programs, which play an important role in the early diagnosis of rare diseases.

Canada's Drug Agency convened an advisory panel[3] whose scope of work included:

- developing guidance around issues related to newborn screening, including a common set of guiding principles for newborn screening in Canada
- exploring a proposed process and criteria for the addition and reassessment of conditions, and a recommendation for a set of conditions for which newborn screening programs in Canada could screen
- when appropriate, identifying the potential need for additional evidence on emerging newborn screening tests and associated interventions through the existing health technology assessment infrastructure at Canada's Drug Agency.

Newborn Screening in Canada

Newborn screening enables earlier detection of serious conditions and rare diseases to offer early treatment, with the aim of improving health outcomes in children. Newborn screening entails testing newborns, often by collecting a small amount of blood from the baby's heel, to identify treatable conditions at an early or asymptomatic stage. As part of public health prevention, it aims to screen all newborns in the general population to identify cases, rather than waiting to identify cases later by family history or clinical symptoms.[11]

Newborn screening in Canada is within the scope of the provincial and territorial governments, as they provide health service delivery for their residents. Because each province and territory governs over its own mandate, newborn screening policies, practices, and processes are not uniform across the provincial and territorial programs.[12] There is variation across jurisdictions in Canada in the governance and use of advisory committees; the conditions screened and procedures to review them; the technologies used; legal frameworks and consent; and treatment and follow-up practices, including funding and access to treatment.[8,13] Some of these differences may be attributable to policies, priorities, and capacity, including resourcing supports, of a province or territory. Other reasons for variation have a scientific basis, such as founder effects or ethnic variations within a province or territory and the prevalence of specific conditions or genetic isolates.[11]

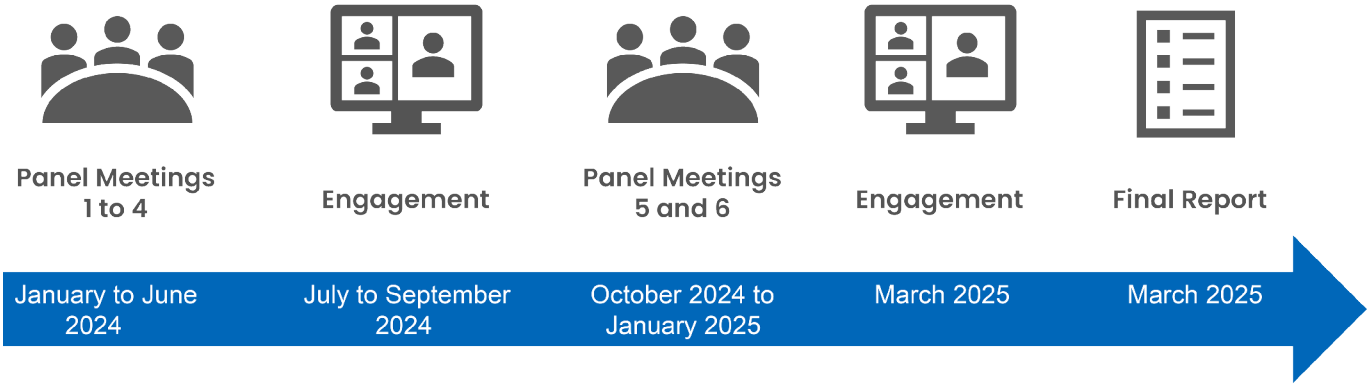
Some progress has been made in envisioning opportunities for pan-Canadian collaboration on newborn screening to enhance consistency of conditions assessed for across Canada. In 2016, an Intergovernmental Newborn Screening Working Group explored areas of pan-Canadian cooperation for newborn screening and made recommendations on a newborn screening list for Canada, consisting of 22 conditions to inform and provide guidance to provincial and territorial newborn screening programs.[14] Similarly, the 2023 joint report by ImmUnity Canada and the Network of Rare Blood Disorder Organizations (NRBDO) made recommendations to improve the consistency of newborn screening across Canada, including establishing a national newborn screening advisory committee.[10] The work of the Newborn Screening Advisory Panel builds off of these advancements.

Advisory Panel Activities and Timeline

Details on the advisory panel members can be found in the About the Advisory Panel Members section.

To develop their guidance, the Newborn Screening Advisory Panel held 6 meetings from January 2024 to November 2024. Figure 1 describes the timeline of the activities of the advisory panel.

Figure 1: Timeline of the Activities of the Newborn Screening Advisory Panel



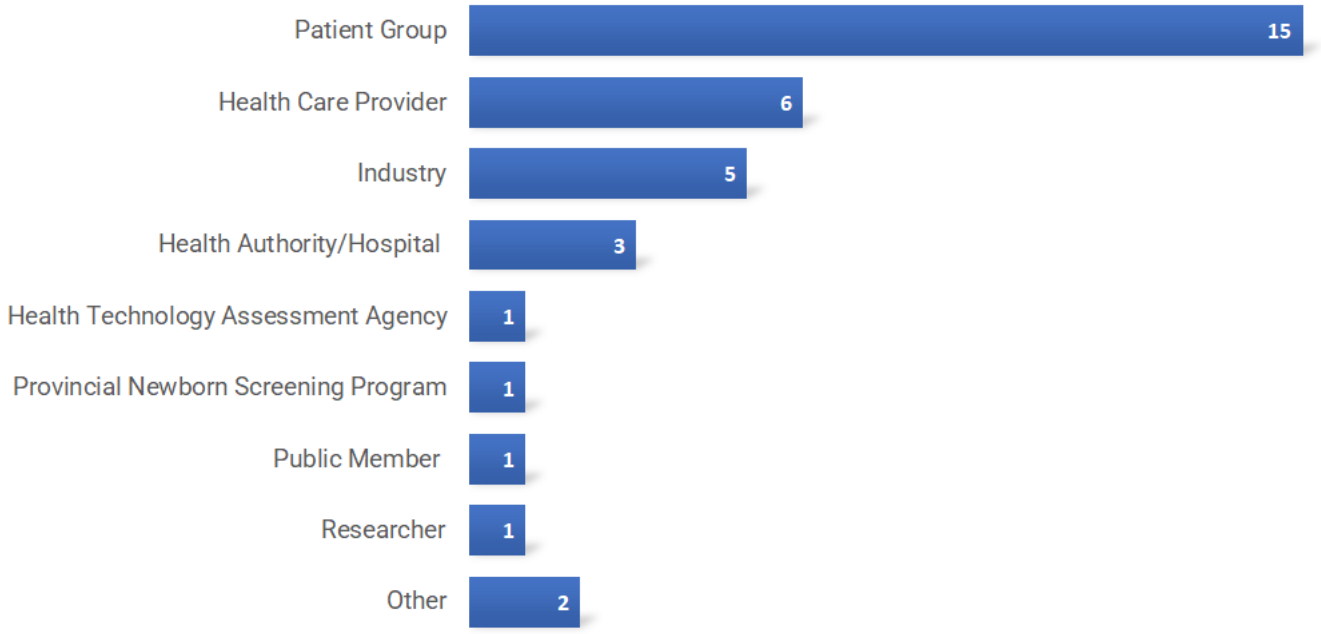
The advisory panel reviewed background information and evidence from a variety of sources, including conversations with international experts in newborn screening and scans of activities related to newborn screening from across Canadian and international jurisdictions. Sources included published peer-reviewed and grey literature sources, and websites from organizations involved in the newborn screening space (e.g., the Canadian Organization for Rare Disorders (CORD)'s Rare Disease Strategy, Canadian and international newborn screening programs, and the US Recommended Uniform Screening Panel, among others). Appendix 1 describes the key literature and information sources that were used. Advisory panel members also drew on and shared their perspectives and experiences as experts. Through discussion and deliberation, the advisory panel came to a consensus on draft guidance and recommendations for a potential pan-Canadian coordinated approach for newborn screening.

Between July 2024 and September 2024, input was invited from interested parties on the advisory panel's discussion paper.[4] In July 2024, a public webinar was held to provide information about the advisory panel's work and included an online written consultation process, as well as focus group discussions. Input from interested parties was sought through an online consultation form, and targeted input from people who worked with or identified as populations made vulnerable by economic and/or social policies through focus groups and key informant interviews. A second public webinar was held in March 2025 to share the input received on the draft guidance and the key deliberations made by the advisory panel.

Engaging With Interested Parties

To gather the perspectives of diverse interested parties on the advisory panel's discussion paper,[4] individuals and organizations were invited to complete an online consultation form either in French or English from July 11, 2024, to September 11, 2024. The online consultation form asked about agreement with and views about each of the components of the discussion paper. A total of 35 online submissions were received from a range of perspectives (refer to Figure 2).

Figure 2: Online Consultations Received by Type of Respondent (N = 35)



Note: The "other" category included a health care ethicist and a member of an academic research network.

The advisory panel wanted to ensure that the perspectives of those who are made vulnerable by social and/or economic policies; those who are disproportionately affected by newborn screening due to higher prevalence of hereditary diseases; and persons who are First Nations, Inuit, or Métis were considered and incorporated into the guidance. Canada's Drug Agency engaged Sage Solutions to conduct 3 distinction-based focus groups with First Nations, Inuit, and Métis participants. The consultant managed recruitment of participants (via direct invitation and social media posts), worked with Canada's Drug Agency on the engagement materials, and facilitated 3 online focus group sessions with a total of 21 participants in September 2024. A report of findings was drafted and validated by sharing the draft report with all participants and providing them with an opportunity to review and provide feedback. The report, titled Consultation Summary From Focus Groups With First Nations, Inuit, and Métis Peoples on Proposed Pan-Canadian Guidance for Newborn Screening Sessions, provides further details describing the participants and findings of the focus group discussions.

Canada's Drug Agency also extended invitations to individuals and organizations who provide community birthing care and who are from or work with underrepresented and underserved populations. We conducted a focus group with 3 participants and interviews with 3 participants. The draft report of findings was shared with all participants to provide an opportunity to validate the description of the themes. Further details can be found in the Consultation Summary From Focus Group and Key Informant Interviews on Proposed Pan-Canadian Guidance for Newborn Screening.

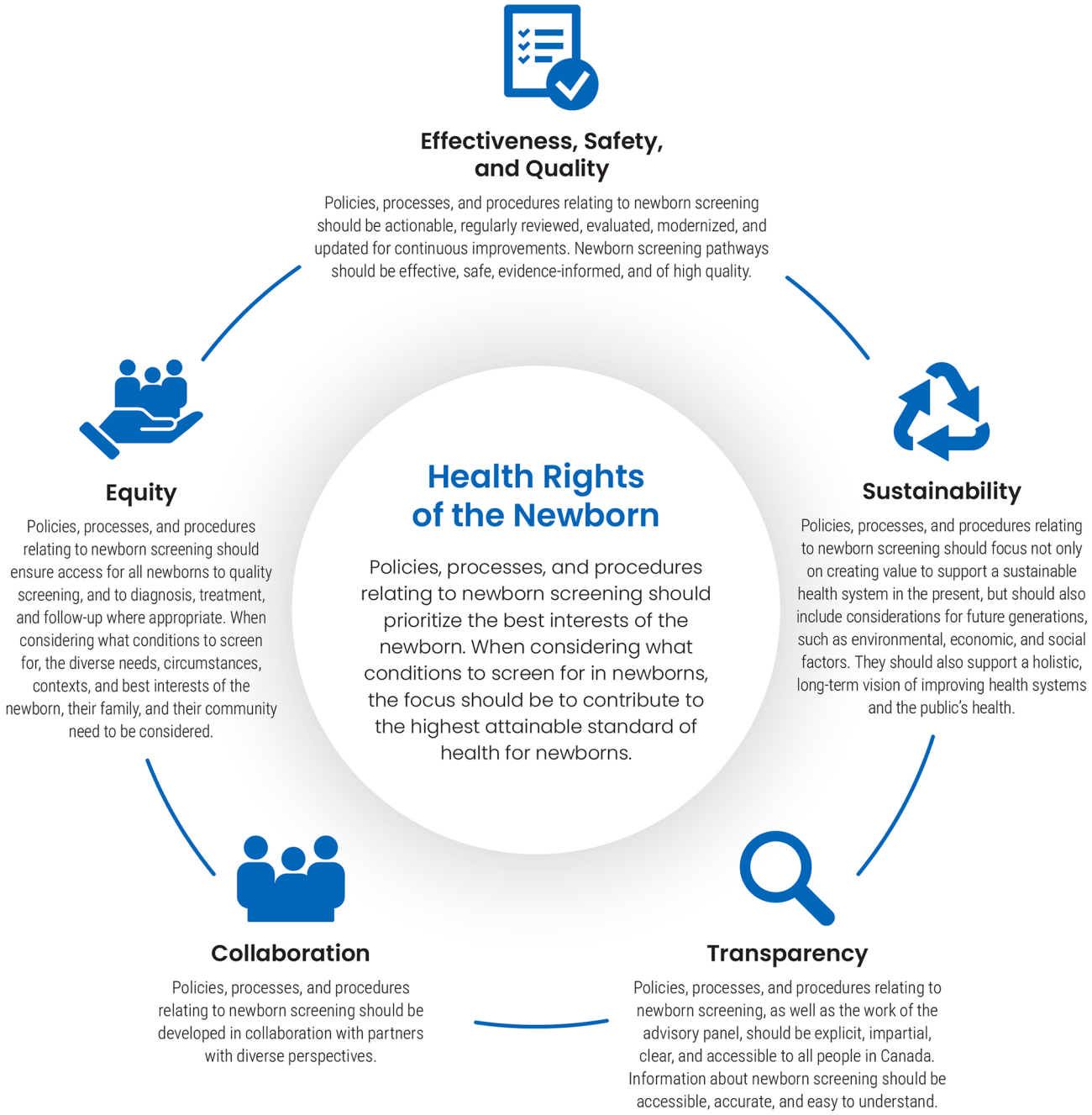
Formulating the Guiding Principles

To establish a foundation for the work, the advisory panel developed a set of guiding principles to inform and shape decision-making for developing processes, criteria, and a proposed list of conditions to screen for in newborns. These guiding principles served as a core set of values that guided the advisory panel's exploratory vision for a potential coordinated newborn screening system and its associated activities. The guiding principles are also intended to shape and inform a pan-Canadian approach to newborn screening. Additional details about the methods for developing the guiding principles are described in Appendix 1.

