December 2, 2021

Dr. Stephen Lucas, Deputy Minister of Health Canada
Deputy Minister's Office, Health Canada
Brooke Claxton Building, Tunney's Pasture
Ottawa, Ontario K1A 0K9

Dear Dr. Lucas;

On behalf of our nine national child and youth health organizations, we are writing today to communicate our urgent and shared concerns related to the pediatric drug file at Health Canada. As we mark the first anniversary of the public release of the Pediatric Drug Action Plan (PDAP), we are alarmed by the lack of tangible progress made since its release, as well as the apparent absence of any modifications or updates to the initial PDAP after our organizations provided substantial feedback on the first iteration. We respectfully submit the following recommendations for action, and look forward to your timely attention to our serious concerns.

Recommendation 1: Establish and publicly commit to specific and transparent deliverables for the PDAP with appropriate resources, clear targets and associated timelines. Continue to engage with pediatric experts to refine priorities and to forward critical initiatives of the PDAP.

The release of the PDAP in November 2020 was considered a significant step forward by the pediatric community. Re-opening an office dedicated to pediatric issues and developing an action plan to address the longstanding regulatory issues specific to pediatric drugs demonstrated a sincere commitment to infant, child and youth health. We welcomed, and continue to enthusiastically support the public acknowledgement that (1) the current receipt of pediatric data for regulatory review is inadequate and should be addressed, (2) unnecessary, time-intensive and costly barriers exist for pediatric clinical trials and should be eliminated, (3) economic challenges complicate the development, marketing and maintenance of a stable and comprehensive pediatric drug supply and

system-level solutions are required, and (4) off-label medication use, and the lack of access to suitable formulations for this population, is a widespread issue that demands policy attention.

Unfortunately, since the public release of the PDAP, there has been no visible progress on the plan. Issues requiring action have been identified, but specific deliverables have not been articulated. Ambitions are clear, but there are no accountabilities in the form of an established timeline. For the Office of Pediatrics and Patient Involvement (OPPI) to achieve its critically important mandate, leadership at the highest levels of Health Canada must appreciate the importance of this work, staffing and other resources must be secured, clear targets and firm timelines must be developed, and all of these efforts must be publicly communicated to the broader child and youth health community.

As leaders in the pediatric community, we are eager to work with Health Canada to advise, amend, and refine the current PDAP priorities. We are willing to consult, collaborate and contribute to all OPPI initiatives. Pediatric clinical, research and regulatory expertise will be essential to ensure focus and to optimize impact.

Recommendation 2: Implement immediate regulatory change to mandate the submission of pediatric data in all drug submissions when pediatric use of a medication can be expected.

We were heartened to read in Gazette Part 1 (July 31, 2021) "that Health Canada intends to amend the Food and Drug Regulations in the spring of 2022", and that "the amendments would give the Minister of Health the ability to impose terms and conditions on drug and medical device authorizations". Specifically, we were encouraged that the first phase of the regulatory proposal will "deliver positive results for Canadians, including improved access to innovative drugs, including drugs for rare diseases and pediatric populations". Moreover, during the recent presentation at the DIA Canadian Conference, Health Canada indicated that it is "implementing a pediatric regulation (with an associated guidance document) that will bring Health Canada in alignment with the Food and Drug Administration (FDA) and European Medicines Agency (EMA) and will require sponsors to develop a pediatric plan and submit the data created by conducting the studies in the plan". This is an important step in the right direction. However, a specific timeline for this regulation has not been communicated. Furthermore, at this same conference, it was announced that the OPPI is also developing a "Sex and Gender-Based Analysis Plus (SGBA Plus) Action Plan". Given the current resources of the OPPI, we are deeply concerned that attempting to advance two Action Plans simultaneously could compromise positive outcomes for both, in the short and the medium-term.

