ANNUAL REPORT

2018 TO 2020

centre de formulations pédiatriques
de la famille Rosalind et Morris Goodman
du CHU Sainte-Justine

The Rosalind & Morris Goodman Family
pediatric formulations centre
of the CHU Sainte-Justine

MESSAGE TO OUR READERS

Since our last Annual Report in 2018, we've revisited our business model, secured financing and continued to work with key stakeholders to improve access to pediatric formulations.

A number of medications on our priority list have been approved and, in some cases, reimbursed by provincial plans. We are now working on a pilot project with a core group of stakeholders, including Health Canada, Reimbursement Agencies and industry to gain marketing authorization and reimbursement for one of the medicines in our priority list. Building on one of the Policy Papers that we published in 2019, we continue to advocate with other stakeholders for a Canadian "Pediatric Framework". With this goal in mind, we are in the process of preparing a summary of pediatric regulations that exist globally and we will be submitting this document not only for publication but also to Health Canada with hopes that they would consider incorporating the "Pediatric Rule" into its Regulatory Reform that is currently underway.

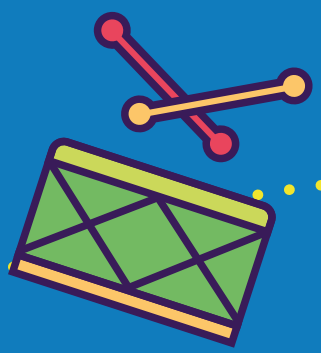
We continued to be engaged with our key stakeholders to increase awareness regarding pediatric formulations in Canada. In December 2019, we participated in the Maternal Infant Child and Youth Research Network's (MICYRN) Annual Conference, we led the Health Summit for the Children Healthcare Canada's Conference and in early February 2020, we organized and led a workshop to discuss a pilot project with key stakeholders. Also in February 2020, we participated in the Université de Montréal Faculty of Pharmacy Centenary celebrations by presenting and participating on a panel at one of their plenary sessions entitled "Medicines and Pediatrics – Unmet Needs". We were pleased to participate in this landmark event for the Faculty.

In the fourth quarter of 2019, we successfully diversified and secured funding for the next few years. We are grateful to both the Morris and Rosalind Goodman Family Foundation as well as to the Sainte-Justine Hospital Foundation for their support and dedication to this important cause.

In conclusion, our efforts, in concert ith key stakeholders, have contributed to providing access to drug formulations adapted to young Canadian patients. We invite you to visit our website, share this Annual Report with colleagues and friends, and follow us on social media in order to keep abreast of our latest news.

We wish you, your colleagues and family members to stay safe and healthy during the pandemic.

The Goodman Pediatric Formulations Team



Overview of the GPFC's Accomplishments and Learnings

Accomplishments

The GPFC worked with an industry partner to support efforts to make available two pediatric medicines to Canadian children in a child-friendly formulation: Amlodipine (a drug to treat hypertension) and Levetiracetam (a drug to treat seizures).

The CHU Sainte-Justine Foundation confirmed a donation in support of the GPFC in addition to the Morris and Rosalind Goodman Family Foundation also providing a second donation to the GPFC.

The GPFC has developed a patient-centric Adaptive Inverted Model along with key stakeholders during an in-person workshop held at the CHU Sainte-Justine in February 2020. The cross-functional Canadian attendees at this workshop decided to test this model with one specific medication that is much needed in pediatrics. This collaboration with all major decision makers in the drug approval and access process along with industry is a first of its kind in pediatrics.

In 2019, the GPFC, recognized for its innovation, research and objectives, became fully integrated into the CHU Sainte-Justine Research Centre.

In 2019, the GPFC led a round table discussion at the Children's Healthcare Canada Annual Conference with the major stakeholders involved in developing, approving, reimbursing and marketing drugs in Canada.

In 2019, through the efforts of the GPFC, new Health Canada regulations will allow priority review to new pediatric drug formulations.

The GPFC continued its advocacy efforts and is supporting Health Canada's Regulatory Reform to introduce more pediatric specific criteria.

What we've learned since inception

The GPFC has confirmed, with real cases, the complexity in the approval of and access to pediatric formulations in Canada, including the lack of harmonization between the different processes.

The Fee for service collaborative model initially offered by the GPFC has provided cases and highlighted the multiple challenges to access pediatric formulations in Canada; however, it was difficult to provide these services with our limited resources. Our partners' satisfaction was generally high with the services provided.