The Recommended Guiding Principles

As a part of the engagement and consultation processes, a draft version of the guiding principles was shared with interested parties for input. The guiding principles were generally accepted, with the majority of the input received related to providing additional details for a specific principle or clarity within the definitions. Appendix 2 contains a high-level overview of the themes of the input received. Upon review and following discussion and deliberation on the input received, the advisory panel recommends 6 guiding principles (Figure 3) — the health rights of the newborn; equity; effectiveness, safety, and quality; transparency; collaboration; and sustainability — to be adopted and used as guideposts for newborn screening policies, processes, and procedures in Canada. The advisory panel elevated the health rights of the newborn as an overarching principle that is central to the activities and decision-making considerations for newborn screening. The guiding principles are intended to be considered collectively, as they influence, balance, support, and, in some cases, build on one another. At times, the principles may be in tension with one another; careful balancing and transparent justification will be required when managing tensions between the respective principles. The advisory panel recognized that ongoing work may be required to refine the detailed application of the guiding principles and to build upon them based on learnings and advances within the newborn screening landscape.

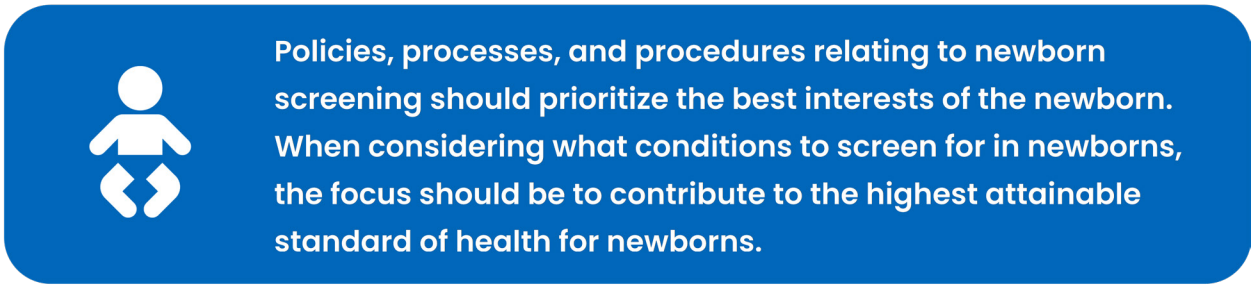
Figure 3: Recommended Guiding Principles and Definitions



Definitions for the Recommended Guiding Principles

Health Rights of the Newborn

Figure 4: Health Rights of the Newborn Definition



While newborn screening policies, processes, and procedures may vary across Canada, the overall aim of newborn screening programs is to find, within the general population, the asymptomatic newborn who has a serious and imminent treatable or preventable condition. Through early identification and treatment, newborn screening can help to reduce or prevent morbidity and mortality associated with these conditions. Reflecting upon the aim of newborn screening, and in keeping with the Convention on the Rights of the Child,[15] the advisory panel concluded that the best interests of the newborn need to be the top priority. Consequently, they recommend that it be an overarching guiding principle for all newborn screening activities to which all other guiding principles should be linked and aligned.

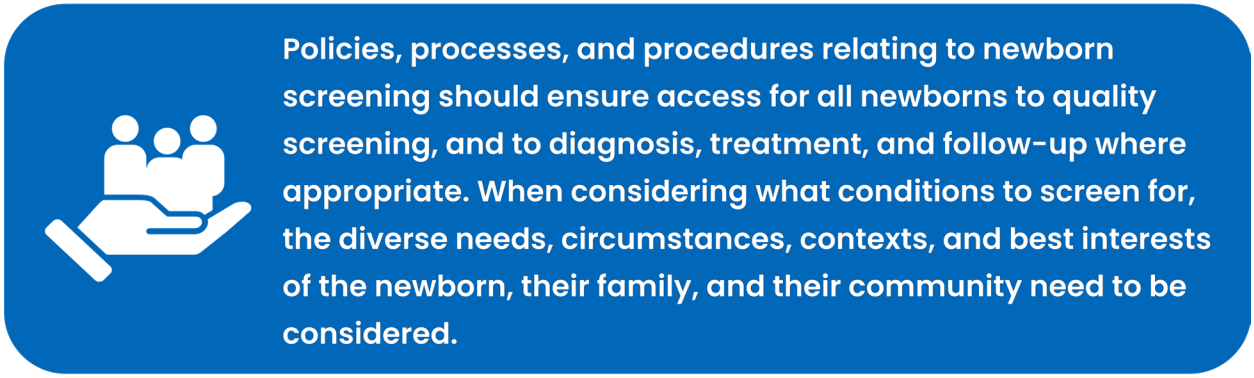
When considering which conditions should be screened for in newborns, the advisory panel felt it was important that newborn screening be for those conditions where there are available interventions and treatments that contribute to the highest attainable standard of health for the newborn.

Interested parties provided input that there ought to be consideration for a holistic concept of health and well-being beyond Western biomedical conceptions of an individual's physical health. In keeping with WHO's definition, the advisory panel recognizes that "health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity."[16] The advisory panel therefore felt that the guiding principle creates space for this broader definition of health.

Input gathered requested that the definition of the health rights of the newborn be expanded to include families and/or caregivers. The advisory panel acknowledges that although family and/or caregivers are not explicitly mentioned in the definition, and that there could at times be competing rights between the newborn and the family and/or caregivers, any policies, processes, and procedures relating to newborn screening should be developed and implemented in a way that respects the needs and perspectives of the family and/or caregivers while still prioritizing the newborn. The advisory panel retained the prioritization of the newborn's best interest in alignment with the Convention on the Rights of the Child.[15]

Equity

Figure 5: Equity Definition



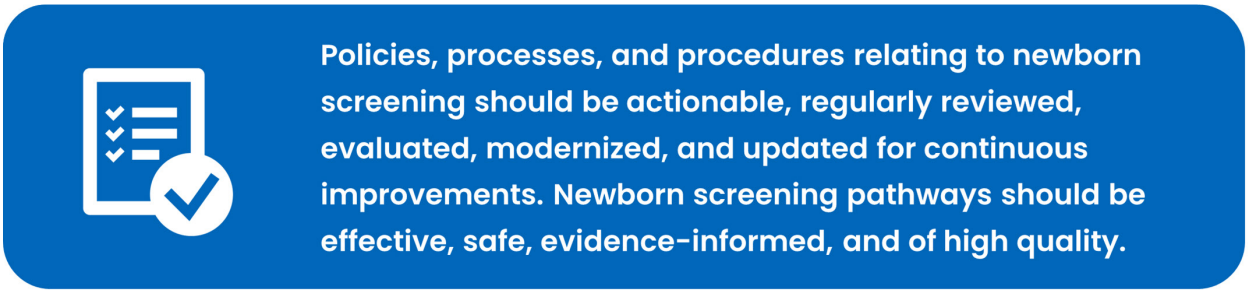
Every newborn in Canada is equally deserving of access to quality screening, diagnosis, treatment, and follow-up interventions and services, where appropriate, as part of newborn screening. The advisory panel acknowledged that many inequities exist within current systems, and their discussions led to the identification of equity as an important guiding principle. In Canada, differences in access currently exist due to the variation in policies, processes, and procedures across newborn screening programs. Variations include, but are not limited to, differences in the number of conditions screened, technologies used, and treatment and follow-up practices.[11,12] These differences in access can have a particular impact on subgroups or subpopulations in Canada. During our engagement with interested parties, we received input highlighting barriers and challenges in accessing newborn screening. An example includes those living in rural or remote communities who may have to travel to access diagnostic services, treatment, or follow-up care relating to a positive newborn screening result. In addition, based on the condition diagnosed, the newborn and the family or caregiver may be away from home for an extended period of time, or may have to consider moving residences to access necessary care. As a result, the definition encompasses the value of equitable access to newborn screening.

The definition also specifies ensuring access for all newborns to quality screening, and to diagnosis, treatment, and follow-up where appropriate. Respondents were seeking additional clarity surrounding the term *quality*. In this context, quality refers to accurate, reliable, relevant, and safe screening, including appropriate collection of the sample, and timely sharing of the results.

Respondents who provided input highlighted the role of the family or caregiver in accessing care for newborns and suggested that the definition of *equity* be expanded to include families and communities. In response to this input, considerations for the diverse needs, circumstances, contexts, and best interests of the newborn, their family, and their community were incorporated into the definition. At times, the best interests of the newborn, their family, and their community may not align; in such instances, the best interests of the newborn are to be prioritized.

Effectiveness, Safety, and Quality

Figure 6: Effectiveness, Safety, and Quality Definition



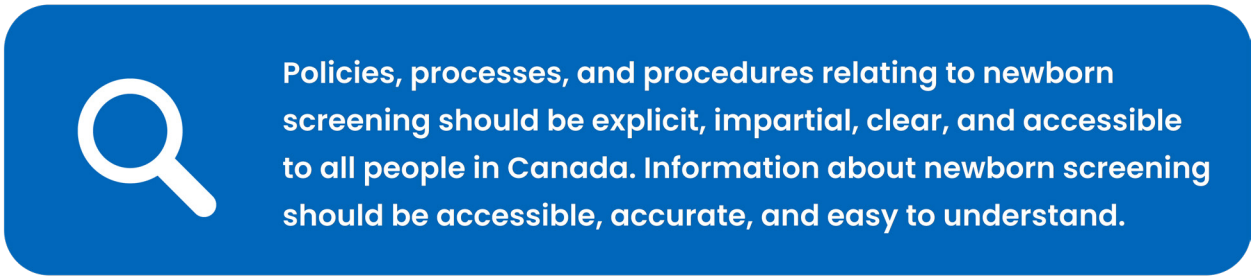
For a condition to be a candidate for newborn screening, evidential information needs to be available that supports its inclusion. This information typically includes: an understanding of the natural history of the condition, an effective newborn screening test, an effective and acceptable intervention, a recognition of societal acceptance of the benefits compared to potential harms, and health systems cost-related considerations.[12] The advisory panel discussed how this information and the available evidence plays a critical role within the development of newborn screening policies, processes, and procedures, and identified effectiveness, safety, and quality as a guiding principle. The term *effectiveness* is intended to include not only clinical effectiveness, but also economic and other considerations, including ethics and implementation. As part of the input received, the advisory panel also discussed and agreed that timeliness is an element of effectiveness when considering newborn screening. They acknowledged that newborn screening care pathways should ensure timely access to screening, diagnosis, and treatment.

When considering the safety of newborn screening, there is the physical safety related to the intervention and testing, but there are also nonphysical and psychological harms that need to be considered. This also speaks to the quality of the testing, as a poorly-performing newborn screening test can result in higher rates of false positives or inconclusive diagnoses, which can lead to more psychological harms to families and caregivers.[17-19] Quality, within this guiding principle, also refers to quality improvement. The advisory panel discussed how newborn screening processes, policies, and procedures will require regular review, evaluation, modernization, and updating. This is due to the rapidly changing and advancing systems within the newborn screening landscape.

In keeping with the overarching guiding principle recognizing the health rights of the newborn, the advisory panel acknowledged that newborn screening pathways should be effective, safe, evidence-informed, and of high quality to support the newborn in reaching the highest attainable standard of health.

Transparency

Figure 7: Transparency Definition



The advisory panel discussed the importance of sharing information about newborn screening in a way that is explicit, factual, impartial, and relevant, so it is understandable and accessible to all people in Canada. They identified that their work and future decisions and processes relating to newborn screening must be transparent. Transparent policies, processes, and procedures support trust and foster accountability by ensuring that decisions relating to newborn screening are visible, understandable, and in the best interests of newborns. Respondents highlighted the importance of openness as an element of transparency. Openness allows everyone access to the same information and enables receiving and applying input from different perspectives. Honest, open, and proactive sharing of newborn screening policies, processes, and procedures is consistent with the advisory panel's vision and stated definition for transparency, and creates a newborn screening system that is accessible and accountable to people living in Canada.

