Canada's Drug Agency
L'Agence des médicaments du Canada
Drugs. Health Technologies and Systems. Médicaments, technologies de la santé et systèmes.

Consultations on Proposed Pan-Canadian Guidance for Newborn Screening: Building the Foundations for Early Detection and Diagnosis of Conditions

IN SUPPORT OF THE NATIONAL STRATEGY FOR DRUGS FOR RARE DISEASES

Index of Respondents

Alberta Precision Labs

1. Do you agree with the proposed guiding principles and definitions?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

No response provided

3. Do you agree with the proposed process for nominating a condition?

No response provided

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4. Do you agree with the proposed process for evidence review?

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5. Do you agree with the proposed processes for deliberating and developing recommendations?

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7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes-in part

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This point could have been applied in a number of places. I understand the need for a Pan-Canadian approach and applaud the work. Would you please consider that some jurisdictions, based on specific populations, may be able to justify NBS for disorders which are not present in all, or even most provinces/territories. While this is a special condition, I would like the inclusion of a proviso stating such. My worry is that various Ministries of Health may rely so heavily on your recommendations that they may discount justifiable internal recommendations/needs.

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

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Please provide your reason(s) and suggested changes, if any.

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9. Do you agree with the proposed pan-Canadian newborn screening list?

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No response provided

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

No response provided

11. Are there any other comments that you would like to share with us?

No response provided

Alnylam Canada ULC

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Primary hyperoxaluria type 1 (PH1) is a rare but serious genetic disorder that leads to the overproduction of oxalate, which can accumulate in the kidneys and other organs, ultimately leading to nephrocalcinosis, damage to other organs, and kidney failure.[1] Early diagnosis and treatment are crucial in managing the disease effectively.[1] Here are several key reasons why PH1 should be added to newborn screening programs:

1. Early Detection Prevents Irreversible Damage

PH1 often presents with kidney stones and kidney failure at a young age, but the damage begins much earlier.[1] Many patients go undiagnosed until significant, irreversible harm to the kidneys or other organs has already occurred. End-stage kidney disease (ESKD) can develop in early childhood and affects 50% of all children at the time of diagnosis.[1,2,3] ESKD can appear as early as age 4 to 6 months and typically before age 12 months, resulting in the need for permanent dialysis or a dual liver-kidney transplant[1,2.3] Newborn screening can detect PH1 before symptoms appear, allowing for early intervention to prevent oxalate buildup and avoid ESKD.

2. Early intervention Can Prevent Kidney Failure

While PH1 is rare, early diagnosis significantly improves treatment outcomes. Traditional management, including high fluid intake, medications, and in severe cases, liver and kidney transplants, are more effective when started early.[1] More recently, the introduction of promising therapies, such as RNA-based treatments (e.g. lumasiran) targeting the root cause of oxalate overproduction provide new options. These treatments are most effective when initiated early, before significant organ damage occurs, which further underscores the importance of early detection. There are several published and unpublished case reports highlighting the benefit of starting treatment early, within hours or days of birth.[4,5,6] Lumasiran was recently included in the list of Common Rare Disease Drugs by Health Canada, meaning patients across the country would have access to a targeted treatment immediately upon diagnosis.

3. Cost-Effectiveness and Healthcare Burden

Not only does early diagnosis and treatment improve outcomes for patients, but it can also result in substantial savings in healthcare costs. Treating advanced kidney failure, including dialysis and organ transplantation, is extremely expensive.[7] Early diagnosis and treatment can help reduce or even prevent these costs by limiting disease progression. Additionally, recent population/immigration patterns in Canada show an increase in individuals with this mutation, indicating a potential bigger impact to our healthcare system in the future. Screening for PH1 can be integrated into existing newborn screening programs with relative ease. Simple biochemical

tests and genetic testing methods can be used to detect elevated oxalate levels or specific gene mutations associated with PH1.

In conclusion, including PH1 in newborn screening programs is a vital step in preventing serious health consequences, improving treatment outcomes, reducing healthcare costs, and supporting affected families. Early diagnosis enables timely intervention that can dramatically change the life trajectory of infants born with this rare disease, turning what could be a fatal condition into a manageable one. This has resonated with physicians across Canada (Mathieu Lemaire – ON, Alex Belotovsky – ON, Dr Auray-Blais, QC). Certain countries, such as Germany, have already begun to initiate country-wide initiatives for newborn screening of PH1. Lastly, PH1 would fit with the other conditions included in the CDA's discussion paper that have an impact on the kidneys (e.g. Tyrosinemia, type I, Homocystinuria, Fabry disease, etc.).

References

1. Milliner, Dawn S., et al. "Primary hyperoxaluria type 1." (2022).

2. Metry, Elisabeth L., et al. "Determinants of kidney failure in primary hyperoxaluria type 1: findings of the European hyperoxaluria consortium." Kidney International Reports 8.10 (2023): 2029-2042.

3. Zhao, Fang, et al. "Predictors of incident ESRD among patients with primary hyperoxaluria presenting prior to kidney failure." Clinical Journal of the American Society of Nephrology 11.1 (2016): 119-126.

4. Taroni, Francesca, et al. "Case Report: effect of lumasiran treatment in a late preterm baby with antenatal diagnosis of primary hyperoxaluria type 1." Frontiers in Pediatrics 11 (2024): 1338909.

5. Méaux, Marie-Noëlle, et al. "The effect of lumasiran therapy for primary hyperoxaluria type 1 in small infants." Pediatric Nephrology 37.4 (2022): 907-911.

6. Hayes, Wesley, et al. "Efficacy and safety of lumasiran for infants and young children with primary hyperoxaluria type 1: 12-month analysis of the phase 3 ILLUMINATE-B trial." Pediatric Nephrology 38.4 (2023): 1075-1086.

7. Manns, Braden, et al. "The cost of care for people with chronic kidney disease." Canadian journal of kidney health and disease 6 (2019): 2054358119835521.

11. Are there any other comments that you would like to share with us?

No response provided

BIOTECanada

1. Do you agree with the proposed guiding principles and definitions?

No response provided

Please provide your reason(s) and suggested changes, if any.

Overall, the guiding principles and definitions are appropriate and reasonable and we strongly agree with placing the health rights of the newborn at the center. There are a few additional considerations:

- Timely diagnosis and treatment are mentioned several times in the document, but the element of timeliness appears to be missing from the guiding principles and definitions. It may align with the principle of 'equity'.
- The 'sustainability' guiding principle refers to the sustainability of the health system, but there is no reference to sustaining adequate and equitable access to newborn screening.

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

- The challenge with this vision is that it falls short of addressing the gap identified in the 'Setting the Context' of the document "Newborn screening policies, practices, and processes across Canada are not uniform as there are currently no standards at the national level." It is unclear how this vision for a coordinated system will improve timely diagnosis and appropriate access to treatments without clear linkages to decision-making. This system is set up to only provide guidance which is likely not sufficient to impact meaningful change.
- The proposed system is complex. There are likely existing frameworks (e.g. NACI/PHAC) that could be adapted for Newborn Screening. Once the current gaps and inconsistencies in which tests are included in newborn screening in each province are addressed, how many novel additions will be added annually? The document cited that "an estimated 60 new transformative cell and gene therapies are predicted to come to the market in the next 10 years" but it is unclear how many of those would fit within a newborn screening paradigm

3. .Do you agree with the proposed process for nominating a condition?

No response provided

Please provide your reason(s) and suggested changes, if any.

- For questions 3-8. It would be helpful to understand the anticipated volume of nominations annually. If it is a small number, this process may be too cumbersome to implement on a small scale.
- Overall, the guidance should take a progressive approach to new screening and testing. If provinces can consider more expansive lists from across the country when screening, even if it is not fully covered on their own lists, it would allow greater health equity for Canadians.

4. Do you agree with the proposed process for evidence review?

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No comment on which conditions should or should not be on the list

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

No response provided

11. Are there any other comments that you would like to share with us?

BIOTECanada commends the efforts of CDA and the advisory panel for their work in providing this guidance document on Newborn Screening, a very important and complex topic. We are heartened to see the link that the Discussion Paper draws between newborn screening and the implementation of the National Strategy for Drugs for Rare Diseases (DRDs), in order to enhance access to DRDs: "As part of setting the foundation for supporting the National Strategy for Drugs for Rare Diseases, there is an opportunity to further enhance systems coordination and equity of access for newborn screening." Equity is of paramount importance; however, it is unclear how this guidance will translate into improved equity of access to newborn screening, or to DRDs more broadly.

While newborn screening is at 100% for some diseases in Canada, many gaps remain and concerted efforts are needed to build up to and beyond these standards across the country. We hope to see the CDA be more ambitious in its newborn screening guidance to enable greater impact on patients as well as health systems. The CDA has a critical role to play as a health system leader and convenor, bringing jurisdictions together and building alignment around newborn screening standards, in order to enable and embed equity for people across Canada.

In addition, while 'sharing records, including patient-level data' was out of scope for this assessment, it would be an ideal opportunity to consider upfront how data on newborn screening could be gathered nationally to inform policies and decision-making in the future. BIOTECanada supports the protection of health information while also recognizing the opportunity for protected and anonymized data to serve better decision-making and access.

The sensitivity concerning health info protection are paramount to every element of the system and industry needs to help uphold that recognition while speaking to how both protection of info and informed decisions can happen.

As the Discussion Paper noted, "Early identification through screening for rare diseases is an important means of assisting with timely and appropriate access to patient supports and treatments." Many Canadian biotechnology companies are developing drugs for rare diseases. In addition, numerous global biotech companies have developed and are bringing to Canada remarkable new drugs and therapeutics to address the healthcare needs of patients with rare diseases. A collaborative implementation process for the National Strategy for Drugs for Rare Diseases is important to enhance the transparency of the process and the development of real-world evidence to inform subsequent decisions regarding drugs for rare disease.

Manufacturers are committed to working with the CDA to improve the decision making to support the assessment and approvals of these vital new therapies for Canadian patients. We also

encourage the CDA to engage with and listen to patient groups to understand the needs around newborn screening and access to drugs for rare diseases.

Canadian CMV Foundation

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No response provided

11. Are there any other comments that you would like to share with us?

On behalf of the Canadian CMV Foundation, along with our multidisciplinary medical advisory committee, parent advisory committee, and healthcare providers across Canada, we urge you to support the inclusion of congenital Cytomegalovirus (cCMV) in the proposed pan-Canadian newborn screening list.

Congenital CMV is the most common congenital infection and the leading non-genetic cause of permanent hearing loss and neurologic disabilities worldwide. Early detection, within the first 21 days of life, opens the door to timely evaluation and treatment, improving long-term outcomes for affected newborns. Because most infections are subclinical at birth, the vast majority of children with cCMV go undiagnosed. Universal cCMV screening can be integrated into the existing infrastructure used for other newborn screening and Early Hearing Detection and Intervention programs across Canada.

Why Universal Screening for cCMV Matters:

- Prevalence and Impact: CCMV is the most common infection transmitted from mother to baby during pregnancy, yet it remains undiagnosed in most cases. If cCMV is detected shortly after birth, the newborn's candidacy for antiviral treatment can be assessed promptly. Interventions including antiviral medications (valganciclovir), close follow-up of hearing, and early provision of support (such as hearing aids and speech/language therapy), can dramatically improve outcomes for infected infants.
- Hearing Loss Risk: cCMV is a leading cause of progressive and late-onset hearing loss. Because late-onset hearing loss is not detected by newborn hearing screening, it typically goes unnoticed for a prolonged period during a critical time for language development. All babies with cCMV need regular audiology follow-ups until age five, ensuring hearing loss is caught early rather than after developmental delays have occurred.
- Missed Diagnoses: Without universal screening, most cases, particularly those that are asymptomatic at birth, are missed. Approximately 15% of asymptomatic infants develop hearing loss later in life. For both cCMV and permanent hearing loss, early detection is critical to mitigating the impact on the child and improving intervention outcomes.

Cost-Effectiveness and Efficiency:

- Universal cCMV screening has been shown to be cost-effective. It reduces the burden of undiagnosed hearing loss and related developmental delays, resulting in long-term healthcare savings. Studies indicate a 12% reduction in hearing loss-related costs when asymptomatic cases are detected early.
- Newborn PCR-based screening programs for other diseases have already demonstrated the possibility for cost savings, and the costs of high-throughput molecular diagnostics will likely continue to decrease. In addition, establishing a universal screening program increases community awareness. Informing pregnant women can reduce the risk of infection. Reducing cases of primary infections would, in turn, reduce the provincial health care burden.
- The success of Ontario and Saskatchewan cCMV programs demonstrates that newborn screening works, leading to earlier diagnosis, better care, improved developmental outcomes for children, and greater community awareness. In recent years, numerous states (including Minnesota and New York) in the U.S. have also successfully implemented universal screening for cCMV.

Community Support and Parent Perspectives:

- The overwhelming majority of parents support cCMV screening. Throughout the first year of Ontario's program, 93% of parents consented to having their newborn screened for cCMV.
- Knowing the cause of their child's condition is very meaningful. A diagnosis provides families with clarity, reduces unnecessary medical tests, and ensures early intervention.

We believe that every child deserves the opportunity for a healthy start in life, and every family deserves the right to know. Universal cCMV screening is not only a proven, cost-effective strategy, but it also aligns with the rights of parents to be informed about their child's health. With existing successful models in place and growing momentum across provinces like Manitoba and Alberta, now is the time for Canada to take this critical step forward.

Sincerely,

Rob Tetrault

President, Canadian CMV Foundation

With unified support from CMV Canada's medical advisory committee:

Marlene Bagatto, AuD, PhD Assistant Professor, School of Communication Disorders & National Centre for Audiology, Western University; Dr. Ari Bitnun, MD Professor of Paediatrics, University of Toronto Physician, Infectious Diseases, Hospital for Sick Children; Dr. Isabelle Boucoiran, MD Co-director, Women and Children Infectious Disease Centre, CHU Sainte-Justine Associate Professor, University of Montreal; Dr. Jason Brophy, MD, MPH Pediatric Infectious Disease Specialist, Clinician Investigator, CHEO Research Institute Associate Professor, University of Ottawa; Dr. Eliana Castillo, MD Associate Professor, Cumming School of Medicine, University of Calgary; Dr. Sharon Cushing, MD Director, Cochlear Implant Program, The Hospital for Sick Children; Dr. Jessica Dunn, MD, MPH Pediatric Infectious Disease Specialist, Alberta Children's Hospital Assistant Professor, Cumming School of Medicine, University of Calgary; Dr. Soren Gantt, MD, PhD, MPH Director, Clinical Research, CHU Ste-Justine, Professor of Microbiology and Pediatrics, University of Montrea;l Dr. Fatima Kakkar, MD Co-director, Women and Children Infectious Disease Centre, CHU Sainte-Justine Associate Professor, University of Montreal Marie Pigeon, MScA Audiologist, Ontario Infant Hearing Program, Children's Hospital of Eastern Ontario; Dr. Rupeena Purewal, MD Pediatric Infectious Disease Specialist, Jim Pattison Children's Hospital Assistant Professor, University of Saskatchewan

With widespread endorsement from Canadian healthcare providers:

Susan Scollie, PhD Chair, Canadian Infant Hearing Task Force Director, National Centre for Audiology Professor, School of Communication Sciences and Disorders, Western University Bonnie Cooke, MClSc, Aud(C) Director of Audiology, Speech-Language & Audiology Canada; Valérie Lamarre, MD Division Chief, Pediatric Infectious Diseases, CHU SainteJustine, University of Montreal; Christian Renaud, MD Pediatrician and Microbiologist, CHU Sainte-Justine, University of Montreal Director, Quebec Blood Bank Services; Jane Bowering, MSc R, Aud(C) Audiologist, Janeway Children's Health and Rehabilitation Center, Newfoundland; Steve J Aiken, PhD Associate Professor, School of Communication Sciences and Disorders, Dalhousie University; Elizabeth Fitzpatrick, PhD Full Professor and Director PhD Program, University of Ottawa Senior Scientist, CHEO Research Institute; Theresa McVea, MSc, Aud(C) Audiologist, Regional Lead, Audiology, Horizon Health Network, New Brunswick; Halen Panchyk, MSc(A) Coordinator, Provincial Newborn Hearing Screening, Saskatchewan Health Authority; Douglas P. Sladen, PhD, CCC-A, Aud(C) Associate Professor, School of Audiology and Speech Sciences, The University of British Columbia; Cheryl Messier, MHSc(A), Aud(C) Infant Hearing Program, Northwest Territories Health and Social Services Authority; Kendell Massier, MSc, Aud(C) Audiologist, Wascana Rehabilitation Centre; Kinley Winter, MSc, CCC-SLP Senior Speech-Language Pathologist, Saskatchewan Pediatric Auditory Rehabilitation Centre

CMV Canada's Parent Advisory Committee Voices Unwavering Support:

Lindsay & Oliver Craig Calgary, Alberta; Lisa & T.J Robinson Innisfail, Alberta ;Andrea McLaughlin Nanaimo, British Columbia; Megan Studd Port Coquitlam, British Columbia; Michelle Tétrault

Winnipeg, Manitoba; Mike George Saint John, New Brunswick; Laija Beaulieu Thunder Bay, Ontario; Pam Foster Orillia, Ontario; Caroline Leroux Montreal, Québec; Catherine Daigle Gatineau, Québec; Brittani & Riley Reid Regina, Saskatchewan; Louise McLelland Rosthern, Saskatchewan

In addition to the 40 names signed on the above letter, and 3,400 signatures on our petition for universal screening, CMV Canada also appealed to community members seeking their input. 43 responses were collected, voicing unanimous support for the inclusion of cCMV on the newborn screening list.