There is unanimous agreement that implementing a pediatric regulation in Canada is an urgent priority. With respect to ensuring access to safe and effective pediatric medications, Canada's regulatory framework remains two decades out-of-step with international best practices. We urge Health Canada to prioritize this critical component of the Action Plan, to provide all of the necessary resources to operationalize this change

and to commit to a specific deadline to execute this vital, and long overdue, aspect of regulatory reform.

Importantly, the pediatric community is sensitive to the commercial challenges of our small market size, as well as the regulatory burden associated with a requirement to review pediatric data with new drug submissions. To that end, we encourage Health Canada to accept the submission of pediatric data in the same form as required by leading international jurisdictions (such as the Pediatric Study Plan (PSP) required by the FDA or the Paediatric Investigational Plan (PIP) as required by the EMA). The leaders of the pediatric community in Canada are willing and eager to work with Health Canada to ensure that the requirements related to the mandatory submission of pediatric data are crafted to optimize positive benefits and minimize any potential harms.

Recommendation 3: Accelerate and expand the use of Trusted Foreign Decisions.

As part of a comprehensive pediatric drug strategy, we urge Health Canada to expand and implement the use of Trusted Foreign Decisions. The recent experience of the COVID-19 Interim Orders (IOs) demonstrates that Trusted Foreign Decision pathways can be both accelerated and streamlined. The requirement in the Trusted Foreign Decisions draft guideline for 15 years of post-market experience in the trusted jurisdiction reflects almost the entire "lifespan" of a pediatric patient, eliminating the opportunity for individual children and youth to access life-sustaining medications throughout this critical developmental window. Moreover, this requirement does not align with what is known regarding the detection of serious safety events, and neglects Canada's responsibility to the global community in terms of participating in appropriate pediatric post-market surveillance. The pediatric community would be keen to explore alternative, pediatric-specific market experience requirements, and would be eager to examine the possibility of flexible Trusted Foreign Decision rules based on risk and disease prevalence. In this regard, in May 2018, Health Canada presented some preliminary thoughts regarding the use of Trusted Foreign Reviews and Decisions. However, since that time, no further details have been released. Again, this lack of progress is concerning.

In addition, we urge Health Canada to generate flexible, agile and innovative pathways to ensure rapid access to life-saving pediatric medications for critical pediatric illnesses and rare diseases. Developing these novel pathways in collaboration with pediatric clinical experts, researchers, patients and their families will ensure an approach that addresses current barriers to timely care and meets the needs of those facing critical illness with viable treatment options available elsewhere.

Summary

The lack of action on pediatric drugs at Health Canada limits the ability of our patients to access new and novel therapies, some that have already been identified as the standard of care elsewhere. Current policies serve to prevent, delay or restrict access to new, safe and effective therapies for Canadian infants, children and youth. The longer we delay, the more children are impacted. The time for action is now.

We respectfully request a formal meeting with you to share our concerns and ideas in greater detail. As a community, we are united in our commitment to executing a progressive pediatric regulatory reform agenda that positively impacts the lives of our patients and their families. We remain confident that we can work together and improve the lives of children and youth and their families.

We very much look forward to your timely response and our future conversation.

Sincerely,

Charlotte Moore Hepburn, MD
Director of Medical Affairs
Canadian Paediatric Society

Geert ‘t Jong, MD, PhD
Chair, Drugs and Hazardous Substances Committee
Canadian Paediatric Society

Andrea Gilpin, PhD, MBA
General Manager
GPFC of the CHU Sainte Justine

Catherine Litalien, MD, FRCPC
Medical and Scientific Director
GPFC of the CHU Sainte-Justine

Thierry Lacaze, MD, PhD
Scientific Director, MICYRN
KidsCAN Trials Lead

Andrew Lynk, MD
President
Pediatric Chairs of Canada

Emily Gruenwoldt
President and CEO
Children’s Healthcare Canada

Michael Rieder MD PhD FRCPC FCAHS FAAP FRCP (Edinburgh)
CIHR-GSK Chair in Paediatric Clinical Pharmacology
University of Western Ontario
Past President
Canadian Society of Pharmacology & Therapeutics