Next Steps

- **Lead the pilot project** using the Adaptive Inverted Model to better understand the challenges, with the goals of developing an innovative and sustainable model for all stakeholders (a win-win) that will translate into accelerated approval of pediatric drug formulations for both old and new drugs.
- **Maintain and expand the internal and external base of engaged stakeholders** as well as reaching out to children and their parents.
- **Continue to lead advocacy efforts** with both federal and provincial governments as well as with key stakeholders.
- **Develop a research program with the Research Centre** of the Sainte-Justine University Hospital aimed at developing innovative pediatric formulations for old off-patent drugs, in partnership with industry.
- **Continue to collaborate with industry** to commercialize pediatric formulations on the GPFC's priority list.

The Goodman Pediatric Formulations Centre

Who We Are

The Goodman Pediatric Formulations Centre (GPFC) of the CHU Sainte-Justine is committed to improving access to child-friendly medicines to ensure efficacy, safety and compliance of medicines for children. To achieve these important and ambitious goals, we have joined together to mobilize a collaboration of researchers, pediatricians and pharmacists with the requisite depth of expertise and breadth of influence. Created in 2016, the GPFC is a group within the CHU Sainte-Justine institution working in a non-for-profit manner towards the accomplishment of its mission.

Our mission

To be the voice of Canadian children of all ages in order to improve access to medicines that meet their needs by creating an environment conducive to the development and marketing of pediatric formulations. In order to build a sustainable Centre, the GPFC works around the following objectives:

Advocacy for the cause along with other pediatric stakeholders at both the provincial and federal governments

Increasing awareness amongst Healthcare Providers and Children's Associations and developing collaborations where possible

Collaborating with industry to support increased access to pediatric formulations in Canada

Increasing the body of knowledge regarding pediatric formulations and compounding

Why do we need a Pediatric Formulations Centre in Canada?

Many medicines used in children are not available in pharmaceutical forms adapted to their needs. Indeed, most oral medications are made for adults as tablets and capsules, which lack dosing flexibility to meet dosage requirements of the spectrum of ages and sizes, ranging from neonates to adolescents. Furthermore, most children under the age of 8 are unable to swallow pills designed for adults. Approved adult forms often need to be modified in some manner to administer the desired dose to children, a process called compounding, and as such are used off-label. When this happens, the adult form is manipulated by either a health care provider, such as pharmacist, or at home by the parents or caregivers (e.g., grinding a tablet and sprinkling it into fluid or food, such as apple sauce). Compounding is commonplace for those medicines that lack adapted pediatric formulations. Click here to watch a short video. Given that compounded medicines are not approved by Health Canada's rigorous process, we do not always know the medication's characteristics. Therefore, it is sometimes difficult to know the exact quantity of the medicine that is absorbed. Furthermore, food vehicle (e.g., apple sauce, juice or yogurt) used to administer these compounded medicines, or to mask the bad taste of some formulations, can alter drug absorption. We strive to contribute to making available convenient and high-quality pediatric products adapted to children's needs. It's important as the formulation can spell the difference between a successful treatment, a therapeutic failure and/or the emergence of adverse drug reactions.

GOALS OF THE CENTRE

1 To facilitate the development and market authorization of safe and effective pediatric drug formulations by:

- Promoting a research-based approach to pediatric formulation development;
- Contributing to a clinical and regulatory environment that fosters pediatric formulation development;
- Contributing to uncovering incentives that could stimulate and attract the development of pediatric formulations;
- Identifying hurdles and challenges in the drug development process as well as in the regulatory landscape and act as a change agent;
- Promoting cost effective treatment for children.

2 To promote safety of medicines administered to children.

- Standardization of key compounding recipes in Québec with the objective of making this initiative Canadian by working with other groups across Canada.

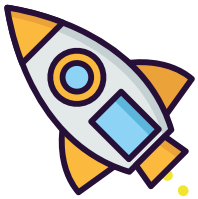
These goals are aligned with a report of the Council of Canadian Academies, "Improving Medicines for Children in Canada". In addition, our mandate supports equal access to pediatric medicines across the country which is aligned with a report of the Pan-Canadian Health Organizations that cited equality as an important attribute to our health care system.

SERVICES OFFERED

The Centre provides the following collaborative services on a "fee for service" basis, which include:

- Clinical, pharmacological and regulatory expertise
- Development of certain reports to assist in clarifying the regulatory and reimbursement pathways
- Consultation services (clinical, business, regulatory, and other)
- Research capacity with clinical investigation unit and trained personnel in pediatrics;
- Expertise in the design and conduct of pediatric pharmacokinetic, efficacy and safety studies
- Supporting advocacy efforts at Provincial, Federal, and international levels.