CMV Canada appealed to community members asking them to share their input on the question of if cCMV should be included on the proposed Pan-Canadian newborn screening list. 43 responses were collected:

“Yes, as a mother of an asymptomatic cCMV baby I think it’s critical that cCMV is added. The research and evidence tells us that early detection is key and that enhanced monitoring of these children provides the best possible outcome should any challenges arrive. While there is added anxiety knowing that my daughter has this scary condition with a whole host of potentially life changing physical and developmental challenges, we firmly feel that we are grateful for the team that’s been supporting us and following our baby girl to ensure any changes are identified early.” Louise McLelland Mother of a baby girl with asymptomatic cCMV, Saskatchewan

“Yes. Our daughter was the first positive-cCMV patient caught under the newborn screening pilot in Ontario. That early diagnosis changed her life forever. It enabled her to have access to therapy (drug, physio, diagnostic testing, speech, auditory, devices) that absolutely changed the direction of her life for the positive. To think this screening is not done everywhere in Canada is criminal. We owe it to our kids and our society to help those who need it the most. cCMV is an awful disease that affects so many kids, let's take action today by improving the odds these kids have less severe effects of its disastrous wake that it leaves on the lives of CMV families.” Will Jones Parent, Ontario

“An enthusiastic yes!! I am so grateful that Ontario has added cCMV to newborn screening. Unfortunately my son was born in 2018, before cCMV was added, so we didn't get the benefit of detection at birth. Here's how we would have benefited from screening and earlier cCMV detection. My son, Emmett, was born appearing perfectly healthy, except he failed his newborn hearing screening. And failed the repeated screening again at 4 weeks of age. At two months old, we first met with an audiologist and learned he had permanent, mild hearing loss in one ear. We were sent home, and returned one month later, at age 3 months, for a follow up. In the course of those 4 short weeks between 2 and 3 months of age, his hearing loss progressed from mild to profound. Deaf in one ear. That's the day we first heard of CMV, and while we received wonderful care from the many doctors and specialists we would be introduced to in the coming days, I need to emphasize that early intervention from birth could have prevented the progression of the

hearing loss. Had valganciclovir been introduced earlier, his hearing may have been saved. The agony of difficult decisions, tremendous guilt and sadness could have been prevented with newborn screening. Not to mention the cost savings! He's now seen by several clinics, and has received a cochlear implant and has regular audiologist visits. While I'm grateful for access to these services, I recognize it's an added cost to our precious health care system. Parents need to know if their child has cCMV so discussions can be had and steps taken where necessary to allow for early intervention! We love our CMV kids and want to do what's best for them. Help us ensure the best possible outcomes for these wonderful kids!" Pam Foster Mother of a child with congenital CMV, Ontario

"100% YES! If it weren't for Saskatchewan testing every newborn, we would not have known the effects it would have on my daughter. The chance I got to know outweighs any risk of not knowing. If there was a question about whether or not someone could tell me that my child was born with a virus that could harm their future… and they could give that child hope with treatment options, ABSOLUTELY I would want to know. Speaking as a mother, there is not a chance in this world where I would want to be left in the dark. As a mother, I strive to give my child the best outcome and chance at a long beautiful life in the best way possible. So if there is a chance that I get to do that, I will. I trust in the medical system, and so should you." Allison Mesenchuk Mother to a daughter with cCMV, Saskatchewan

"Yes; early diagnosis leads to early support for children and families which, ultimately, leads to better health outcomes for children impacted by cCMV. As we know, cCMV has a large spectrum of potentially devastating health & developmental impacts on children and often, without early screening, children go home and do not show signs or symptoms until later in life (as was the case with my son). This leads to a long and emotional journey of trying to find out why their child suddenly is going deaf or why their child isn't reaching certain milestones (flipping over, walking, etc.), among many other impacts. This leads to caregivers having to make appointments, not knowing where to go or what is happening, long waitlists, and many referrals that also take time. I did not find out my son had cCMV and this was the cause of brain white matter abnormalities, his deafness, and his balance & motor deficits until he was around 5 years old. This is completely unnecessary & ultimately means less support and later interventions, which can significantly impact children's growth and development. Despite passing his infant hearing screening at 2 months old, my son started to become deaf when he was around 8 months. Unfortunately, he was not diagnosed with deafness until he was over a year old, as I had to call and make an appointment with a local audiologist. Their waitlist was a year long, but were kind enough to get us in within a few months due to my concerns. Getting the surgery for cochlear implants for my son then took over a year to schedule. This means he was over 3 years old before he could hear. Due to missing those critical speech and language years, my son is behind with speech & communication which has affected him greatly socially and with his education. Knowing early means early interventions and supports set up for families and children. Given cCMV is the

leading cause of childhood hearing loss and is more common that other well known childhood disabilities such as down syndrome and spina bifida, why would we NOT screen for this at birth? I cannot wrap my head around why this would not be considered to be part of screening at birth and feels like a fight. It is infuriating as a parent to a child who would be so much farther ahead in life and development had this been part of screening at his birth." Laija Beaulieu Mother to a son with cCMV, Ontario

"Yes! I have personal family experience with a newborn being diagnosed and having to watch all it entailed in their new life has been hard to watch. A lot of their suffering could have been prevented with proper screening. It is a simple test to include in general screening. If we work on screening and prevention measures, the burden on the Healthcare system lessens. Screening and early treatment can help prevent multiple unnecessary physician visits, blood work, prescriptions, imaging, and other tests." Nicole Loran Cousin's baby was diagnosed late. Still not sure of final outcome

"Yes, without the screening in Ontario, my daughter would have gone on undetected and without the care she needs to grow and develop." Claire Riopelle Mother, Ontario "Yes, it should. Universal screening is particularly important for asymptomatic babies. Monitoring these asymptomatic children for developmental delays, hearing loss, and autism is important for early intervention (particularly with the current health care provider crisis that is causing lengthy multi-year waitlists)." Rebekka Mom to an asymptomatic CMV baby, Ontario "Yes - universal screening gives the opportunity to treat cCMV with antivirals that have been shown to reduce risk of SNHL. Otherwise, we may miss the opportunity to treat asymptomatic children that go on to lose hearing later in childhood." Anonymous Parent to a son with cCMV, Nova Scotia

"Yes, if it wasn't for newborn screening we never would have known my daughter had cCMV. She did not have typical physical symptoms or newborn blood work indices as cause for concern and it was only after further investigation following a positive screen that she met criteria for symptomatic cCMV. Without newborn screening she would not have gotten the treatment she needed and at the time point where it is shown to have benefit (within 1 month of birth). We are very grateful that Saskatchewan has universal newborn screening and drug treatment publicly available. We now have a happy and healthy 22 month old who has negative tests for hearing loss and developmentally doing well. If it wasn't for early detections, diagnosis and treatment, I'm not sure we could say the same. As a healthcare worker, I am very disappointed that this is not discussed as part of regular prenatal care and education." Brittani Reid Mother of baby with cCMV, Saskatchewan

"YES. My daughter is deaf in her left ear and has some slight scarring on her brain. She was born with a symptomatic case, and had 6 months of antiviral treatment. We are so incredibly thankful for our province that has the CMV screener and having access to Dr.Brophy who supported us

throughout the whole process and gave incredible care to our daughter. ” Samantha Wilson Mother to a daughter born with cCMV, Ontario

“Absolutely! It would help reassure parents, give proper treatment and support! It would answer a lot of unanswered questions and comfort parents. This should absolutely be added as a screening at birth. If parents know, then they can take precautionary measures and get the immediate support they need. It would reduce stress and improve outcomes of babies. ” Brigitte Mother to a daughter born with cCMV, Quebec

“Yes! Before my daughter was diagnosed, I hadn’t even heard of CMV. It is a leading cause of infant disability and why it’s not on the list already is beyond me. If it’s that common, but no one knows about it, it should be screened for. We have gone through so much with our daughter and we need to advocate to have this done.” Emma Winston Mother, Ontario

“Yes, CMV should be part of the newborn screening list. The earlier a child can be identified as having potential difficulties with development, the sooner intervention can begin. Earlier intervention usually leads to better outcomes in my experience.” Anonymous Parent to a son with cCMV, Ontario

“Yes. My son was born with cCMV and he would have not been diagnosed had the immunologist not noticed his abnormal immune results and did further testing. This led to him being eligible for early drug treatment, physiotherapy, speech therapy and occupational therapy- all services we wouldn’t qualify for without a diagnosis. But more importantly, because of this early diagnosis leading to these services, we are giving him the best chance at developing important life skills during these early years of life.” Anonymous Mother to a son with cCMV, British Columbia

“YES! Because then our children can start treatment right away. All expecting moms should also be informed about the dangers of cCMV.” Megan Studd Mom of cCMV baby, British Columbia

“Yes, because there are prophylactic measures to reduce long term complications.” Alisha Dartige Aunt, Saskatchewan

“Yes, cCMV can have major life altering side effects that affect children throughout their lifetime. I had never heard about CMV until my niece was diagnosed. This is a terrifying disease that should absolutely be screened for.” Michelle Aunt of a child with CMV, Saskatchewan

“Yes, my sister's daughter was born with cmv (at the same time I was two months pregnant). Why would we not spread awareness and provide treatment to the children that need it?” Samantha Herrick Auntie, Saskatchewan

“Yes, early diagnosis is essential. Parents need to know early so medication can help these newborn babies.” Patricia Pizzuto CMV Grandma, Saskatchewan

"Yes, my granddaughter was tested at birth and is doing great. If newborns are not tested at birth, it is often too late for them to get the treatments that could protect them." Philip Pizzuto CMV Granddad, Saskatchewan

"Yes. It is important to screen for CMV so parents with toddlers who may have been sick during pregnancy can have peace of mind that their newborn is healthy. More information and awareness of CMV should also be made available." Jessica Loran Friend to CMV Mom, Saskatchewan

"Yes. Then medication can be given, if needed. If it is not known that your infant has CMV until after your child has symptoms, it is too late to prevent them." Anonymous

"Yes, congenital CMV should be added to the newborn screening list. Adding CMV screening will help parents know if their baby was born with the virus. The general population is unfamiliar with CMV and do not understand the potential side effects that a child born with CMV may face throughout their life. I, myself, was unaware of CMV until my friend's newborn tested positive for CMV. Fortunately, in Saskatchewan, CMV is part of newborn testing and thankfully my friend's daughter was able to start immediate treatment. It is frightening that the potential and long term side effects of CMV are blindness, deafness, behavioural, psychological and physical issues and many parents are unaware of these side effects. I one hundred percent support the addition of CMV testing to the Canadian newborn screening list." Amber Panchuk Friend to CMV parents, Saskatchewan

"Yes, it is important for families to know and understand the effects that this virus can have." Leah Mesenchuk Grandmother, Saskatchewan

"Yes. CMV should be added to the proposed pan-Canadian newborn screening list, as the earlier CMV is detected, the sooner it can be addressed and the better the ultimate outcome for the child." Anonymous

"Yes, it could help with early intervention for many children. I want to see change." Kerri Despres Son was born with severe cCMV, New Brunswick

"Yes, it would be a very interesting prevention tool and would allow the mother who has never been infected with CMV before their pregnancy to be informed of the risks and precautions to take to avoid such an infection during pregnancy. I was infected with CMV early in my second trimester of pregnancy and my daughter was born with congenital CMV infection. Raising pregnant women's awareness of the existence of CMV and of ways to prevent infection would help reduce the number of infections. This awareness is more important if the woman has other children at an early age. In addition, pregnant women with a first CMV infection could benefit from follow-up to better document transmission factors and develop medical/medication approaches to prevent transmission to babies. Follow-up of infected fetuses and babies would also enable

better documentation of the disease. Having access to this information would certainly have helped us to make a better-informed decision when the time came to decide whether or not to continue the pregnancy. As things stand, with so little known about the disease, all approaches are almost experimental (antiviral drugs taken during pregnancy, antiviral drugs taken by the infant, etc.). The approach, when experienced, is anything but reassuring." Caroline Mailloux Maman, Quebec

"Absolutely. I wish I would have known about it when I was pregnant and could have been extra cautious with having a toddler in my home and working in a school. My daughter was born with cCMV and it was caught late. Now she is completely deaf in both ears." Kristin CMV Mom, Alberta

"Absolutely! Jasper's diagnosis has been pivotal in connecting us with support and resources to help our baby thrive. It not only helps us to understand certain presentations or behaviours thus fostering a better relationship with our son, but also connects us with the knowledge and support to help him navigate through life as optimally as possible." Rylea Bromley CMV Mom, Ontario

"Yes. Our son was born in Nov. 2021 in Ontario. If it weren't for the universal newborn screening including cCMV, we would have had no idea that our son was sick until he was much older. Since we were diagnosed early, we were able to get him on an antiviral medication to protect his hearing and have access to so many resources to help his development. Although he still has challenges, he is doing incredible, because of the support he receives." Jennifer Gagne Parent, Ontario

"Yes, early detection gives children with cCMV the best outcome. It is just a Band-Aid solution until a cure (ie. vaccine) is available. The outcome and sequela of those affected by cCMV can be devastating. Before families are even able to manage the consequences that cCMV can have on their child, they need to know if their child has cCMV. The first step, while a cure is being discovered, is to ensure that these children are identified and treated as soon as possible." Anonymous Parent to a child with congenital CMV, Ontario "

"Yes, CMV should be added to the newborn screening list across Canada." B.G. Alberta "

"Yes - early detection can be vital in decreasing negative side effects." Noelle Friend to CMV Mom, Saskatchewan

"Yes." Tati cCMV aunt, Saskatchewan

"Yes!" Rebecca Loran CMV Cousin, Saskatchewan

"Yes." Anonymous

"Yes." Christine Beaulac Friend to CMV parents, Saskatchewan

"Yes." Nicolette Godwin Aunt to CMV child, Saskatchewan

“Yes.” Laura Shirley Saskatchewan

“Yes.” Chelsey Friend to CMV parents, Saskatchewan

Canadian MPS Society

1. Do you agree with the proposed guiding principles and definitions?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

No response provided

3. Do you agree with the proposed process for nominating a condition?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

4. Do you agree with the proposed process for evidence review?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes-in part

Please provide your reason(s) and suggested changes, if any.

I agree in part with the proposal for further evidence review because I strongly believe that MPS Type I should be added to the pan-Canadian newborn screening list immediately. Several compelling reasons support this stance:

The inclusion of MPS I in the newborn screening panels in Ontario and Alberta has proven successful. Both provinces have demonstrated the feasibility and efficacy of early detection through newborn screening, leading to timely interventions that significantly improve patient outcomes. This regional experience serves as a valuable precedent, highlighting the tangible benefits of screening for MPS I.

Substantial evidence supports the benefits of early detection and intervention for MPS I. Early diagnosis through newborn screening allows for timely treatments, such as hematopoietic stem cell transplantation (HSCT) and enzyme replacement therapy (ERT), which can prevent or mitigate severe complications, particularly neurological damage. This early intervention can significantly enhance the quality of life and lifespan of affected individuals, underscoring the critical importance of early detection.

The United States has also recognized the importance of early detection of MPS disorders. MPS Types I and II have been added to the Recommended Uniform Screening Panel (RUSP) in many states across the country. This inclusion has facilitated the early identification and treatment of affected infants, allowing for improved health outcomes and quality of life. The U.S. experience provides a robust international example of the benefits of including these conditions in newborn screening programs, reinforcing the urgency and importance of similar measures in Canada.

A further evidence review could result in delays in adding MPS I to the screening list, potentially leading to delayed diagnosis for Canadian children. Such delays can have severe consequences, as the progressive nature of MPS I means that the longer the condition goes undiagnosed and untreated, the greater the likelihood of irreversible damage. Early screening and intervention are crucial to preventing health deterioration and preserving the potential for a better quality of life for affected children.

While a thorough evidence review is always important, the existing evidence, along with the experiences in Ontario, Alberta, and the United States, strongly supports the immediate inclusion of MPS I in the pan-Canadian newborn screening program. Further delays in implementation could harm children who would benefit from early diagnosis and treatment. Therefore, I advocate for swift action to add MPS I to the newborn screening list, ensuring that all Canadian children have the best chance for timely and effective care.

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Based on the advisory panel's discussion regarding the need for early awareness of potential emerging conditions not yet screened for in Canada, I recommend the inclusion of Mucopolysaccharidosis Type II (MPS II) in the pan-Canadian newborn screening program. This recommendation is grounded in the experiences of other countries that have already incorporated MPS screening into their newborn screening panels. Including MPS II aligns with the proactive approach of monitoring emerging conditions, especially those with potential treatments in development.

United States: MPS I and MPS II are included in the Recommended Uniform Screening Panel (RUSP) in many states. This inclusion has facilitated the early identification and treatment of affected infants, improving health outcomes and quality of life.

Japan: Japan has included MPS II in its newborn screening program, recognizing the importance of early detection and treatment to manage the disease effectively.

Taiwan: Taiwan has implemented newborn screening for MPS I, MPS II, and other lysosomal storage disorders. The country's comprehensive screening program has led to early diagnosis and intervention, preventing severe disease progression.

Emerging conditions, such as MPS II, that are being screened for in other countries, that have existing treatments, or have potential treatments in the pipeline should be closely monitored. These conditions often have treatments under development or are already available in clinical settings, making early diagnosis critical for maximizing the benefits of intervention.

A notable aspect of MPS II is the availability of Enzyme Replacement Therapy (ERT), specifically idursulfase (Elaprase), which has been shown to help manage symptoms and improve the quality of life for individuals with the condition. Additionally, there are advancing clinical trials targeting the neuronopathic phenotype of MPS II. These trials aim to address neurological symptoms that ERT cannot manage, offering hope for more comprehensive treatment options in the future.

Given the global trend of including various types of MPS in newborn screening programs and the potential for emerging treatments, I recommend that MPS II be added to the pan-Canadian newborn screening list. This proactive approach will help identify affected infants early, allowing for timely intervention and improved outcomes, consistent with global best practices in newborn screening.

11. Are there any other comments that you would like to share with us?

Thank you for your commitment to a pan-Canadian Newborn Screening Program.

Canadian PKU and Allied Disorders (CanPKU+)

1. Do you agree with the proposed guiding principles and definitions?

Yes-in part

Please provide your reason(s) and suggested changes, if any.

This response is on behalf of our patient organization. Thank you for identifying a core problem: the lack of standards pan-Canadian or otherwise for governance, advisory functions, and criteria for conditions to be considered for newborn screening. We think we missed an opportunity to elucidate the multiple elements of newborn screening programs and systems which include elements outside the newborn screening laboratory. A newborn screening system or program should explicitly include parental, public and provider ongoing education, sample collection and delivery, point-of-care screening (for example, pulse oximetry for critical congenital heart defects and audiometric testing for hearing loss, with more to come as science and technology continues to develop), short-term follow-up, diagnostic determination, disease management and continual evaluation. The proposed guiding principles and definitions can and should be improved by: 1. changing the headline on Health Rights of the Newborn to include the Wellbeing of the Newborn with a definition of wellbeing to encompass optimizing health and life outcomes for each newborn. 2. Expanding the concept of Sustainability from the potential for silo thinking focusing on health system sustainability which can be seen to risk de-emphasizing that the purpose of the health system is to sustain human life, nurture human development, and optimize life and health outcomes, Sustainable should include sustainability of newborn lives. 3. Transparency is a good start but can be improved by including the value of openness. This is especially important when applied to processes. Yes recommendation-making and decision-making processes should be open and accessible to all interested persons as they are in other jurisdictions outside Canada. 4. Collaboration should include a clear and comprehensive definition of who are the "partners". We did not see a definition of partners. 5. Equity mentions "quality screening" but we do not see a definition of "quality". Nor do we see a definition of "best interests" of newborns. We suggest that Equity discussion be expanded to include the highest attainable state of health and wellbeing. Table 1 at Collaboration mentions "partners" under proposed definition yet mentions " interested parties" under rationale, without a definition or description of partners or interested parties. At Sustainability, Table 1 under Rationale discusses the needs and rights or future generations. We ask what about current generations? At Transparency in Table 1 under Rationale, we ask that the value of openness of processes and procedures be added. This proposal seems to be missing the opportunity and could be enhanced by suggesting ways and means to address the postal

code lottery (aka inequities) across Canada of access to newborn screening. The proposed pan-Canadian list of NBS conditions is unclear on its value judgements: is it akin to minimum wage, minimum standard approach or is it setting targets or even aspiration goals? The draft does not provide a solid answer to the question. The proposed list if used as a minimum could do real harm to newborns and their families if it contributes to defunding or delisting conditions being screened beyond the "minimum wage" concept.

