

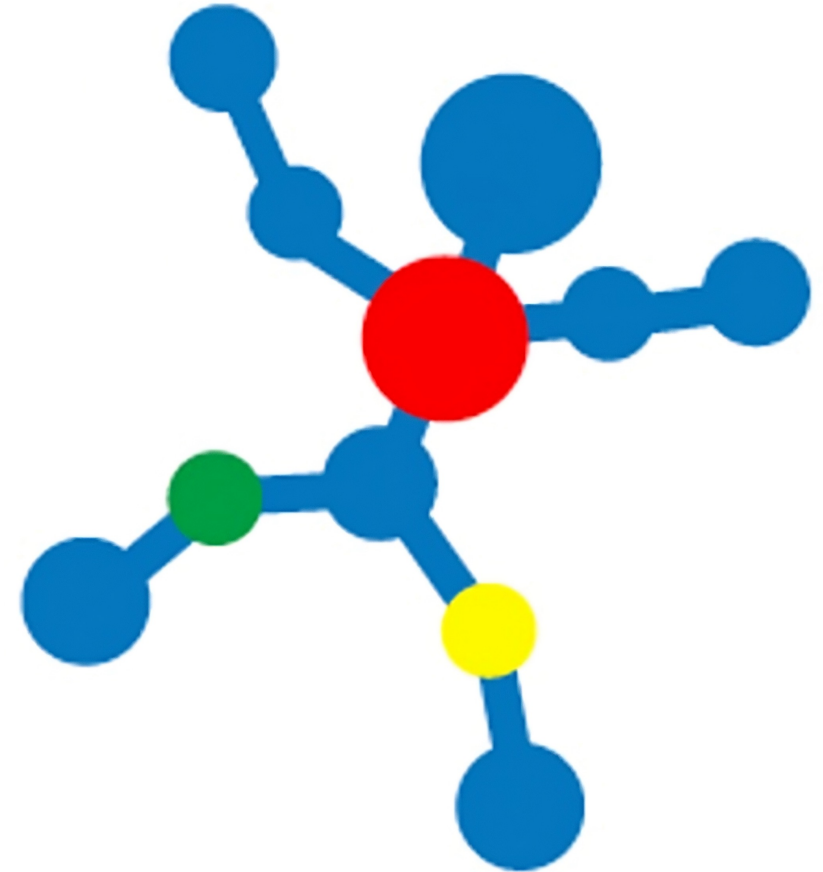
Time for a Paediatric Drug Regulatory Framework in Canada

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On behalf of the Goodman Paediatric Formulations Centre (GPFC)

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Relevant Objectives

- What are the Canada-specific **challenges** associated with ensuring safe and effective on-label prescribing for infants, children and youth?
- What **future opportunities** would further enhance Canada's drug regulatory framework to ensure paediatric patients benefit from the same safety, efficacy, availability and access standards as adults?