MAIN ACHIEVEMENTS FOR 2018-2020



Policy & Stakeholder Engagement

Over the last two years the GPFC has directly supported advocacy efforts towards regulatory and reimbursement agencies and continued to align with key pediatric associations and groups across the country.

Health Canada

Since January 2018, in response to consultations, the GPFC wrote 8 advocacy letters with other organizations having a focus in pediatrics, asking for the inclusion of pediatric specific regulations:

- Use of Foreign Decisions (February 2018)
- Accelerated Review (May 2019)
- Cost Recovery Fee Structure (January 2018, August 2018)
- Regulatory Modernization consultation (September 2019)
- Pharmacare (September 2018 and December 2018)
- Agile Regulations (September 2019)
- Interim Order for Respecting Clinical Trials with COVID (May 2020)
- Letter to advocate for pediatric specific considerations during the Patented Medicines Product Review Board (PMPRB) reform (August 2020).

Results from the advocacy and responses to the above consultations were two –fold. First, pediatric considerations were included in the following three drafted guidances:

- “Accelerated Review” guidance
- “Use of Foreign Decisions” guidance
- “Agile Regulation” guidance

as Health Canada is in the process of its regulatory reform, pediatric considerations such as instituting a “Pediatric framework” in Canada is being considered (see below).

In the 2019 Health Canada Annual report, which was published in September 2020, we highlight the mention of the importance of pediatric formulations by Dr. Supriya Sharma, Chief Medical Advisor, Health Canada.

« The health system is also evolving. For example, in 2019 we approved several new pediatric formulations for our youngest, and most vulnerable, Canadians. These formulations mean that healthcare professionals no longer have to rely on the longstanding practice of using medicines approved for adults. »

Reimbursement Agencies

The Centre, along with its partners, advocated for more harmonization with Health Canada decisions by providing case examples to illustrate challenges with pediatric medications and formulations. In October 2019, L'Institut National d'excellence en santé et en services sociaux (INESSS) acknowleged the Policy Paper led and written by the GPFC and the Canadian Paediatric Society (CPS) by referencing the policy paper in one of its listing recommendations. In addition, the GPFC had multiple interactions with the Canadian Agency for Drug Technology in Health (CADTH) regarding pediatric medications and formulations.

Federal Minister of Health

Federal Minister of Health, in a letter, acknowledged the need for more pediatric formulations to be made available in Canada.

Participation in the Université de Montréal Faculty of Pharmacy Centenary Plenary

Dr. Catherine Litalien, Medical and Scientific Director for the GPFC, presented during one of the celebratory plenary sessions hosted by the Faculty of Pharmacy to celebrate its centennial. Dr. Jean-Marie Leclerc, Executive Director for the GPFC, participated as a panelist with several key stakeholders in the health care industry. The event was concluded with a presentation from Dr. Lionel Carmant, delegate Minister for Health and Social Services, who was the guest of honour for the event.

Advocacy Leadership in Pediatric Community with Authorship of Two Regulatory Policy Papers

Together with the Canadian Paediatric Society (CPS), we wrote a position statement focusing on the changes needed at the provincial and federal levels to improve access to pediatric medications and formulations. The Policy paper was endorsed by 17 associations across Canada and recently cited by INESSS in its recommendation for reimbursement of glycopyrrolate oral solution.

One of the major changes proposed in this policy paper is the institution of a Canadian pediatric framework where Health Canada would require the submission of pediatric data in the product monograph when use in children is expected.

With federal discussions underfoot regarding the development of a National Pharmacare program, the GPFC also contributed to an article on National Pharmacare (Link here) as it relates to pediatrics.

Increasing Awareness of Challenges of Pediatric Formulations amongst Key Stakeholders

The GPFC developed strong ties with other pediatric support groups: CPS, The Hospital for Sick Children, KidsCan and MICRYN, Children's Healthcare Canada, Pediatric Chairs of Canada, Canadian Childhood Cannabinoid Clinical Trials (C4T), to name a few.

In February 2020, the GPFC led a workshop along with Dr. Michael Rieder, CIHR-GSK Chair in Paediatric Pharmacology, Western University, to work on a pilot project with representatives from the manufacturing, regulatory, reimbursement and listing areas from major stakeholders in drug commercialization and market access process. The workshop was attended by over 20 representatives and a summary of the event can be found here. From this larger group a smaller core team has been struck to work on a pilot project. This pilot project is expected to restart in the fall of 2020 as the COVID pandemic took the attention of many people on the core team.