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

This proposal could be improved by explicitly saying a goal is to reduce duplication of efforts among P/Ts. Figure 2 talks about "accountability" yet this proposal does not address a key question: who appoints people to the various committees. This should be consciously elucidated. Table 2 could be improved at Equity by clarifying what "quality" and "best interests" mean. At Transparency, it could be improved by adding "openness" of processes such as committee hearings. As drafted, the language enables closed doors and closed processes. At Sustainability, the fit for purpose consideration of sustainability of newborn lives and wellbeing should be added. At Table 3, the Expert Review Committee should be refined by expanding membership to include relevant lived experiences of families as raising a child with a condition subject to newborn screening includes developing a special kind of expertise. Also Transparency and Openness would include more than public engagement (also undefined). At Quality, Standards and Education, the proposal to coordinate and support a pan-Canadian NBS data repository is excellent and sorely lack today. A very significant omission in Table 3 is the lack of recognition of the emerging roles and jurisdictions of indigenous governance and health organizations. Enhancing and delivering a robust pan-Canadian NBS system involves active measure to reconcile with our indigenous peoples and nations, not just P/T health ministries. No single "expert" review committee of 5-8 multi-disciplinary members can include the necessary and sufficient medical and scientific knowledge to consider newborn screening across the 11,000 or so (and growing) number of rare, ultra-rare and nano-rare conditions. Thought should be given how best to constitute subject-matter relevant expert review committees. Open deliberations can and will protect the proposed pan-Canadian NBS processes from self-inflicted harms caused by "experts" deliberating and recommending based on incomplete or less relevant expertise. Openness can help us move towards the goal of evidence-based decisions and away from eminence-based processes and outcomes.

3. Do you agree with the proposed process for nominating a condition?

Yes-in part

Please provide your reason(s) and suggested changes, if any.

To reduce duplication of efforts and to improve the timeliness of evidence review and recommendation-making, a NBS consideration should not wait for an application (complete or otherwise) on certain conditions such as when a P/T or indigenous agency adds a condition to its NBS program or when a new therapeutic is under consideration by Health Canada for an indication or condition which can meet NBS criteria on a prima facie basis, that is on the face of readily available information. The devastating report of the Ontario Ombudsman on NBS in that province, 2005, entitled, "The Right to be Impatient", is evidence of the preventable harms that come from health system failure and/or health system inertia is the face of better science, better technology, better screening, better diagnosis and better interventions. We need a commitment for NBS programs to avoid doing harms to newborns by being slow to learn, adapt and adopt new ideas, new evidence and new opportunities to improve health and wellbeing outcomes of newborns. Figure 3 and Table 4 at Step 2 should clarify who screens a nomination for completeness. Step 4 should elucidate who makes a recommendation. Step 6 should say who conducts the evidence review. Step 9 should articulate with whom the draft recommendation will be shared for feedback. Table 4 at Step 1 should define what "availability" means for both a screening test and effective treatment. Linkage to guiding principles should include transparency and openness. The entire nomination process and each step should include a target for how much time each are to take. It seems ironic that the only mention of timelines is in the final bullet in Table 4 at Steps 4 & 5 under description and features which proposes a prespecified timeframe for resubmission. Open meetings should be the gold standard for accountability and transparency.

4. Do you agree with the proposed process for evidence review?

No

Please provide your reason(s) and suggested changes, if any.

Wow, the proposal would set up roadblocks, delays and institutionalize duplicative work if a full evidence review is to be the expected or required when such work has already been done by competent others, in other countries, regions, provinces or states, which perhaps have greater evidence review resources and subject-matter expertise and experience than available in the current pan-Canadian context. Let's cut the red tape but don't cut it length-wise. We need a new

kind of wait time metric to identify how long it takes from first jurisdiction on the planet to implement adding a condition to NBS until 50% and 100% of newborns across Canada have the life-altering benefits of NBS for that condition. When we start measuring that metric, the postal code lottery of wait times for adding new conditions will help drive reforms on an ongoing basis. Table 5 at Step 6 under Description and features could be improved by explicitly adding both health system savings (if any) and productivity gains to the 3rd last bullet on evidence review. The second last bullet about engagement with public and affected families needs rework to expand opportunities for openness in the steps of the review process. Finally add transparency and openness to the list of values/principles under the final bullet on linkages.

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes-in part

Please provide your reason(s) and suggested changes, if any.

At Step 7, the phrase "consensus-style voting process" needs work for clarity. It seems to be fudge language as drafted. The bullets about deliberations under Description and Linkages should be rethought to elucidate the principles of transparency and openness, with deliberations being open to the public except under very limited circumstances. The concept of "readiness to implement" needs elucidation. The final bullet about implications beyond NBS needs elucidation.

6. Do you agree with the proposed process for engagement and communication?

Yes-in part

Please provide your reason(s) and suggested changes, if any.

Table 7 at Step 9 speaks of "eligible parties". A definition of eligible needs clarity. At Step 10, issuing a recommendation needs clarity. Now is a good time to operationalize the combined principles of accountability, transparency and openness. Votes on the final recommendation should be taken openly and recorded for the record.

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

No

Please provide your reason(s) and suggested changes, if any.

Wilson & Junger criteria are more robust than this proposal indicates. The evidence to support alterations or deletions to those criteria is lacking. Most egregious would be in Table 9 to delete criteria 2 about latency or early symptomatic stage under-recognizing the opportunities for early therapeutic intervention to prevent harms and maximize well-being. Criteria 2 has been found relevant by most NBS programs world-wide. Why propose becoming outliers on this criterion?

In the discussion at page 28 in the fifth bullet about acceptance of test, diagnosis and treatment, the language presented begs the question: accepted by whom? Elucidate please.

At Table 8, the principles should be recrafted as we discuss earlier. Under Equity there, what does facilities "across Canada" mean? Taken the wrong way, this could rationalize delays and thus contribute to substantial harms to newborns and society.

At Table 9, the changes proposed to the 4th criterion seem well-covered by the existing term "suitable" and any nuances of robust, scalable, safe, precise and validated can best be examined in evidence review. Criteria 7 contains the first mention in this draft of "better health outcomes". This is a central shortcoming of the draft and needs attention earlier and consistently in the proposal. Criteria 8 mentions "across Canada" without clarity on what that means or could be interpreted or misinterpreted to mean.

Removal of W&J criteria 9 flies in the face of global NBS real-world policy, practice and evidence. Again, why propose to become an outlier. The fundamental importance of NBS is to address the known shortcomings of the pre-NBS case finding. When irreversible harm takes place before the onset of clinical signs or symptoms at whatever stage of life, then that is the compelling logic of doing population screening including surveillance, select or general depending on specific factors, including NBS of our target population. These proposed deletions and alterations to the Wilson & Junger criteria are highly problematic.

The suggested application of the principle of equity should not be a reason to slow down the too-few early adopters in Canada of new science, technology and therapeutics, including regional or localized customizations.

On criteria 10, impacts should be considered beyond just budget. Those other impacts should include health system and societal impacts.

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

Good learnings from Australia on this point.

9. Do you agree with the proposed pan-Canadian newborn screening list?

No

Please provide your reason(s) and suggested changes, if any.

This proposal seems based on a faulty assumption: that a current absence of uniform NBS across the jurisdictions of Canada is a good reason to warrant a review. See table 13. This assumption lacks evidence and is not fit for purpose.

The proposed list of 25 pan-Canadian conditions is old news with the exception of adding Spinal Muscular Atrophy (SMA) otherwise based on the 2016 list worked up by officials under the auspices of the P/T Health Ministers. Here we are 8 years later and where is the (slow) metric of progress on addressing this example of the postal code lottery? How many babies died or are damaged for life because of this example of health systems sclerosis? That is the real-world of the harms engendered by the status quo.

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Wow, this proposed list of potential conditions for NBS is underwhelming and hopefully can be easily evergreened. It makes no sense to exclude MPS 4 and MPS 6 which have drugs approved by Health Canada available. It makes no sense to exclude biopterin deficiencies (BH4) which are ultra-rare but devastating conditions ascertained by NBS discovery of PKU-mimicking abnormal levels of the amino acid phenylalanine and diagnosed differentially as part of the short-term follow-up element of a robust NBS system. The irony is that a key treatment is readily available (sapropterin) and funded by every F/P/T health drug program for BH4 patients found by NBS across Canada even though the indication is off-label.

Table 12 needs to include critical congenital heart defects and hearing loss to be consistent with best practices globally,

There is an opportunity in this proposal to be more forward looking and to take on the challenge of futureproofing the state of newborn screening for every newborn in Canada.

11. Are there any other comments that you would like to share with us?

Appendix 2, Table 16 should be augmented to include critical congenital heart defects and hearing loss to be reflect the principles of diversity, equity, inclusiveness and completeness.

Thanks for your kind consideration of these perspectives.

Cystic Fibrosis Canada

1. Do you agree with the proposed guiding principles and definitions?

Yes

Please provide your reason(s) and suggested changes, if any.

Cystic Fibrosis Canada supports the guiding principles. One principle in particular – equity – is paramount to Canadians with CF.

According to the Cystic Fibrosis Foundation:

"Research shows that children who receive CF care early in life have better nutrition and are healthier than those who are diagnosed later. Cystic fibrosis can affect people of every race and ethnicity, and all children should undergo newborn screening as well as follow-up sweat testing at a CF Foundation-accredited care center after a positive newborn screen. Early diagnosis and treatment can:

- Improve growth
- Help keep lungs healthy
- Add years to life"

In 2021 Trikafta, a life-changing drug for CF, was made available to people aged 12 years and older who have the most common mutation that leads to cystic fibrosis, F508del. Access was then expanded to those 2 years of age and older who have this mutation. This represents about 90% of the CF population in Canada.

However, this drug can treat an additional 4-5% of the Canadian CF population who have rare mutations, and it was only recently, in 2024, that Health Canada, the CDA, INESSS and our public drug programs started to contemplate access for those who have certain rare mutations.

Cystic Fibrosis Canada held focus groups to inform our advocacy efforts to expand access and heard from families whose children were missed by newborn screening because their mutations were not included on newborn screening panels. While all provinces and territories screen newborns for cystic fibrosis, some individuals with rare mutations continue to fall through the cracks. These people may face significant challenges in being diagnosed late with more advanced disease than those diagnosed at birth and given access to standard of care treatments early.

<Our child with CF> was diagnosed when <they were> 3 weeks old, kind of a fluke, which was really amazing. That was in 1997 when <they were> born.

My parents lost a child when he was 11 months old in 1959 and my dad was a pharmacist and he went into medical school after that and they became aware of this disease that became <known as> cystic fibrosis. My dad had an article that he read and thought that that sounded like <the symptoms> they were dealing with.

…he was very healthy and got a cold and went into the hospital. Both of my parents did not anticipate him passing away. In fact, they both weren't there when he did, which was very sad in my family. And so, they always suspected that he had cystic fibrosis.

So, <our child> was diagnosed with CF when <they were> three. I had a lot of trouble nursing my older daughter, so when <our child with CF> was born, I just said I'm not gonna go through that again. They had lactation consultants at the hospital at that time and they helped me. They actually came to my home and nursing actually with <our child with CF> turned out completely different and went really well, but <our child with CF> wasn't responding and gaining weight. So basically, failure to thrive.

And so, at three weeks of age, that lactation consultant said to me: “I don't want to alarm you, but there's no reason why your baby should not be gaining weight. I think you should go back to your doctor”.

And that's when my mom intervened and said, “you know what? I want this baby tested for cystic fibrosis”. I thought my mom was out of her mind. She had that sense from the previous experience that she went through.

But we did go back to the doctor and that's how <our child received> a kind of fluky diagnosis at three weeks of age, which was a blessing. – Parent of a child with CF that lives with a rare mutation

Receiving “fluky” diagnoses was a theme among those in our focus groups:

And I think and I know the system is quite complicated for newborn screening and it's not perfect and all of that. But there is a piece there that if you are really saying that you're looking at a person and you're saying this is precision medicine or an individual person, you would <think to> look at the biological parents.

And so, once we got the sweat test, we had to repeat it a few times. It took I think four months to finally find the mutations. It took a long time, I was told. I thought I wasn't sure what the time usually takes, but they couldn't find them. But I think back now and I say, well, if they had said, well both parents of are of <our heritage’s> descent, what's the most common mutation in <the

country we came from>? Most likely one of them would have been <the mutation my child has> and it is.

And so race was just sort of erased from all of it. And I think that's the piece that really bothers me. I think, you know… it's that color blindness, right, which is systemic racism. And so that was a big p

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

Cystic Fibrosis Canada applauds the proposed model, but it must have teeth. Newborn screening for cystic fibrosis was first made available in Alberta in 2007. Most provinces and territories adopted newborn screening for CF by 2014. However, Quebec did not implement newborn screening for CF until 2017, a decade after Alberta.

A 2016 Canadian study compared newborns that had been screened to those that had not been. The study found that:

"…patients were diagnosed earlier and had their first clinic visit at a younger age. Pancreatic insufficiency was less common in NBS patients. The incidence of Pseudomonas aeruginosa and Staphylococcus aureus were lower in NBS patients. After adjusting for age at clinic visit, gender, pancreatic status, and Pseudomonas aeruginosa infection status, mean z-scores for weight-for-age and height-for-age were higher in NBS patients, with no differences in BMI-for-age."

In the proposed approaches document, the advisory panel agreed that "the right of the newborn to achieve the highest attainable state of health should be granted primacy and viewed as an over-arching principle for all screening activities". We agree too, which is why a collaborative model must have requirements for all jurisdictions to participate actively in this important work.

CFTR mutation prevalence has regional and cultural distributions in Canada. For example, one mutation is quite rare broadly in Canada but very common among those with cystic fibrosis of Hutterite communities in Western Canada. Other mutations are very common in Quebec but rare in the West. Still others are more common in South American, Middle Eastern or African populations but quite rare among those of European decent. All jurisdictions must be at the table to ensure that screening panels capture the complexity of diseases like cystic fibrosis and are relevant to all regional populations.

3. Do you agree with the proposed process for nominating a condition?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

4. Do you agree with the proposed process for evidence review?

Yes-in part

Please provide your reason(s) and suggested changes, if any.

Yes, this seems fair but should require all jurisdictions to participate in these processes.

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Yes, this seems fair but should require all jurisdictions to participate in these processes.

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

Yes, Cystic Fibrosis Canada supports this direction and welcomes increased engagement and communication efforts. This is especially important to ensure that the voices of those who live with rare and ultra-rare mutations that lead to CF are heard and supports the advisory committee's equity principle.

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes-in part

Please provide your reason(s) and suggested changes, if any.

For the most part, yes, Cystic Fibrosis Canada agrees with the criteria. However, we recommend that criterion 10 – considering the cost of screening, diagnosis and treatment against the cost of not doing so – must be used with great caution. In our case, cystic fibrosis may be expensive to screen, diagnose and treat, but the human impact of not doing so is tremendous.

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes-in part

Please provide your reason(s) and suggested changes, if any.

Similar to our response for question seven, removal of newborn screening tests must be done with an abundance of caution. The criteria seem thoughtful, but any criteria that deal with cost must be considered in relation to benefit: some diseases may be costly to screen, test and treat but catching them early through screening can change and save lives.

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

Cystic Fibrosis Canada is pleased to see CF on the list. Newborn screening has had a tremendous impact on the ability to treat newborns for CF which has resulted in better health outcomes. With the availability now of highly effective treatments that can be started at a young age, NBS is more important than ever to ensure that people with CF in Canada live long and healthy lives.

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Cystic Fibrosis Canada reserves comment on this question. This discussion should be left to experts in newborn screening.

11. Are there any other comments that you would like to share with us?

We thank the advisory panel for their thoughtful deliberations and would be pleased to comment further on the impact that NBS for CF has had on infants. Should the advisory panel need to reach out to experts in screening for CF in the future, we can provide names and contact information.

Global Action Network for Sickle Cell & Other Inherited Blood Disorders

1. Do you agree with the proposed guiding principles and definitions?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

Yes, in Table 3, under the proposed committees, we agree with the proposed composition of the different committees and the proposed coordinated model. However, it would serve for improved transparency and clarity if this section could also address the recommended committee selection process, especially on how the information to recruit the standing, ad-hoc, or time-limited committee members would be disseminated. For instance, would the members be handpicked or would a call to submit an interest for the NBS advisory council be shared with the public?

3. Do you agree with the proposed process for nominating a condition?

Yes

Please provide your reason(s) and suggested changes, if any.

4. Do you agree with the proposed process for evidence review?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

No

Please provide your reason(s) and suggested changes, if any.

The proposal by the advisory panel to adopt 8 of the 10 criteria from Wilson and Jungner with modifications is okay except for the modifications proposed by the panel. We have listed below the two proposed modifications with issues on the proposed modifications.

1. Create additional clarification that eligible conditions are those that manifest in early life (i.e., neonatal period, infancy, or early childhood) as opposed to those later in life (e.g., adolescence or adulthood) or carrier status:

Carrier status for some conditions such as sickle cell disease (the most common monogenetic blood disorder in Canada and globally) is currently screened in many provinces. While a province such as Ontario currently provides the result of the sickle cell trait (SCT) screening to families upon request, provinces such as the Maritimes and Alberta, not only screen for it but also automatically inform the families of the newborn of their babies' carrier status.

Since 2019, the Sickle Cell Awareness Group of Ontario has been working with the NSO and the Ministry of Health to ensure automatic disclosure of newborns' carrier status paired with counselling is the way forward in Ontario.

Sickle Cell Trait (SCT) is not a disease and having it means that the individual has inherited the sickle-cell gene from one of their parents[1].

Most people with SCT do not have any symptoms of SCD. However, some people with SCT experience complications of SCD, such as pain crises2. In their extreme form and rare cases, the following conditions could be harmful for people with SCT:

- Increased pressure in the atmosphere (which can be experienced, for example, while scuba diving)[2]
- Low oxygen levels in the air (which can be experienced, for example, when mountain climbing, exercising extremely hard in military boot camp, or training for an athletic competition)[2]
- Dehydration (when one has too little water in the body)[2]
- High altitudes (which can be experienced, for example, when flying, mountain climbing, or visiting a city at a high altitude)[2]

Additionally, there are a few rare health problems that may affect people with SCT.[2]

Hematuria

Sometimes people with SCT experience blood in the urine, a condition called hematuria. This can be a sign of a serious medical condition, so it requires a thorough medical evaluation. In very rare cases, blood in the urine may be associated with a rare type of cancer that affects the kidney called renal medullary carcinoma[2].

SCT and athletes

Some people with SCT are more likely than those without SCT to experience heat stroke and muscle breakdown when doing intense exercise, such as competitive sports or military training under unfavorable temperatures (very high or low) or conditions (such as high humidity)[2].

SCT is a significant public health concern, as, without routine screening and awareness among the general public, the number of individuals affected by Sickle Cell Disease will continue to rise, creating a significant burden on families, as well as the healthcare system as a whole[2].