Compounding

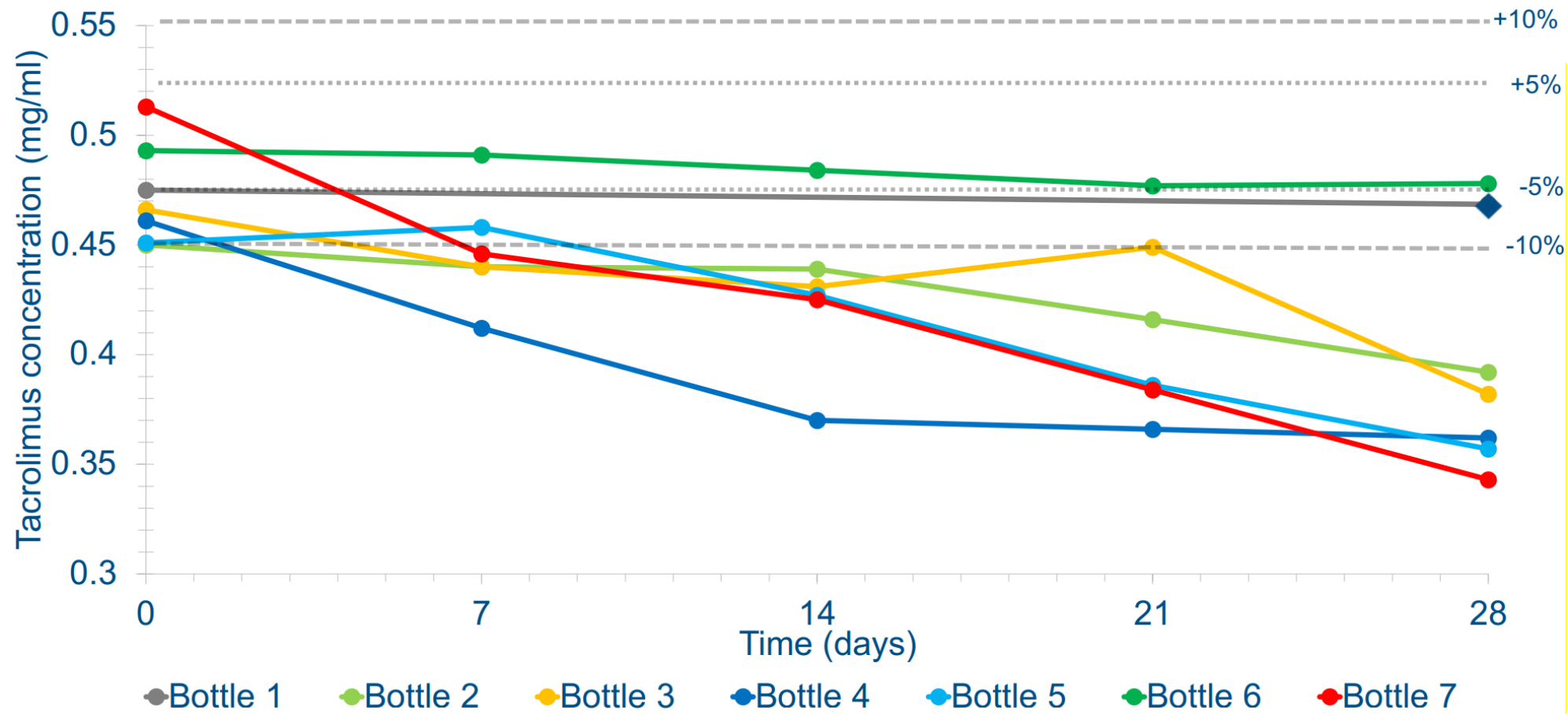


Bioavailability

- HIV drug lopinavir/ritonavir (*Best 2011*):
 - Crushed tablets (mixed with pudding) vs. whole tablets
 - Mean 40% reduction AUC (5-75%)