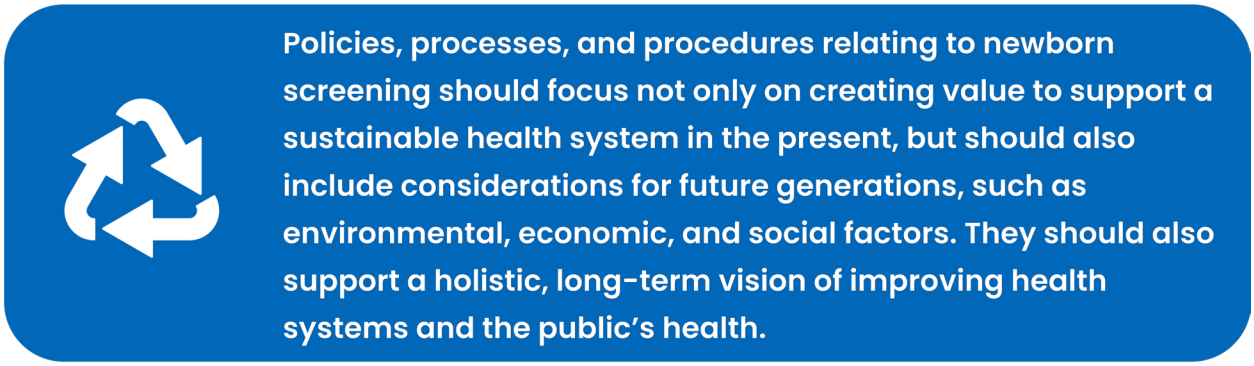
Collaboration

Figure 8: Collaboration Definition

When the advisory panel considered future newborn screening policy, process, and procedure development, they recognized that collaboration across multiple perspectives will be required to ensure that the values and diverse perspectives of individuals and organizations across Canada are embedded within newborn screening systems. In addition, the advisory panel acknowledged that early, inclusive, and meaningful engagement is important to further support collaborative efforts. During the course of engagement activities, it became evident that additional clarity was required for the term *partner*, which was used within the collaboration definition. *Partner* is intended to describe any individual or organization that is interested in collaborating, including but not limited to people with lived and living experience of a condition, caregivers of individuals with the condition, clinicians, policy-makers, researchers, manufacturers, advocacy groups, community organizations, and government.

Sustainability

Figure 9: Sustainability Definition



Within the next 10 years, researchers are projecting a large influx of rare disease treatments and new health technologies to the market, which has the potential to disrupt newborn screening.[9] Bearing this in mind, the advisory panel identified a need for newborn screening policies, processes, and procedures to consider sustainability of health systems, not only for current generations but also considering the needs and rights of future generations. While newborn screening activities should prioritize the best interests of the newborn, long-term planning and strategy should support program viability and better anticipate future health care challenges and needs. To support the long-term vision of improving newborn screening systems in Canada, it will also be important to consider the environmental, economic, and societal factors that could impact, positively or negatively, the newborn screening landscape.

Recommendation

The advisory panel recommends that the guiding principles be considered when developing and implementing policies, processes, and procedures related to newborn screening.

Short-Term Recommendation (1 to 2 Years)

- Adopt the guiding principles to support a pan-Canadian approach to newborn screening in Canada.

A Future Coordinated Approach for Newborn Screening in Canada

Building a Case for a Pan-Canadian Coordinated Approach for Newborn Screening

There is currently no centralized governance structure for newborn screening in Canada. As the administration and delivery of health care is a provincial and territorial responsibility, each province and territory has its own governance structure. Some provinces and territories rely on the knowledge and infrastructure of other jurisdictions, including advisory committees that review and make decisions on adding or reassessing conditions. Depending on the jurisdiction, there may not be a transparent pathway surrounding decision-making to add or reassess a newborn screening condition.

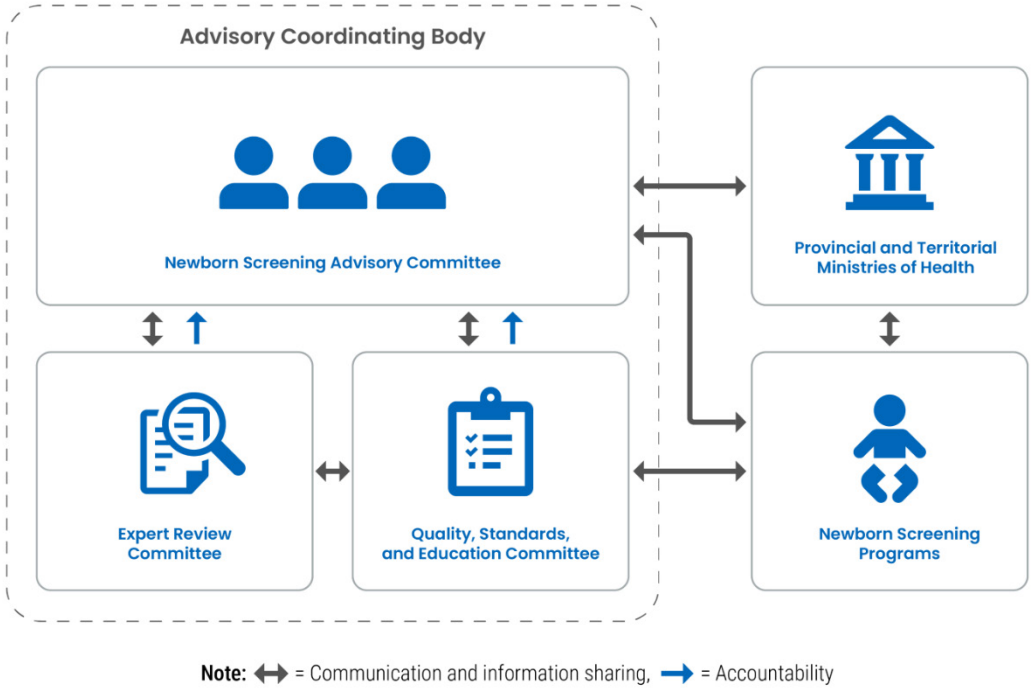
The advisory panel felt that having a centralized coordinating function for newborn screening guidance would enhance the standardization and uniformity of newborn screening policies, practices, and procedures across Canada by improving equity in access and addressing differences in economies of scale. A coordinated system can enable efficiency in process and use of resources (e.g., avoid duplication of efforts), mitigate risks for individual programs, facilitate quality improvement, and support anticipation of and collective response to new challenges within the newborn screening landscape. The advisory panel saw opportunities for such a coordinated model to support pan-Canadian collaboration on expert advice, implement quality initiatives, and support education and engagement activities that would support jurisdictions and newborn screening programs in adapting to ongoing changes.

A Proposed Pan-Canadian Coordinated Approach for Newborn Screening

The advisory panel explored a high-level vision for a coordinated pan-Canadian governance model for newborn screening. As part of the advisory panel's discussion, various examples of governance structures for newborn screening programs (i.e., from the US, Australia, Ontario, and British Columbia) were reviewed and summarized. Additional details on the methods, sources consulted, and approach are described in Appendix 1. The advisory panel identified functions that could be aligned and enhanced through a pan-Canadian coordinated structure including processes for adding and reassessing conditions, establishing and maintaining the Recommended Pan-Canadian Newborn Screening List, education, and quality improvement activities.

Upon reviewing and discussing various governance structures and approaches for newborn screening in Canada and internationally, the advisory panel proposed a governance structure (Figure 10) that included an advisory coordinating body (composed of a newborn screening advisory committee; an evidence review committee; and a quality, standards, and resourcing committee), with involvement from newborn screening programs and provincial and territorial ministries of health. A more detailed explanation of potential roles for each of the committees is included in Appendix 3.

Figure 10: Illustrative Example of a Potential Coordinated Newborn Screening System



Importantly, the advisory panel developed a recommended governance model that recognizes the autonomy of provinces and territories and the importance of their ability to tailor newborn screening to meet the unique needs of the populations within their respective jurisdictions. Input received through engagement activities highlighted opportunities to further involve and embed provincial and territorial decision-makers in the development of pan-Canadian newborn screening guidance. The advisory panel responded to this by recommending the inclusion of representatives of provinces and territories to act as observers on the proposed committees to better understand the information and context of the committees' work.

To avoid duplication, the advisory panel recommended that the functions, composition, and responsibilities of the proposed committees align with the processes for adding or reassessing conditions for the Recommended Pan-Canadian Newborn Screening List. This requires setting clear mandates, functions, and accountabilities for the different committees, and ensuring collaboration and communication across committees, newborn screening programs, and provinces and territories. The advisory panel also proposed opportunities to embed the guiding principles within the structure and functions of the governance model. Additionally, opportunities to pilot a secretariat support function for newborn screening programs across Canada by working in collaboration with a pan-Canadian health organization, such as Canada's Drug Agency, should be considered. A longer-term vision should consider how the 3 proposed committees could be housed within an existing organizational structure. This could be explored by considering different model examples, including learning about the operation models of the National Advisory Committee on Immunization hosted by the Public Health Agency of Canada, or considering the governance model within a pan-Canadian organization, such as Canada's Drug Agency.

The advisory panel acknowledged the importance of ensuring decision-makers, including provincial and territorial ministries of health, are engaged in the proposed newborn screening advisory committee. Input highlighted the need to keep committee structures streamlined, with no more than 1 or 2 committees or subcommittees, to ensure effectiveness, efficiency, and timeliness. The advisory panel acknowledged that the governance model should seek to ensure efficiency and streamlined processes whenever possible. Respondents also pointed to opportunities for connections between the proposed coordinating model with community-based organizations and patient groups. The advisory panel recognized the importance of engaging with the public and patients, and articulated opportunities for engagement in committee composition and function (refer to Appendix 3 for further details). Similarly, the advisory panel revisited the committee compositions and functions at a high level to highlight opportunities to engage representatives from provinces and territories.

Recommendations

The advisory panel recommends developing a potential collaborative model for pan-Canadian coordination of newborn screening.

Short-Term Recommendations (1 to 2 Years)

- Develop and implement a pan-Canadian governance model for guidance for newborn screening by working with and building from existing organizations. This could be explored by piloting a secretariat support function for guidance for newborn screening programs across Canada by working in collaboration with a pan-Canadian health organization, such as Canada's Drug Agency, to evaluate and learn.
- Explore and establish opportunities to engage with and educate the public about newborn screening, in collaboration with other organizations.
- Assess the need for and feasibility of a pan-Canadian data repository and a centralized resource and laboratory reference centre to provide Canadian-specific data and information to support newborn screening programs and laboratories.

Medium-Term to Long-Term Recommendations (3 Years or More)

- Further develop the proposed pan-Canadian newborn screening governance model to enhance coordination for newborn screening in Canada by establishing and convening expert committees, such as a newborn screening advisory committee; an expert review committee; and a quality, standards, and education committee.
- Establish the groundwork for a pan-Canadian data repository by convening interested parties and decision-makers to work toward purpose; participation; and data governance, protection, and sharing. These activities should be done in collaboration with national Indigenous health organizations and organizations representing underserved communities.

Enhancing Newborn Screening Processes

To consider mechanisms that could be used to add or reassess conditions from the Recommended Pan-Canadian Newborn Screening List, the advisory panel explored and proposed a series of process steps that could be applied. The advisory panel began by reviewing processes that are in current use among newborn screening programs for adding or reassessing conditions. Relevant Canadian and international sources were identified (described in Appendix 1) and used to inform advisory panel discussions about proposed processes to add or reassess conditions for a recommended pan-Canadian newborn screening list.

The proposed processes were intended to outline an approach to identifying and selecting conditions for consideration, gathering and assessing available evidence and information, considering the input of interested parties, and communicating recommendations. The recommended guiding principles were used to inform discussions about the processes and steps necessary to appropriately consider conditions for addition to the Recommended Pan-Canadian Newborn Screening List, or reassessment (which could include removal from the list). A draft version of the proposed processes was shared with interested parties as a part of an online consultation. The proposed processes are outlined as follows and illustrated in Figure 11, and described in detail in Appendix 4. For more detail about the input received as a part of the online consultation, please refer to Appendix 5.

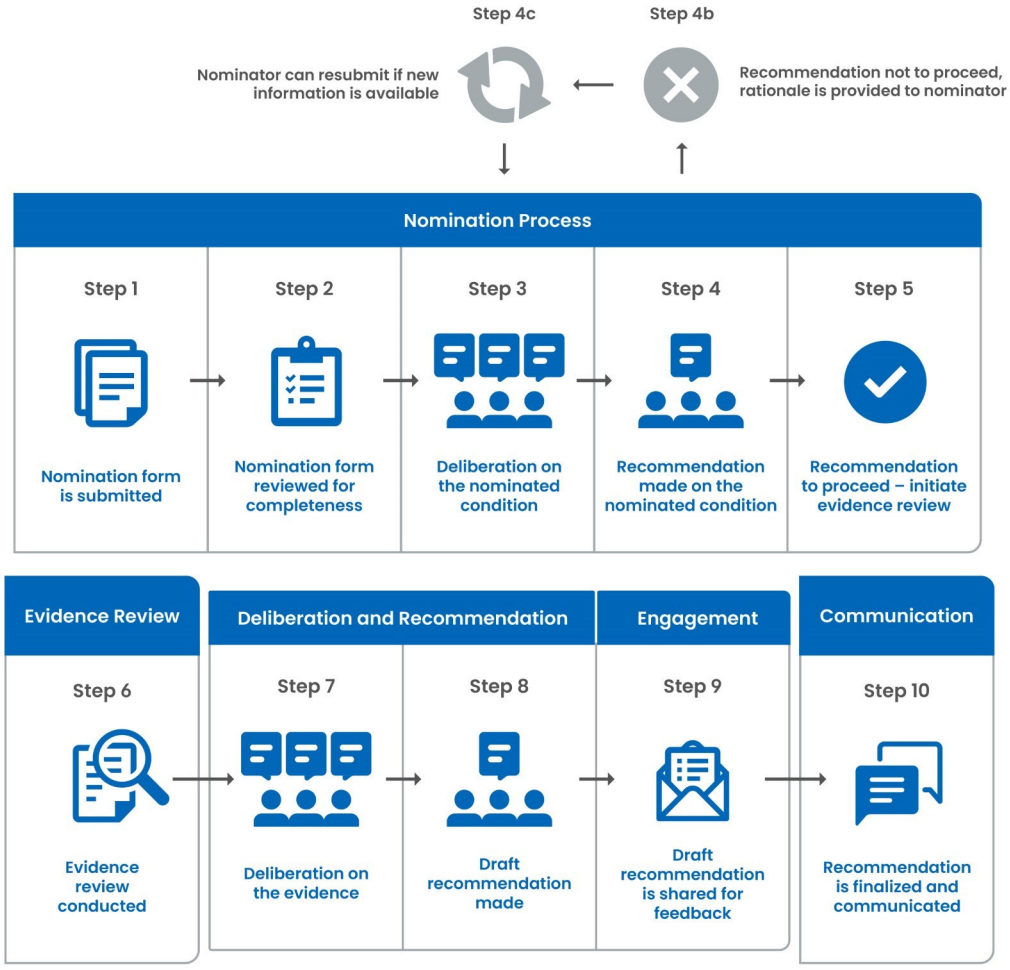
Proposed Processes

The advisory panel proposed 4 key sequential and dependent processes that could inform the addition or reassessment of a condition for a recommended pan-Canadian newborn screening list:

- a process to nominate conditions for review
- an evidence review process
- a process to inform deliberation and the development of a recommendation for the newborn screening condition under review
- a process to inform communication and engagement with interested parties.

