Written Testimony of Tara Sander Lee, Ph.D.
Senior Fellow and Director of Life Sciences, Charlotte Lozier Institute

House Judiciary 1 Committee, North Carolina
May 2021

To the Honored Members of the House Judiciary 1 Committee,

Thank you for the opportunity to testify on HB 453, the Human Life Non-Discrimination Act.

I am a scientist with over 20 years' experience in basic science research and clinical medicine. My education and experience involve a PhD in Biochemistry from the Medical College of Wisconsin followed by postdoctoral training at Harvard Medical School and Boston Children's Hospital in molecular and cell biology. I held faculty appointments at the Medical College of Wisconsin and the Children's Research Institute, with a focus on the pathologic mechanisms of childhood disease. My clinical experience includes appointments as Scientific Director of Molecular Diagnostics at Children's Hospital of Wisconsin and Children's Specialty Group with credentialed hospital privileges. I also served as a molecular pathology inspector for the College of American Pathologists and scientific consultant for various entities. I am testifying in my capacity as a scientist, with expertise in molecular genetics and diagnostic testing, and as a senior fellow and director of life sciences at Charlotte Lozier Institute.

The purpose of this bill is to prevent eugenic discrimination and induced termination of a pre-born child based on race, sex, or the presence or presumed presence of a genetic abnormality like Down syndrome. Down syndrome is a trisomy disorder genetically caused by the presence of an extra copy of chromosome 21. This genetic anomaly occurs at conception, when the man's sperm fuses with a woman's egg to form a single-cell embryo—the creation of a new, totally distinct, integrated organism or human being.[1] Most children with Down syndrome survive to birth, often with medical conditions, such as congenital heart defects, eye disease, thyroid disease, and hearing loss. With appropriate medical care, children born with Down syndrome can lead healthy, happy lives with an average life expectancy of 60 years.[2]

---

[1] Ronan O'Rahilly and Fabiola Müller, *Developmental Stages in Human Embryos: Including a Revision of Streeter's "Horizons" and a Survey of the Carnegie Collection* (Washington D.C.: Carnegie Institution of Washington, 637, 1987); and The Endowment for Human Development. Available at: https://www.ehd.org/prenatal-summary.php

[2] National Association for Down Syndrome. Available at: https://www.nads.org/resources/facts-about-down-syndrome/#:~:text=However%2C%20with%20appropriate%20medical%20care,into%20their%20sixties%20and%20seventies.

The frequency of Down syndrome in the population is estimated to be 1 in 700 live births.[3] And the Center for Disease Control estimates that each year, 6,000 babies are born with Down syndrome in the United States.[4]

Down syndrome can be diagnosed in a newborn baby at birth or shortly thereafter. However, early prenatal screening and testing for Down syndrome are targeting babies inside the womb for destruction based on their presumed risk for trisomy 21. Some view the ability to detect trisomy 21 in the first trimester as a "benefit" so that "decisions regarding pregnancy termination may be made at a time when services are more readily available."[5] A survey in Australia found that 97% of women who had already undergone non-invasive prenatal screening had a personal interest in using a cell-free prenatal screening test to identify a Down syndrome trait and 43% of women were likely or definitely likely to terminate a pregnancy if the result came back positive (38% were unsure).[6]

HB 453 is needed to protect babies diagnosed or at risk of trisomy 21 against disability discrimination through abortion. There is well-documented evidence in the U.S. and abroad showing that babies are being aborted at an alarming rate after receiving a "positive" prenatal trisomy 21 result.

In the U.K., a 1999 study found a 92% abortion rate for children diagnosed in the womb with Down syndrome.[7] Maxwell and co-workers reported a 93% abortion rate in Western Australia for babies diagnosed in the womb with Down syndrome.[8] De Graaf and colleagues looked at the Down syndrome population throughout Europe and found that there were 50% fewer babies born with Down syndrome looking back 40 years up to 2015, and that just over the period of 2011-2015, abortions decreased the Down syndrome population in Europe by a rate of 27%.[9,10]

---

[3] Mai CT, Isenburg JL, Canfield MA, Meyer RE, Correa A, Alverson CJ, Lupo PJ, Riehle-Colarusso T, Cho SJ, Aggarwal D, Kirby RS. National population-based estimates for major birth defects, 2010–2014. *Birth Defects Research.* 111(18): 1420-1435, 2019

[4] Centers for Disease Control and Prevention (CDC), Data and Statistics on Down Syndrome. Available at: https://www.cdc.gov/ncbddd/birthdefects/downsyndrome.html.