Purity, Potency, Content, Stability



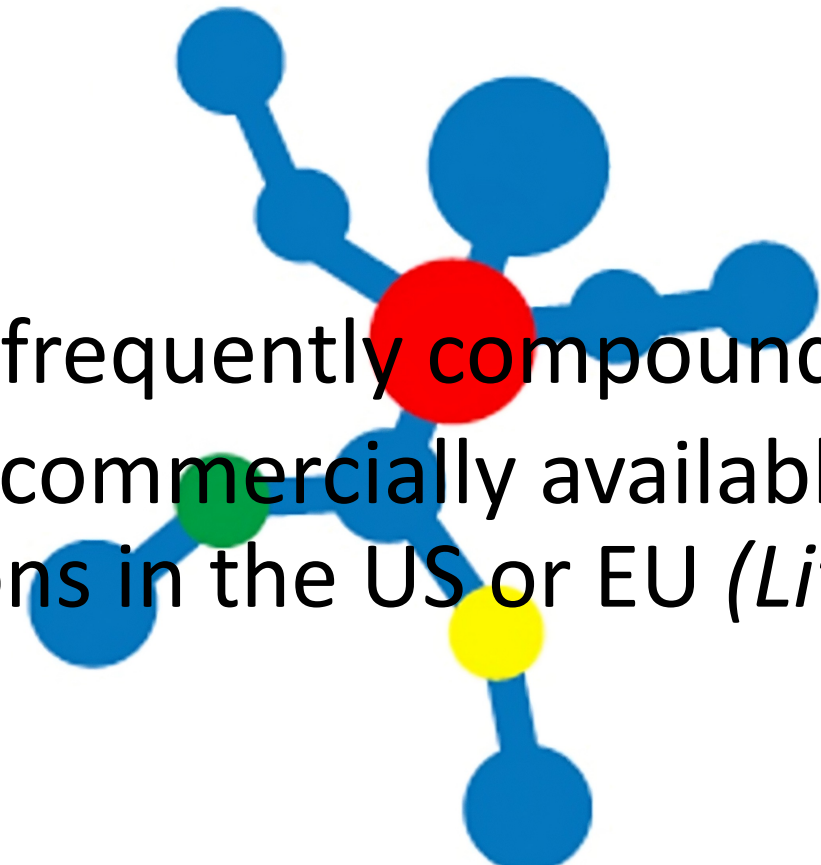
Extent of Problem in Canada

- 2007-2016: **60%** of new drugs for children <6 years unavailable in child-friendly formulation (*Raja 2020*)
- CHUSJ (*Landry 2023*):
 - **1/4** enteral drugs compounded
 - **1/2** of hospitalized children prescribed at least one compounded drug
- Compounding errors → **35%** of harmful medication incidents in children (*ISMP Canada 2022*)



Parents find son's lifeless body after pharmacy switches sleep medication for toxic dose of another drug





~50% of frequently compounded oral liquid medications are commercially available as child-friendly formulations in the US or EU (*Litalien 2020*)

Our Mission

**Improving access to commercialized
child-friendly medicines**

Our Mandate

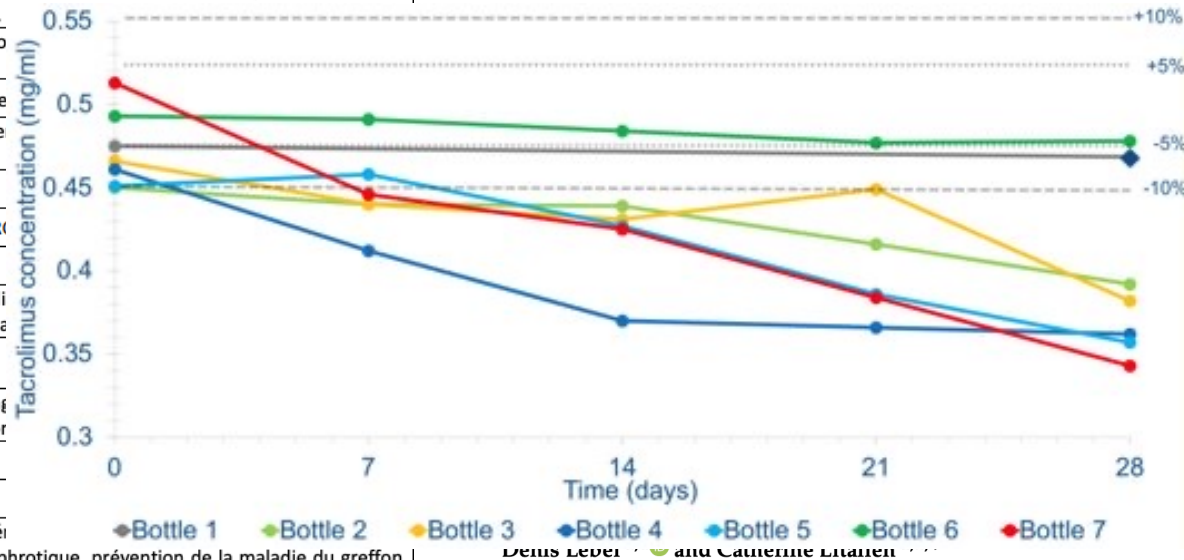
- To **facilitate market authorization** of paediatric drug formulations in Canada by:
 - Identifying and communicating **unmet paediatric formulation needs** to key stakeholders
 - Contributing to a favorable **clinical and regulatory environment**
 - Contributing to **uncovering incentives** for manufacturers and life science organizations
 - Promoting **cost effective** treatments for children
- To **promote safety** of medicines administered to children