Given the foregoing, we must ensure that sickle cell trait screening is included in the list of conditions already screened for (as is the case in some Canadian provinces) or in the least, the list of conditions identified for further review.

2. In Table 8, under the guiding principle of “Collaboration”, the linkages to draft guiding principles could be slightly amended to add counselling to the collaborative services to read “ …from screening to identification to treatment and counselling”.

3. Table 9: We agree with the Wilson and Jungner recommendation that the condition must be an important public health problem and do not agree with the panel's recommendation that the condition must lead to morbidity/mortality in children.

References

1. https://www.sicklecellanemia.ca/

2. https://www.cdc.gov/sickle-cell/sickle-cell-trait/index.html

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

No

Please provide your reason(s) and suggested changes, if any.

A. Given that sickle cell trait is currently being screened for in most Canadian provinces (though disclosure processes differ), it should have been included on the conditions on the pan-Canadian newborn list.

B. While sickle beta thalassemia is on the conditions on the pan-Canadian newborn list, the universally screened (beta0, HbH) is not on this list. We believe that this is an oversight and seek that the pan-Canadian newborn list should be updated with these two conditions.

Furthermore, we are recommending that given the high frequency of trait status for thalassemia and hemoglobinopathies, including testing of carrier status of thalassemia is extremely important[3]. It provides an important opportunity for education and a potential reduction in the number of future newborns (out of ignorance) with thalassemia. Overall, it supports this panel's vision of addressing the health rights of the newborn.

It is also important to note that:

1) Beta thalassemia major manifests clinically as jaundice, growth, retardation, hepatosplenomegaly, endocrine abnormalities, and severe anemia requiring lifelong blood transfusions. Newborn screening would allow these infants to be detected early and referred to the appropriate clinics and physicians for treatment and prevent infants from falling through the cracks, especially those with Thal intermedia with moderate symptoms that if untreated can cause longer-term issues like extra-medullary hematopoiesis (EMH). This type of screening aligns with the goal of prioritizing the health rights of the newborn.

2) Approximately 5% of the worldwide population has a variation in the alpha or beta part of the hemoglobin molecule. Particular ethnic groups are more likely to be affected, with between 5% and 30% of these populations experiencing symptoms of thalassemia. With the increase in immigration from countries with high prevalence of thalassemia and these families settling in all areas across Canada including smaller cities and rural areas, it's important that screening is done for newborns so the health rights of the newborn can be preserved. The Thalassemia Foundation of Canada has heard from hematologists that their smaller clinics have grown largely due to new immigrants, including children born in Canada.

References

1 Langlois S, Ford JC, Chitayat D; CCMG PRENATAL DIAGNOSIS COMMITTEE; SOGC GENETICS COMMITTEE. Carrier screening for thalassemia and hemoglobinopathies in Canada. J Obstet Gynaecol Can. 2008 Oct;30(10):950-959. English, French. doi: 10.1016/S1701-2163(16)32975-9. PMID: 19038079.

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

No response provided

11. Are there any other comments that you would like to share with us?

Inherited blood disorders are genetic blood disorders and screening for them will support awareness and education that might reduce the overall cost of treatment of these conditions in Canada. The Global Action Network for Sickle Cell & Other Inherited Blood Disorders is recommending that the advisory panel consider including additional inherited blood disorders outside of hemoglobinopathies in the National newborn screening program.

HAE Canada Inc

1. Do you agree with the proposed guiding principles and definitions?

Yes-in part

Please provide your reason(s) and suggested changes, if any.

Yes; however, we would emphasize that collaboration includes the perspective of patient/family partners and highlight the importance of meeting the family where they are and taking into consideration aspects such as cultural perspectives, and barriers to services once the diagnosis is made or the initial testing is complete. If follow-up testing and treatment is needed, we encourage providing funding to support families with barriers to access these services (e.g., transportation, parking, etc.).

Partnering with community-based organizations in each community will be crucial as a serious diagnosis may start the need for more information, support and programming for the family.

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

We would add there needs to be connections with and funding for the various community-based organizations and patient advocate groups that support these families when dealing with a new diagnosis. There is concern that this can still result in a "Postal code lottery" for newborn screening, as we see with reimbursement approval for drugs.

3. Do you agree with the proposed process for nominating a condition?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

4. Do you agree with the proposed process for evidence review?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

Yes, and we would add that the treatment not only be effective but that it would be accessible to all without barriers.

We appreciate that the "societal and other considerations" section is included. In relation to the part that states "the cost of case finding should be economically balanced in relation to possible expenditure on medical care as a whole", we hope this is acknowledging that sometimes more money has to be spent up front when screening for health conditions. The aim would be that the early intervention up-front costs would reduce the negative health and developmental impacts,

thus lowering costs associated with caring for a child or adult who is having health crisis due to an unknown condition.

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Hereditary Angioedema Type 1 and 2, as this can be determined with a simple blood test and the hope that one day there will be an established test for Hereditary Angioedema with normal C1.

Dravet syndrome is another condition that would benefit from newborn screening. While it is recognized that genome sequencing / genetic testing is way done the road, if there was a way to stop the seizures before they start, and control them early, maybe a child's quality of life could be increased and reduce the burden on families and the health and social systems.

11. Are there any other comments that you would like to share with us?

We would like to reiterate the importance of services and treatments to support families.

For parents with children with serious chronic illnesses, it is often very hard to navigate the system. There is a lack of services everywhere and if this could be part of the implementation plan, as well as social and emotional support for families, this plan would be more beneficial.

Individual Respondent 1

1. Do you agree with the proposed guiding principles and definitions?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

No response provided

3. Do you agree with the proposed process for nominating a condition?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

4. Do you agree with the proposed process for evidence review?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

I'd like to see DNA screening for Hypovitaminosis D and macular degeneration. I have genes for both.

11. Are there any other comments that you would like to share with us?

No response provided

Individual Respondent 2

1. Do you agree with the proposed guiding principles and definitions?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

No response provided

3. Do you agree with the proposed process for nominating a condition?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

4. Do you agree with the proposed process for evidence review?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Would recommend inclusions of all clinically significant hemoglobinopathies (i.e., HbSD, HbH, rather than just HbSS, HbSC and HbSbthal)

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

No response provided

11. Are there any other comments that you would like to share with us?

No response provided

Individual Respondent 3

1. Do you agree with the proposed guiding principles and definitions?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

I agree with the principles but feel there should be further discussion and recognition that at times, these principles will be at odds with each other. The paper does define the health rights of the newborn as a primary consideration (which I agree with) but even here, the health rights of individual newborns could be in conflict (affected infants vs false positive cases). With a diversity of opinions on the advisory committee, there may need to be further guidance on how to weight these principles in the decision-making process.

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

I think a significant shortcoming currently is the apparent absence of the actual payor (the provincial or territorial Ministries of Health) in this process. If decision-makers from the ministries of health are not actively engaged in this process, with input into this coordinated system, we run the risk of creating a structure with reduced practical value. In the end, the newborn screening programs will require provincial/territorial engagement and funding to implement any of the recommendations produced by this committee.

3. Do you agree with the proposed process for nominating a condition?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

The proposed process is reasonable but the criteria for initial evaluation of a nominated condition needs further clarification. We run the risk of being flooded with inappropriate nominations if the criteria are not clear to the nominator from the start, so there can be a certain degree of self-assessment prior to a submission. There also needs to be consideration of a sustainable funding

structure for the nomination process and the corresponding administrative burden associated with it.

4. Do you agree with the proposed process for evidence review?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

I think this document could provide some more discussion of the intended scope and criteria for the evidence review process. Specifically, the health economics piece is only mentioned in passing and it is critical to have at least a broad estimate of costs associated with screening and treatment as part of the evaluation. .

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes

Please provide your reason(s) and suggested changes, if any.

Considerations for ongoing monitoring of diagnosed patients should also be added to the section discussing "screening and diagnostic testing that may have implications beyond newborn screening." This could include laboratory testing, but also medical imaging and other clinical assessments (physiotherapy, psychoeducational assessments, etc.)

6. Do you agree with the proposed process for engagement and communication?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

There should be some discussion of potential conflicts of interest and their disclosure in this engagement process (e.g. disclosure of industry funding for advocacy groups, or industry relationships for care providers).

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

1) "Child" may need to be more clearly defined (e.g. onset of symptoms before age X for a significant proportion of those affected). 2) The concept of a latency period (added to point 3) may need to be more clearly discussed. I'm concerned that the need to have some degree of a pre-symptomatic period or reversibility of symptoms has been lost.

2) For the added NSO criteria, there may need to be some discussion that the benefits and harms may be ascribed to different individuals (net benefit for the population vs net benefit for the individual).

3) For treatments, there needs to be a comment on the availability of treatment/intervention to the population screened.

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Consideration of whether or not a condition is screened in another jurisdiction can be problematic if the original decision to add the condition in that other jurisdiction was not well justified.

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Avoid the use of "secondary target". If the condition is secondary, it is, by definition, not a target. Consider using "secondary condition".

For consistency, CPTII and CACT should be listed as secondary conditions in the Yukon (to mirror the BC panel).

Critical congenital heart disease is a condition that warrants being on the list for a full evaluation.

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

This discussion paper avoids the massive issues and opportunities posed by DNA-based, or "genomic" newborn screening. This is a clear emerging approach to screening with the potential to force a fundamental change in the way we assess candidate conditions. A condition-by-condition review of hundreds of potential candidates is not feasible with the structure being proposed and it is a glaring omission to not address this in some way. Its complicated and full of practical and ethical issues but newborn screening programs are going to have to face this in the near future and this body seems to be the appropriate venue to begin to coordinate those assessments.

11. Are there any other comments that you would like to share with us?

I was surprised not to see any discussion of the assumed consent model of newborn screening and the assumptions that are implicit in this model, with respect to the guiding principles. This becomes relevant as we move toward considering conditions with more variable or delayed onset, more invasive therapies, or as mentioned above, the prospect of genomic newborn screening.

Individual Respondent 4

1. Do you agree with the proposed guiding principles and definitions?

No response provided

Please provide your reason(s) and suggested changes, if any.

The framing of the principle “Health Rights for Newborns” is powerful. Rights language is loaded in that it implies obligations and responsibilities. But the rationale provided for this on page 12 is not really rationale – it doesn’t give reasons to justify why this should be the paramount consideration. Maybe it should be, but we need to understand the reasons for this. Why is this more important than any other life stage? And what kind of “right” is this? What grounds it? How does it compare against other rights? • I think it might be helpful to articulate a bit how these values are in tension and what difficult balancing will have to occur in making decisions about newborn screening. • For example, the overall argument of the approach seems to be that there are new treatments for rare diseases available, there is a diversity in approaches to newborn screening which leads to inconsistency in access, consistency of access is an important value and goal, the approach is designed to improve this consistency. This argument makes sense. However, it is important to recognize that seen on its own in this way, it would lead to proliferation of diagnostics and treatments and be silent on the opportunity cost of investing in these areas. While sustainability is mentioned in a value, the tension between sustainability and seeking equity and pursuing the health rights of the newborn aren’t really illuminated – which I think is important especially because it seems to me there will be a direct conflict between health rights of a newborn and sustainability. • The articulation of the principle of equity is inclusive and hard to argue with. I wonder though, if it would be helpful to say a bit about the types of inequity that exist (beyond provincial jurisdiction) and what this commitment is to in those contexts. I also notice that equity seems to be addressed procedurally in many places (having diverse perspectives inform deliberation). This is excellent and important. But the substantive dimension is also an important – which groups are being treated inequitably and how should we deal with the relative claims of these groups? • The rationale provided for this value is also not really rationale but a statement that equity is important. Many of the statements in the rationale column are not really rationale, but restatements of the importance of the principle. (As opposed to why these are so important.)

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

: Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening? • I think an important role of the Newborn Screening Advisory Committee should also be to add values oversight/assurance of integrity of decisions against guiding principles. If agreed, then this will require systematic methods to ensure. Otherwise it could easily get lost. • A few questions: o Whose responsibility will it be to align the newborn screening strategy with the values of the broader EDRD strategy? o Who will define and monitor consistent understanding of the equity principle?

3. Do you agree with the proposed process for nominating a condition?

No response provided

Please provide your reason(s) and suggested changes, if any.

I would advocate that the criteria used throughout the process should ensue from the principles.

4. Do you agree with the proposed process for evidence review?

No response provided

Please provide your reason(s) and suggested changes, if any.

I would advocate that the way evidence is categorized, evaluated and deliberated upon at all stages of the process, should correspond to the way the principles are being dealt with and the criteria that ensue from the principles. (E.g. in Step 7 on page 20, Step 6 on page 22, etc.)

An overarching problem for this work will be the lack of diversity-related data available. This larger issue should be named and steps to address should be called for. For example, the ability to undertake Step 6, bullet 5 on page 22 will be hampered by the lack not just of data and data gathering systems, but of shared understanding about what data should be gathered.

5. Do you agree with the proposed processes for deliberating and developing recommendations?

No response provided

Please provide your reason(s) and suggested changes, if any.

I also suggest that principles of deliberation should be spelled out somewhere – what expectations are there for how deliberation will structured and facilitated? (E.g. Step 3 on p 22) This is hinted at in Step 7 on page 24. But just having a decision matrix will not be enough. Principles of deliberation using the tools will also be required to ensure inclusive, systematic, values-focused discussion and decision making.

6. Do you agree with the proposed process for engagement and communication?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

No response provided

11. Are there any other comments that you would like to share with us?

Thank you for the opportunity to provide feedback on this important work. Overall I believe this is a very solid document and I especially appreciate that it is clearly principle-driven and very methodically thought through. The grounding is in general very solid and the methods align with and manifest the principles well. I share my comments without any ulterior motive, only to supporting greater integrity in the work. Some of these reflections may be too detailed for the level at which the paper is being developed. In this case, and assuming they are seen as constructive and useful, where the comments are too detailed or go beyond the scope of the project team, it may be useful to share them with appropriate downstream leaders. The one overarching comment I wish to make is that I believe the principles that guide the various initiatives seeking to improve drug decision-making should align, if not be the same. I believe it would be helpful if this point could be made by the leaders of the Newborn Screen initiative as well.

Individual Respondent 5

1. Do you agree with the proposed guiding principles and definitions?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

No response provided

3. Do you agree with the proposed process for nominating a condition?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

4. Do you agree with the proposed process for evidence review?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

I believe the evidence for MPS I is strong enough to move this from table 13 to Table 12. We are consistently diagnosing patients with this condition late. For Hurler patients, early treatment and

transplant in the first months of life is essential to improve the outcome. However, there patients are often diagnosed late in the first year at which time there may be irreversible changes. Transplant after 2 years of age is too late to prevent the neurological sequelae.

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

I am happy to see that MPS II and MPS III are there but I think there is a big whole with respect to Morquio A and Maroteaux Lamy syndrome. These are two diseases I would add to the emerging conditions. Morquio A syndrome has a founder effect in Quebec and as such, is one of the more frequent MPS disorders in Canada. Maroteaux Lamy is not frequent but early management is essential to outcome. Many of the patients that I follow with Morquio A have gone through a diagnostic odyssey of 5-10 years. Long delays in diagnosis results from lack of knowledge of these rare diseases and leads to delay in treatment. Furthermore, many of these patients are faced with surgeries that occur prior to a known diagnosis which puts them at high risk of complications secondary to their anesthetic risks.

11. Are there any other comments that you would like to share with us?

I commend you for this effort which has been a long time coming.

Individual Respondent 6

1. Do you agree with the proposed guiding principles and definitions?

Yes

Please provide your reason(s) and suggested changes, if any.

Agree the work of the advisory committee should be informed by the guiding principles recommended. It is important that the health rights of the newborn is central to the guiding principles.

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

I would suggest a representative from the provincial/territorial ministries of health be included on the newborn screening advisory committee. Though healthcare is the jurisdiction of the provinces/territories, I would also suggest including a representative from the federal government in some capacity, particularly to allow collaboration with the national rare disease strategy.

I am supportive of knowledge transfer and education being included in the framework.

3. Do you agree with the proposed process for nominating a condition?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

4. Do you agree with the proposed process for evidence review?

Yes

Please provide your reason(s) and suggested changes, if any.

Evidence review should include analysis of health economic factors.

Evidence review should address the impact and management of secondary conditions that may be picked up by screening, and incidental findings.

Accessibility of treatments should also be considered in the evidence review, for example, this was a consideration with implementation of SMA screening.

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes

Please provide your reason(s) and suggested changes, if any.

I agree that transparency and ability to solicit stakeholder review from the public is essential.

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

For criteria 4, footnote b - I would be cautious requiring test values be known and a cut off level agreed. For example, this was not the case for TREC analysis for SCID screening. There is no standardized assay, measurement value or cut off for TRECs. 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.

Criteria 8 - consider adding 'resources,' services and facilities should be available for screening, diagnosis and treatment. This would include financial and personnel resources.

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

Hemoglobinopathy screening also picks up most cases of beta thalassemia major. Suggest review of whether this condition should be included as a primary condition for hemoglobinopathy screening, similar to Hgb SS, SC and Sbthal.

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Consider adding conditions screened for in some jurisdiction due to a high incidence/founder mutations in specific ethnic populations living in those jurisdictions. Evidence review of whether there should be a recommendation to expand screening for these conditions to other jurisdictions where the specific ethnic populations live may be beneficial. Conditions include ZAP70 deficiency, IKBKB deficiency and purines.

11. Are there any other comments that you would like to share with us?

I would strongly suggest engaging the provincial/territorial ministries of health early in this process and garnering their input and support.

Canada has unique and significant challenges with screening, diagnosis and treatment of newborns in rural/remote regions. Under the guiding principle of equity I would suggest the

advisory committee consider these challenges and advocate for resources and quality improvements to reduce these barriers.

For Appendix 2 - I would suggest adding a description of what jurisdictions each newborn screening lab covers, i.e. illustrate which labs perform screening for the territories, maritime provinces and Newfoundland. No response provided

Also consider adding to Appendix 2 conditions that are screened for in some jurisdictions due to the presence of specific ethnic populations, i.e. ZAP70, IKBKB, purines. Would also add KREC screening for SK.

Individual respondent 7

1. Do you agree with the proposed guiding principles and definitions?

Yes

Please provide your reason(s) and suggested changes, if any.

Ensure the safety and transparency with the uniform guidelines. It helps to collaborate and prioritize the needs for the health of newborns.

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

It is important to have an unified processes and criteria to enhance the efficiency in processes and utilities the resources that we have. It helps to improve the quality; and provides and protects the neonatal outcomes. It was great for the committee to include different resources and countries to have a boarder aspect of ideas and views prior to develop our own model for the processes and criteria across Canada.

3. Do you agree with the proposed process for nominating a condition?

Yes

Please provide your reason(s) and suggested changes, if any.

It is equal and fair in the nomination process. It is ensure the appropriateness conditions and information with the right target population in the screening process.

4. Do you agree with the proposed process for evidence review?

Yes

Please provide your reason(s) and suggested changes, if any.

Well done.