The proposed processes are illustrated in Figure 11 with details presented in Appendix 4.

Figure 11: Illustration of Proposed Processes to Add or Reassess a Condition for a Pan-Canadian Newborn Screening List



Input on the proposed processes was summarized (Appendix 5) and informed the development of recommendations.

Discussion and Input That Informed the Recommended Processes

Nomination Process

The advisory panel recommended that the nomination process should be available and accessible to all people living in Canada, demonstrating its adherence to the guiding principles of the health rights of the newborn, equity, and collaboration. The advisory panel also stated that nominations should align with the predefined criteria, be complete, and be supported by appropriate and sufficient evidence, in alignment with the guiding principle of effectiveness, safety, and quality. In addition, the advisory panel agreed that decisions about whether a nomination proceeds to evidence review should be justified and communicated publicly, to optimize opportunities for collaboration and ensure transparency. Similarly, to ensure transparency and

collaboration, nominations should be made public, which would also mitigate the potential for duplicate nominations and unnecessary effort.

Input received on the proposed nomination process indicated the importance of requiring conflict of interest disclosures for those submitting nominations, to ensure transparency. Additional input offered suggestions for implementing the nomination process, which was out of scope for this phase of the work but will be considered in future phases.

Evidence Review Process

The advisory panel acknowledged and agreed that the evidence review is designed to identify and summarize the potential benefits and harms of screening to newborns, demonstrating its adherence to the guiding principle of the health rights of the newborn. The advisory panel also agreed that the evidence review must be informed by the predefined criteria for adding or reassessing conditions, which will support the guiding principle of effectiveness, safety, and quality.

Discussions by the advisory panel, as well as input received on the proposed processes, emphasized the importance of an evidence review process that is inclusive of experts, those with lived and living experience, and the public, supporting the guiding principles of equity and collaboration. Additional input specified that the evidence review team should include expertise specific to the rare disease under consideration and representation from the jurisdictions within which newborn screening for the proposed conditions are being considered for implementation.

Deliberation and Recommendation Process

The advisory panel agreed that deliberations should be informed by the criteria and a structured approach to ensure that the guiding principles of the health rights of the newborn; effectiveness, safety, and quality; and collaboration are manifested. In addition, public deliberations would be a key feature of this process, embodying the guiding principle of transparency. To ensure alignment with the guiding principles of equity, collaboration, and sustainability, the recommendation process would consider variation among populations, capacities, and resources within and across provincial and territorial jurisdictions.

Input received on the proposed deliberation and recommendation process underscored the importance of requiring expertise specific to the rare disease under consideration; ensuring representation from all jurisdictions; as well as consideration of short-term and long-term implications for newborns, families, and health systems. The advisory panel agreed that these features should be included in the proposed deliberations and recommendations process, demonstrating the guiding principles of effectiveness, safety, and quality; collaboration; and sustainability.

Engagement and Communication Process

The advisory panel discussed and agreed that draft recommendations for a newborn screening condition should be made publicly available to ensure all relevant feedback is solicited, considered, and incorporated, demonstrating the guiding principles of the health rights of the newborn, transparency, equity, and collaboration. Input received on the proposed process suggested that conflict of interest disclosure should be mandatory for all parties providing feedback on the recommendations to further ensure transparency.

Recommendations

The advisory panel recommends a test-and-learn approach to the proposed processes to review newborn screening conditions as follows.

Short-Term Recommendation (1 to 2 Years)

- Pilot the proposed processes for adding a condition by conducting an evidence review on a candidate condition and developing recommendations. This would provide learnings for coordination among interested parties and explore the development of a secretariat support function.

Medium-Term to Long-Term Recommendation (3 Years or More)

- Establish and apply a nomination process for adding or reassessing conditions for the Recommended Pan-Canadian Newborn Screening List.

Criteria for Adding and Reassessing Conditions

Importance of Establishing Criteria

Many jurisdictions in Canada and internationally use explicit predefined criteria as part of deliberations and to make recommendations to add or reassess a condition on a newborn screening list. Criteria can enhance deliberations and recommendations by providing a transparent standard that can be applied consistently and can help ensure that recommendations to add or reassess a condition are legitimate, impartial, and inclusive.[20] They can support consistency in deliberative reasoning and decisions and advance transparency by making the rationale for recommendations to add or reassess a condition explicit.

To support future decision-making on expanding the proposed pan-Canadian newborn screening list, the advisory panel developed criteria for adding conditions to and reassessing conditions on the Recommended Pan-Canadian Newborn Screening List. These criteria are intended to be used in the deliberations and recommendations process of adding or reassessing a condition. They can also be adapted and used during the nomination process. The advisory panel felt it important to note that these criteria will likely need to be refined over time and should be revisited to ensure their continued relevance and appropriateness, particularly in light of emerging technologies such as genomic sequencing. The advisory panel also recognized that there needs to be further work done on establishing deliberative processes to support the use of the criteria in making recommendations.

Developing the Criteria

To develop the proposed criteria for adding or removing conditions from the Recommended Pan-Canadian Newborn Screening List, the advisory panel reviewed the criteria from several key newborn screening programs, including those in Canada and internationally (refer to Appendix 1). The advisory panel discussed opportunities to modify several existing criteria — including collapsing some criteria for operational feasibility — and identified ways to embed the draft guiding principles into the criteria to add a condition to the Recommended Pan-Canadian Newborn Screening List. For reassessing a condition, the advisory

panel drew on considerations for removing a condition as conceptualized in Australia's Newborn Screening Framework[6] as it covered the key relevant considerations and could be adapted for Canada. The advisory panel solicited input on the proposed criteria through engagement activities and reflected on and modified the proposed criteria in response to the input received.

Criteria for Adding a Condition

The advisory panel considered Wilson and Jungner's[5] 1968 criteria for screening programs developed for WHO to still be relevant and foundational for newborn screening programs; however, they recognized that these criteria are not specific to newborn screening, and as such need to be tailored and adapted to be relevant.

The advisory panel recommended adopting 8 of the 10 criteria from Wilson and Jungner with modifications (Table 1). The modifications include being more specific in the articulation and interpretation of the criteria, and were made drawing on how the criteria are expressed and interpreted by other newborn screening programs in Canada and internationally. The advisory panel received input from engagement activities on many of the specific criteria for adding a condition. Some of those consulted strongly felt that the original Wilson and Jungner criteria were sufficient and should not be modified; however, the advisory panel felt it was necessary to tailor and update the original criteria for the current context of newborn screening. Input was also solicited on how the criteria will be interpreted and operationalized and pointed to the need to have deliberation methods that allow for clarity between opinions and transparency in interpreting and applying the criteria. The advisory panel agreed, and this need was reflected in their recommendations for further work on deliberative processes. Further details on the input received for the modified criteria can be found in Appendix 6. Additional specific input was received on the following considerations:

- Input noted the need to ensure that the focus of the criteria was on those conditions that arise in early life and that are preventable or treatable. The advisory panel modified the criteria to clarify that eligible conditions are those that manifest in early life (i.e., in the neonatal period, infancy, or early childhood). Carrier testing for conditions and testing for those that manifest in later in life (e.g., during adolescence or adulthood) are not eligible.
- Input suggested that it is important to account for there being a *benefit* of screening to the newborn, and not the *convenience* of screening. The advisory panel clarified in the criteria that the benefit of screening is intended to apply to newborns.
- Input sought clarity on how the criteria will account for regional and jurisdictional variability in populations and condition incidence, particularly in subpopulations who are frequently underserved or underrepresented. The advisory panel felt that the modified criteria allowed for this variation. They recognized that the population of Canada is increasingly diverse[8] and that there is often limited evidence about the incidence of many conditions and/or screening targets within cultural or ethnic subpopulations, which is an important consideration when making recommendations about specific conditions.
- Input suggested that the concept of a presymptomatic or latency period was not clear in the proposed criteria. As it is a key feature of the rationale of newborn screening (i.e., detecting at-risk

or asymptomatic newborns), the advisory panel modified the criteria to ensure that this dimension was clear.

Table 1: Original Wilson and Jungner Principles for Screening and Recommended Modifications Made by the Advisory Panel

Wilson and Jungner's criteria[5]	Recommended modified criteria
Condition	
The condition is an important public health problem.	The condition should be serious and one that arises in children and/or leads to morbidity and mortality in childhood.
There should be a recognizable latent or early symptomatic stage.	Removed. The advisory panel indicated that this criterion is not relevant to newborn screening, and elements (e.g., natural history) are captured by the next criterion (epidemiology of the condition).
The natural history of the condition, including development from latent to declared disease, should be adequately understood.	The epidemiology (including incidence and variation across regions and jurisdictions) and natural history (including the latent or presymptomatic stage) of the condition should be adequately understood. Differences in the incidence and variation in test performance in subpopulations, particularly those who are underserved or underrepresented, should be characterized and adequately understood.
Test	
There should be a suitable test or examination.	There should be a robust, scalable, safe, and validated screening test.
The test should be acceptable to the population.	The screening test, diagnosis, and treatment should be socially and ethically acceptable to health professionals and the public.
This is an additional criterion adapted from Newborn Screening Ontario.	The benefits of screening should outweigh the physical and psychological harms caused by the screening test (including the sample collection), diagnostic procedures, and treatment.
Treatment[a]	
There is an agreed policy on whom to treat as patients.	There is an agreed policy on the further diagnostic investigation of newborns with a positive screening test result. There should be agreed evidence-based policies covering appropriate treatments and the cases in which they can be offered.
There should be an accepted treatment for patients with recognized disease.	There should be an effective treatment or intervention for newborns identified through early detection, with evidence of early treatment leading to better health outcomes and reduced morbidity and/or mortality than late treatment.
Other considerations	
Facilities for diagnosis and treatment should be available.	Services and facilities for diagnosis and treatment should be available to newborns who are screened.
Case-finding should be a continuing process and not a "once and for all" project.	Removed. The advisory panel indicated that this criterion is not relevant to adding a condition to a pan-Canadian newborn screening list.

Wilson and Jungner's criteria[5]	Recommended modified criteria
The cost of case-finding (including diagnosis and treatment of patients who are diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.	The budgetary impact of case-finding (including screening, diagnosis, and treatment) should be considered in relation to not screening.

[a]The term *treatment* is used in this table to refer to health care (including drugs, medical devices, and clinical and therapeutic interventions such as diets) that is intended to alter the course of and/or improve a child's or newborn's health.

Considerations for Reassessing a Condition

With the establishment of the recommended newborn screening list, there will be a need to reassess conditions on the list. Reassessment is an important part of ongoing quality initiatives in health care.[21,22] In the context of newborn screening, it looks to ensure that there is value in screening a condition in terms of health benefits and harms, and for opportunities to improve screening test performance. A reassessment may result in changes to the way screening is conducted for a condition but there also could be no changes made. Rarely, a recommendation could be made to remove a condition that was previously recommended, unless there are concerns that the harms substantially outweigh the benefits of screening. The advisory panel recognized the need for future work to develop processes for reassessing a condition at a pan-Canadian level.

As part of the scope of current work, the advisory panel considered examples of deliberative frameworks that support the reassessment of a condition that could lead to the potential for removal. The advisory panel recommends adopting the modified questions for reassessing a condition established by Australia's Newborn Bloodspot Screening Framework,[6] which outlines 1 of the few public processes for reassessing and potentially removing a condition from a newborn screening list. These 13 questions cover similar domains to those in Wilson and Jungner's criteria.[5]

The advisory panel modified the questions by adding whether the condition, if reassessed, would meet the criteria to be added to the Recommended Pan-Canadian Newborn Screening List. They also modified the questions to consider how a condition might be removed as a primary target, but in some cases could still be identified through the screening test results for another condition. As part of their process of developing the considerations for reassessing a condition, they reviewed input received on the considerations for reassessment. By and large, input from respondents supported drawing on the learnings of Australia's approach. The proposed considerations for reassessing a condition from a pan-Canadian newborn screening list include the following:

- When was screening initiated for this condition and why?
- What is the rationale for removing the condition from screening? Provide relevant information that draws on current screening experience and a review of literature to support removal.
- Would the condition meet the criteria for adding a condition to the list at this time?
- What is the incidence in Canada? Is this determined clinically or through screening studies in Canada or other countries?