Knowledge Creation

Médicament ¹	Exemples d'utilisation(s) en pédiatrie
6-Mercaptopurine ^{2,3}	Colite ulcéreuse, maladie de Crohn, leucémie lymphoïde aigue
Baclofène	Spasticité
Clobazam ³	Épilepsie, prévention des convulsions fébriles
Dexaméthasone	Asthme aigu, croup, pharyngite/amygdalite reliée au VEB, désordre rhumatologiques/immuns, désordres endocriniens, désordres hématopoïétiques/ néoplasiques,
Dompéridone	Gastroparésie, désordres de la motilité gastro-œsophagien (RGO)
Gabapentin	Épilepsie, douleurs neuropathique
Hydrocortisone	Insuffisance surrénalienne, hypofonction physiologique
Hydroxyurée ²	Anémie falciforme
Esomeprazole ³	Œsophagite érosive associée au RGO
Lévothyroxine ⁵	Hypothyroïdie
Métronidazole ⁴	Infections anaérobies, amibiase, diarrhée inflammatoire de l'intestin, giardiase
Phytonadione ⁶	Hypoprothrombinémie, maladie de la déficience en vitamine K
Rifampicine ⁴	Méningite à H. Influenzae /méningite (et prévention), infection par le corps
Sildénafil	Hypertension pulmonaire
Sotalol ⁵	Arythmie
Tacrolimus ^{2,5}	Prévention de rejet de greffe rénal, hématopoïétiques, syndrome néphrotique, prévention de la maladie du greffon contre l'hôte
Topiramate ²	Épilepsie, migraines

Pediatric drug data in Canadian drug monographs: a descriptive analysis

Preeya Raja MSc PharmD, Mark Duffett PhD, Maryann Mazer-Amirshahi PharmD MD PhD, Anthony K. Chan MBBS, Samira Samiee-Zafarghandy MD



Ending at a Canadian: A Cross-

el Kraus^{1,2}, Marie-Élaine Métras⁴,

Advocacy

Providing Suitable Pediatric Formulations for Canadian Children: A Call for Action

Catherine Litalien, Julie Autmizguine, Antoine Carli, Denis Giroux, Denis Lebel, Jean-Marie Leclerc, Yves Théorêt, Andrea Gilpin, and Sophie Bérubé

Can J Hosp Pharm. 2020;73(4):247-56

Time for a regulatory framework for pediatric medications in Canada

Andrea Gilpin PhD MBA, Sophie Bérubé BPharm MSc, Charlotte Moore-Hepburn MD, Thierry Lacaze-Masmonteil MD PhD, Samira Samiee-Zafarghandy MD, Michael Rieder MD PhD, Emily Gruenwoldt MHA, Stuart MacLeod MD PhD, Catherine Litalien MD

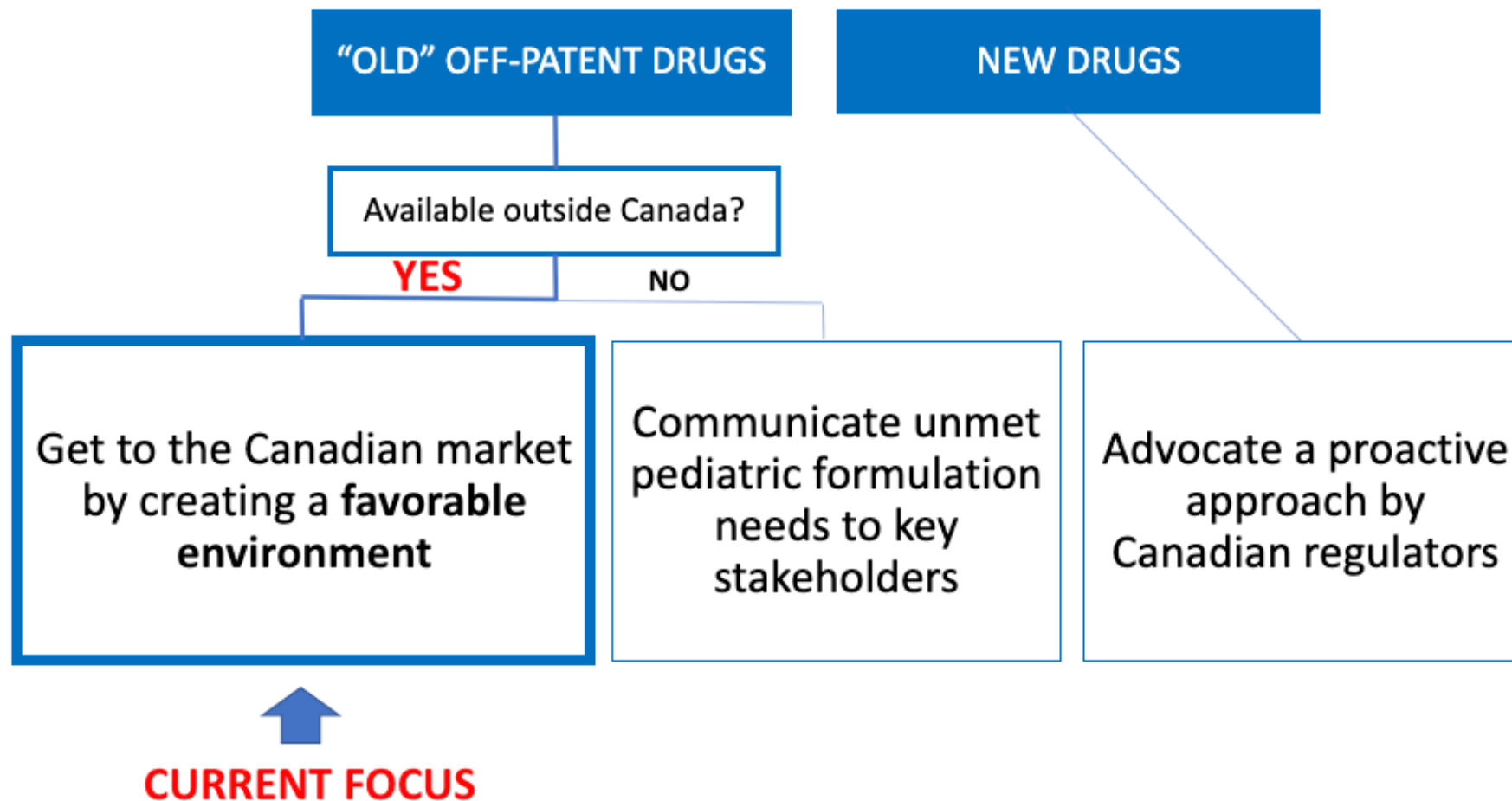
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Response to the Standing Committee on Health Study on Children's Health