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes

Please provide your reason(s) and suggested changes, if any.

The deliberation process enhances the transparency and increase the engagement among the committee members and the public.

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

The process for engagement and communication helps to eliminate bias and improve the equality outcomes which include the diversity of people, regardless their age, gender and background.

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

It enhances the equality, transparency , safety, quality and collaboration.

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

It improves the cost and enhance the benefit.

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

The new proposed list is more comprehensive, details and in-depth. The advisory panel will be able to explore further the 9 uniform conditions with a full evidence review along with the proposal principles and criteria.

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

The modern world changing a lot and genes and mutated frequently. We may not be able to capture all the conditions. Some populations may not be able to access their service, new immigrants, indigenous people, etc. will affect our changes.

11. Are there any other comments that you would like to share with us?

Well done overall. Thanks all the work behind the program.

Individual respondent 8

1. Do you agree with the proposed guiding principles and definitions?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

No response provided

3. Do you agree with the proposed process for nominating a condition?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

4. Do you agree with the proposed process for evidence review?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes-in-part No response provided

Please provide your reason(s) and suggested changes, if any.

I think all those in table 13 should be in table 12. There is ample evidence of benefit from early diagnosis for these conditions, which are already included in NBS in many developed nations with expert and competent advisory boards.

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

No

11. Are there any other comments that you would like to share with us?

No response provided

Individual respondent 9

1. Do you agree with the proposed guiding principles and definitions?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

I have a level of cynicism when it comes to the provincial ministries of health. While I know that they are a key member of the team (as they provide the funding), I have also found that they are often the bottleneck in making meaningful changes to newborn screening programs. Having been involved in the care of a family who had a child who died of a condition that could have been picked up on NBS but that the government had previously denied funding for NBS expansion to include this condition, I hope that this new coordinated model will help the ministries put newborns ahead of the budget

3. Do you agree with the proposed process for nominating a condition?

Yes

Please provide your reason(s) and suggested changes, if any.

I really appreciate that this nomination process is open to all, including families and/or their advocates.

4. Do you agree with the proposed process for evidence review?

Yes

Please provide your reason(s) and suggested changes, if any.

I am glad that the guidelines emphasize the inclusion of people with lived experience on their expert panel, as they are, indeed, experts at living with or caring for someone with the condition.

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes

Please provide your reason(s) and suggested changes, if any.

I hope that one of the conditional recommendations includes: "Committee re-review in 2 years" or something to that effect.

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

Having families with lived experience on this committee will help ensure that the relevant people or organizations are made aware of the recommendations being open for comment. There should be some sort of communications plan for how to ensure rare disease organizations can notify their members that recommendations are available for review; this should not just be left to chance.

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

I have some apprehensions about point 10. With the extremely-high costs of many new emerging therapies, the cost of treatment could out-weigh the cost of screening, diagnosis and care for some conditions. This has more to do with the pharmaceutical companies than the value of those children's lives.

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

No response provided

11. Are there any other comments that you would like to share with us?

I appreciate all of the great work done by the advisory panel members.

Individual respondent 11

1. Do you agree with the proposed guiding principles and definitions?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

For consideration: Health rights of the newborn. With genetics there needs to be consideration to the rights of the probands families as part of the principles. Consider that reporting sickle cell trait could reveal non-paternity. Alternatively, a positive screening in a female for an X-linked condition, such as G6PD, could identify that the father is affected.

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

My only comment is in reference to the two boxes outside the advisory coordinating body (i.e. provincial and Territorial Ministries of Health and NBS programs). Although this point might be too granular, these external bodies are likely composed of their own unique structures. So communication from the advisory coordinating body might require different point of contact in each province. Also note that, I am aware that not all provinces have clearly defined groups to coordinate with.

3. Do you agree with the proposed process for nominating a condition?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

4. Do you agree with the proposed process for evidence review?

No

Please provide your reason(s) and suggested changes, if any.

The membership for the evidence review should be specified and the inclusion of certain experts considered mandatory rather than ad hoc. There have been cases where lab representation was excluded from NBS evidence review resulting in a misinterpretation of the literature and therefore erroneous conclusions.

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes

Please provide your reason(s) and suggested changes, if any.

Either the Evidence Review or Deliberation process should include required expert membership. In my opinion this membership requirements are best addressed at the Evidence Review step.

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

The addition of 'explicitly need for the net benefit to screening...' is brilliant. There is increasing signs that screening might be a benefit even when an approved treatment is not available. Consider the Sanfilippo A trail (LYS-SAF302) that failed its efficacy targets. However, the study identified that early treatment provided on compassionate grounds had positive outcomes. This suggests that NBS might be needed to support a clinical trail.

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Branch chain keto-acid dehydrogenase deficiency

CARD11 and Zap70 deficiency

MT-RNR1 variant cochleotoxicity from aminoglycoside treatment

11. Are there any other comments that you would like to share with us?

No response provided

Individual respondent 12

1. Do you agree with the proposed guiding principles and definitions?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

While I agree that the overarching principle must be health rights of the newborn, the health impacts on society of proposed changes to NBS must also be considered. The document discussed guidance from NBS Ontario as to "weighing the harms and benefits to newborns AND society" and these societal considerations should also be included in the guiding principles. This is particularly important when considering later onset conditions, a number of which are in the list of conditions for review. The impact of proposed NBS changes throughout the patient lifecycle needs to be a guiding principle of this work and this language needs to be adjusted throughout the report. Also, to say that drugs/treatments for rare diseases are out of scope for the panel is misleading - the panel will not be evaluating these treatments (which would be done by HTA groups) but must take into consideration the availability and efficacy of therapies - if no effective treatment exists, this may impact the recommendation in terms of NBS.

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

The P/T should not be external to the coordinating body - they need to be part of the coordinating body in order to provide information relevant to decision making such as availability of resources for patient follow up and therapy etc. I believe that the CDA also should be integral to both the Advisory Committee and the Expert Review Committee to assist with identified priorities such as horizon scope and discussions on when there is a need for generating additional evidence.

3. Do you agree with the proposed process for nominating a condition?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

I agree that individuals should be able to submit nominations but might suggest a threshold that a nomination must come from more than a single individual - for example, nominations from individuals could require 3 or more nominators. This is to avoid excessive volume of nominations. I feel strongly that full conflict of interest disclosures should be required for all nominators and these COI must be included in the public information (with names removed). The COI must ask for all sources of funding for individuals and organizations even if such funding was not specifically directed to preparation of the nomination document. Also, although there is a later section outlining considerations for conditions to be removed from the NBS panel, it is not clear to me how conditions are nominated for removal.

4. Do you agree with the proposed process for evidence review?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

As above, the evidence review needs to identify and summarize potential benefits and harms to patients across the lifecycle, not just for newborns (as per the NBS Ontario statement referenced above). It is my strong suggestion that the Advisory Panel and Expert Committees routinely include a member whose role is to represent the adult patient perspective and this is separate from members who represent the roles of patients and parents. When you ask parents what they are willing to risk in order to get a diagnosis for their children, they will risk everything. However, when you ask adult patients with later onset conditions if they would have wanted to know earlier, they often do not, citing concerns over the impact of early diagnosis of a later onset condition on their mental health (particularly relevant to teens), job opportunities, insurance implications etc. Thus, specifying "lived and living experience" is not sufficient - need to have representation across the life span of this experience.

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Recommendations for conditions recommended for addition to the panel should specifically include timelines for implementation. Whilst I understand that recommendations from the committee are non-binding, making the playing field for NBS more level across Canada involves

not just agreeing to add conditions to the panel in each P/T but actually doing so. The fact that NBS for SMA is not yet in place in all P/T despite the availability of highly effective therapies for several years is a good example where delays in NBS have very seriously impacted patient health. Including recommendations on timelines for implementation is another reason that P/T representation should be included within the Advisory Panel so that P/T can provide input on what is feasible.

6. Do you agree with the proposed process for engagement and communication?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Feedback from stakeholders should include detailed COI statements which will be public as discussed above.

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Criterion 1 should be modified to keep language consistent with that in the discussion on page 28 (above Table 8) - "the condition should be serious and one that is manifest early in life (neonatal period, infancy, or early childhood"

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

I believe that Fabry disease and Gaucher disease clearly are conditions that should not be considered for NBS. They do not normally cause serious morbidity in early childhood. There is ample published literature for Gaucher disease showing that some patients may not need treatment for several decades if at all. There is a randomized trial for Fabry disease in the primary prevention setting showing no benefit. I believe that consideration of XALD for inclusion must include a discussion about risks/benefits of reporting in males only. Such sex-based considerations have not been discussed in the document but principles on this should be developed as there are other conditions where this may be an issue

11. Are there any other comments that you would like to share with us?

I believe that the Public Health Agency of Canada might be a better home than the CDA as could build on existing infrastructure and be operational faster. However, as discussed above, CDA needs to be integral part of the review process, particularly for horizon screening, impact of early therapy, and need for evidence generation.

Individual respondent 13

1. Do you agree with the proposed guiding principles and definitions?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

No response provided

3. Do you agree with the proposed process for nominating a condition?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

4. Do you agree with the proposed process for evidence review?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

No response provided

11. Are there any other comments that you would like to share with us?

Good Afternoon,

I want to offer feedback and be heard on the necessity of adding adrenoleukodystrophy to the Proposed Pan-Canadian Newborn Screening List. A valid test has been available for over a decade, and it is now successfully screened for in 45 American states.

Rationale for Adrenoleukodystrophy (ALD) Newborn Screening (NBS) in Canada

Overview of ALD:

X-linked adrenoleukodystrophy (X-ALD) is a rare peroxisomal neurodegenerative disorder that, due to mutations on the ABCD1 gene, result in the accumulation of saturated very long-chain fatty acids (VLCFA), which cause damage to the central and peripheral nervous system and the endocrine organs, such as the adrenal cortex and the testes. It has a broad phenotype range affecting young boys, adolescent males, and male and female adults. 35% of boys are affected by the progressive and devasting cerebral phenotype, with death usually occurring between 2 to 4 years after the onset of symptoms.

https://ojrd.biomedcentral.com/articles/10.1186/1750-1172-7-51

http://www.mdpi.com/2409-515X/2/4/15

The purpose of Newborn Screening is early diagnosis of boys with X-ALD, which is essential for preventing the loss of life due to adrenal insufficiency and for the timely therapy of the childhood cerebral form of X-ALD with Hematopoietic Stem Cell Transplant (HSCT). It has secondary outcomes allowing the detection of siblings and other relatives with ALD.

The primary benefit of NBS is the saving of life by monitoring a child from birth through systematic follow-up and detecting the early onset of adrenal insufficiency and/or cerebral ALD, thus allowing for steroid replacement and HSCT. Important secondary benefits of NBS are establishing the foundation of genetic counseling, eliminating the diagnostic odyssey, are the genesis of research, the beginning of a thorough understanding of the fundaments of this disorder, achieving enormous financial savings in health, emotional, and medical costs, obviate

unnecessary fear, anxiety, depression and emotional turmoil due to elongated prognoses until the correct diagnosis is finally made as ALD in whatever form.

https://www.ncbi.nlm.nih.gov/pubmed/27338599

https://www.ncbi.nlm.nih.gov/pubmed/27337030

http://www.mdpi.com/2409-515X/2/4/15

X–linked adrenoleukodystrophy is the most common peroxisomal disorder affecting the adrenal cortex and the central nervous system (brain inflammation and spinal cord/ peripheral neuropathy). (Ann B. Moser et al Int. J. Neonatal screening 2016).

http://www.mdpi.com/2409-515X/2/4/15

Adrenal Insufficiency (AI) was found to be undiagnosed in 80% of neurologically asymptomatic boys with ALD, and they already had impaired adrenal function (Dubey et al. 2005). Unrecognized adrenal insufficiency frequently results in morbidity and even mortality. Early detection of AI is vital, and close monitoring for detecting cerebral ALD is essential. NBS will achieve these aims.

https://www.ncbi.nlm.nih.gov/pubmed/15812458

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3101278/

There is an extremely reliable, high throughput LC-MS/MS 1-hexacosanoyl-2-lyso-sn-3-glycero-phosphorylcholine(C26:0-lysoPC) Screening Test which not only identifies ALD Adrenal but picks up peroxisomal biogenesis disorders, Zellweger spectrum, single enzyme defects of the peroxisomal FA oxidization (peroxisomal acyl-CoA oxidase 1 (ACOX1) and D-bifunctional protein deficiency (HSD1B4), acyl-CoA binding domain-containing protein 5 (ACBD5)deficiency, the “contiguous ABCD1 DXS1357E deletion syndrome” (CADDS) and Aicardi Goutières Syndrome (AGS). The analysis can easily be multiplexed with an MS/MS method of newborn screening test for Krabbe, Pompe, Hurler, Gaucher, Fabry, and Niemann-Pick A/B diseases. This testing offers the choice to detect these disorders and take advantage of early detection and the therapeutic opportunities. Precision medicine is demanding that we deliver a higher performing and broader base of screening where we use 6-plex 10-plex or even 24-plex modes. We must have a more efficient and cost-effective system that uses current technologies.

https://www.nature.com/articles/gim201668

https://www.nature.com/articles/gim2017194

https://news.mayomedicallaboratories.com/files/2016/09/LSDXALDbyMSMS_Tortorelli_ClinChem2016.pdf

https://www.ncbi.nlm.nih.gov/pubmed/25481105

https://www.ncbi.nlm.nih.gov/pubmed/24875301

https://www.ncbi.nlm.nih.gov/pubmed/22766634

https://www.ncbi.nlm.nih.gov/pubmed/21325949

After a positive NBS diagnosis for cerebral ALD adoption and implementation of the established guidelines as set out in the literature published by Doctors Raymond, Moser, Fatemi, Engelen, Kemp, Visser, Wanders, Aubourg and Bwee Tien Poll-The, is absolutely essential. The proven biomarker for cerebral ALD is the MRI which needs to be done yearly until 3 years of age and every six months between the ages of 3 and 12 years and annually thereafter. Any sign of symptoms within that period requires an immediate MRI knowing that cognitive dysfunction is at least 6 to 12 months away as proven by serial monitoring. Corticosteroid replacement therapy is essential of course for those with AI. There is a curative therapy for ALD in the form of an allogenic Hematopoietic Stem Cell Transplant (HSCT). There is a 95% 5-year survival rate year as compared to 54% to those untreated. Survival and neurological outcome of ccALD patients after HSCT is clearly superior compared to untreated patients.

The MRI is the most accurate, predictive and cost-effective biomarker for cerebral ALD. The world ALD physician-scientist community is in unanimous agreement about the benefit of serial MRI's for boys up to 12 years of age.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3503704/

https://www.ncbi.nlm.nih.gov/books/NBK1315/

https://www.ncbi.nlm.nih.gov/pubmed/17618834

https://www.ncbi.nlm.nih.gov/pubmed/28976817

https://www.ncbi.nlm.nih.gov/pubmed/28375456

This is an enormous amount of money and the financial savings realised through early intervention and disease awareness are substantial and the ongoing gathering of scientific knowledge is priceless.

Economic analysis for ALD NBS in Washington State USA shows a benefit/cost ratio of 5.83. The use of this technology can and will save the lives of our children, improve their quality of life (QoL) and return vast sums of money into the health systems of Australia. The cost of the NBS test is between $2-$8.00 and the return in dollar value is in the millions of dollars per annum.

http://adrenoleukodystrophy.info/clinical-diagnosis/newborn-screening

http://leukodystrophyresourceresearch.org/wp-content/uploads/2013/08/Avoiding-the-Misdiagnosis-of-Adrenoleukodystrophy.pdf

https://www.aphl.org/conferences/proceedings/Documents/2017/NBS%202017/23Thompson.pdf

http://n.neurology.org/content/75/8/718.full

https://www.ncbi.nlm.nih.gov/pubmed/23953952

https://www.allianz.com.au/life-insurance/news/cost-of-critical-illness

http://www.ausstats.abs.gov.au/ausstats/subscriber.nsf/0/9C2B94626F0FAC62CA2577FA0011C431/$File/44300_2009.pdf

https://www.cdc.gov/ncbddd/musculardystrophy/research.html

https://www2.deloitte.com/au/en/pages/economics/articles/economic-analysis-motor-neurone-disease-australia.html

http://www.mda.org.au/wp-content/uploads/media/publicity/Executive_Summary_Economic_study_of_muscular_dystrophy.pdf

Summary:

ALD has a proven NBS test with a proven curative HSCT therapy and gene therapy for patients without a match on the registry. A subset of male patients develops the fatal cerebral demyelinating disease (cerebral ALD) before the age of 18 years. The age of onset of cerebral ALD cannot be predicted. A newborn male patient has a 35–40% risk of developing cerebral ALD between the ages of 3 and 18 years, but cerebral ALD can also occur in adulthood. Allogeneic hematopoietic stem cell transplantation (HSCT) is curative for cerebral ALD, provided the procedure is performed in an early stage of the disease before extensive MRI white matter abnormalities are present12. Unfortunately, this therapeutic window is often missed.

Patients with ALD are asymptomatic at birth. A study in neurologically asymptomatic young boys with ALD revealed that 80% had unrecognized adrenal insufficiency (Dubey et al. 2005).

Multiplexing this test is an established procedure and offers amortized costs and additional savings to genetic laboratories and health departments. Test performances have been greatly improved by those that adopt the globally available free Collaborative Laboratory Integrated Reports (CLIR) tool developed at the Mayo Clinical Genetics Laboratory, which has reduced false positives to 0.024%. This worldwide database program is an upgraded version of the R4S tool.

It is very difficult to see how this could be not be accepted to the NBS panel in Australia as it meets all the established criteria and generates substantial financial, emotional and medical expenditures. There is a clear and defined benefit to the baby from birth which is more than reasonably balanced against financial and other costs. The test is proven, suitable and can be multiplexed and there are well established systems to deal with the diagnostic testing, counselling, treatment and follow up for all identifiable patients. There is a body of expertise in ALD existing within Canada who can and do consult with their overseas colleagues in the US and thereby maintain their currency in this rare disorder.

INESSS

1. Do you agree with the proposed guiding principles and definitions?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

No response provided

3. Do you agree with the proposed process for nominating a condition?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

4. Do you agree with the proposed process for evidence review?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

No response provided

Please provide your reason(s) and suggested changes, if any.

No response provided

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

No response provided

11. Are there any other comments that you would like to share with us?

Bonjour, je vous transmets les commentaire de l'équipe de dépistage de l'INESSS.

Nous avons lu le document du Comité consultatif fédéral sur le dépistage néonatal. Nous n'avons que peu de commentaires à formuler sur le modèle organisationnel proposé (trois comités : aviseur, expert, qualité/éducation) ainsi que sur les principes décisionnels guidant les travaux de ces comités. Les principes scientifiques énoncés (tableau 9) correspondent généralement au consensus accepté dans ce domaine d'évaluation des technologies.

Nous pensons qu'il sera essentiel que toutes les parties prenantes, notamment les provinces (et les territoires) soient représentées au niveau de cette organisation.