Supported Partners in their Health Canada Applications

- Two much needed pediatric formulations on the GPFC priority list submitted in 2017 and 2018, by one of the GPFC's partners, have been approved by Health Canada and recently launched on the Canadian market. Link to announcements: Amlodipine and Levetiracetam.
- We have accompanied two international companies to Health Canada to obtain guidance on the regulatory submission pathway. The GPFC provided its clinical, patient and pharmacy expertise which contributed to clarifying the submission pathway for these companies.

Determination of the Percentage of Active Prescriptions Requiring Compounding

Even though compounding is a common practice in pediatrics, the importance of this issue in a pediatric health care center is not well described.

The main objective of the cross-sectional study conducted during summer of 2020 was to determine the percentage of active prescriptions requiring compounding that are administered enterally compared to global active prescriptions dispensed in a day for patients aged 0 to 18 hospitalized at Sainte-Justine University Hospital (CHUSJ). Secondary objectives are to determine the percentage of hospitalized patients receiving at least one prescription for a compounded formulation, to identify the characteristics of these patients and those of their medication.

Results of the study will be available in the fall of 2020 and will be subsequently published.

Data collection was performed by a first-year medical student through a grant for student work learning integration program from BioTalent who subsidized 75% of the student's salary for 16-weeks.

PARTICIPATION IN SCIENTIFIC PUBLICATIONS

Since January 2018, in addition to the two policy papers cited above, the GPFC has contributed to a number of scientific articles/posters.

Litalien C., Autmizguine J., Carli A., Giroux D., Lebel D., Leclerc JM., Théorêt Y., Gilpin A., and Bérubé S. **Providing Suitable Pediatric Formulations for Canadian Children: A Call for Action.** Can J Hosp Pharm. 2020; 73(4):247-256

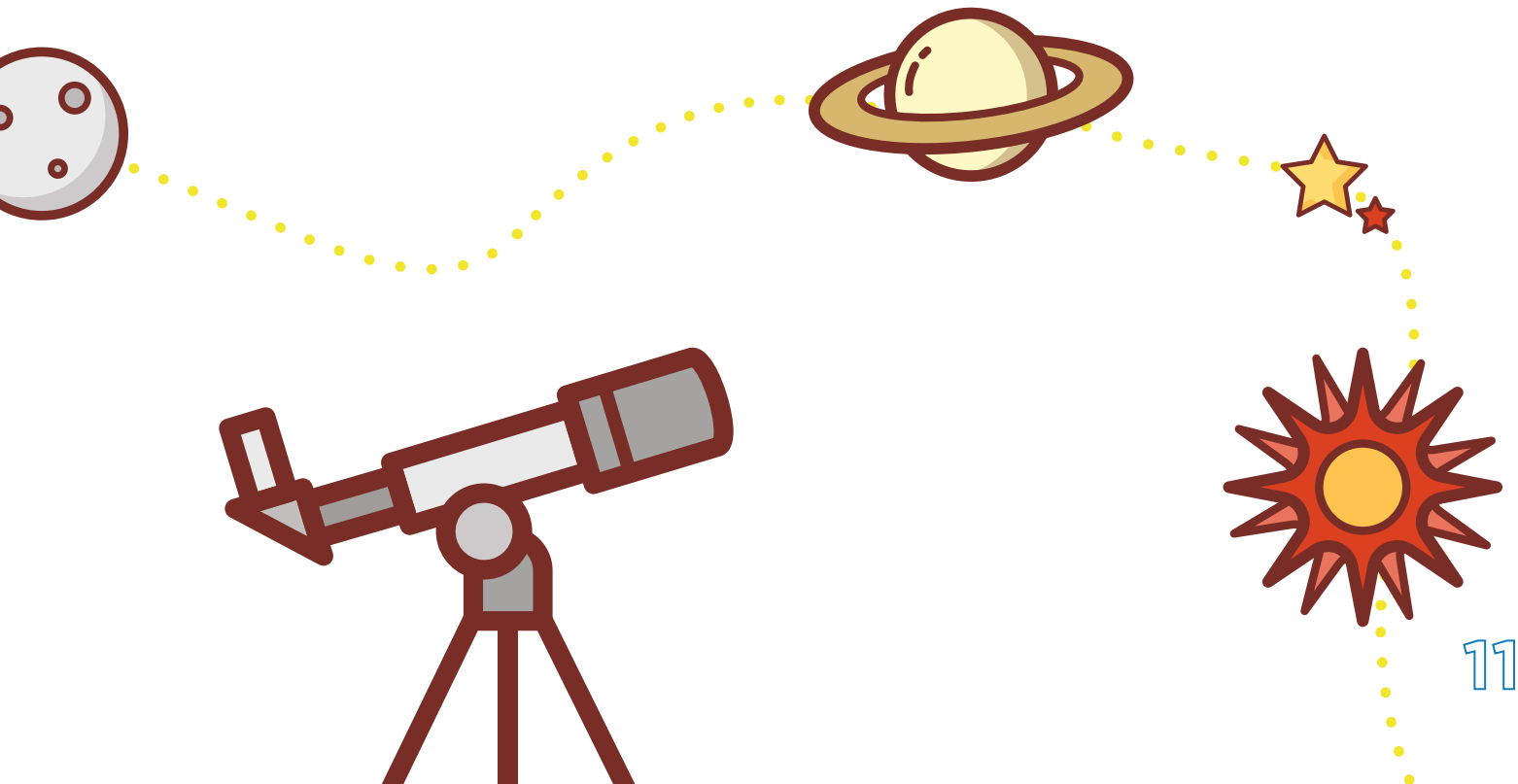
Preeya R., Duffett M., Mazer-Amirshahi M., Patel A., Gilpin A., Litalien C., Chan A.K., van den Anker J., Lacaze-Masmonteil T., Samiee-Zafarghandy, S. **Pediatric drug data in Canadian drug monographs: a descriptive analysis"**. CMAJ OPEN. 2020; 8(3) E529 Link.