The Institute of Safe Medication Practices Canada (ISMP Canada) and the Goodman Pediatric Formulations Centre (GPFC) of the CHU Sainte-Justine with support from CAH Advocates Canada and Children's Healthcare Canada, are pleased to jointly submit to the House of Commons Standing Committee on Health's study of children's health.

Our Strategy

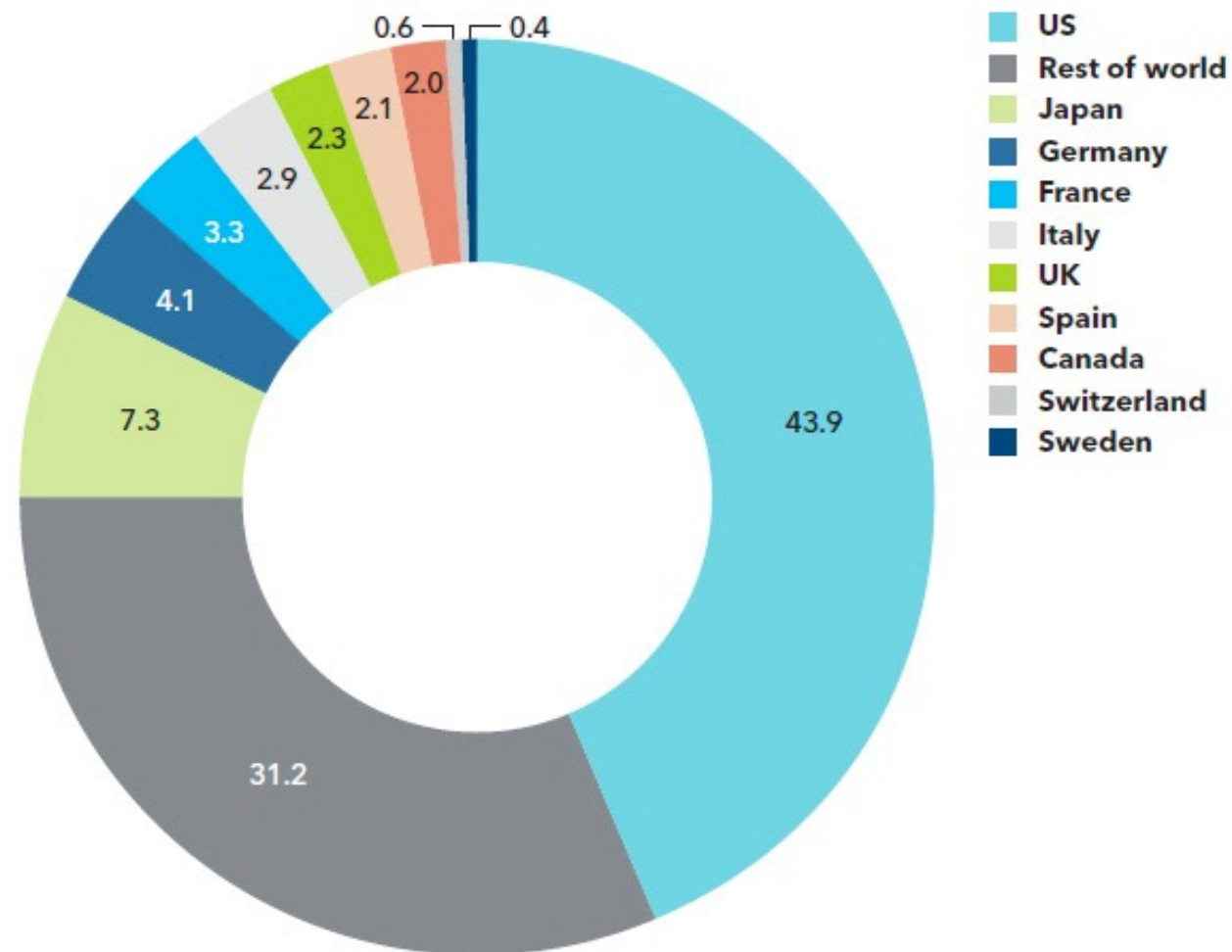


Canada-Specific Challenges

- Small market size
- Outdated regulatory framework
 - Lack of incentives
- Reimbursement

Small Market Size

- ~ 2% global market share
- Paediatric drugs: <10%



Outdated Regulatory Framework

- USA:

- 2002: Best Pharmaceutical for Children Act (BPCA)
- 2003: Pediatric Research Equity Act (PREA)
- 2005: FDA BPCA Pediatric Formulation Initiative



- EU:

- 2007: EU paediatric Regulation
- 2007: Paediatric-use marketing authorisation (PUMA)
- 2007: European Paediatric Formulation Initiative (EuPFI)



- WHO:

- 2007: Make Medicines Child Size
- 2016: Global Accelerator for Paediatric Formulations (GAP-f)



Outdated Regulatory Framework

- **Canada:**

- 2014 Improving Medicines for Children in Canada
- 2016 GPFC
- **No paediatric rule**
- **No trusted foreign review policy**
- **No harmonization of regulations with other jurisdictions**
- **No incentives for formulations for old, off-patent drugs**
 - On-patent: 6-month market exclusivity, 8-year data protection





Future Opportunities - Research

- Shared international approach for formulation development
 - International inventory of needs (dynamic)
 - International standards for compounding
