March 3, 2022

Dr. Stephen Lucas, Deputy Minister of Health Canada
Deputy Minister's Office, Health Canada
Brooke Claxton Building, Tunney's Pasture
Postal Locator: 0906C
Ottawa, Ontario K1A 0K9

Dear Dr. Lucas,

This letter responds to the update on the Pediatric Drug Action Plan (PDAP) presented at the DIA Canadian annual meeting on October 20, 2021 by Dr. Alysha Croker, Director, Office of Pediatrics and Patient Involvement (OPPI), now the Center for Policy, Pediatrics and International Collaboration. In particular, this letter provides commentary on the National Priority List (NPL) proposed during this conference. As outlined in this presentation, the purpose of this NPL is to develop, alongside with major pediatric stakeholders, a list to ensure that appropriate medications and formulations are prioritized in PDAP. The objective cited is two-fold: first, to identify approximately 10 products with a new list to be developed every 2-5 years, and second, for Health Canada to identify the appropriate review pathway to support the commercialization of those listed products.

Children are not miniature adults and failure to appreciate this has resulted in tragedy. the relative lack of availability of pediatric dosage forms can lead to treatment failure or adverse events in children. The Council of Canadian Academies published a report in 2014 entitled, “Improving Medicines for Children in Canada,” which outlines the challenges in treating pediatric patients in detail[1]. Approved adult formulations often need to be modified in some manner to administer the appropriate dose to children, and as such, are used off-label. Compounding is the process by which an adult form is manipulated by a health care provider, or others, to adapt the adult form to be used in children; this can increase risk of errors. Even though the practice of compounding is regulated by provincial pharmacy regulatory authorities and is essential to give young children access to medication they require, it should not be considered an equivalent surrogate for a pediatric formulation approved by Heath Canada.

The ideal is to have commercial pediatric formulations available for Canadian children. In many cases, commercialized pediatric formulations exist in other jurisdictions, such as in the United States and in Europe[2]. However, oftentimes, these commercial pediatric

[1] Improving Medicines for Children in Canada, 2014, Council of Canadian Academies.
[2] Litalien C, Autmizguine J, Carli A, Giroux D, Lebel D, Leclerc JM, Théorêt Y, Gilpin A, Bérubé S. Providing Suitable Pediatric Formulations for Canadian Children: A Call for Action. Can J Hosp Pharm. 2020;73(4):247-256.

formulations are not marketed in Canada, leaving an already vulnerable and unaddressed population without access to the commercially available pediatric formulations.

In an effort to bridge this gap, the Goodman Pediatric Formulations Centre (GPFC), working with the pediatric community, has developed a priority list of 17 medications, listed on page 7, that we feel **must be** made commercially available in child-friendly formulations for Canadian children. All 17 medications are available either in the United States or in Europe in a commercial form suitable for children, and we believe that continuing to use the compounded form in Canada represents unnecessary – and unjustifiable - risks to Canadian children. We feel, that given that the medications on this list are currently available in other jurisdictions, this first list is a great place to begin the NPL initiative outlined by the OPPI.

We recommend Health Canada to evaluate the pediatric needs separately from those of adults and we encourage using the priority list developed by the GPFC, endorsed by the pediatric community, **as a starting point**.

Health Canada is also exploring incentives to encourage development of pediatric medicines in the areas of infants/neonates, pediatric formulations, and for pediatric-only diseases. A comprehensive policy paper on this important issue[3] was published in 2019. In December2021, we submitted a letter, which fully supports the recommendations in the aforementioned policy paper and outlines the key issues faced in pediatrics. We would like to take this opportunity to reiterate that the following recommendations would have the greatest impact:

- The urgency to **identify dedicated resources, a budget and a time frame to accomplish the objectives outlined in the PDAP**. We cannot accept another year to plan the Pediatric Drug Action Plan: we must move to action. On average, the drugs on the priority list have been on the Canadian market for adults for a median of 40 years.

- The federal government should establish a permanent, dedicated, appropriately funded **Expert Paediatric Advisory Board** ('EPAB') to review, guide, and co-ordinate activities related to paediatric medication approvals, associated clinical research, and reimbursement activities.

- Introduction of a **Pediatric Rule** for new medications –namely, a requirement that manufacturers must submit for a pediatric indication and develop a pediatric formulation when use in pediatrics is anticipated. A similar system exists in the US and Europe and has shown proven success.

[3] https://cps.ca/documents/position/improving-paediatric-medications

- Allowing Canadian pediatric submissions to rely on **Trusted Foreign Decisions** from other jurisdictions without requesting additional information or data. This mechanism should be available to manufacturers as soon as the medications are approved in those trusted jurisdictions. Moreover, alignment with the provinces to ensure provincial listing is crucial. In particular, this could be used for many of the medications on the GPFC priority list and for any medication that has been on the market for some time but not approved for a pediatric indication.

- **Pediatric specific-fees** for submitting a pediatric indication or formulation to Health Canada which would be considerably less that the cost of a regular submission. This would greatly help the backlog of medications that are old and for which there is neither a pediatric indication on the Canadian monograph nor a commercialized pediatric formulation in Canada.

