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

DIA

Canada Needs a Pediatric Framework to Best Serve our Children

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#Canada21

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Children are Not Mini-Adults

Children’s Unique Needs for Medication Formulations

- Metabolize drugs differently
- Developmental stages may mean variable drug responses
- Efficacy and safety may not be known or studied
- Drug may be not be of an optimal concentration for ideal dosing volume
- Drug excipients (alcohol/sugars)
- Dose administration may be difficult
- Stability and bioavailability unknown

Polling Question 1:

- What percentage of pediatric prescriptions fall outside of the regulatory approval?
  - 25%
  - 43%
  - 57%
  - 75%
  - 83%

Importance of On-Label Prescribing

- On-label prescribing means:
  - Clinical studies
  - Bioavailability and stability data
  - Pharmacovigilance databases
  - Pharmaceutical manufacturing practices
  - Better adherence due to pediatric formulations (taste)

Polling Question 2:

- What percentage of new drug approvals are only indicated in adults?
  - 32%
  - 48%
  - 52%
  - 65%
  - 80%

Canadian Children Are Second-Class Citizens

- We do not have many of the approved commercial child-friendly formulations that other countries have
- A recent study indicated that between 2007 and 2016 more than 80% of all new active substances were only approved in adults
- There is not enough commercial interest to market these formulations in Canada but there is a tremendous need

Patel et al. (Arch Dis Child, 2019)

Why Do These Formulations Not Exist in Canada?

- Mid to small market size
- Regulatory and reimbursement path (perceived to be) unclear
- Reimbursement landscape is complex and cumbersome
- No incentive for investment
- Many drugs are off-patent

The GPFC is a non-profit that is advocating in these areas to make change and to facilitate bringing these medicines to Canadian children.

We Have to Resort to Compounding

- Many pediatric formulations exist in the United States and Europe but are not commercialized in Canada

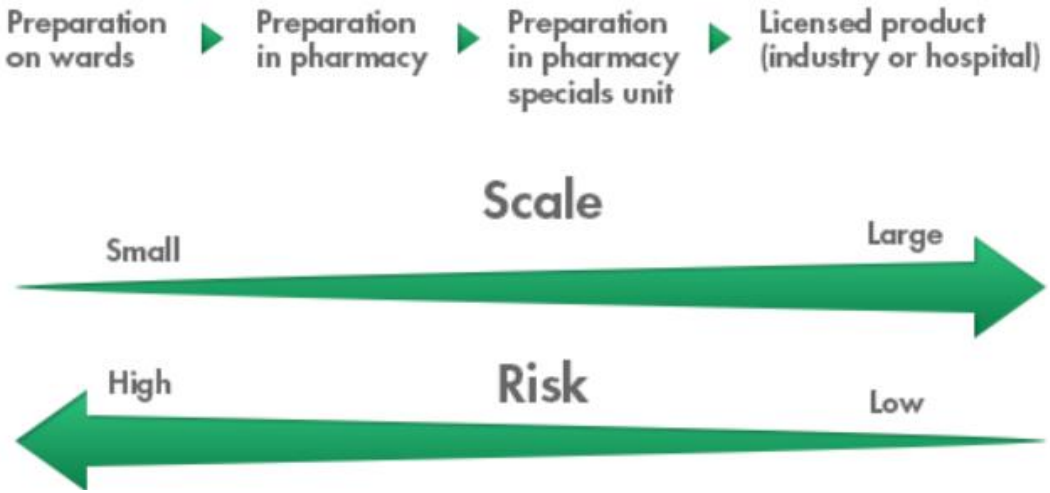
Resulting in…

- Compounding of the medication at the pharmacy
- Off-label use to adapt the adult form to an appropriate child-friendly form

As many as 75% of all pediatric prescriptions may fall outside regulatory approval in Canada.

Compounding is not Without Risk

- Modification of adult form is needed, requiring human manipulation
- Physicians often are unaware that a compounded medication has been used
- Adverse events are not reported (off-label)
- Safety and bioavailability are often not studied



Polling Question 3:

- What data can be missing when using a compounded formulation? Choose all that apply.
  - Stability
  - Source of medication
  - Compounding recipe
  - Bioavailability
  - Bioequivalence of compounded form with commercial form
  - Quality control measures
  - Any food effect
  - Adverse event reporting