 - Harmonized research standards
 - WHO Paediatric Regulatory Network
 - Relationship building



The Time is Now for Regulatory Change

- **Paediatric rule**
 - Mandate paediatric safety & efficacy data
 - Paediatric indications and formulations
 - Data and market protection
- **Trusted Foreign Decisions pathways**
 - Reasonable market experience requirements
- **Innovative fee structures**
 - Reduced rates for paediatric medications
 - Accelerated review
 - Orphan drug designation/some form of protection for medication identified as meeting a critical need (NPLPD)

Paediatric Drug Action Plan

Vision: Children and youth (aged 0-17) in Canada have access to the medicines they need in age-appropriate formulations

We propose to work across Health Canada, other governmental departments, and with our external (national and international) partners to accomplish the following three goals:

1.

Increase the **development** of essential pediatric medicines and formulations

2.

Improve **access** to pediatric medicines and formulations

3.

Provide more information to people in Canada

NEW DRUGS

6-month market exclusivity

“OLD” OFF-PATENT DRUGS



NOTHING

NEW DRUGS

Trusted foreign decision pathway

Paediatric Rule

Optimize market exclusivity

“OLD” OFF-PATENT DRUGS

Trusted foreign decision pathway

Innovative Fee Structures &
Incentives

NPLPD

Our Team



Left to right: Denis Lebel, Sophie Bérubé, Hélène Roy, Ginette Piteau, Dr. Catherine Litalien and Dr. Raphaël Kraus

Select References

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