Kathy Brodeur-Robb
Executive Director
C-17 Council

Lauren Kelly PhD, MSc, CCRP
Scientific Director
Canadian Childhood Cannabinoid Clinical Trials Network

CC: **David Lee**, Chief Regulatory Officer, Health Canada
Supriya Sharma, Chief Medical Advisor, Health Canada
Pierre Sabourin, Assistant Deputy Minister, Health Products and Food Branch, Health Canada
John Patrick Stewart, Director General, Therapeutic Products Directorate
Celia Lourenco, Director General, Biologics and Genetic Therapies Directorate
Alysha Crocker, Office of Pediatrics and Patient Engagement

About MICYRN and KidsCAN Trials

MICYRN is a federal not-for-profit, charitable organization founded in 2006 to build capacity for high-quality applied health research. It now links 20 maternal and child health research organizations based at academic health centres in Canada; is affiliated with more than 20 practice-based research networks; provides support to new and emerging teams; and has established strong national and international partnerships.

About the Goodman Pediatric Formulations Centre of the CHU Sainte-Justine

The GPFC has the mandate to improve access to child-friendly medicines in Canada. We are the only Centre in Canada whose objective is to facilitate the development of, safe and effective age-appropriate formulations for children. The GPFC operates as a not-for-profit organization, whose exclusive goal is to support the well-being of children by facilitating the availability of formulations adapted to their needs. Even though the GPFC works closely with hospitals, health care providers and industry, our positions and actions are completely independent of these third parties.

About Children's Healthcare Canada

For Canadian leaders in children's healthcare, we are the only national association that enables local improvements and contributes to system-wide change by building communities across the full continuum of care. Our members deliver health services to children and youth, and include regional health authorities, children's tertiary/quaternary and rehabilitation hospitals, community hospitals, children's treatment centres and home/respite care providers.

About the Pediatric Chairs of Canada

We are the national network of academic leaders in paediatric medicine strengthening the future of paediatrics and improving the health outcomes of all children, by working together to advance evidence-based care, education and research.

About the Canadian Paediatric Society

The Canadian Paediatric Society is the national association of paediatricians, committed to working together to advance the health of children and youth by nurturing excellence in health care, advocacy, education, research and support of its members. Founded in 1922, the CPS represents more than 3,600 paediatricians, paediatric subspecialists, paediatric residents and others who work with and care for children and youth.

About the CIHR-GSK Chair in Paediatric Clinical Pharmacology

The CIHR-GSK Chair in Paediatric Clinical Pharmacology is the only endowed Chair in Paediatric Clinical Pharmacology in Canada and is dedicated to the goal of conducting clinically impactful research with the goal of ensuring effective and safe drug therapy for children in Canada and beyond.

About the Canadian Society of Pharmacology and Therapeutics

The Canadian Society of Pharmacology and Therapeutics (CSPT) is a national not-for-profit charitable organization that aims to foster the application of educational and research excellence to drug discovery and therapeutic choice. CSPT is recognized for its involvement with the Royal College of Physicians and Surgeons of Canada fellowship training program in Clinical Pharmacology and Toxicology, as well its support of graduate/postdoctoral trainees and academic researchers across the country.

About the C17 Council-Children' Cancer & Blood Disorders

The C17 Council is an organization composed of the institutionally appointed heads of the sixteen pediatric hematology, oncology, and stem cell transplant programs across Canada. We represent the interests of children and adolescents with cancer and blood disorders and act as an authoritative Canadian voice.

About the Canadian Childhood Cannabinoid Clinical Trials

C4T is an academic-led team of parents, doctors, pharmacists, nurses and scientists who are studying medical cannabis used by children. Our goal is to move cannabinoid use from the era of anecdote to evidence to treat health concerns in children.