- What positive and negative impacts would removing this condition have on the screening program (e.g., in terms of the impact on families, on the laboratory, on perinatal service providers)?
- What would be the clinical implications of removing the condition from screening? Include reference to the burden of disease associated with the condition, including morbidity and mortality, and the spectrum of disease.
- Are there other risks of removing this condition from screening (e.g., impact on the ability to detect other conditions; impact on the family, including future reproductive risk; community concerns)?
- Is the condition screened internationally?
- Would removal of this condition from screening have any other implications for the quality of the program?
- Are there any alternatives to removal (e.g., alterations to cut-offs, further follow-up testing)?
- For the current testing protocol, comment on the clinical and analytic validity, sensitivity, specificity, false-positive rate, false-negative rate, positive predictive value, and negative predictive value.
- Is the test part of an assay that tests for multiple targets simultaneously (i.e., multiplexed)? Does its removal affect the detection of other treatable (i.e., secondary) conditions? Will it continue to be identified as a secondary target by screening of another primary condition?
- Does testing identify other conditions (clinical or of unknown significance)?
- What would be the cost implications of removing the test?

Recommendations

The advisory panel recommends the following with regards to the criteria for adding a condition and the considerations for reassessing conditions on the recommended pan-Canadian list.

Short-Term Recommendation (1 to 2 Years)

- Adopt the proposed criteria and processes for adding and reassessing a condition for the Recommended Pan-Canadian Newborn Screening List. This would include developing transparent deliberative processes to support recommendations for adding or reassessing a condition.

Medium-Term to Long-Term Recommendations (3 Years or More)

- Evaluate and refine the criteria for adding and reassessing conditions on the pan-Canadian newborn screening list.
- Develop a process for reassessing conditions on the Recommended Pan-Canadian Newborn Screening List and prioritize conditions for reassessment.

Recommended Pan-Canadian Newborn Screening List

Building Toward a Recommended Pan-Canadian Newborn Screening List

To identify potential candidate conditions that could be considered for a recommended pan-Canadian newborn screening list, the advisory panel first considered what conditions are being screened for in Canada. It is important to note that comparing the number of screening conditions across newborn screening programs can be challenging because of differences in how newborn screening conditions are reported and defined. A table outlining the newborn screening conditions and which jurisdictions provide screening can be found in Appendix 7. Upon review of the different conditions screened for across Canada, the advisory panel made a deliberate decision to focus on primary conditions for the list and acknowledged that future work should include the development of pan-Canadian case definitions, including laboratory screening parameters, and approach for identifying secondary conditions. A secondary condition refers to a condition that is identified as a part of the differential diagnosis of a condition that is screened.[23]

The advisory panel also considered previous newborn screening work that was done at the pan-Canadian level in 2016.[14] A list of 22 conditions for newborn screening were recommended to the ministers of health. Additional details about the 2016 pan-Canadian newborn screening work, including the proposed list of conditions to screen for, can be found in Appendix 8.

The Recommended Pan-Canadian Newborn Screening List

The recommended newborn screening list is proposed as a foundation to foster discussion and decision-making, leading to more consistent newborn screening in Canada. In response to clarification requests from respondents, the advisory panel emphasized that the list is not intended to impose additional obligations or defund screening for any conditions that are already adopted by newborn screening programs, nor is it intended to deter programs from considering the addition of new conditions to their program. It is important to note that newborn screening programs and decision-makers for provinces and territories retain their autonomy and the ability to tailor their program to their local needs.

The advisory panel identified an opportunity to build on the work of the Intergovernmental Working Group, as the conditions that were proposed in 2016 have been adopted, or are in the process of being adopted, by most newborn screening programs in Canada. The advisory panel recommended that the list of 22 conditions from 2016 be adopted as the starting point for the Recommended Pan-Canadian Newborn Screening List, with a few modifications. The first modification is to separate sickle cell disease into 3 subtypes, and the second modification is to add spinal muscular atrophy to the list, as it is the only condition that has been added to all newborn screening programs since 2016. Additional details regarding these modifications can be found in Appendix 8.

The Recommended Pan-Canadian Newborn Screening List is provided in Figure 12 and includes 25 conditions. While the advisory panel agreed that the recommended list of conditions is a starting point, the advisory panel acknowledged that the conditions on the recommended list will require further review to support the development of case definitions and guidance on best screening practices. In addition, the

advisory panel noted that even if a condition is currently being recommended for the proposed pan-Canadian newborn screening list, this will not preclude it from being reviewed or reassessed in the future.

Figure 12: The Recommended Pan-Canadian Newborn Screening List

List of 25 conditions for inclusion on the Recommended Pan-Canadian Newborn Screening List

- Argininosuccinic aciduria
- Biotinidase deficiency
- Carnitine uptake deficiency
- Citrullinemia, type I
- Classic galactosemia
- Classic phenylketonuria
- Congenital adrenal hyperplasia
- Cystic fibrosis
- Glutaric acidemia, type I
- Hemoglobin S beta thalassemia disease (sickle cell beta thalassemia)
- Hemoglobin SC disease
- Hemoglobin SS disease (sickle cell anemia)
- Isovaleric acidemia
- Long-chain hydroxyacyl-coenzyme A dehydrogenase deficiency
- Maple syrup urine disease
- Medium-chain acyl-coenzyme A dehydrogenase deficiency
- Methylmalonic acidemia (cobalamin disorders)
- Methylmalonic acidemia (methylmalonyl-coenzyme A mutase deficiency)
- Primary congenital hypothyroidism
- Propionic acidemia
- Severe combined immunodeficiencies
- Spinal muscular atrophy
- Trifunctional protein deficiency
- Tyrosinemia, type I
- Very long-chain acyl-coenzyme A dehydrogenase deficiency

During the advisory panel's review of conditions that are screened for across Canada, 9 conditions were identified as not being uniformly screened. The advisory panel discussed these 9 conditions to explore if they should be added to the Recommended Pan-Canadian Newborn Screening List or if additional information was required to make a recommendation. Because of the variation in screening practices, differences in populations across jurisdictions, evidence considerations, and the rarity of some of the conditions, the advisory panel concluded that all 9 conditions should undergo further evidence review to determine if they should be added to the Recommended Pan-Canadian Newborn Screening List. The advisory panel noted that future evidence reviews should be guided by the guiding principles and the criteria that are outlined in this report. Figure 13 includes the list of conditions that require further evidence review.

Through the online consultation, respondents submitted input to consider adding different conditions to the recommended newborn screening list, and the list of conditions requiring an evidence review. Additional details addressing the input received can be found in Appendix 9.

Figure 13: List of Conditions That Require Further Evidence Review

- 3-hydroxy-3-methylglutaryl-coenzyme A lyase deficiency
- Carnitine acylcarnitine translocase deficiency
- Carnitine palmitoyltransferase I deficiency
- Carnitine palmitoyltransferase II deficiency
- Congenital cytomegalovirus (hearing loss risk factor)
- Guanidinoacetate methyltransferase deficiency
- Homocystinuria
- Mucopolysaccharidosis, type I
- X-linked adrenoleukodystrophy

Recommendations

The advisory panel recommends the following with regard to the Recommended Pan-Canadian Newborn Screening List.

Short-Term Recommendations (1 to 2 Years)

- Adopt the Recommended Pan-Canadian Newborn Screening List as a starting foundation to foster discussion and decision-making, leading to more consistent newborn screening across Canada.
- Work with experts to develop pan-Canadian case definitions for primary newborn screening conditions to facilitate a common language and understanding across newborn screening programs.

Anticipating Emerging Conditions for Newborn Screening in Canada

Emerging Newborn Screening Conditions

The advisory panel recognized that it is important to have proactive strategies in place to monitor and anticipate emerging newborn screening conditions. With new and emerging health technologies, it becomes imperative to anticipate emerging newborn screening conditions. Anticipating the need to review conditions enables more strategic and proactive decision-making, supports the appropriate allocation of resources, and helps to prioritize and manage potential condition review requests. By anticipating and monitoring emerging conditions when new information becomes available or a new treatment comes to market, the system may be ready and primed to support efficient and timely decision-making. As a starting point, the advisory panel

considered an emerging condition to be a condition that has been added to or is under review by a newborn screening program in another country and is not currently screened for by any jurisdiction in Canada. It also includes conditions that have treatments in the pipeline that should be monitored.

The advisory panel discussed some of the emerging newborn screening conditions and asked for input through the online consultation, focus group discussions, and key informant interviews. Based on the input received, a list of examples of emerging conditions that may be candidates for further monitoring has been compiled and is included in Appendix 10. For transparency, all conditions suggested have been included. The emerging conditions list is not meant to be exhaustive or comprehensive; rather, it is intended to represent a starting list of conditions that may benefit from monitoring. Future work will be required to develop a process for maintaining the list, including adding, prioritizing, and monitoring the conditions.

Recommendations

The advisory panel recommends the following with regard to the emerging conditions for newborn screening.

Short-Term Recommendation (1 to 2 Years)

- Leverage existing processes within pan-Canadian health organizational capacity to develop a process for horizon scanning to anticipate candidate conditions for newborn screening in Canada.

Medium-Term to Long-Term Recommendation (3 Years or More)

- Continue to build on the horizon scanning service to anticipate and expand the list of emerging conditions and technology trends in newborn screening such as genomic sequencing.

Other Considerations

Through the course of the advisory panel's work, several out-of-scope topics were raised, either through advisory panel discussions or by the input received as a part of engagement with interested parties. Although these elements were out of scope, the advisory panel acknowledges that they are important within the broader context of newborn screening and have implications for newborn screening in Canada. Specifically, the advisory panel felt it would be important to highlight the following topics for future work:

Other types of newborn screening methods: While the focus of the advisory panel's Recommended Pan-Canadian Newborn Screening List is on bloodspot screening for primary conditions, there are many other types of newborn screening methods that can be used to identify the need for further diagnosis of a condition in Canada. There are a few point-of-care and home monitoring tests that are offered in select jurisdictions (e.g., pulse oximetry for critical congenital heart disease, and monitoring feces colour to detect biliary atresia). Hearing tests are another common newborn screening method and are often administered by a separate newborn hearing screening program. Lastly, some jurisdictions perform targeted screening, where a certain condition is looked for in a certain population or by special request. Because there are multiple methods that can be used within newborn screening tool kits, the advisory panel encourages future work to consider opportunities to collaborate and coordinate newborn screening beyond bloodspot screening.

Genomic sequencing: Genomic sequencing technologies are emerging as having the potential to allow for the simultaneous detection of multiple rare disease conditions, and their application to newborn screening is being studied by newborn screening programs internationally. While genomic sequencing was out of scope for the advisory panel's work, it is important to acknowledge that this technology is rapidly evolving and will impact newborn screening in the future. Genomic sequencing brings forward opportunities and challenges. Opportunities include the ability to screen for additional treatable diseases and the potential to enable research and support innovation. It may increase the ability to add new conditions to newborn screening with minimal resources. Conversely, it is recognized that a number of ethical and social issues present challenges when working with genomic data, such as data privacy, informed consent, diagnostic uncertainty, and the lack of representativeness of genomic databases for people of all genetic ancestries. Specific to newborn screening, genomic sequencing will likely require changes in the consent model (i.e., informed versus implied or opt-out consent). There are also ethical concerns related to screening newborns for conditions that may present later in life. The advisory panel indicated that there is a pressing need to explore genomic sequencing and its potential impact on newborn screening as more information, through national and international pilot studies, becomes available. A part of this exploration should include public engagement and input on this important topic.

Laboratory infrastructure: Laboratory infrastructure considerations should be explored as a part of the implementation considerations. When proposing the expansion of the number of conditions screened for by a program, there are many components that need to be in place to operationalize the expansion. These include, but are not limited to, having the necessary equipment, technological systems (including laboratory information systems), operating processes, physical space, and staff expertise (in the lab and clinical experts for managing a positive screening result and providing care). Having the proper laboratory and clinical infrastructure is critical to ensure that any changes to newborn screening are integrated appropriately.

Data sharing, privacy, and quality metrics: When proposing the example for a coordinated newborn screening model, the advisory panel identified a need for data sharing, quality indicators, and standards. There is currently no infrastructure for cross-provincial and territorial newborn screening data collection and data analysis to inform quality improvement. While data sharing was considered out of scope, the advisory panel recognizes the importance of standardized and integrated data systems where monitoring and evaluation of lab data and patient outcomes can take place and support multijurisdictional decision-making. The Canadian Public Health Laboratory Network was identified as an example of a model of success in integrated data collection across provinces and territories to inform advances in select disease areas in public health. Processes for maintaining privacy need to be developed and established, with early engagement with the public as an important step. Quality metrics were identified as an important initiative, as newborn screening programs currently have no way of sharing laboratory methods, optimal laboratory cut-off values, and performance of diagnostic algorithms. Developing quality metrics at a national level can further support quality, safety, and equity of screening across the country.

Educational materials: The advisory panel identified the importance of developing educational materials, for both health care providers and the public, within the potential functions for the quality, standards, and education committee. Input received through engagement activities identified that clinicians, people who

are pregnant, and parents desire standardized and accessible educational materials on newborn screening, particularly given the expanding number of conditions that are being screened for. While the exploratory model is not intended to provide detailed descriptions of the potential functions of the proposed committees, the advisory panel wanted to highlight that the development of such educational materials for both clinicians and patients would need to be culturally appropriate and available in multiple languages.

Conclusion

As an independent advisory panel making nonbinding recommendations to support pan-Canadian collaboration around newborn screening, we are grateful to Canada's Drug Agency and the Government of Canada's National Strategy for Drugs for Rare Diseases for the opportunity to be part of this discussion.