[5] Rink, B.D. and M.E. Norton, *Screening for fetal aneuploidy.* Semin Perinatol, 2016. 40(1): p. 35-43.

[6] Bowman-Smart H, et al. 'Is it better not to know certain things?': views of women who have undergone non-invasive prenatal testing on its possible future applications. *J Med Ethics* 2019;45:231–23

[7] Mansfield C *et al*. Termination rates after prenatal diagnosis of Down syndrome, spina bifida, anencephaly, and Turner and Klinefelter syndromes: a systematic literature review, *Prenatal Diagnosis* 19, 808, 1999

[8] Maxwell S *et al.,* Impact of prenatal screening and diagnostic testing on trends in Down syndrome births and terminations in Western Australia 1980 to 2013, *Prenatal Diagnosis* 35, 1324–1330, 2015; doi: 10.1002/pd.4698

[9] de Graaf G *et al.*, Estimation of the number of people with Down syndrome in Europe, *European Journal of Human Genetics* published online 31 October 2020, doi: 10.1038/s41431-020-00748-y

[10] de Graaf G *et al.*, Factsheet: People living with Down syndrome in Europe: BIRTHS AND POPULATION, 11 November 2020, accessed at: https://go.downsyndromepopulation.org/europe-factsheet

In the U.S., a 2012 review of the literature on this topic found a range from 61% up to 93% of those diagnosed with Down syndrome in the womb who were aborted.[11] More recent data show that abortion accounts for a 33% reduction in the number of babies with Down syndrome born in 2014. This means that in recent years there were 33% fewer babies with Down syndrome born in the U.S. than could have been.[12]

In 2009, Skotko posed the question of whether the new, non-invasive prenatal testing would mean babies with Down syndrome would slowly disappear.[13] In less than a decade, his question was answered. In 2017, Iceland reported that it was on pace to virtually eliminate Down syndrome through abortion.[14] Denmark was the first country to institute a national screening program, and it has seen Down syndrome births drop dramatically.[15] Denmark is moving closely on the heels of Iceland, getting ever closer to "eliminating" Down syndrome in their population.[16]

Standard prenatal screening for Down syndrome is often performed during the first and second trimester to calculate the risk of having a baby with trisomy 21. Maternal age, serum analyte screening for biochemical markers (such as the triple screen or quad screen), and fetal nuchal translucency (NT) measurement are considered first-line screening.[17] However, these standard screening tests do not accurately predict the risk of Down syndrome. There is a high false-positive rate of incorrect reporting (a negative result is reported as positive) ranging from 1-14% and incredibly low positive predictor values (PPV, the proportion of positive test results that are true positives) of 4.2%.[18]

Traditional screening for trisomy 21 may be combined with other DNA screening and diagnostic testing, usually between 10-18 weeks gestation, to increase the chance of correctly predicting a Down syndrome risk. Diagnostic DNA tests can be performed using fetal samples obtained via amniocentesis and chorionic villus sampling. These tests are accurate, but the means to obtain

---

11 Natoli JL *et al.*, Prenatal diagnosis of Down syndrome: a systematic review of termination rates (1995–2011), *Prenatal Diagnosis* 32, 142–153, 2012; doi: 10.1002/pd.2910

12 de Graaf G *et al.*, Estimates of the live births, natural losses, and elective terminations with Down syndrome in the United States, *American Journal of Medical Genetics* Part A 167A, 756-776, 2015, doi: 10.1002/ajmg.a.37001

13 Skotko BG, With new prenatal testing, will babies with Down syndrome slowly disappear? *Arch Dis Child* 94, 823-826, 2009; doi: 10.1136/adc.2009.166017

14 Julian Quinones and Arijeta Lajka, "What kind of society do you want to live in?": Inside the country where Down syndrome is disappearing, CBS News August 14, 2017, accessed at: https://www.cbsnews.com/news/down-syndrome-iceland/

15 Lou S *et al.*, National screening guidelines and developments in prenatal diagnoses and live births of Down syndrome in 1973-2016 in Denmark, *Acta Obstet Gynecol Scand* 97, 195-203, 2018; doi: 10.1111/aogs.13273

