February 2, 2022

Dear Legislature,

I am an Advisory Board Member for the Northwest Regional Newborn Screen Program, as well as a consultant to the Newborn Screen Program, and a clinical geneticist at OHSU. However, I am submitting this testimony outside of my professional roles, but as an individual to share my thoughts and experiences that would pertain to House Bill 4109.

Firstly, I am proud of the work the state's Advisory Board has been able to accomplish since 2019, and I thank you for the vision you had when you voted to have the advisory board created. This board is made up of a diverse group of representatives of their profession and life's passion, knowing that **each member does not only speak for themselves but for the groups they represent.** Though the members come from different backgrounds, they listen and work together because of a shared passion for newborn screening. The members of the board are FOR newborn screening, and NOT adversaries. The board **works towards the best solution to address the needs of ALL newborns and families in the state, as well as the health providers that have to support them**.

In regards to amendments as drafted in House Bill 4109, Section 1:

- Page 1, Lines 15-23 regarding removal of "representative of a statewide association of …", as an advisory board member, I appreciate that board members are chosen representatives of their fields, so that we are not listening to just the loudest voice in the room, but the measured voice of the entire association of profession.
- Page 1, Line 15-16 regarding "a federally recognized tribe in Oregon that uses the services of", I do like that addition, but this should be an additional member and not to replace the "representative of an entity that contracts with" the lab, as the lab services NBS for not just Oregon, but Guam, New Mexico, and other entities. We should keep their voices intact.
- Page 2, Line 12, regarding term of office being 2 years instead of 4, honestly, I think that will make it harder for us to recruit, if we have to recruit a new member every 2 years. There is a benefit to having a historical references of topics discussed, and I believe the current Advisory Board structure allows for that with staggering of 4 year terms to make sure the board's recommendations are consistent and more productive, and not re-discussing the same points, over and over.
- Page 2, Lines 21-23, regarding the deleted language, "One chairperson must be a voting member and the other chairperson must be the manager of the Northwest Regional Newborn Bloodspot Screening Program or the manager's designee. The manager or manager's designee must be a nonvoting member", the co-chair that is a non-voting manager allows the board to perform the administrative burden for the Advisory Board and allows for improved coordination of meetings and gathering of information that the Advisory Board has requested. This should remain in place in order for the board to function.
- Page 2, Line 27, regarding meeting four times per calendar year, I think that's going to be challenging. The board is already meeting 3 times a year since 2019, with agreements to call a meeting if something comes up. Finding a day/time that works with 13 member's schedule and to reach quorum is difficult.

In regards to amendments of House Bill 4109, Section2:

(1) **The state's advisory board does not have the resources and time to reach out to each of the 10 states or more, as proposed, and review each of their rational, methods, and results** on a

piloted newborn screen for a condition NOT on the RUSP. This is also not always published information, nor do other states have the resources at times to provide the data analysis. The state's Advisory Board cannot judge whether another state's newborn screening program is working well for that state, and having 10 states that have already added the disease does not always translate to something that will work well for the people of Oregon.

(2) **The state's advisory board does not have the resources and time to do the comprehensive and rigorous science, economic, and ethics review** (both published and unpublished) that the federal Advisory Committee on Heritable Disorder of Newborns (ACHDNC) does when they review a condition nominated for the RUSP. The advisory board relies upon the ACHDNC's recommendations and review first, in order for them to determine if it can be applied to the state. While sometimes the process can be long, when the science is CLEARLY there in terms of sensitivity and specificity of a screen, as well as treatment, the ACHDNC can move quickly to approve, as such was the case with spinal muscular atrophy (SMA).

I also want the board to be fiscally responsible so as to not take away resources that should otherwise be applied for the state's actual Newborn Screening purposes. As it stands in the past two years, I hear from the state lab's continued challenges to meet major goals of the program, including timeliness of critical results, facilitation of dried blood spots returned to the state in an equitable manner (not just for urban but also rural settings), updating its reporting infrastructure (they are still using fax machines) and to be up-to-date with conditions ALREADY recommended on the RUPS, such as X-ALD (x-linked adrenoleukodystrophy) and SMA (spinal muscular atrophy).

Finally, my heart goes out for the families struggling w/ Krabbe disease. As a clinician, I have seen the ravages of this disease, as well as the devastating consequences when newborn screening is rushed and not reviewed properly by the medical scientists and health providers that have to guide these families through the toughest times of their newborn's lives. I completed my pediatric and genetics training in NY state, when the state was the first in the nation to implement Krabbe NBS in 2006.

As a first year genetics fellow, I met a family whose baby was screened positive for Krabbe, with two mutations predicting infantile disease. However, because there was limited data on bone marrow transplant for Krabbe at the time (no longitudinal studies of those w/ infantile Krabbe that have received bone marrow transplant, only case reports), we could not promise that bone marrow transplant would be a cure, and were unclear what the outcome would be, whether there will be continued deficits. Because of lack of scientific knowledge at the time, and the baby appeared well, the family left without a bone marrow transplant work-up, choosing to take their own chances. The family returned with this infant 6 months later, in the throes of this disease, with severe spasms causing a lot of pain, but only comfort care could be provided at that point. The baby eventually died. A year later, another newborn from this couple also had the same condition. This time, they chose bone marrow transplant, and the child died from complications from the bone marrow transplant. Though I do not know the full details, I suspect because of the family's ethnic background, it was hard to find a really good cord blood match, and baby died of severe graft-versus-host disease.

During my training years, I also met scores of families who were screened positive for Krabbe, but was not determined to have infantile Krabbe, and were told "perhaps your child may

develop Krabbe disease sometime in the future". We subjected these babies to multiple testing, brain MRI, lumbar puncture, repeated anesthesia for various other tests like nerve conduction studies. There is a certain harm to that, not to mention anxiety that the families face every time they come in for a follow-up check.

Fast forward 15 years, we're finally able to find a promising biomarker that can better predict infantile Krabbe disease, and to understand how to make a better decision on who should get a bone marrow transplant, how fast this needs to be done (within a month), and what long-term consequences can still occur (peripheral neuropathy and motor difficulties). I have hope for Krabbe NBS screening now, and I await eagerly for the ACHDNC's review. We've come a long way, but the science was not there 15 years ago, and many families suffered the consequence of that.

I share with you my lessons learned: The science must catch up to our passion, before we can implement newborn screen for a condition. If we do not convince the health provider that has to be on the journey with these families, that there is good science behind the NBS process, the screen will fail its purpose. While we all have passion about catching disease early and to be proactive, this has to be tempered with hard-to-get evidence and strategy. Good scientific discovery takes time, and cannot be rushed, particularly for rare disorders. The RUSP assures we have that down, at least, and this process SHOULD NOT be circumvented. For the families affected, NBS cannot come soon enough, because statistics do not apply to them (they are the 1 in a 100,000 in this cruel lottery), and science has shown its limitations to them in the most disturbing way. As a clinician and scientist, my job is to hear these families' voices, and use that to propel further research. That is the best way we can address their urgency.

As a legislature, it's your job to hear your communities' needs as well, and I applaud this governing body for listening to all of our needs and being aware of the impact of rare diseases in our communities.

Amy C. Yang, MD