The nonbinding recommendations were built upon learnings from existing programs and processes, and were developed to advance newborn screening in Canada and in support of the National Strategy for Drugs for Rare Diseases. As this work continues, the advisory panel noted that it was important to highlight the need to continue to engage with members of the public, interested parties, and decision-makers in newborn screening. Engaging with people who live across Canada, including those who are affected by social and/or economic policies as well as individuals and representatives who are First Nations, Inuit, or Métis, will continue to be important for newborn screening programs to act in accordance with the guiding principles.

With the anticipated increase of new treatments for rare diseases, there is an opportunity to prepare for the potential corresponding increases in the number of conditions that could be screened for in newborns. The advisory panel and the individuals who participated in the engagement activities strongly felt that newborn screening is an important public health matter and that these recommendations can advance the dialogue for decision-makers and directly contribute to the early identification of newborns with serious and rare diseases, improving access to timely and appropriate intervention.

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Appendix 1: Approach, Assumptions, and Limitations

Please note that this appendix has not been copy-edited.

Approach

- To support the development of the guiding principles, the process to add or reassess a condition, and the criteria for deliberations and recommendations on adding or reassessing a condition, Canada's Drug Agency supported the advisory panel with relevant publicly available information and published literature.
- A staff information specialist conducted a literature search on key resources including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, the International Health Technology Assessment Database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search approach was customized to retrieve a limited set of results, balancing comprehensiveness with relevancy.
    - The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. Search concepts were developed based on the elements of the research questions and selection criteria. The main search concepts were newborn screening programs and equity, evidence-based medicine, decision-making, or principles. The search was completed on September 19, 2023, and limited to English-language documents published since January 1, 2018.
    - Search results were screened by 1 reviewer experienced in citation screening in Endnote. Citations selected for potential full-text retrieval were those that were relevant to newborn screening program policy and decision-making. The focus was on selecting citations that were described in the title and/or abstract a focus on principles for newborn screening criteria and decision-making for newborn screening, including ethical, legal or social issues, emerging conditions, and perspectives and experiences from collaborators.
- For the guiding principles, 6 key sources were drawn upon: CORD,[24] Canada's Rare Disease Strategy,[2] Quebec's newborn screening program reference framework,[25] Australia's National Policy Framework for Newborn Screening,[6] the US Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC)'s decision matrix,[26] and the key principles for newborn screening from Rare Diseases Europe (EURORDIS).[27]
- Potential opportunities for a coordinated model of newborn screening were developed using key sources including the composition, terms of reference, and reporting structures of newborn screening advisory committees in British Columbia,[28] Ontario,[29] the US,[30] and Australia,[31] and the process of adding or removing conditions in those same jurisdictions. Information was supplemented with relevant published literature as appropriate.
- The criteria for adding or reassessing a condition drew on published literature and 3 key examples of publicly available criteria for advisory committees in Ontario, the US, and Australia (Table 2).

Table 2: Canadian and International Sources of Decision-Making Criteria for Adding Conditions to a Proposed Newborn Screening List

Source	Purpose
Wilson and Jungner's criteria[5]	Wilson and Jungner's principles of screening, first published in 1968, are cited as the foundational criteria for many public health screening programs, including newborn screening programs.
Dobrow et al., 2018[32]	Dobrow and team aimed to build on Wilson and Jungner's initial criteria and conducted a systematic review of principles used in public health screening, then used a consensus-based approach to develop a consolidated set of criteria.
Newborn Screening Ontario, high-level criteria from Form 3[33]	These criteria are used to guide the evidence review and the committee deliberations on the evidence when making recommendations on a condition for screening in Ontario.
ACHDNC	The ACHDNC uses key questions and topics[34] to guide the evidence review. A different set of questions is used in deliberations on recommendations that evaluate net benefit, certainty of those benefits, system readiness, and feasibility.
Australia's Newborn Bloodspot Screening Framework[6]	Australia uses these criteria to guide their evidence review and the deliberations on the evidence when making recommendations on a condition for screening in Australia.

ACHDNC = Advisory Committee on Heritable Disorders in Newborns and Children.

- As a part of engagement activities, a discussion paper was shared and interested parties were invited to share their input through an online consultation form. Focus group and key informant interviews were conducted to seek input from birth care providers that brought their experiences as people from or working with people who were affected by economic and/or social policies. In addition, Canada's Drug Agency contracted Sage Solutions to conduct focus groups discussions with individuals from First Nations, Inuit, and Métis communities. All of the input received was reviewed and considered by the advisory panel.

Assumptions

- The guiding principles, exploratory outline of a coordinated model for newborn screening, proposed processes and criteria to add or reassess a condition, and the proposed pan-Canadian approach are being advanced as a first step with recognition that there will be a need for modification should they be considered and adopted in future for implementation.
- Inequities in outcomes can be affected by inequities in access to screening but can also affect those who do access newborn screening. This can be for several reasons, including difficulties accessing diagnostic services, delays in accessing care, challenges accessing treatment. Inequities can also arise where the benefits of newborn screening are not realized by a population. This can include scenarios where the clinical and analytic validity of a particular screening target differs for a specific population, for example where the genetic variants that contribute to a condition differ in type or distribution by population. Where appropriate, activities outlined incorporated the use of the Equity Checklist for HTA (ECHTA).[35] Efforts were made to ensure there was inclusive, diverse, and equitable representation among experts and interested persons engaged in this project, aligned with our commitment to inclusivity, diversity, equity, and accessibility (IDEA).[36]

- Additionally, Canada's Drug Agency acknowledges the critical need for Indigenous perspectives in health care systems in Canada. In both historical and ongoing ways, Indigenous Peoples and communities in Canada have been excluded from and/or harmed by medical research and have faced systemic racism and prejudice within health care systems. We commit to reconciliation,[37] and as part of our journey toward reconciliation, we created space and committed resources to ensure Indigenous voices were heard and influenced this work.
- Coordination of efforts including having a proposed common list of conditions to screen in future would not infringe upon the authority and the responsibilities of respective parties, including newborn screening programs and provincial and territorial ministries of health decision-makers.

Limitations

- The identification of guiding principles, their definitions and existing processes and criteria for adding or reassessing conditions for newborn screening relied on a limited literature search and iterative selection process that were done at a point in time, and any updates since the search period were not included in the discussion by the advisory panel.
- While the advisory panel was composed with considerations of diversity, the perspectives of the advisory panel members are not reflective of all perspectives and opinions relevant to newborn screening in Canada. Engaging with members of the public and interested parties to elicit their perspectives on the advisory panel's proposals was intended to address this limitation.
- These limitations were addressed by prioritizing transparency of, and collaboration on, the final outputs of the work (i.e., consulting broadly and soliciting public input to ensure there was opportunity to identify as broad a set of inputs and perspectives as possible).
- Other limitations include the difficulties accounting for variation in newborn screening programs across Canada.

Appendix 2: Summary of Input on the Guiding Principles

Please note that this appendix has not been copy-edited.

Interested parties who provided responses shared their input on a draft version of the guiding principles. Input was gathered through an online questionnaire, focus group discussions, or key informant interviews and is summarized online. During these engagement activities, respondents generally expressed their agreement with the guiding principles proposed by the advisory panel. Most of the input received related to clarifying elements of the definitions. The advisory panel reviewed and discussed the input and subsequently made changes to the guiding principles. Some of the themes that arose from the input include:

- incorporating considerations for the family or caregivers and communities
- incorporating a focus on the well-being of the newborn and holistic care
- providing additional details surrounding the definition of terms, such as quality and partners
- addressing additional barriers and challenges to access
- incorporating concepts such as timeliness and openness
- acknowledging that tension can exist between the guiding principles
- clarifying that the guiding principles are intended to be considered collectively, and can build on one another
- clarifying the purpose of the guiding principles.

At times, the input received did not lead to changes; for example, to a specific definition because it was addressed in another section of the report, or the input was out of scope for inclusion. Some examples of such comments that were out of scope included providing specific details on how the guiding principles will be weighted and operationalized or sought details relating to funding of the conditions.

Appendix 3: Additional Information: Vision for a Future Coordinated Model for Newborn Screening in Canada

Please note that this appendix has not been copy-edited.

Considerations for Committee Composition and Functions

When recruiting members for various committees, the advisory panel indicated that it will be important to include a diversity of perspectives and represent dimensions of diversity, including but not limited to women; Indigenous Peoples; and persons of all races, places of origin, religions, abilities, sexual orientations, and gender identities and expressions. There also may be specific jurisdictional considerations relating to equity that should be considered when identifying potential committee members.

The advisory panel recommended, for specific committees, there may be a need for specialized subcommittees, either standing or ad hoc or time-limited, to address specific tasks; this will ensure the required activity is executed with the appropriate expertise. While noting the need for varying experts, the advisory panel also recognized the need to manage recruitment on different committees due to the limited pool of expertise in newborn screening, which may result in experts having to serve on multiple committees at a pan-Canadian and local level. If such a model is explored in the future, there could be opportunities to further consider the operations and process to leverage existing expertise without putting undue burden on these experts (for example, examining and reducing any potential duplication of efforts within these processes).

Table 3 describes the proposed committees and their composition and function.

Table 3: A Potential Coordinated Model for Newborn Screening in Canada: Committee Composition and Functions

Proposed committee	Potential composition	Potential functions
Newborn screening advisory committee	The committee may be composed of 5 to 15 multidisciplinary members. Such a committee would be required to have diverse representations, perspectives, and expertise (e.g., laboratory experts, clinical experts, people with lived and living experience, allied health care providers, ethicists, representatives from newborn screening programs, and so on) and could have observers from provincial and territorial ministries of health.	The potential responsibilities of this committee may include: • providing oversight and advising committees, including the integrity of decisions and implementation of guiding principles • providing strategy and intelligence in newborn screening policy landscape • maintaining records of newborn screening adoption • reviewing and deliberating draft recommendations • making and communicating recommendations • providing a coordinated forum for communication with newborn screening programs and Provincial and Territorial Ministries of Health • building relations within the broader drugs for rare disease space • conducting consultations with the public.

Proposed committee	Potential composition	Potential functions
Expert review committee	The committee may be composed of 5 to 8 multidisciplinary members with the potential need for additional smaller expert subcommittees or working groups of 3 to 4 members. The membership of the expert review committee could include, but is not limited to, clinician experts, laboratory scientists, health economists, ethicists, experts in health technology assessment, experts in public health, experts in public engagement, a member of the public, and people with lived and living experience.	The potential responsibilities of this committee may include: • reviewing nomination forms • conducting horizon scans to detect emerging newborn screening conditions • completing evidence reviews on newborn screening conditions or new screening technologies • conducting public engagement • drafting recommendations.
Quality, standards, and education committee	The committee may be composed of 5 to 8 multidisciplinary members with the potential need for additional smaller expert subcommittees or working groups of 3 to 4 members. The membership of the quality, standards, and education committee could include, but is not limited to, knowledge translation and communication experts, data management administrators, newborn screening laboratory and clinical experts, health care policy and standards administrators, population and public health experts, ethicists, and people with lived and living experience.	The potential responsibilities of this committee may include: • providing guidance on best practices, standards, definitions, key performance indicators, and follow-up for newborn screening programs • providing support for developing protocols or proposals for newborn screening programs • coordinating and supporting a newborn screening data repository • developing educational materials and providing learning opportunities for health care providers and the public.
Newborn screening programs	Representatives from the newborn screening programs	The potential role of newborn screening programs may include: • communicating program needs • sharing information about their program data • providing input on nominations and recommendations • observing on the newborn screening advisory committee.
Provincial and territorial ministries of health	Representatives responsible for newborn screening funding decisions within the provincial and territorial ministries of health	The potential role of provincial and territorial ministries of health may include: • communicating priorities relating to newborn screening • reviewing screening recommendations to make funding decisions for their respective jurisdictions • observing on the newborn screening advisory committee.

Appendix 4: Recommended Processes to Add or Reassess Conditions for a Pan-Canadian Newborn Screening List

Please note that this appendix has not been copy-edited.

The advisory panel recommended 4 sequential and dependent processes.

Nomination Process

Step 1: Nomination Submitted

The advisory panel recommended that nominations would be open to the public, including individuals (e.g., patients, clinicians), groups or organizations (e.g., patient advocacy groups, provincial and territorial ministries of health), and submitted nominations would be made publicly available. The advisory panel agreed that conflict of interest disclosure should be a requirement of the nomination submission process. The nomination forms used in the submission step of the process would be designed to balance accessibility with comprehensiveness.

Step 2: Nomination Reviewed

The advisory panel recommended that, once submitted, the nomination would be reviewed for completeness. Nominations with missing information would be returned to the nominator for completion. Nominations deemed to be complete would advance to the next step.

Step 3: Nomination Deliberated

The advisory panel recommended that the nomination form would be reviewed for alignment with the predefined criteria and deliberations would take place as to whether the nomination should advance to an evidence review.

Steps 4 and 5: Recommendation Regarding Whether to Proceed With an Evidence Review

The advisory panel recommended that the outcome of the nomination review would be communicated to the nominator and made public, including a rationale for the decision. Whereas nominations deemed to align with the criteria would proceed to evidence review, those nominations that may not proceed to evidence review could be resubmitted within a prespecified time frame if new information becomes available.

Alignment of the Nomination Process With the Guiding Principles

The public availability, accessibility and comprehensiveness of the nomination submission step demonstrates adherence to the guiding principles of transparency, equity, collaboration and effectiveness, safety and quality. The requirement for a complete nomination that aligns with the criteria demonstrates the guiding principle of effectiveness, safety, and quality. Decisions concerning whether a nomination proceeds to evidence review are communicated publicly, aligning with the guiding principles of collaboration and transparency.