Notons aussi que l'application des principes scientifiques proposés (tableau 9) demeure souvent très difficile à implanter à cause de la rareté des maladies impliquées. Le petit nombre de cas disponibles ne permet généralement pas la conduite d'essais randomisés, et les preuves scientifiques demeurent souvent indirectes, fondées sur la pathophysiologie et les jugements d'experts. Une méthode d'arbitration de ces opinions devra être prévue.

Notons aussi que les principes décisionnels invoqués (tableau 1), notamment celui de la primauté des intérêts des nouveau-nés (Health rights of the newborn) devront forcément être mis en équilibre avec d'autres principes comme celui de l'intérêt des familles et des communautés. Encore ici, des arbitrages complexes, invoquant des perspectives et des valeurs diverses, devront être mis en place. Il serait utile d'initier une réflexion sur les mécanismes qui seront utilisés pour aborder ces questions.

Le fait que l'organisation proposée agira au niveau fédéral imposera des contraintes quant à l'applicabilité des recommandations au niveau des provinces. Une certaine duplication sera inévitable entre les travaux effectués au niveau fédéral et ceux des provinces (par exemple par l'INESSS). Quant aux chois des maladies, il serait important de ne pas seulement recensé les maladies dépistées, mais tous les travaux d'évaluation qui auraient menés à des évaluations de non recommandation, pour comprendre les arguments ayant menés à ces décisions. Le délai d'obtention des résultats de dépistage est un élément important et toutes les provinces n'ont pas les mêmes capacités au niveau des laboratoires. Certaines maladies ont des présentations

cliniques très précoces pour lesquelles les résultats de dépistage pourraient ne pas être obtenus en temps opportun.

Nous recommandons aussi une approche plus systématique dans l'analyse des travaux internationaux. On devrait par exemple s'assurer d'inclure les documents d'évaluation produits en français, comme ceux de la France.

Nous espérons que ces commentaires pourront contribuer à votre réflexion et nous demeurons disponibles pour d'autre échanges.

Innovative Medicines Canada

1. Do you agree with the proposed guiding principles and definitions?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

The recommended guiding principles look acceptable. The only concern is related to the ability for equity to be achieved if there is no mechanism to ensure consistent coverage of screening/tests across the provinces and territories. There are clear examples, i.e. SMA where there is inconsistent coverage across the country leading to inequities in screening and diagnosis of children across the country

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

Would suggest that PHAC act as the coordinating body for the advisory panel. PHAC has expertise with screening and surveillance and arguably are better linked to the health care delivery system.

Would suggest that you streamline the committee structure and include representatives from the provinces and territories and newborn screening programs on the advisory council so that they are involved in the decision-making process and therefore more likely to adopt the committees' recommendations.

Would also suggest that the committee structure keep as streamlined as possible with no more than one or two committees or subcommittees to ensure effectiveness, efficiency and alignment to timelines.

3. Do you agree with the proposed process for nominating a condition?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

The process seems reasonable, but it would be helpful to have more details about potential timelines. For example, will the review take months, years? It might be helpful to consider having a proactive iterative approach where there is a yearly review of the evidence on new and emerging tests and recommendations made on this basis instead. The other concern is about all the work being done to review nominations and make recommendations, without there being a mechanism to ensure that the recommendations are adopted across the provinces and territories. Finally, it might be worth considering a mechanism for special access to screening/testing for those babies that have high risk factors while the evidence review is taking place

4. Do you agree with the proposed process for evidence review?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

No comment, looks reasonable

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

As mentioned before, we strongly suggest that the newborn screening advisory committee include representatives from the provinces and territories and newborn screening programs to ensure that they are involved in the evidence review and recommendations development to ensure a greater likelihood that the jurisdictions will take up the recommendations.

6. Do you agree with the proposed process for engagement and communication?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Would be helpful to have more detail on who the eligible parties are that can provide feedback. To ensure a diversity of perspectives and experiences, would suggest keeping the eligible parties as broad as possible.

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No comments

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No comments

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

It is a bit surprising that only one new condition is being proposed in addition after eight years, given the advancements in the science. Additionally, given that the adoption of the 2016 list varies widely across the provinces/territories there needs to be strategies in place to ensure that there is better uptake and implementation of the recommendations on this new list.

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

No response provided

11. Are there any other comments that you would like to share with us?

No response provided

JDRF Canada

1. Do you agree with the proposed guiding principles and definitions?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

No Recommendations.

3. Do you agree with the proposed process for nominating a condition?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

A. One of the pieces of information required in the nomination form is the "availability of effective treatment". This could be clarified further to define what an effective treatment is. For example, is an effective treatment anything that prevents death from the condition, or may an effective treatment prevent/cure/improve the condition? Can education be considered an effective treatment if it helps prevent further complications due to the condition?

B. Some thought should be given at this stage to the cost of screening in case it is overly prohibitive. As it stands, cost is not considered until the Wilson and Jungner criteria stage, but it may be pertinent to include an estimate of screening costs in the nomination form.

4. Do you agree with the proposed process for evidence review?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Agree, with one suggestion and several queries:

Suggestion: In the proposed evidence review process (Table 5), it is stated: “There may be opportunities to engage members of the public and people with lived and living experiences during the review process.” We strongly encourage a change to this proposed process to ensure that this is always part of the review process, as follows: “Members of the public and/or people with lived and living experiences during the review process will be engaged as part of the review process.”

Queries:

A) The process for assessing benefits and harms refers to the health rights of the newborn, but the psychological harms associated with diagnosis of many conditions will fall to the parents, guardians, and/or family members of the newborn. How will this be taken into account?

B) How will equity be addressed if the majority of evidence to support screening of a condition has been done in a specific population (ex., white, European-ancestry)? Will screening be considered equitable if a test may be more representative or accurate for one population over another?

C) How will the evidence review committee reach out to the public and ensure that relevant stakeholders are informed of the ongoing review? For example, reaching out to patient advocacy groups to ensure that they (as well as the community they serve) are engaged.

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Step 9 indicates that “eligible parties” will be able to provide feedback, but no explanation is given as to what/who would constitute an eligible party.

Would new information received during the engagement and communication stage send the recommendation back for further review? What are the potential impacts of engagement at this stage?

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Agree, with a few queries:

A. The modifications to Wilson and Jungner include "Account for having a benefit of screening in newborns and not just convenience of bloodspot screening." Can this be clarified. What would a 'benefit of screening in newborns' entail? For example, does a treatment from birth need to be available? Would early education of the parent/caregiver/guardian count as a benefit? If the testing could wait until age 1 or 2, is the cost-effectiveness to the health care system a reasonable benefit?

B. Criterion 6 states that "there is an agreed policy on the further diagnostic investigation of newborns with a positive screening test result". We would like to flag that this may be a case of 'the chicken or the egg', that is, the creation of a policy for further diagnostic investigation may not be in place until the condition is being considered for newborn screening.

C. Criterion 7 states that "There should be an effective treatment or intervention…". Could this include education that has been shown to reduce long-term complications, and/or the potential to take part in clinical trials for preventative therapies?

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Type 1 diabetes (T1D). Screening for T1D has been enabled by decades of research showing that autoimmunity causing clinical (i.e., insulin-requiring) T1D develops over months or years preceding a clinical diagnosis. Briefly, T1D begins with polygenic risk conferred largely by specific genetic variants related to immune function (known as HLA haplotypes), with smaller effects conferred by a large number of other genes. An individual's genetic risk of T1D can be determined by applying genetic risk scores. Using a genetic risk score (GRS) that includes genes associated with T1D, the population most at benefit for further screening can be further identified. For individuals with high genetic risk (stage 0), one or more environmental triggers (mostly unknown) throughout life then trigger beta cell dysfunction and initial autoimmune attack on pancreatic beta cells. Autoimmunity against beta cells involves a cascade of immunological events involving multiple immune cell types, and its occurrence can be measured by the presence of two or more circulating islet autoantibodies in the blood (stage 1). With progressive damage to beta cells, remaining beta cells have a harder time meeting the insulin demands of the body, and blood glucose begins to become dysregulated (stage 2) – but the individual is still asymptomatic. The early, asymptomatic stages are where intervention (via education and potentially disease-modifying therapies with the potential to delay the need for insulin therapy) are crucial to limit the long-term impacts of the condition. With further damage to beta cells, which can in some cases be accelerated by a precipitating event such as a common viral infection, the body's demands for insulin exceed what remaining functional beta cells can provide. Blood sugar rises quickly and dangerously, leading to a clinical diagnosis of T1D (stage 3). Screening with genetic risk scores (at birth), autoantibody testing (in childhood), and educational intervention has the ability to almost eliminate the incidence of diabetic ketoacidosis (DKA) at diagnosis (Barker et al., 2004; Elding Larsson et al., 2011; Hekkala et al., 2018; S. Hummel et al., 2023; McQueen et al., 2020), a traumatic, life-threatening and costly complication that is seen in approximately 40% of pediatric T1D diagnoses in Canada (60% during the COVID-19 pandemic) (Ho et al., 2021). Moreover, identifying children at risk of clinical T1D allows individuals and families to prepare for insulin therapy and eases psychosocial distress around the time of diagnosis.

Research and engagement underway by a pan-Canadian consortium focused on pediatric T1D screening is likely to generate evidence to inform an application for newborn screening within 4-5 years.

11. Are there any other comments that you would like to share with us?

Table 3, expert review committee. Add consultation with patient advocacy groups at this stage (in addition to conducting public engagement).

Muscular Dystrophy Canada

1. Do you agree with the proposed guiding principles and definitions?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

No response provided

3. Do you agree with the proposed process for nominating a condition?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

4. Do you agree with the proposed process for evidence review?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Please add Duchenne muscular dystrophy and Pompe disease to the proposed pan-Canadian newborn screening list.

11. Are there any other comments that you would like to share with us?

Introduction:

We welcome the release of this guidance document; particularly as clinical experts as well as people with neuromuscular conditions and their families have been calling for a national strategy to establish clear guidelines and standards for newborn screening programs for more than a decade. The discussion paper on newborn screening by the Canadian Drug Agency raises important issues, but it overlooks several critical areas that must be addressed if we are to move forward effectively, especially in the context of rare and ultra-rare neuromuscular condition.

Ensuring Flexibility and Innovation in Newborn Screening:

There are several novel treatments and therapies for rare diseases likely to enter the market within the next five years, including many targeting neuromuscular conditions that could benefit from newborn screening. This presents a significant opportunity, and it is essential that the "Proposed Pan-Canadian Newborn Screening List" focuses on establishing national minimum standards, not maximums. If this distinction is not made clear, we risk stifling innovation and discouraging provinces like Manitoba and Ontario, which have historically led the way by adding conditions based on real-world evidence (RWE). Decisions grounded in RWE must be carefully managed to avoid creating overly rigid frameworks that limit flexibility and responsiveness to new, emerging innovations.

Consideration of "Out of Scope" Issues:

To achieve meaningful progress in newborn screening, it's essential to address issues beyond the immediate scope of this document. Specifically, laboratory infrastructure and processes are paramount to the success of screening programs. For example, ensuring that the proper facilities exist, such as Molecular Genetics Labs (MGLs), is critical to screening conditions like DMD and Pompe disease, which are predicted to become part of an increasing number of NBS

Network of Rare Blood Disorder Organizations (NRBDO)

1. Do you agree with the proposed guiding principles and definitions?

Yes

Please provide your reason(s) and suggested changes, if any.

These guiding principles will be a strong foundation for a national newborn screening program and a helpful filter that can be revisited while making decisions related to processes, criteria, and a list of conditions for newborn screening.

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

No

3. Do you agree with the proposed process for nominating a condition?

Yes

Please provide your reason(s) and suggested changes, if any.

We especially support that nominations can come from patients and patient groups, not just healthcare providers or provinces.

4. Do you agree with the proposed process for evidence review?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

We also support the Thalassemia community in requesting that Thalassemia be added to this list and the Sickle Cell community in requesting that sickle cell trait be considered for this list.

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Not that we are aware of

11. Are there any other comments that you would like to share with us?

It is exciting to see this work moving forward. We look forward to next steps. Thank you for the opportunity to participate in the consultation.

Neuromuscular Disease Network for Canada

1. Do you agree with the proposed guiding principles and definitions?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

No response provided

3. Do you agree with the proposed process for nominating a condition?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

4. Do you agree with the proposed process for evidence review?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

No response provided

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Duchenne muscular dystrophy

Pompe disease

While the discussion document emphasizes the need for evidence, it doesn't fully consider the emerging landscape of genomic technologies. We need to consider how next-generation sequencing (NGS) technologies could be integrated to handle multiple conditions, rather than tackling them one by one, which would significantly delay implementation. Additionally, some neuromuscular diseases are currently suitable for newborn screening due to their identification through a sensitive biochemical assay or a specific mutation, such as the deletion of SMN1 exon 7 in SMA. However, most neuromuscular diseases lack a specific biomarker or common molecular defect, making them incompatible with existing NBS platforms, which rely primarily on biochemical markers. For example, congenital myasthenic syndromes is not detectable by current NBS technologies. CMS involves mutations in multiple genes, and low-cost treatments like salbutamol and pyridostigmine can prevent sudden death or disability during an often-lengthy diagnostic journey. CMS cannot be identified through current biochemical NBS methods. Biomarker based DMD NBS is also non-trivial, and is particularly associated with false positives. NGS is likely a significantly more effective strategy for this condition. As discussed above with the examples of CMS and DMD, identifying these disorders at birth will require more advanced techniques, such as whole-exome or targeted sequencing. The Committee should take into account the potential benefits of incorporating whole-exome and next-generation sequencing into newborn screening protocols

11. Are there any other comments that you would like to share with us?

Response to the Pan-Canadian Guidance for Newborn Screening: Building the Foundations for Early Detection and Diagnosis of Conditions

About Muscular Dystrophy Canada and The Neuromuscular Disease Network for Canada:

This response was authored by Muscular Dystrophy Canada (MDC) and investigators of the Neuromuscular Disease Network for Canada (NMD4C), a collaborative network of clinicians, researchers, and patient representatives who together are dedicated to advancing care, research, and policy for individuals with neuromuscular disorders. MDC and NMD4C bring leading experts in the field together to provide informed perspectives on critical healthcare initiatives, such as newborn screening, with the aim of ensuring equitable access to innovative disease modifying

therapies (DMT)and improving the lives of those affected by neuromuscular conditions across Canada.

Neuromuscular diseases encompass a heterogeneous group of over 400 disorders with a wide range of clinical presentations. Until recently, disease-modifying treatments were limited for most of these conditions. Advances in understanding the underlying pathophysiology with subsequent preclinical and clinical research have led to the development of transformative therapies, showing remarkable effects not only in acquired, inflammatory diseases, but also in genetic disorders such as spinal muscular atrophy (SMA), and Pompe disease. Encouraging early results have also been seen in conditions like limb girdle muscular dystrophies, X-linked myotubular myopathy, and Duchenne muscular dystrophy (DMD), with some DMT already receiving regulatory approval for DMD in jurisdictions outside of Canada.

Due to their rarity and complexity, neuromuscular diseases are often diagnosed after significant delays, during which time irreversible damage to the peripheral nervous system can occur, reducing the effectiveness of early treatments. This prolonged diagnostic journey can lead to years, even decades, of reduced quality of life before an accurate diagnosis and appropriate treatment are provided. As of a few weeks ago, there is 100% adoption of newborn screening for SMA across all Canadian provinces and territories. There was a 4-1/2 year delay between the adoption of SMA into NBS programs between the first adopting province (ON in January 2020) and the most recent provinces (NS, NB, PEI in August 2024). We advocate the need for harmonized national newborn screening recommendations, similar to the USA's Department of Health and Human Services' Recommended Universal Screening Panel (RUSP) recommendations, that may provide a more streamlined, evidence-based recommendations at a national level, facilitating more equitable and timely adoption, and avoiding the redundant reviews and staggered implementation that was observed with SMA. Despite this, achieving full screening within four years was an impressive outcome, made possible by patient advocacy, evidence-based efforts, and national collaborations led by Muscular Dystrophy Canada alongside implementation and readiness projects led by clinicians and researchers at local/provincial levels.

Introduction:

We welcome the release of this guidance document; particularly as clinical experts as well as people with neuromuscular conditions and their families have been calling for a national strategy to establish clear guidelines and standards for newborn screening programs for more than a decade. The discussion paper on newborn screening by the Canadian Drug Agency raises important issues, but it overlooks several critical areas that must be addressed if we are to move forward effectively, especially in the context of rare and ultra-rare neuromuscular conditions.

Ensuring Flexibility and Innovation in Newborn Screening:

There are several novel treatments and therapies for rare diseases likely to enter the market within the next five years, including many targeting neuromuscular conditions that could benefit from newborn screening. This presents a significant opportunity, and it is essential that the "Proposed Pan-Canadian Newborn Screening List" focuses on establishing national minimum standards, not maximums. If this distinction is not made clear, we risk stifling innovation and discouraging provinces like Manitoba and Ontario, which have historically led the way by adding conditions to their newborn screens based on evidence review and real-world evidence processes (RWE). Decisions grounded in RWE must be carefully managed to avoid creating overly rigid frameworks that limit flexibility and responsiveness to new, emerging innovations. There should be a minimum standard set of recommendations such that there is equitable access to NBS and its benefits for individuals in all provinces. This would have prevented the delays in adoption of NBS for SMA in some provinces, and the application of NBS for this condition has enable life altering early access to treatment. At the same time, individual provinces should be allowed the freedom to innovate, and to explore NBS for additional diseases based on RWE and to develop new technical approaches.

Consideration of "Out of Scope" Issues:

To achieve meaningful progress in newborn screening, it's essential to address issues beyond the immediate scope of this document. Specifically, laboratory infrastructure and processes are paramount to the success of screening programs. For example, ensuring that the proper facilities exist, such as Molecular Genetics Labs (MGLs) as well as Biochemical Genetics Labs (BGLs) and other functional testing labs, is critical to screening conditions like DMD and Pompe disease, which are predicted to become part of an increasing number of NBS panels in the near future. Without addressing these foundational aspects, any advancements in screening will be severely limited by downstream bottlenecks.

Without full transparency into the bilateral agreements under the National Rare Disease Strategy, it is difficult to assess the potential success of this proposed national screening list and process. In other words, without a focused effort and investment in the logistics and individual processes of individual newborn screening programs and laboratories, and without clear understanding of the per province mandate that would accompany minimum national standards, the proposed plan is unlikely to bring about significant change. Critical issues such as infrastructure for sample processing, responsibility for managing these processes, and the transport of samples to labs must be addressed. To make a meaningful impact, this guidance document should align with provincial funding through the Rare Disease Federal Strategy to ensure streamlined processes and equitable access nationwide with uniform adoption of accepted screening lists.

Patchwork Implementation:

While a national newborn screening list will help reduce inequities, we do not expect it will dramatically alter adoption timelines. All provinces should be encouraged to adopt similar processes to avoid inequitable and irregular rollouts, which result in inconsistent clinical care across the country. A truly national approach is essential to ensure equity in newborn screening and clinical care. Province-by-province decision-making has historically led to patchwork implementation, as demonstrated recently with SMA.