Canadian children deserve optimal care. Moving forward with this proposed list is a first, much needed, step which may complement the Health Canada's NPL plan.

Thank you for your attention in this matter. The pediatric community supports Health Canada's efforts and it would be our pleasure to assist in any way possible to accelerate implementation of the Pediatric Drug Action Plan.

Sincerely,

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

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

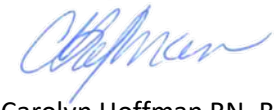
Thierry Lacaze, MD, PhD
Scientific Director, MICYRN
KidsCAN Trials Lead

Michael Rieder MD PhD FRCPC FCAHS FAAP
FRCP(Edinburgh), CIHR-GSK Chair, Paediatric Clinica
Pharmacology, UWO and Past PresidentCanadian
Society of Pharmacology & Therapeutics

Emily Gruenwoldt
President and CEO
Children's Healthcare Canada

Lauren E Kelly PhD, MSc, CCRP
Clinical Trials Director and Scientist, Children's Hospital Research Institute of Manitoba
Scientific Director, Canadian Childhood Cannabinoid Clinical Trials (

Kathy Brodeur-Robb
Executive Director
C-17 Council



Carolyn Hoffman RN, BSN, MN,
CEO
ISMP Canada

Andrew Lynk MD MSc FRCPC D.Litts (Hon)
Chief of Pediatrics, IWK Health Centre Halifax Nova Scotia
Chair of Pediatrics, Dalhousie University Department of Pediatrics, Faculty of Medicine
President, Pediatric Chairs of Canada
Consultant Pediatrician, Cape Breton Regional Hospital Sydney Nova Scotia

Cc: David Lee, Chief Regulatory Officer, Health Canada
Supriya Sharma, Chief Medical Advisor, Health Canada
Nancy Hamzawi, Assistant Deputy Minister, Health Products and Food Branch, Health Canada
John Patrick Stewart, Director General, Therapeutic Products Directorate, Health Canada
Celia Lourenco, Director General, Biologics and Genetic Therapies Directorate, Health Canada
Elizabeth Toller, Director, Health Care Innovation Secretariat, Strategic Policy Branch, Health Canada
Alysha Croker, Director, Centre for Policy, Pediatrics and International Collaboration, Health Canada

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 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 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's 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.

About the Institute for Safe Medication Practices Canada

The Institute for Safe Medication Practices Canada (ISMP Canada) is an independent national not-for-profit organization committed to the advancement of medication safety in all healthcare settings. ISMP Canada works collaboratively with purposeful partners to promote safe medication practices.

GPFC Priority List regarding most needed commercial child-friendly formulations for use in Canadian children

Dated: March 2022

Medication[1]	Examples of Uses in Pediatrics
6-Mercaptopurine[2,3]	Ulcerative colitis, Crohn's disease, acute lymphoid leukemia,
Baclofen	Spasticity
Clobazam[3]	Epilepsy, febrile convulsions prevention
Dexamethasone	Acute asthma, Croup, EBV related-pharyngitis/tonsillitis, rheumatologic/immune disorders, endocrine disorders, hematopoietic/neoplastic disorders, anti-emetic (oncology)
Domperidone	Gastroparesis, esophageal motility disorders, anti-emetic (oncology), gastroesophageal reflux disease (GERD)
Gabapentin	Epilepsy, neuropathic pain
Hydrocortisone	Adrenal insufficiency, congenital adrenal hyperplasia, physiologic replacement
Hydroxyurea[2]	Sickle cell anemia
Esomeprazole[3]	Erosive esophagitis associated with GERD, Helicobacter pylori eradication
Levothyroxine[5]	Hypothyroidism
Metronidazole[4]	Anaerobic infections, amebiasis, Clostridium difficile diarrhea/colitis, giardiasis, inflammatory bowel disease, trichomoniasis, balantidiasis,
Phytonadione[6]	Hypoprothrombinemia, hemorrhagic disease of newborn (prevention), Vitamin K deficiency
Rifampicin[4]	H.influenzae/meningococcal meningitis (prevention), tuberculosis (prevention and treatment), mycobacterium avium complex infection, endocarditis
Sildenafil	Pulmonary hypertension
Sotalol[5]	Arrythmia
Tacrolimus[2,5]	Prevention of renal/hepatic/cardiac/hematopoietic stem cell graft rejection, nephrotic syndrome, graft-vs-host disease prevention
Topiramate[2]	Epilepsy, migraines (prevention)

1 Medications were selected as a priority if they had commercial forms available in either the US or Europe

2 Cytotoxic product manipulated by the parents OR for which the extemporaneous preparation requires the use of a fume hood (Class 3)

3 These products have the option to undergo "tablet-splitting" or the available strength doesn't allow for a flexible dosage.

4 The compounded preparation has a bad taste which affects the adherence to treatment, especially taking into account that this product often has to be administered several times a day

5 Narrow therapeutic index: A preparation error or a modification in the recipe (i.e. a change in excipients or in the active ingredient) can potentially lead to serious consequences on the efficiency and/or safety of the product

6 No oral formulation available in Canada