Evidence Review Process

Step 6: Evidence Review Conducted

The advisory panel recommended that the approach to the evidence review would be informed by the recommended guiding principles and would consider the potential benefits and harms of screening for the nominated condition in newborns. The evidence review would identify, assess, critically appraise and summarize the available information and evidence describing the condition, available screening tests, treatment, and societal and other considerations. Additional information may be included as part of this step where there is, for example, uncertainty in the availability of evidence to support eligibility or a full evidence review.

The scope, detail, and timeline for completion of the evidence review will be contingent upon practical, technical, and methodological considerations. The evidence review may be conducted by a time-limited or commissioned working group, including potential ad hoc members with clinical or other expertise and/or experience with the condition (e.g., clinicians, researchers, people with lived and living experience, and provincial/territorial decision-makers). There may be opportunities to engage members of the public and people with lived and living experiences during the review process.

The evidence review working group would use the criteria to consider the evidence and the net benefit of screening for the condition to make a draft recommendation whether to add the condition to the proposed pan-Canadian newborn screening list.

Alignment of the Evidence Review Process With the Guiding Principles

The evidence review is designed to identify and summarize potential benefits and harms to newborns, which supports the guiding principle of prioritizing the health rights of the newborn. The evidence review is also informed by the criteria for adding and reassessing conditions, which aligns with the guiding principle of effectiveness, safety, and quality. The evidence review process is inclusive of experts, those with lived and living experience, and the public, which supports the guiding principles of equity and collaboration.

Deliberation and Recommendation Process

Step 7: Evidence Review Deliberated

The advisory panel recommended that the proposed newborn screening advisory committee will deliberate on the net benefit of screening for a condition, as described within the evidence review, and consider proposed recommendations using the criteria for adding or reassessing a condition to or from the proposed pan-Canadian newborn screening list. The deliberations will include diverse perspectives and will be structured to ensure that all criteria and relevant information are considered. The deliberations could be made public, and meeting minutes would be made publicly available.

Step 8: Recommendation Drafted

The advisory panel recommended that the proposed newborn screening advisory committee would refine and propose draft recommendations (including justification and rationale), which would generally focus on whether to add the nominated condition to the proposed pan-Canadian newborn screening list, or to reassess a condition already on the list. Draft recommendations could also address the need for generating additional evidence (e.g., when the net benefits to the newborn for a condition remain unclear), optimal types of screening tests, the need for developing clinical guidance for the diagnosis and treatment of a condition when it is not recommended for addition, and/or the need to consider screening and/or diagnostic testing that may have implications beyond newborn screening.

If any conditional recommendations were issued, an outline describing what would be needed to satisfy the conditions would also be provided.

Alignment of the Deliberation and Recommendation Process With the Guiding Principles

The deliberations will be informed by the criteria and a structured approach, demonstrating adherence to the guiding principles including the health rights of the newborn, effectiveness, safety, and quality, and collaboration. The deliberations will be publicly available, which aligns with the guiding principle of transparency. The draft recommendations will consider variations in populations, capacities, and resources within and across provincial and territorial jurisdictions, supporting the guiding principles of equity, collaboration, and sustainability.

Engagement and Communication Process

Step 9: Engagement

The advisory panel proposed that draft recommendation(s) would be made publicly available and eligible parties would be able to provide feedback.

Step 10: Communication

The advisory panel proposed that input and feedback be made publicly available, collated, and incorporated into the recommendations, as appropriate. Any final recommendations would be issued by the proposed newborn screening advisory committee, made publicly available, and communicated to health decision-makers across Canada’s provinces and territories.

Alignment of the Engagement and Communication Process With the Guiding Principles

Draft recommendations would be made publicly available to ensure all relevant feedback is solicited, considered, and incorporated, which support the guiding principles of the health rights of the newborn, transparency, equity, and collaboration.

Appendix 5: Input on the Proposed Processes

Please note that this appendix has not been copy-edited.

Table 4: Summary of Input Received on the Proposed Processes and the Advisory Panel's Responses

Proposed processes and steps	Summary of input received[a] and response
Nomination Step 1: Nomination submitted Step 2: Nomination form reviewed Step 3: Nomination form discussed and deliberated Steps 4 and 5: Recommendation for or against an evidence review	**General input received** • Conflict of interest disclosure should be mandatory for nominators. **Response to input** • The advisory panel agreed that mandatory conflict of interest disclosure for nominators should be incorporated into the proposed nomination process.
Evidence review Step 6: Evidence review conducted	**General input received** • The evidence review team should include: ◦ expertise specific to the rare disease under consideration ◦ expertise specific to lived/living experience ◦ representation from the jurisdictions ◦ public input. • Available evidence from other jurisdictions should be eligible for consideration. **Response to input** • The advisory panel agreed that the evidence review team should include the representation suggested and that available evidence from other jurisdictions should be eligible for consideration as part of the proposed process.
Deliberation and recommendations Step 7: Deliberation Step 8: Recommendations	**General input received** • Expertise specific to the rare disease under consideration should be included in the process of deliberation and recommendations. • Expertise specific to lived or living experience should be included in the process of deliberation and recommendations. • Representation from jurisdictions should be included. • Deliberations should consider short-term and long-term implications for newborns, families, and health systems. **Response to input** • The advisory panel agreed on the suggested expertise, representation and implications that should be included in the proposed deliberations and recommendations process. The advisory panel also recognized that resourcing capacity, timelines and operational feasibility would need to be taken into account.
Engagement and communication Step 9: Draft recommendation published for feedback Step 10: Recommendation finalized and communicated	**General input received** • Conflict of interest disclosure should be mandatory for those providing feedback. **Response to input** • The advisory panel supported the idea that mandatory conflict of interest disclosure for those providing feedback could be incorporated into the proposed engagement and communication process.

[a]All input received was reviewed and considered for inclusion in the report; however, not all of the input received is summarized in Table 4. Some of the input received did not apply to a specific process or step, applied to another section of the report, or was out of scope for this report but relevant for future consideration.

Appendix 6: Input on Criteria for Adding a Condition and Responses

Please note that this appendix has not been copy-edited.

Table 5 details the initially proposed criteria, input received from the online consultations, focus groups, and key informant interviews, and the modifications made by the advisory panel.

Table 5: Input on the Proposed Criteria for Adding a Condition and Advisory Panel Responses

Wilson and Jungner's criteria[5]	Proposed modification to criteria	Input	Response to input
Condition			
The condition is an important public health problem.	The condition should be serious and 1 that arises in children and/or leads to morbidity and mortality in childhood.	"Child" may need to be more clearly defined (e.g., language used later in the report "manifest early in life (neonatal period, infancy, or early childhood)"). Do not agree that the condition must lead to morbidity or mortality in children – could exclude consequences or symptoms that can be prevented can often appear in later in life. (i.e., Wilson's disease). From focus groups: good to focus on children and serious disease as it leads to support for newborn screening (vs. a broader scope).	Childhood defined more clearly; "*arises early in life (neonatal period, infancy, or early childhood).*"
There should be a recognizable latent or early symptomatic stage.	Removed. The advisory panel indicated that this criterion is not relevant to newborn screening and elements (e.g., natural history) are captured by criterion 3.	Do not remove this criterion or ensure that criterion #2 is in fact covered in #3: need to ensure that the recognition of the concept of latency or early/ presymptomatic stage that creates opportunities for early therapeutic intervention to prevent harms and maximize well-being.	Latent or presymptomatic stage added to the next criterion (i.e., natural history).
The natural history of the condition, including development from latent to declared disease, should be adequately understood.	The epidemiology (including incidence and variation across regions and jurisdictions) and natural history of the condition should be adequately understood. Differences in the incidence and variation in test performance in subpopulations, particularly in equity-deserving groups, should be characterized and adequately understood.	The concept of a latency period needs to be more clearly discussed – there needs to be some degree of a presymptomatic period or reversibility of symptoms has been lost. Differencing perspectives on the value and impact of statement that acknowledges differences in subpopulations: some felt it was unclear what this would require, others (particularly focus group participants) felt it is necessary to account for changes in demographics.	Add "and natural history of the condition *(including the latent or presymptomatic stage)*…"

Wilson and Jungner's criteria[5]	Proposed modification to criteria	Input	Response to input
Test			
There should be a suitable test or examination.	There should be a robust, scalable, safe, precise, and validated screening test.	The change is unnecessary; proposed changes well-covered by the existing term "suitable" and any nuances of robust, scalable, safe, precise, and validated can best be examined in evidence review.	Remove "precise."
The test should be acceptable to the population.	The screening test, diagnosis, and treatment, should, on balance, be socially and ethically acceptable to health professionals and the public.	No input provided.	No change.
This is an additional criterion adapted from Newborn Screening Ontario.	The benefits of screening should outweigh the physical and psychological harms caused by the screening test (including the sample collection), diagnostic procedures, and treatment.	Define benefit: benefit to whom? (To individuals? To society?) Is screening (information and education provided to positive cases) beneficial? Is potential for enrolment in a clinical trial a benefit? Whose perspective gets to define benefit?	Add "benefits of screening to the newborn" to be clear focus is on health of the newborn.
Treatment			
There is an agreed policy on whom to treat as patients.	There is an agreed policy on the further diagnostic investigation of newborns with a positive screening test result. There should be agreed evidence-based policies covering which newborns should be offered treatment and the appropriate treatment to be offered.	Diagnostic policies can be developed once newborn screening is in place.	No change.
There should be an accepted treatment for patients with recognized disease.	There should be an effective treatment or intervention for newborns identified through early detection, with evidence of early treatment leading to better health outcomes and reduced morbidity and/or mortality than late treatment.	Does effective treatment or intervention include education that has been shown to reduce long-term complications, and/or the potential to take part in clinical trials for preventive therapies? Does effective treatment have to be Health Canada–approved? From focus group participant: What is "effective"? What if there is only moderate change over the long term? What if it improves quality of life?	No change.
Other considerations			
Facilities for diagnosis and treatment should be available.	Services and facilities for screening, diagnosis, and treatment should be available across Canada.	Different perspectives in the value and impact of this criterion: Serious concerns were expressed that	Removed "across Canada," added "to newborns who are screened."

Wilson and Jungner's criteria[5]	Proposed modification to criteria	Input	Response to input
		it could be interpreted as requiring services or facilities be available everywhere in Canada for a condition to be added, which would limit provinces' and territories' ability to add conditions and fails to recognize regional differences (e.g., founder effects). Others expressed support for this, agreeing there needed to be consistency in what care is provided across Canada. Focus group participants worried about the sustainability of care for families, in terms of noninsured costs and travel burden.	
Case-finding should be a continuing process and not a "once and for all" project.	Removed. The advisory panel indicated that this criterion is not relevant to adding a condition to a pan-Canadian newborn screening list.	The concept of "surveillance" is still important where irreversible harm takes place before the onset of clinical signs or symptoms, which is the compelling logic of doing population screening including surveillance, select or general depending on specific factors, including newborn screening of our target population.	No change.
The cost of case-finding (including diagnosis and treatment of patients who are diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.	The budgetary impact of case-finding (including screening, diagnosis, and treatment) should be considered in relation to not screening.	Suggest removing; too much missing information, costs are high but so is human need. Add monitoring to the costs of case-finding. Impacts beyond budget should be considered (i.e., should include health system and societal impacts). This criterion aligns with the guiding principle of sustainability, and it is important to consider.	No change.
Not applicable	Footnote A: The term *treatment* is used in this table to refer to health care (including pharmaceuticals, medical devices, and clinical interventions) that is intended to alter the course of and/or improve a person's health.	What about non–health care interventions (e.g., special diets, formula, and so on) that can prevent or delay further morbidity or change the course of a condition?	Add "clinical and therapeutic interventions such as diets."
Not applicable	Footnote B: The additional consideration for this can include the distribution of test values in the target population should be known	Could bar screening for a disorder that had not been studied in such a way that the distribution of test values is known in advance. The definition of 'suitable cut-off' for	Remove footnote B

Wilson and Jungner's criteria[5]	Proposed modification to criteria	Input	Response to input
	and a suitable cut-off level defined and agreed, and, if the screening test includes a test for mutations, the criteria used to select the subset of mutations to be covered by screening, if all possible mutations are not being tested, should be clearly set out.	a screening test is dependent upon factors (instrumentation, location, seasonality) that are outside the scope of consideration when adding a condition. Remove this criterion – e.g., T-cell receptor excision circles analysis for severe combined immunodeficiency screening: there is no standardized assay, measurement or cut-off value. Each jurisdiction has had to develop their own cut-off values, and most have adjusted the cut-off over time as the programs have gained more experience and data with their specific assay.	

Appendix 7: Newborn Screening Across Canada

Please note that this appendix has not been copy-edited.

There are 8 newborn screening programs in Canada, some programs cover multiple jurisdictions. The current programs include:

- the Alberta Newborn Screening Program, which provides screening for Alberta, the Northwest Territories, and Nunavut (Kitikmeot)
- Newborn Screening BC, which provides screening for British Columbia and Yukon
- the Manitoba Newborn Screening Program which provides screening for Manitoba and Nunavut (Kivalliq)
- the Maritime Newborn Screening Program, which provides screening for New Brunswick, Nova Scotia, and Prince Edward Island
- the Newborn Screening Program in Newfoundland and Labrador
- Newborn Screening Ontario, which provides screening for Ontario and Nunavut (Qikiqtaaluk)
- Quebec's Neonatal Blood and Urine Screening Program
- Saskatchewan's Universal Newborn Screening Program.