The Need for National Guidance:

A national body to define minimum standards in newborn screening is a good idea but must be executed with caution. The proposed process risks becoming another bureaucratic layer that may further slowdown or even prevent progress. Instead, we should focus on using the lessons from the Recommended Uniform Screening Panel (RUSP) in the U.S. process, which is highly evidence-based, but apply it in a way that speeds up decision-making in Canada. It raises the question of why the U.S.A's RUSP and Canada cannot share their evidence reviews, given that both processes are focused on ensuring the highest standards of care for newborn screening. Sharing evidence reviews would streamline the decision-making process, reduce duplication of efforts, and accelerate the adoption of new screening technologies. Collaboration between the two systems would allow both countries to benefit from each other's expertise and resources, ensuring that the most up-to-date and comprehensive data is considered when making decisions about which conditions to include in newborn screening panels. This could lead to more timely and consistent care across jurisdictions, ultimately improving outcomes for patients with rare diseases.

Financial Considerations and Funding Allocation:

The current funding structure across provinces must be revisited. Provinces need the will to implement changes, and financial incentives should be restructured to support rapid adoption of new technologies and processes. Such funding and forecasting must take in to account the increased burden on specialty providers, who will be anticipated to evaluate and monitor patients during pre symptomatic periods identified by NBS based diagnoses

Inclusion of Neuromuscular Disease Experts:

The committee responsible for the development of the Guidance Document did not include neuromuscular experts. It also did not include clinical experts in the treatment from other relevant rare disease areas. As a result, key conditions may have been overlooked in the proposed iteration of the National Screening List. Given the significant advancements in treatment options for certain neuromuscular diseases and the potential for early interventions to drastically improve patient outcomes, it is critical that conditions such as these are considered. Engaging with

neuromuscular and other relevant disease experts in future deliberations would ensure that the list is more comprehensive and reflective of current therapeutic developments.

Implementation and the Role of Emerging Technologies:

While the discussion document emphasizes the need for evidence, it doesn't fully consider the emerging landscape of genomic technologies. We need to consider how next-generation sequencing (NGS) technologies could be integrated to handle multiple conditions, rather than tackling them one by one, which would significantly delay implementation. Additionally, some neuromuscular diseases are currently suitable for newborn screening due to their identification through a sensitive biochemical assay or a specific mutation, such as the deletion of SMN1 exon 7 in SMA. However, most neuromuscular diseases lack a specific biomarker or common molecular defect, making them incompatible with existing NBS platforms, which rely primarily on biochemical markers. For example, congenital myasthenic syndromes is not detectable by current NBS technologies. CMS involves mutations in multiple genes, and low-cost treatments like salbutamol and pyridostigmine can prevent sudden death or disability during an often lengthy diagnostic journey. CMS cannot be identified through current biochemical NBS methods. Biomarker based DMD NBS is also non-trivial, and is particularly associated with false positives. NGS is likely a significantly more effective strategy for this condition. As discussed above with the examples of CMS and DMD, identifying these disorders at birth will require more advanced techniques, such as whole-exome or targeted sequencing. The Committee should take into account the potential benefits of incorporating whole exome and next-generation sequencing into newborn screening protocols.

Conclusion:

While the discussion paper outlines important aspects of newborn screening, it fails to address critical issues related to infrastructure, national standards, and the integration of emerging technologies. A broader approach is needed—one that encourages innovation, addresses systemic lab issues, and ensures equitable implementation across all provinces. The goal should be to create a national framework that sets minimum standards while allowing for the necessary flexibility to adopt new treatments and technologies as they become available. We must ensure that the system is prepared for the future and free from rigid processes that prevent timely advancements.

Contributing Authors: Homira Osman, PhD Pranesh Chakraborty, MD James Dowling, MD, PhD Stacey Lintern, CHE Hanns Lochmuller, MD Alex MacKenzie, MD, PhD Hugh McMillan, MD Maryam Oskoui, MD Kathryn Selby, MD

Newborn Screening Ontario

1. Do you agree with the proposed guiding principles and definitions?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

- Equity – This part of the statement is unclear: "When considering what conditions to screen for in newborns, their diverse needs, circumstances, and best interests need to be considered."
    - How would the panel suggest this concept be operationalized? Could an example be provided?
    - The rationale for this portion of the equity statement effectively repeats it: "When decisions regarding newborn screening are made, the newborn's diverse needs, circumstances and best interests need to be considered."
- Sustainability – Consider removing reference to 'environmental' consideration. Environmental assessments of screening process are not routine, and do not stand on par with social and economic considerations.
- Our greatest concern about this discussion paper (applicable to multiple questions) is the lack of clarity on the means to correct 'differences in the conditions screened and access to screening across the county?'
    - Is the 'proposed pan-Canadian newborn screening list' going to be communicated as a minimum standard or as a target? Will this list be the most limited screen, because everyone can do it, an 'average' screen, or the most advanced screening practices in the country?
    - This work of the advisory panel has the potential to be misused to limit existing screening programs and innovation in screening if you do not directly address this. A province could potentially justify attempts to defund screening programs if they exceed the 'proposed pan-Canadian newborn screening list.'

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

- Figure 2 - Newborn screening programs are accountable to the P/T MOHs in addition to sharing information with them.
- Figure 2 - The panel should also clarify how and why the proposed NSAC would engage in direct communication and information sharing with a P/T MOH in the absence of the provincial screening organization. This would be appropriate when the NBS program was housed within the provincial or territorial MOH but not otherwise. It should also be explicit that the role of any communication with MOH would be to encourage the support and expansion of screening programs.
- Expert review committees (whether for consideration of new screening or analysis of existing screens) should be selected ad hoc. Content experts and those with lived experience will not be uniform across diseases. Although this point is considered in Table 5 and described below Table 3, I would recommend you explicitly state this in Table 3.

3. Do you agree with the proposed process for nominating a condition?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

- We would propose that in addition to nomination, two actions should automatically nominate a condition for a review:
    - The condition is added to the screen by any province or territory.
    - There is a new rare disease drug or gene therapy application in Canada for a condition that may meet NBS criteria.

4. Do you agree with the proposed process for evidence review?

No

Please provide your reason(s) and suggested changes, if any.

- Is a full evidence review required when another group has already completed this? Could existing evidence reviews (from another national authority or provincial group) be considered and voted upon? Could we agree to partner globally on evidence review? These steps could reduce the burden on the proposed advisory committee and expert review committee.
- Can disorders be considered as a class? For example, if there were a set of inherited disorders that used a shared methodology (enzymatic analyses or genotyping for example) that had similar pathologies (all forms of MPS3 for example) could these be co-evaluated?

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Will the NSAC propose methodologies for the screens or not? It is not clear.

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

No

Please provide your reason(s) and suggested changes, if any.

The Wilson and Jungner criteria have provided a longstanding framework for evaluating screening. You can write about how you intend to apply them but should not modify foundational principles. Of particular concern.

- Wilson and Jungner criterion 2 – This criterion should be retained, as it provides the opportunity for therapy.

- Wilson and Jungner criterion 3 – The statement “Differences in the incidence and variation in test performance in subpopulations, particularly in equity-deserving groups, should be characterized and adequately understood” is problematic. It fails to define subpopulations or what activities would fulfill this requirement. The original statement should be preserved.
- The change to criterion 4 is unnecessary. The intention of the original covers this point. Footnote b is concerning, as it could bar screening for a disorder that had not been studied in such a way that the distribution of test values was known in advance. Furthermore, the definition of ‘suitable cut-off’ for a screening test is dependent upon factors (instrumentation, location, seasonality) that are outside the scope of consideration of a new disease.
- The change to criterion 8 may have unpredictable consequences as noted above. ‘Across Canada’ is not defined, and this could be construed to force all provinces to cover the most limited set of disorders. This criterion also fails to consider regional variation, where screening may be needed in one area because of a founder population but not Canada-wide.
- The removal of criterion 9 does not consider its full meaning. It is not just about the timing of case finding. Wilson and Jungner also write about the concept of ‘surveillance’ and these issues are still important.
- The principle of equity, as currently written, could be construed to prevent the adoption of screening for a condition in one region of Canada because of a lack of treatment option in any other region of Canada. This may have consequences for the introduction of screening that are not intended, especially without an exact definition of ‘across Canada.’ The statement of this principle also fails to recognize that there may be legitimate purpose to region-specific variations in the operation of NBS programs.

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

No

Please provide your reason(s) and suggested changes, if any.

The proposed list should be reviewed as individual disorders. The panel has created it from the 2016 list, adding the uniformly screened conditions and then SMA. The generation of this list should be taken as future work, considering these conditions and others that are currently screened for in Canada as a starting point.

- Some disorders need to be better defined. Our primary target of screening for CAH is infants with salt-wasting forms, not simple virilizing disease. The target for MPS1 is Hurler, but not Scheie.
- The panel has equated a lack of uniform screening across Canada with a requirement for further review (Table 13). There is no justification for this equivalence. Indeed, newborn screening for cCMV was already the subject of a CDA review and this is not mentioned.

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Although the conditions listed are not objectionable, this list should not be static. The nomination process, to be transparent, should permit any stakeholder to propose the consideration of a disorder.

11. Are there any other comments that you would like to share with us?

This discussion paper was funded through the National Strategy for Drugs for Rare Diseases but makes little effort to describe how screening for new disorders supports the goals of the NSDRD. This is a missed opportunity.

Perinatal Services BC, PHSA

1. Do you agree with the proposed guiding principles and definitions?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

No response provided

3. Do you agree with the proposed process for nominating a condition?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

4. Do you agree with the proposed process for evidence review?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

As with all other health areas, having members of the public involved is good and provides different perspective, but it also comes with a bias perspective. It is much harder for a parent / family to see the larger bigger picture for population health level decision making when their focus is solely on their affected child for e.g. And rightly so. Their opinion is import but I don't think it can supersede the larger issues at play in a public health care system. There have been many times when it does and a champion care provider or champion family notify the media and make a lot of noise and then the gov't reacts. Can be a good result, but does not reflect a good decision-making process.

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

No response provided

11. Are there any other comments that you would like to share with us?

As more treatments become available, there will be more nominations for newborn screening. This is good. But also requires funding. Newborn screening panels can not just continue to grow without very thoughtful deliberation. Every screen costs the screening lab and the downstream system as a whole. Holistically looking at the system is very important. Removing conditions from the panel has to be part of this as technology changes. Deciding where to invest - prenatal carrier screening, newborn biochemical screening, molecular genomic screening / testing - all have parts of play but we don't want to overlap too much and compete for same resources.

E.g. if SMA carrier screening prenatally is available, do we also offer newborn screening for the same condition? This could lead to pregnancies and newborns being screened twice.

Regroupement québécois des maladies orphelines

1. Do you agree with the proposed guiding principles and definitions?

Qui

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

1) Est-ce que les évaluations pour ajouts de maladies vont continuer dans les provinces? Par exemple, par l'INESSS au Québec? Il me semble qu'il y aurait alors dédoublement du travail. Et si les recommandations sont contradictoires??

2) Est-ce qu'il serait pertinent d'inviter les représentants des programmes provinciaux au "Expert Review Committee" ou les personnes - dans les provinces - qui sont responsables d'évaluer les maladies à dépister?

3) On veut harmoniser à travers le Canada, mais "en conservant leur [les provinces et territoires] autonomie et le pouvoir d'adapter les programmes à leurs besoins". Si "leurs besoins" font référence à des considérations budgétaires, l'harmonisation est peut-être utopique. Cela irait à l'encontre des principes des "droits des nouveau-nés" au Canada et de l'équité. Étant donné l'investissement proposé via la Stratégie canadienne pour les médicaments pour maladies rares, pourquoi ne pas avoir alloué les sommes nécessaires pour "compléter les programmes de dépistage néonatal des provinces et territoires" selon la liste proposée de maladies (Tableau 12)? Sommes permettant l'achat d'équipements et l'embauche de ressources humaines.

Cependant, si les "besoins" concernent la prévalence d'une maladie ou l'absence d'une sous-population cible, cela est justifiable.

3. Do you agree with the proposed process for nominating a condition?

Oui

Please provide your reason(s) and suggested changes, if any.

Veuillez expliquer votre réponse et proposer des modifications, le cas échéant. Toujours mon questionnement quant aux évaluations faites séparément dans les provinces et qui pourraient être contradictoires.

4. Do you agree with the proposed process for evidence review?

Oui

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Oui

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

Oui

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Oui

Please provide your reason(s) and suggested changes, if any.

No response provided

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Oui, en partie

Please provide your reason(s) and suggested changes, if any.

Veuillez expliquer votre réponse et proposer des modifications, le cas échéant. Considérant les maladies déjà dépistées au Canada (et qui ont certainement fait l'objet d'une évaluation pour être inscrites sur un panel de maladies dans une province ou territoire), il est étonnant de considérer leur retrait. À moins 1) qu'on démontre une absence systématique de dépistage de la maladie due à une faible incidence ou 2) qu'il y ait un changement de technologie ayant un impact significatif sur le coût du dépistage.

9. Do you agree with the proposed pan-Canadian newborn screening list?

Qui, en partie

Please provide your reason(s) and suggested changes, if any.

Veuillez expliquer votre réponse et proposer des modifications, le cas échéant. Pour les neuf (9) affections que l'on veut réviser, est-ce que l'évaluation des provinces qui ont font le dépistage n'est pas suffisante pour les inclure aujourd'hui?

Le seul critère qui pourrait être évalué est l'incidence dans une province/territoire spécifique.

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Il y a plusieurs maladies lysosomales proposées.

Je me questionne sur l'absence des MPS IV (Morquoi) et MPS VI (Maroteaux-Lamy) étant donné qu'il y a aussi un traitement pour ces maladies. Incidence? Efficacité du traitement?

Notez qu'au Québec, nous avons une prévalence plus élevée de la maladie de Morquio que dans les autres provinces. Par contre qu'en est l'incidence au cours des dernières années?

Enfin, avec l'avènement des nouvelles technologiques génomiques, je pense qu'à court ou moyen terme, il faudra penser à cibler beaucoup plus de maladies génétiques pour lesquelles il y a un

traitement (et traitement ne signifie pas toujours "médicament"; il peut y avoir d'autres traitements ou interventions possibles pour éviter le décès ou réduire la morbidité). Un autre avantage d'un tel dépistage étendu est la réduction du délai de diagnostic qui entraînerait des économies dans le réseau de la santé, libérerait du temps de médecins et allégerait l'angoisse des familles.

11. Are there any other comments that you would like to share with us?

Merci au Comité pour ce travail exhaustif.

Sanofi-aventis Canada Inc.

1. Do you agree with the proposed guiding principles and definitions?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

- The guiding principles are indeed essential for shaping the overall direction of the program's development. There remains some ambiguity in their practical application that needs to be addressed. Greater clarity will be required on what standards will be put in place to ensure these pillars are upheld.
- To ensure continuous quality improvement in newborn screening programs, it would be important that the advisory panel's recommendations to the Federal, Provincial, and Territorial (FPT) governments are not merely advisory. Implementing and monitoring these improvements effectively requires a more robust framework. Additionally, there should be greater transparency of the FPT's decision-making process.
- Further, while the health rights of the newborn are central to panel's activities and decision making, the scope of these rights should be more clearly defined. Will these rights include screening for conditions that do not involve severe morbidity, mortality, or disability, or for those that can be actioned upon but with uncertain or short-term benefits? It might be worth considering whether the concept of "actionable" should be incorporated under the health rights of the newborn.
- Lastly, if funding for implementing recommendations is out of scope, will the advisory panel provide guidance to the FPTs on how to prioritize their recommendations when it is not feasible to fund all screening tests?

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

- Choosing between the CDA and PHAC as the coordinating body points to the need for enhanced communication between the two organizations, especially given their respective mandates. It seems crucial that both organizations remain actively involved.

- Furthermore, while sharing records, including patient-level data, is noted as out of scope for the advisory panel (as mentioned on page 7), there's an apparent contradiction on page 17 (Table 3), where a potential responsibility of the Quality, Standards, and Education Committee is to coordinate and support "a pan-Canadian newborn screening data repository."
- Greater clarity is needed on whether the coordinating body will be empowered to drive this change or even monitor measurable performance indicators if data sharing is explicitly out of scope. Based on Figure 2, the coordinated model should explicitly include a communication strategy directed towards the public and healthcare professionals (HCPs). If it aligns with the scope of the model, considering a ministerial action to ensure effective and well-integrated communication would be beneficial.
- Adopting a best practice example where Federal, Provincial, and Territorial (FPT) bodies routinely share information beyond specific topics like vaccinations, and communicable diseases would be helpful than developing guidelines from scratch.
- Another suggestion is to simplify the model to facilitate its implementation. Currently, there seem to be multiple committees with potentially overlapping mandates. Consolidating these committees could enhance efficiency.
- Finally, regarding the CDA potentially taking on this responsibility, it would be important to assess whether they have the necessary capacity and capabilities to do so effectively.

3. Do you agree with the proposed process for nominating a condition?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Overall, the nomination process is well-structured and bears similarities to a drug HTA submission. However, there should be greater clarity on the criteria used to add or remove a condition and how these criteria will be weighted. Additionally, more clarity is needed around the timeline for each step of the process. For consideration, A significant concern is the lack of rare disease prevalence data in Canada, which could impact the effectiveness of the nomination process.

4. Do you agree with the proposed process for evidence review?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

While a review process is essential, there are several areas that require further clarification.

- What level of evidence will be accepted or denied during the review?
- Clarification is also needed on how the net benefit of screening will be defined, and whether there will be a common threshold for the number-needed-to-screen to avoid a poor outcome that will be applied to all nominated conditions. In the absence of a common threshold, how will the process vary?
- The definition of "actionability" in the context of a positive screen is also unclear. Does "actionable" mean that a diagnostic test or treatment only needs to exist somewhere in the world, or must it be funded by the Federal, Provincial, and Territorial (FPT) governments to be considered actionable?
- Moreover, the timelines for each step of the process should be specified. It would be helpful to clarify what evidence is necessary for both the nomination and the review stages. Is the nomination process akin to a pre-screening, and does it require the same or different levels of evidence?

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

- It is recommended to combine the advisory committee and evidence group to save time and shorten the overall process. Additionally, clarification is needed on how the need for and cost of ongoing diagnostic tests and treatments will be factored into deliberations and recommendations, especially in comparison to conditions where a one-time treatment is sufficient.
- The target timelines for each step in the process should also be outlined. Furthermore, please clarify how the deliberation committee will be formed for each review. Will there be a deliberative framework, particularly as there is mention of a decision matrix.
- Lastly, it would be helpful to understand how the evidence required for removing a condition will differ from that for adding one. It seems impractical for any stakeholder to gather and present evidence to remove a condition, especially given the lengthy process involved.

6. Do you agree with the proposed process for engagement and communication?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

While the overall process for engagement and communication appears viable and quite similar to HTA reviews, there are some points that need clarification. Specifically, it's unclear who the permitted parties will be to provide feedback on the draft recommendations, and whether there will be an opportunity for re-deliberation based on the feedback received. Besides, will there be an opportunity to provide feedback prior to the review?