Sushko K., Litalien C., Gilpin A., Mazar-Amirshahi M. Chan AK., van den Anker J., Lacaze-Masmonteil T., Samiee-Zafarghandy S. **Topical Nitroglycerin Ointment as Salvage Therapy for Peripheral Tissue Ischemia in Neonates Infants: a Systematic Review**. Submitted in May 2020 to the Can Med Assoc J.

Huntsman, R.J, Kelly, L.E., Alcorn, J., Appendino, P., Bélanger, R.E., Corley, S., Crooks, B., Finkelstein, Y., Gilpin, A., Lewis, E., Jacobs-Levin, J., Litalien, C., Meier, S., Moore-Hepburn, Cl, Oberlander, T., Rassekh, R., Repetski, A.E., Rieder, M., Shackelford, A., Siden, H., Siefert, B., Szafron, M., 't Jong, G.W., Vaillancourt, R. **Improving the Canadian Medical Cannabis Regulations to better serve paediatric patients.** Submitted in September 2020 to Can Med Assoc J.

Gilpin A. Bérubé S, Leclerc JM, Litalien C. **An Urgent Need for Canada to Have Access to Commercial Pediatric Formulations: Children Deserve the Same Standards as Adults.** Eupfi 2019.

Landry EK, Gilpin A. Bérubé S.,Lebel D., Litalien C. **Age-Appropriate Formulations at Any Cost? A Canadian Case Example.** Eupfi 2020



Secured Philanthropic Funding for the GPFC

With the generous support of the Sainte-Justine Hospital Foundation and the fulfillment of the funding commitment from the Morris and Rosalind Goodman Family Foundation, the GPFC now has funding for the next few years to accomplish its mandate.

What's Next in 2020 and 2021

With the COVID pandemic, the GPFC has taken the opportunity to publish and has participated in with other collaborators. We have also identified 7 key studies that we will undertake in the next few years to provide more data regarding pediatric formulations and compounding in Canada. Since March 2020, we have initiated one of these studies (previously described) to evaluate the percentage of compounded medications prescribed to children hospitalized at the CHU Sainte-Justine on two randomly selected days (in summer and winter of 2019-2020). Our team will continue to collaborate on and lead studies that will generate more information to inform stakeholders of the impact of not having child-friendly formulations in Canada.

Working with pediatric interest groups across Canada, the GPFC will continue its advocacy efforts to improve access to pediatric medications. With this objective in mind, it will support the development of a pediatric framework at Health Canada and will write a report benchmarking other jurisdictions to support the implementation of a Pediatric Rule in Canada.

The GPFC will work with the cross sectional core group to advance its pilot project in 2020-21. With a particular medication in hand, we will collaborate with key stakeholders to identify the areas that are unclear or unnecessarily complex for regulatory approval, reimbursement and commercialization. The core group consists of individuals from the GPFC, Health Canada, INESSS, generic and branded companies, as well as several key associations.

ACKNOWLEDGMENTS

The GPFC wishes to express particular thanks to the CHU Sainte-Justine for its contribution in kind which proved indispensable for the proper functioning of the Centre's activities. We wish to thank the CHU Sainte-Justine Foundation and the Rosalind & Morris Goodman Family Foundation for their support, as well as Frédérique Pelletier-Morin for the graphic design of this Annual Report. We are fortunate to have many individuals who are moved by our mandate and who provide to the GPFC their advice, support and expertise, in kind. We could not be where we are today without all of these supporters of the GPFC.

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