Comparing the number of screening conditions across newborn screening programs can be challenging because of differences in how newborn screening conditions are reported and defined. Newborn screening programs typically categorize the conditions they screen for into 3 separate groups. They include primary or core conditions, secondary conditions, and targeted screening. Typically, a primary or core condition is a condition that has a newborn screening test that is specifically designed to assess whether a newborn may be at risk for having the condition. A secondary condition identifies a condition where newborn screening is not specifically designed to identify it, but the condition is found through screening for a primary condition. Lastly, targeted screening is when screening is provided to a specified subset of the population or by request. It can be difficult to compare the number of primary screening conditions across newborn screening programs in Canada because some programs consider conditions as primary conditions while other programs consider the same conditions as secondary conditions or provide targeted screening. Discrepancies in terminology can also add complexity to comparing screening across programs, as different jurisdictions refer to and define disorders, deficiencies, or conditions screened in different ways. Table 6 provides an overview of the conditions that are screened for through bloodspots by newborn screening programs in Canada. To support consistency with the condition counts, the advisory panel decided to focus on primary conditions that are identified through bloodspot screening for the Recommended Pan-Canadian Newborn Screening List.

Table 6: Conditions Screened Through Dried Bloodspot Newborn Screening Across Canada (Updated January 2025)

Condition	BC	AB	SK	MB	ON	QC	NB	PE	NS	NL	NU			YT	NT
											Qik	Kit	Kiv		
3-hydroxy-3 methylglutaryl-coenzyme A lyase deficiency	No	Yes	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes
Argininosuccinic aciduria	Yes	Dev	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Dev	Yes	Yes	Dev
Biotinidase deficiency	Yes	Yes	Yes	Yes	Yes	Targ	Yes	Yes	Yes	Rev	Yes	Yes	Yes	Yes	Yes
Carnitine acylcarnitine translocase deficiency	Sec	No	Yes	Yes	Sec	Sec	Yes	Yes	Yes	Yes	Yes	No	Yes	Sec	No
Carnitine palmitoyltransferase I deficiency	No	No	Yes	Yes	Sec	Sec	Yes	Yes	Yes	Yes	Yes	No	Yes	No	No
Carnitine palmitoyltransferase II deficiency	Sec	No	Yes	Yes	Sec	Sec	Yes	Yes	Yes	Yes	Yes	No	Yes	Sec	No
Carnitine uptake deficiency	Yes	Yes	Yes	Yes	Yes	Dev[a]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Citrullinemia, type I	Yes	Yes	Yes	Yes	Yes	Sec	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Classic galactosemia	Yes	Yes	Yes	Yes	Yes	Targ	Yes	Yes	Yes	Rev	Yes	Yes	Yes	Yes	Yes
Classic phenylketonuria	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Condition	BC	AB	SK	MB	ON	QC	NB	PE	NS	NL	NU			YT	NT
											Qik	Kit	Kiv		
Congenital adrenal hyperplasia	Yes	Yes	Yes	Yes	Yes	Dev	Dev	Dev	Dev	Rev	Yes	Yes	Yes	Yes	Yes
Congenital cytomegalovirus: hearing loss risk factor	No	Dev	Yes	No	Yes	No	No	No	No	No	No	Dev	No	No	Dev
Cystic fibrosis	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Glutaric acidemia, type I	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Guanidinoacetate methyltransferase deficiency	Yes	Dev	No	No	Yes	No	No	No	No	Yes	No	Dev	No	Yes	Dev
Hemoglobin S beta thalassemia (sickle cell beta thalassemia)	Yes	Yes	Dev	Yes	Yes	Yes	Yes	Yes	Yes	Rev	Yes	Yes	Yes	Yes	Yes
Hemoglobin SC disease	Yes	Yes	Dev	Yes	Yes	Yes	Yes	Yes	Yes	Rev	Yes	Yes	Yes	Yes	Yes
Hemoglobin SS (sickle cell anemia)	Yes	Yes	Dev	Yes	Yes	Yes	Yes	Yes	Yes	Rev	Yes	Yes	Yes	Yes	Yes
Homocystinuria	Yes	No	No	Yes	Yes	Dev[a]	No	No	No	Yes	Yes	No	Yes	Yes	No
Isovaleric acidemia	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Condition	BC	AB	SK	MB	ON	QC	NB	PE	NS	NL	NU			YT	NT
											Qik	Kit	Kiv		
Long-chain hydroxyacyl-coenzyme A dehydrogenase deficiency	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Maple syrup urine disease	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Medium-chain acyl-coenzyme A dehydrogenase deficiency	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Methylmalonic acidemia (cobalamin disorders)	Yes	Yes	Yes	Yes	Yes	Dev[a]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Methylmalonic acidemia (methylmalonyl-coenzyme A mutase deficiency)	Yes	Yes	Yes	Yes	Yes	Dev[a]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Mucopoly-saccharidosis, type IH	Dev	Dev	No	No	Yes	No	No	No	No	Rev	Yes	Dev	No	Dev	Dev
Primary congenital hypothyroidism	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Propionic acidemia	Yes	Yes	Yes	Yes	Yes	Dev[a]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Condition	BC	AB	SK	MB	ON	QC	NB	PE	NS	NL	NU			YT	NT
											Qik	Kit	Kiv		
Severe combined immunodeficiencies	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Rev	Yes	Yes	Yes	Yes	Yes
Spinal muscular atrophy	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes[b]	Yes	Yes	Yes	Yes	Yes
Trifunctional protein deficiency	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Tyrosinemia, type I	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Very long-chain acyl-coenzyme A dehydrogenase deficiency	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
X-linked adreno-leukodystrophy	No	No	No	No	Dev	No	No	No	No	No	No	No	No	No	No

AB = Alberta; BC = British Columbia; Dev = in development; Kit = Kitikmeot; Kiv = Kivalliq; MB = Manitoba; NB = New Brunswick; NL = Newfoundland and Labrador; NS = Nova Scotia; NT = Northwest Territories; NU = Nunavut; ON = Ontario; PE = Prince Edward Island; QC = Quebec; Qik = Qikiqtaaluk; Rev = under review; SK = Saskatchewan; Sec = secondary; Targ = targeted; YT = Yukon.

Notes: “Yes” denotes a primary screened condition (i.e., a stated target of the screening program). “Sec” (“secondary”) denotes a secondary screened condition (i.e., not a stated target, but anticipated to be detected as a result of screening). “Targ” (“targeted”) denotes a condition targeted to a specific population (i.e., the screening is provided to a specified subset of the population or by request). “Dev” (“in development”) denotes a condition that has been approved for funding and screening is in development. “Rev (“under review”) denotes a condition that is formally being reviewed for inclusion. “No” denotes a condition that is not screened (i.e., the condition has not been formally considered or has been reviewed and declined as a target).

[a]Conditions will be screened for as of April 28, 2025.

[b]Screening is a part of a pilot program; funding will expire in May 2025.

Appendix 8: The 2016 Recommended Canadian Newborn Screening List of Conditions and Modifications

Please note that this appendix has not been copy-edited.

2016 Recommended Canadian Newborn Screening List of Conditions

In 2016, an Intergovernmental Working Group made recommendations for a pan-Canadian list for newborn screening and prepared a report for the ministers of health. The Intergovernmental Working Group developed a newborn screening list through a consensus-based approach. During their deliberations, the members drew upon the Wilson and Jungner criteria and considered test performance, treatment options, benefits of care on newborn health, and information from the different newborn screening programs. The principle of fairness of access to newborn screening across Canada was an overarching theme in their discussions. The list of 22 conditions that were recommended for the Canadian list by the Intergovernmental Working Group in 2016[7] included:

- argininosuccinic aciduria
- biotinidase deficiency
- carnitine uptake deficiency
- citrullinemia, type I
- classic galactosemia
- classic phenylketonuria
- congenital adrenal hyperplasia
- congenital hypothyroidism
- cystic fibrosis
- glutaric acidemia, type I
- isovaleric acidemia
- long-chain hydroxyacyl-coenzyme A dehydrogenase deficiency
- maple syrup urine disease
- medium-chain acyl-coenzyme A dehydrogenase deficiency
- methylmalonic acidemia (methylmalonyl-coenzyme A mutase)
- methylmalonic acidemia (cobalamin A and B disorders)
- propionic acidemia
- severe combined immunodeficiency
- sickle cell disease (which includes hemoglobin SS, hemoglobin SC, and hemoglobin S beta thalassemia)
- trifunctional protein deficiency

- tyrosinemia, type I
- very long-chain acyl-coenzyme A dehydrogenase deficiency.

Modifications to the 2016 Recommended Canadian Newborn Screening List of Conditions

The advisory panel recommended that the list of 22 conditions from 2016 be adopted as the starting point for the Recommended Pan-Canadian Newborn Screening List, with a few modifications.

The first modification is to separate sickle cell disease and count each of the 3 different subtypes of this condition. Different newborn screening programs have different approaches for counting sickle cell disease, and some programs include sickle cell conditions within the broader group of conditions known as hemoglobinopathies. On the 2016 recommended Canadian newborn screening list, sickle cell disease was counted as 1 condition, but there are different subtypes of the condition that are identified through the newborn screening process. In the US, they separate and count each subtype of sickle cell disease.[23] To provide clarity and align with international standards, it was recommended to split out this condition into the 3 subtypes for the Recommended Pan-Canadian Newborn Screening List.

The second modification that the advisory panel made to the recommended newborn screening list was to expand the list to include uniformly screened conditions that have been added to newborn screening programs across Canada after the original 2016 list was proposed. One new condition, spinal muscular atrophy, was identified as in the process of being screened for across all jurisdictions in Canada and is recommended for inclusion on the Recommended Pan-Canadian Newborn Screening List.

Appendix 9: Input Received Regarding the Recommended Pan-Canadian Newborn Screening List of Conditions

Please note that this appendix has not been copy-edited.

Through the online consultations, input received requested the addition of all 9 conditions to the Recommended Pan-Canadian Newborn Screening List without additional evidence review. Some respondents also voiced their disagreement in the use of variation in screening practices as a reason to suggest further evidence review. The following were the conclusion and reasons made by the advisory panel on why evidence review is needed for these 9 specific conditions:

- **Variation in screening practices:** While variations in screening practices may be due to a program not having the opportunity or resources to review a particular condition, variations may also be due to newborn screening programs removing a condition from their program, programs reviewing a condition and making the decision not to add the condition, or a program counting a condition as a secondary condition rather than a primary condition. Understanding the variation and the reason for these differences is required before recommending the addition of a condition to the Recommended Pan-Canadian Newborn Screening List.
- **Differences in populations across jurisdictions:** Canada is diverse, and every jurisdiction has their own unique subpopulation. For some conditions there is a need to review how the condition, and its variants, impact different populations in Canada before recommending screening across all jurisdictions.
- **Rarity of the condition**: Some conditions are extremely rare; therefore, it may be beneficial to consider newborn screening data and prevalence from Canada before recommending screening for all jurisdictions.
- **Evidence considerations:** While a thorough review of the evidence was out of scope for the advisory panel, there are conditions on the list of conditions requiring an evidence review that would benefit from a robust evidence review due to conflicting evidence reports or knowledge of new evidence that could impact screening practices.

It is also important to note that newborn screening programs and the evidence within this space is changing constantly. While the recommendation, at this point in time, is for the conditions to remain on the further evidence review list, this may change as the newborn screening landscape evolves and more information becomes available.

We also received recommendations to include conditions from the emerging conditions list (e.g., Pompe disease, Duchenne muscular dystrophy, mucopolysaccharidosis type 2) on the recommended pan-Canadian list. We also received requests to add Wilson's disease to the list of conditions that require an evidence review. The objective for seeking this information is to support health systems readiness and movement toward more consistent access to newborn screening across Canada. The inclusion of the emerging conditions list is intended to identify conditions that may be considered for the proposed pan-Canadian

newborn screening list in the future. The conditions noted by respondents are all included on the emerging conditions list.

We also received recommendations to include other hemoglobinopathies on the recommended pan-Canadian list. Previously on newborn screening lists, sickle cell disease was represented as 1 condition. In keeping with the nomenclature from international sources, sickle cell disease was broken into 3 specific subtypes for the Recommended Pan-Canadian Newborn Screening List. As a part of sickle cell disease screening, different subtypes were not included on the pan-Canadian newborn screening list because they were identified and considered by some newborn screening programs as secondary conditions. The advisory panel did not include secondary conditions as a part of their work and have acknowledged a need to consider secondary conditions in the future.

Appendix 10: Emerging Conditions for Newborn Screening in Canada

Please note that this appendix has not been copy-edited.

The emerging conditions for consideration for newborn screening in Canada include:

- adenosine deaminase deficiency
- Batten's disease
- biopterin deficiencies (BH4)
- branch chain keto-acid dehydrogenase deficiency
- caspase recruitment domain family member 11 (CARD11)
- Dravet syndrome
- Duchenne muscular dystrophy
- Fabry disease
- Gaucher disease
- hereditary angioedema type 1 and 2
- hypophosphatasia and achondroplasia
- hypovitaminosis D
- IKBKB deficiency and purines
- Krabbe disease
- macular degeneration
- metachromatic leukodystrophy
- MT-RNR1 variant cochleotoxicity from aminoglycoside treatment
- mucopolysaccharidosis, type 2
- mucopolysaccharidosis, type 3
- mucopolysaccharidosis, type IVA
- mucopolysaccharidosis, type VI
- Niemann-Pick disease, type A and B
- Pompe disease
- primary hyperoxaluria type 1
- type I diabetes
- Wilson's disease
- Wiskott-Aldrich syndrome
- X-linked agammaglobulinemia
- zeta-associated protein 70 (ZAP70) deficiency.

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Questions or requests for information about this report can be directed to Requests@CDA-AMC.ca.