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

- The proposed criteria are well-considered, but transparency should also extend to the relative weighting of each criterion for adding a condition to the list.
- Clarification is needed on how the effectiveness of screening in improving a newborn's health will be assessed in the absence of real-world evidence for the test.
- In Table 9, bullet 10, it would be beneficial to include the budgetary impact of monitoring within the overall cost of screening, diagnosis, and treatment, compared to not screening.
- Point 7 in Table 9 mentions the need for an accepted treatment for patients with the condition.
- Further clarification is necessary on what "accepted" refers to—whether it means treatments that are approved or those that are both approved and funded. Also, a typo is identified in Table 9 where it states "the condition should be serious and 1..."; the "1" should be replaced with "one."

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

The considerations outlined seem reasonable; however, there is a need for clarity regarding the relative weight assigned to each factor in the final decision-making process. While the process for adding a condition is well-defined, the procedure for removing a condition remains unclear. It would be beneficial to know if there will be a consultation process for removing a condition.

Additionally, clarification is needed on the priority order for the questions listed in Table 10.

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Understanding the criteria used to select these nine tests for the evidence review would be beneficial. It would also be helpful to know the rationale for including SMA on the list, as this could provide useful insights for evaluating other conditions. For instance, conditions like Pompe disease, which can be halted in progression with early diagnosis and treatment, might benefit from similar consideration in future reviews.

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Exploring potential emerging conditions with limitations in blood test screening could be valuable. Conditions such as hypophosphatasia and achondroplasia might also warrant consideration. Moreover, further information is required on how the conditions listed in Table 14 be incorporated into the proposed screening list? It would be helpful to understand what additional evidence is required for their inclusion.

11. Are there any other comments that you would like to share with us?

In addition to newborn screening, it is important to consider screening guidance for diseases that may arise outside of the newborn setting. Early detection of such diseases can significantly improve patient and caregiver quality of life and reduce the burden on public healthcare systems. For instance, screening for Type 1 Diabetes at a young age, before symptoms develop, could help mitigate the severe impacts associated with a symptomatic diagnosis.

- It would also be beneficial to explore whether longitudinal data can be collected for newborns who are screened and diagnosed but choose to opt out of treatment. This data could enhance understanding of the natural history of rare diseases.
- There is still some uncertainty about how the newborn screening (NBS) program can benefit Canadian patient registries, data generation, and access to innovative therapies. The link between these elements and the NBS program needs further clarification.
- While significant progress has been made in advancing the NBS program in Canada, there is still much work to be done. The proposed list of conditions primarily reflects the outdated 2016 list, with only one new addition and no clear rationale for its inclusion.
- More clarity is needed regarding the process for removing a condition from the list and who would initiate this process, as it seems unlikely that any stakeholder would take on this responsibility.
- Finally, given the powerful role of NBS in combating devastating diseases, it would be useful to explore ways to measure its long-term benefits effectively.

Takeda Canada Inc.

1. Do you agree with the proposed guiding principles and definitions?

Yes

Please provide your reason(s) and suggested changes, if any.

Takeda Canada Inc. (Takeda) commends Canada's Drug Agency (CDA) for its forward-thinking approach in setting the foundation for a coordinated and standardized approach to newborn screening as part of the National Strategy for Drugs for Rare Diseases. We applaud CDA's efforts in initiating this critical discussion and its openness to feedback, which are crucial for achieving timely diagnoses and better health outcomes for newborns across Canada. This initiative represents a significant step towards equity, effectiveness, and sustainability in our healthcare system, especially for patients with a rare disease. Takeda is proud to contribute to this vital dialogue, as patients are our top priority.

For the guiding principle on “Collaboration”, the definition of “partners” and “interested parties” should be clarified to include all stakeholders (e.g. provincial drug plans, patient advocacy groups, medical associations, pharmaceutical industry associations, etc.) to ensure diverse perspectives are included.

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

Takeda is supportive of the proposed approach and model that supports alignment of process and criteria across Canada while allowing jurisdictions to customize based on local needs.

While diverse representation is important, there is a noticeable overlap of representatives between different proposed committees and programs (e.g. clinical experts, laboratory experts, public health experts, etc.). Takeda suggests having a single diversely represented central committee, such as the Newborn Screening Advisory Committee, but with the option to consult subject matter experts on an ad-hoc basis. Having a single central committee balances the need for broad expertise and minimize potential duplication of efforts. For this approach, the central committee should focus on supporting alignment of process and criteria via recommendations and allow jurisdictions to customize newborn screening programs based on local needs.

In the discussion report, meeting frequency between the Advisory Coordinating Body, regional Ministries of Health and newborn screening programs is not mentioned. Takeda suggests establishing a meeting frequency to permit continuity of discussion and collaboration

3. Do you agree with the proposed process for nominating a condition?

Yes

Please provide your reason(s) and suggested changes, if any.

Step 1 - Nomination submitted:

- Suggest forms are available in English and French.
- Suggest various ways to submit a nomination to provide equitable access for submissions: digital, fax, mail.
- Suggest revising to 'potential availability of effective treatment' as a mandatory criterion for nomination or nomination for review. Some Newborn screening (NBS) tests or technology take time to establish prior to availability of effective treatment.

Step 2 and 3 - Nomination form reviewed, discussed and deliberated: timing?

- Suggest providing expected time window for review/discussion/deliberation and decision. This will help nominators with expectations on turn-around.
- Suggest having a system that weights the supporting information to allow for objective assessment for prioritization.

Step 4 and step 5 - Recommendation for or against an evidence review:

- Suggest calling out the opportunity for the nominator to provide additional information and the opportunity to add further explanations for the nomination besides the initial input form after the first round of discussion and deliberation for nominations deemed not to proceed.
- If a nomination is added or removed, suggest that a clear rationale is provided as to why the condition is added/removed.

4. Do you agree with the proposed process for evidence review?

Yes

Please provide your reason(s) and suggested changes, if any.

Strongly suggest leveraging experts in specific rare disease areas to support the evidence review process is a must. Current language is that the experts "may be" called upon and suggest changing to "will be".

- Suggest information of NBS tests/programs of each nominated disorder/disease from other countries with official national NBS program / strategies (e.g. USA, Australia, New Zealand, Italy, The Netherlands, Norway, Germany, Denmark) should be added to the review as supportive evidence.
- Suggest possible time windows and deadlines to complete a review to be communicated to the nominator prior to initiation of the review.
- The net benefit criteria should be defined in detail prior to implementing the process.

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes

Please provide your reason(s) and suggested changes, if any.

Takeda agrees with the proposed approach of deliberating on the net benefit of screening for developing a recommendation.

- Suggest leveraging both a decision matrix and consensus voting during deliberation for objective and standardized decision making. Similar to the current deliberation process of health technology assessment, ad hoc consultation with experts should be permitted if required.
- Sharing detailed meeting minutes publicly permits all stakeholders to clearly understand the deliberation and recommendation, aligned with the principle of "Transparency". If the final recommendation has changed from the draft, suggest providing the rationale and a list of information that was available or not available to explain the decision so that it will help with future submissions if evidence package changes.
- For step 7, there appears to be a minor discrepancy in the first bullet under "Description and Features". It is unclear what the type of "recommendations" will be made by the Evidence Review given its role is to assemble an evidence package for deliberation by the Newborn Screening Advisory Committee. Therefore, additional clarification is needed.

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

Takeda agrees with the proposed process and suggest all parties should have the opportunity to provide feedback on a draft recommendation to align with the principle of equity and collaboration. Also, public communication of upcoming draft recommendation in the CDA's weekly newsletter would best allow interested stakeholders to prepare and participate.

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

Criteria #1: Important to define severity of morbidity that deems the condition 'serious'.

Criteria #3: 'adequately understood' may be different among diseases that are rare or ultra-rare. It's important to operate within certain flexibility when considering 'adequately understood', but a definition would help.

Criteria #4: Important to define what a 'validated' tests is. What validation is considered adequate?

Criteria #7: Suggest to 'broaden' the criteria to a potentially effective treatment or intervention instead. Consider the flexibility to add a new condition for NBS when adequate clinical data of a new medication (ph2/ph3) is available prior to Health Canada approval so that the public and private sector can adequately prepare (enough lead time) for a new screening test being implemented prior to treatment availability.

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

When providing what positive or negative impacts would removing this condition have on the screening program, suggest being clear not to list monetary/budget impacts.

- When asking if the condition is screened internationally, ask to provide a list of the other countries.
- Suggest combining Question 7 and Question 9.
- Suggest removing Question 10 about cost of case finding, as this may be a question that can't be answered due to the lack / missing of full cost and budget impact information.

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

Takeda agrees with the overall proposed pan-Canadian newborn screening list (Table 12).

- Although there are 9 conditions (Table 13) not currently uniformly screened in Canada, some have been thoroughly evaluated by experts in the field and by newborn screening committees (www.newbornscreening.on.ca).
- There should be a 'fast-track' review process to determine if they could be added to the proposed pan-Canadian newborn screening list. For example, guanidinoacetate methyltransferase deficiency, homocystinuria and mucopolysaccharidosis type 1 are all conditions currently being screened in Ontario and have gone through the Newborn Screening Ontario Advisory Council's formal review process (//www.newbornscreening.on.ca/en/about-us/nso-governance and //www.newbornscreening.on.ca/en/results/screen-positive-results/disease-information/). For cases such as these, a fast-track process should exist to expedite recommendations and use the evidence package from these committees to avoid duplication of efforts

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Takeda agrees with the other emerging conditions for consideration in their final report (Table 14) and has no additional comments and suggestions for consideration.

11. Are there any other comments that you would like to share with us?

It is estimated that one in 12 Canadians live with a rare disease[1] and approximately 80% of rare disease are genetic in origin.[2] Early access to genetic screening testing is crucial for precise diagnosis and to inform clinical decision-making, leading to timely and effective treatment. Unlike traditional sample evaluation, next-generation sequencing (NGS) allows rapid and efficient analysis of multiple genes concurrently. Therefore, Takeda recommends CDA to consider the potential impact (risks / benefits) a newborn sequencing strategy could have on the earlier diagnosis and treatment of a significantly broader range of rare diseases versus current NBS approaches.

Takeda also encourages CDA to review other published Canadian sources for recommendation on NBS, such as the 2023 report and recommendations for federal and provincial/territorial policymakers prepared by ImmUnity Canada and the Network of Rare Blood Disorder Organizations (NRBDO).[3]

References

1. Health Canada. "Building a National Strategy for High-Cost drugs for Rare Diseases: a Discussion Paper for Engaging Canadians." Retrieved August 23, 2024 from: https://www.canada.ca/en/health-canada/programs/consultation-national-strategy-high-cost-drugs-rare-diseases-online-engagement/discussion-paper.html

2. Health Canada. "About orphan drugs and rare diseases." Retrieved August 23, 2024 from: https://www.canada.ca/en/health-canada/services/licences-authorizations-registrations-drug-health-products/regulatory-approach-drugs-rare-diseases/about-drugs-rare-diseases.html

3. Network of Rare Blood Disorder Organizations (NRBDO). "A 2023 report and recommendations for federal and provincial/territorial policymakers". Retrieved August 23, 2024 from: https://www.nrbdo.ca/uploads/8/5/3/9/8539131/newborn_screening_report_jan_2023_for_web.pdf

Wilson Disease/Key Proteo

1. Do you agree with the proposed guiding principles and definitions?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

No

3. Do you agree with the proposed process for nominating a condition?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Yes and… reiterating the opportunity to provide evidence as described in Table 4 with the initial nomination form in step 4. Followed by more in depth evidence once in step 6

4. Do you agree with the proposed process for evidence review?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Yes and confirming that the decision matrix will include both short term AND lifetime impact and burden to patient, families and system.

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Yes, and…ensuring that criterial #2 is in fact covered in #3. I am unclear about symptom recognition and impact as outlined. Wilson disease, a rare genetic disorder where the liver lacks a protein to remove excess copper from the system, symptoms sometimes appear in early childhood but also later in life - typically late teens and early 20s. However by the time the disease is diagnosed, the patient will have suffered significant liver, neurological and/or psychiatric damage. I would hope that the criteria doesn't just include conditions that appear in early childhood as many patients suffer for years in silence until they are diagnosed as young adults or older adults. By this time, patients suffer so much damage (typically to their liver and/or brain) that treatments (which are available) are not effective.

Further, for Wiskott Aldrich some symptoms appear early and are “treated” improperly due to improper diagnosis. As a result, the long-term health and viability is impacted by the delayed screening and diagnosis, though symptoms may not be severe immediately after birth.

Wiskott-Aldrich syndrome is a hereditary immunodeficiency disorder characterized by abnormal antibody (immunoglobulin) production, T-cell (lymphocyte) malfunction, a low platelet count, and eczema. Because the number of platelets is low, bleeding problems, usually bloody diarrhea, may be the first symptom. Eczema also develops at an early age.

Susceptibility to viral and bacterial infections, particularly of the respiratory tract, is increased because immunoglobulin levels are low and T cells malfunction. The risk of developing cancers (such as lymphoma and leukemia) and autoimmune disorders (such as hemolytic anemia, inflammatory bowel disease, and vasculitis) is increased.

Life expectancy is shortened. Premature death results most often from bleeding, but it may result from infections, autoimmune disorders, or cancers.

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Yes and…

In reviewing the criteria throughout the paper, we are noting the value in adding screening for multiple disorders due to the significant burden of delayed screening and diagnosis, including morbidity and mortality. This burden could be avoided through novel and accessible methods such as proteomic based screening from dried blood spots. Specifically seeking to add:

Wilson disease to be added to the list for 9 other conditions requiring evidence review. Currently, the state of Washington in the US is reviewing an application from Key Proteo and Dr. Sihoun Hahn (a doctor specializing in Wilson disease) who has developed an assay to test newborns for Wilson disease. He completed a pilot project in Washington state and tested his NBS assay on more than 20,000 newborns. His test is also currently being reviewed by the Food and Drug Administration (FDA). Dr. Hahn and Key Proteo have had positive discussions with the FDA and Washington state on NBS for Wilson disease. There is a lot of literature on the details and values of the assay which we appreciate the opportunity to share.

Wilson disease. Babies with Wilson disease begin accumulating copper from birth. It's a slow and gradual buildup of copper until it reaches toxic levels that result in significant liver, brain, neurological and psychiatric conditions. Left untreated it is fatal or severely damaging the individual with Wilson disease. However, there are 3 highly effective treatment options that can assist the body in removing excess copper - trientine, penicillamine (both are chelators) and zinc (blocks absorption). There are also two clinical trials underway that offer gene editing to correct the defective gene. These trials are showing great promise. The good news is if / when Wilson disease is detected early, they can be treated and live long, healthy lives.

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10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Yes any. As noted in the response to question #9 there are several disorders that we recommend considering and adding to the NBS.

11. Are there any other comments that you would like to share with us?

I applaud the care and effort invested to date. Newborn screening offers equitable access to early detection, diagnosis and treatment to all. With the evolution of newborn screening methods, such as proteomic-based testing of dried blood spots additional conditions can be screened early AND treated. And therefore, as new accessible screening methods are approved, more newborns can be tested for more high-burden conditions. And that the program and guidelines developed are nimble enough to allow patient groups to nominate new conditions. Thank you.

Wilson Disease/Key Proteo

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Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

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No

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Yes-in-part

Please provide your reason(s) and suggested changes, if any.

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No response provided

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No response provided

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8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

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10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Yes any. As noted in the response to question #9 there are several disorders that we recommend considering and adding to the NBS.

11. Are there any other comments that you would like to share with us?

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Wilson Disease Association

1. Do you agree with the proposed guiding principles and definitions?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

2. Do you have any specific changes that you would recommend for the proposed approach to the potential coordinated structures for newborn screening?

No

3. Do you agree with the proposed process for nominating a condition?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

4. Do you agree with the proposed process for evidence review?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

5. Do you agree with the proposed processes for deliberating and developing recommendations?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

6. Do you agree with the proposed process for engagement and communication?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

7. Do you agree with the proposed criteria for adding a condition to a proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

Yes but I am unclear about when symptoms should appear. For Wilson disease, a rare genetic disorder where the liver lacks a protein to remove excess copper from the system, symptoms sometimes appear in early childhood but also later in life - typically late teens and early 20s. However, by the time the disease is diagnosed, the patient will have suffered significant liver, neurological and/or psychiatric damage. I would hope that the criteria doesn't just include conditions that appear in early childhood as many patients suffer for years in silence until they are diagnosed as young adults or older adults. By this time, patients suffer so much damage (typically to their liver and/or brain) that treatments (which are available) are not effective.

8. Do you agree with the proposed considerations for removing a condition from a proposed pan-Canadian newborn screening list?

Yes

Please provide your reason(s) and suggested changes, if any.

No response provided

9. Do you agree with the proposed pan-Canadian newborn screening list?

Yes-in-part

Please provide your reason(s) and suggested changes, if any.

I would like Wilson disease to be added to the list for 9 other conditions requiring evidence review. Currently, the state of Washington in the US is reviewing an application from Key Proteo and Dr. Sihoun Hahn (a doctor specializing in Wilson disease) who has developed an assay to test newborns for Wilson disease. He completed a pilot project in Washington state and tested his NBS assay on more than 20,000 newborns. His test is also currently being reviewed by the Food and Drug Administration (FDA). Dr. Hahn and Key Proteo have had positive discussions with the FDA and Washington state on NBS for Wilson disease. There is a lot of literature on the details and values of the assay which I am happy to share. Babies with Wilson disease begin accumulating copper from birth. It's a slow and gradual buildup of copper until it reaches toxic levels that result in significant liver, brain, neurological and psychiatric conditions. Left untreated it is fatal or severely damaging the individual with Wilson disease. However, there are 3 highly effective treatment options that can assist the body in removing excess copper - trientine, penicillamine (both are chelators) and zinc (blocks absorption). There are also two clinical trials underway that offer gene editing to correct the defective gene. These trials are showing great promise.

10. Are there other emerging conditions that you would recommend the advisory panel consider in their final report?

Yes Wilson disease. Again, the state of Washington is considering to add Wilson disease to its newborn screening panel. Dr. Sihoun Hahn has presented a comprehensive case to support his petition. He will soon be approaching other states in the USA. I am happy to provide his submission for your review, demonstrating the effectiveness of his assay and the potential to identify babies with Wilson disease. Because Wilson disease is a silent disease as the body slowly accumulates excess copper, symptoms don't appear until later in childhood or early teens. By then, significant liver and/or brain damage has already occurred. Because there are three highly effective treatment options (trientine, penicillamine and zinc) plus following a low-copper diet, the disease can be managed if children are diagnosed early enough - before damage occurs. And with two gene editing clinical trials underway, another very exciting treatment option may be in the pipeline in a few years.

11. Are there any other comments that you would like to share with us?

I applaud the work you have already done. I hope that we can expand conditions tested as newborns. I hope the program and guidelines developed are flexible enough to allow patient groups to nominate new conditions. Thank you.