16 Sarah Zhang "The Last Children of Down Syndrome. Prenatal testing is changing who gets born and who doesn't. This is just the beginning." *The Atlantic* December 2020; accessed at: https://www.theatlantic.com/magazine/archive/2020/12/the-last-children-of-down-syndrome/616928/

17 Rink, B.D. and M.E. Norton, *Screening for fetal aneuploidy. Semin Perinatol*, 2016. 40(1): p. 35-43.

18 Bianchi, D.W. et al., DNA sequencing versus standard prenatal aneuploidy screening. *N Engl J Med* 370:9, 2014.

fetal samples for DNA testing from the amniotic sac and placenta are invasive and carry their own risks for pregnancy loss.[19]

A new, advanced method of non-invasive prenatal screening (NIPS; also known as NIPT) is on the market, reducing the need for invasive techniques. NIPS uses cell-free fetal DNA (also known as cffDNA) found in the maternal circulation to screen for chromosomal aneuploidy such as trisomy 21. Scientists can detect cell-free fetal DNA from a mother's blood sample as early as 4 weeks and 5 days after fertilization.[20] Cell-free fetal DNA is consistently detected from seven weeks[21], remains level between 10 and 21 weeks,[22] steadily increases after 24 weeks, peaks at birth, and then declines postpartum.[23] NIPS is the predominant method used in both low- and high-risk patients and is endorsed by all major medical organizations to be used as the "primary test in all women".[24]

Once the cell-free DNA sample is collected, NIPS uses advanced molecular techniques to determine a child's genetic susceptibility to Down syndrome.[25] Various platforms analyze cell-free fetal DNA fragments across the whole (or part) of the genome using next generation sequencing (NGS), targeted sequence analysis, and array-based techniques. NGS platforms that screen fragments from the entire genome can be reliable, specific, and sensitive with a reported failure rate of 0.1% (inconclusive result) and false-positive rate of <0.1%.[26]

NIPS may be less invasive compared to amniocentesis and CVS, but it is far less accurate and is not diagnostic, because the cell-free fetal DNA that is collected is fragmented. Therefore, NIPS can only report whether the patient's results *are consistent with* an increased risk for trisomy 21 that causes Down syndrome. Even with the most comprehensive molecular platform (i.e., NGS, array technology), NIPS will never be a diagnostic test that can definitively report a person's known risk of having Down syndrome.

With any clinical laboratory test, especially NIPS, there are inherent limitations. No test or screen will always perform the way it should 100% of the time. From my own experience

---

19 Rink, B.D. and M.E. Norton, *Screening for fetal aneuploidy. Semin Perinatol* 40(1): p. 35-43, 2016

20 G. S. Dawe *et al*., Cell migration from baby to mother. *Cell Adhesion & Migration* 1:19-27, 2007.

21 *ibid*

22 Wapner, R.J and Dugoff, L. *Prenatal diagnosis of congenital disorders*, in Creasy and Resnik's *Maternal-Fetal Medicine: Principles and Practice 8th Edition*, R., Resnik, Lockwood, C.J., Moore, T.R., Greene, M.F., Copel, J.A., and Silver, R.M., Editor. 2019, Elsevier: Philadelphia, PA. p. 506.

23 H. Ariga *et al*., Kinetics of fetal cellular and cell-free DNA in the maternal circulation during and after pregnancy: implications for noninvasive prenatal diagnosis. *Transfusion* 41:1524-30, 2001

24 Wapner, R.J and Dugoff, L. *Prenatal diagnosis of congenital disorders*, in Creasy and Resnik's *Maternal-Fetal Medicine: Principles and Practice 8th Edition*, R., Resnik, Lockwood, C.J., Moore, T.R., Greene, M.F., Copel, J.A., and Silver, R.M., Editor. 2019, Elsevier: Philadelphia, PA. p. 510.

25 ACOG Committee on Genetics, Committee Opinion No. 640: Cell-Free DNA Screening For Fetal Aneuploidy. *Obstet Gynecol.* 126(3): p. e31-7, 2015

26 Illumina Verifi Prenatal Test: https://www.illumina.com/clinical/reproductive-genetic-health/nipt/sendout-testing-for-labs.html

directing a genetic testing lab for almost 10 years—the DNA test is never 100% accurate every time. Underlying conditions can limit NIPS performance and interfere with test results including placental mosaicism, maternal chromosomal abnormality, vanishing twin, organ transplant, etc. Incorrect reporting due to erroneous results, technical problems, and lab errors (i.e., false positives, false negatives, mixed specimens, mislabeling, etc.) is also a possibility.