Four Pronged Problem – All Needing Different Solutions

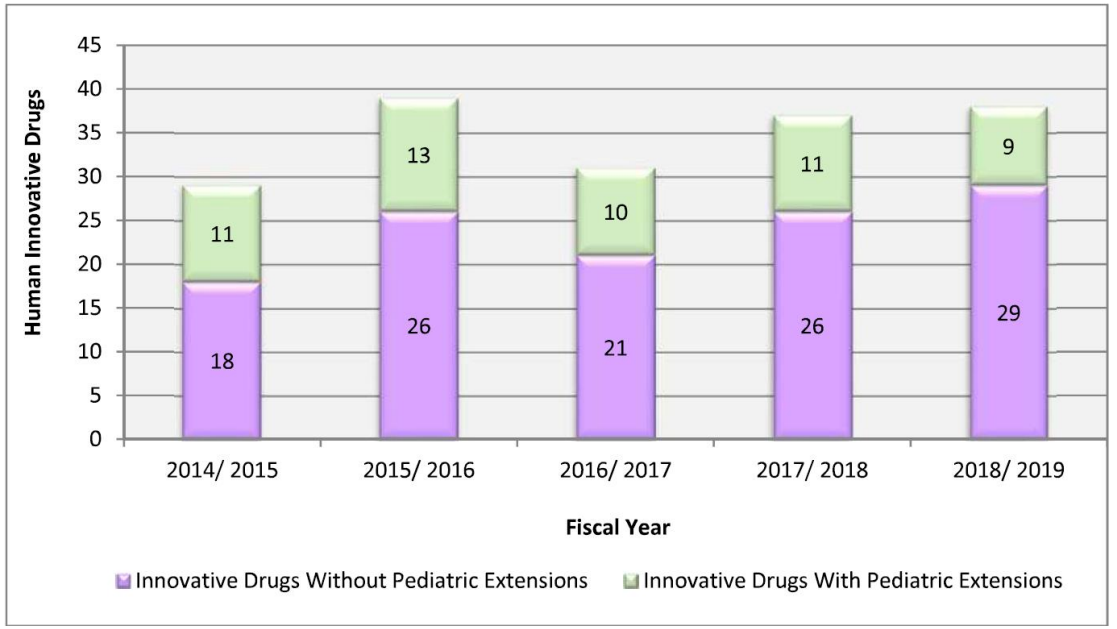
- Existing adult medications that do not have a pediatric indication or formulation in Canada
- New drug submissions – when use in pediatrics is anticipated
- Old off-patent drugs where there is no (or little) commercial interest
- Encouraging research in pediatric pharmacotherapy – including compounding

Regulatory Requirements & Incentives for Pediatric Medicines

Country/ Region	Population (millions)	Requirement	Incentive
US (FDA)	329	Yes PREA/FDASIA	Yes BPCA/FDASIA
Europe (EMA)	> 500	Yes	Yes
Switzerland	8.5	New law relating to pediatric development to be implemented	Yes (to be implemented)
Australia (TGA)	25	Information regarding EU or US development pediatric programs must be provided for new registration	No
Japan	126	No	Yes
Canada (HC)	37	No	Yes *(for NDS only)*

Canada Does Have an Incentive – But it's Insufficient

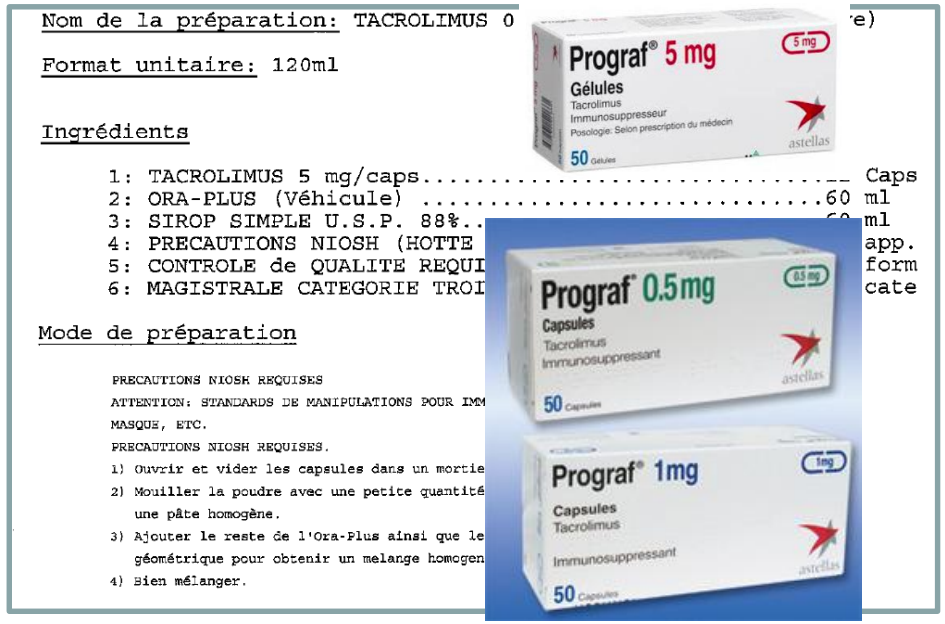
- Since 2006, Health Canada offers a 6-month extension for data protection to innovator companies if the manufacturer provides evidence for a pediatric label indication.
- The success of this incentive alone has been limited
- There are no incentives for older, off-patent, drugs



Statistical Report FY2018-19, Table 14, Page 15.

An Example: Tacrolimus

- 8 month old liver transplant recipient admitted for severe hepatic failure secondary to acute rejection
- Tacrolimus blood level found to be extremely low
- During hospitalization, his tacrolimus blood level returned within a therapeutic range
- Lack of adherence by the mother was suspected along with parental neglect



An Example: 6 Mercaptopurine

- Treatment of leukemia – usually 18-36 months
- Only available as 50 mg tablet
- No dosing flexibility
- Caregiver need to compound 2x per day
- Cytotoxic drug
- Commercial liquid available in US and Europe

Approaches to Solving this Problem

Regulatory Reform

Advocating for the requirement of the submission of pediatric data when use of medication in pediatrics is anticipated.

Proposing Inverted Model

Beginning from patient need (rather than commercial) by developing a list of prioritized medications where a child-friendly commercial form is needed.

Standardization of Compounding

Standardizing compounding recipes to reduce human error.

We Leave you with a Video that Provides the Challenges from a Parental Point of View

https://youtu.be/4kDxlhabb7I

Andrea Gilpin, Ph.D, MBA, ICD.D
General Manager
Andrea.Gilpin.hsj@ssss.gouv.qc.ca

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