Past pregnancies may also interfere with the NIPS result. Some studies have shown that cell-free fetal DNA is rapidly cleared from the maternal blood, with 100% clearance within 1-2 days postpartum[27,28], suggesting that fetal DNA from past pregnancies should not interfere with current tests. However, other studies have found the persistence of fetal DNA for decades in the mother.[29,30]

NIPS limitations will affect correct result reporting and interpretation. One widely utilized NIPT screening test on the market has a positive predictive value (PPV) of 81%, meaning that there is a significant chance that a positive test result is NOT a true positive.[31] But even this reported PPV value is deceiving, because PPV is based on test sensitivity, specificity, *and* the prevalence of the condition in the population being tested. Because the prevalence of Down syndrome increases with maternal age, PPVs will be higher in patients of advanced maternal age (>35 years old) and will likely increase when other aneuploidy risk factors are known (*e.g.*, ultrasound abnormalities).[32]

A comprehensive study across 21 different centers in the United States, which included 1,914 women (mean age, 29.6 years), observed much lower positive predictor values of 45.5% for trisomy 21. This indicates that a significant proportion (over 50%) of "positive" test results for Down syndrome may not be truly positive when screening women mostly at low risk.[33] For this reason, the authors from this study highlight the "need for follow-up diagnostic testing to confirm true positive results before decisions are made about irrevocable clinical intervention."[34] They know that a woman might tragically abort her child based on an erroneous and incorrect NIPS lab result.

There are significant medical advancements that use prenatal screens and tests to heal and not harm the developing baby. The perinatal revolution has made it possible to perform

---

[27] A. Kolialexi *et al*., Rapid Clearance of Fetal Cells from Maternal Circulation After Delivery. *Ann N Y Acad Sci* 1022, 113-8, 2004

[28] Y. M. D. Lo *et al*., Rapid Clearance of Fetal DNA from Maternal Plasma. *Am. J. Hum. Genet*. 64:218–224, 1999

[29] D. W. Bianchi *et al*., Male progenitor cells persist in maternal blood for as long as 27 years postpartum. *Proc Natl Acad Sci USA.* 93:705-708, 1996

[30] Invernizzi P. *et al.*, Presence of fetal DNA in maternal plasma decades after pregnancy. *Human Genetics*, 110(6): 587-591, 2002.

[31] Norton ME *et al.*, Cell-free DNA Analysis for Noninvasive Examination of Trisomy, *New England Journal of Medicine* 372, 1589, 2015; doi: 10.1056/NEJMoa1407349

[32] National Society of Genetic Counselors, NIPT/Cell free DNA screening predictive value calculator. Available at: https://www.perinatalquality.org/Vendors/NSGC/NIPT/;

[33] Bianchi, D.W. et al., DNA sequencing versus standard prenatal aneuploidy screening. *N Engl J Med* 370:9, 2014.

[34] *ibid*

interventions on the preborn before birth while still in the womb, through neonatal and fetal surgeries, potential pharmaceutical treatments as well as cell-based and genetic therapies.[35] There is even evidence that babies with Down syndrome may one day benefit in the future from research of a prenatal treatment with neuroprotective peptides or fluoxetine that can prevent learning deficits, correct intellectual disability, and even improve cognitive performance in a Down syndrome mouse model.[36]

We need to consider these young individuals as equally valued human lives. Eliminating young lives is not the answer to eliminating disease and disability once a risk of the disorder is identified.[37] Destroying the patient is not curative medicine. Such acts become a modern-day form of eugenics.

HB 453 would provide necessary, distinct protections for developing human beings at risk for Down syndrome, preventing discrimination based on genetics or disability. Thank you for the opportunity to contribute to the discussion on this important issue.

---

[35] Malloy C *et al.*, The Perinatal Revolution, Issues in Law and Medicine 34, 15-41, 2019

[36] Guidi, S., et al., *Prenatal pharmacotherapy rescues brain development in a Down's syndrome mouse model.* Brain, 2014. **137**(Pt 2): p. 380-401; and Incerti, M., et al., *Prenatal treatment prevents learning deficit in Down syndrome model.* PLoS One, 2012. **7**(11): p. e50724.

[37] Chuck Donovan, Eliminating Down Syndrome Children Is Not Something to Be Proud Of, The Daily Signal Aug. 16, 2017, accessed at: https://www.dailysignal.com//print?post_id=351821