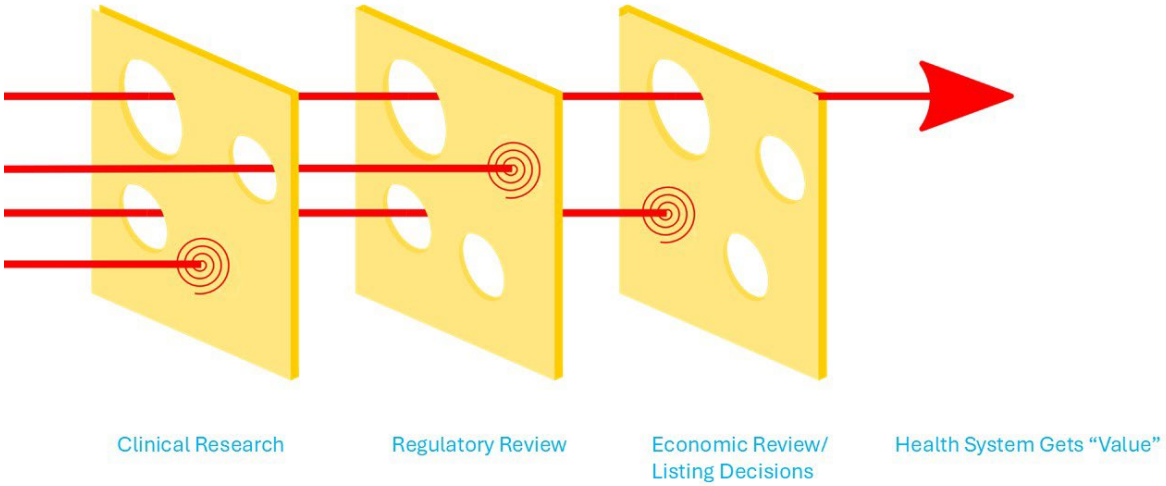
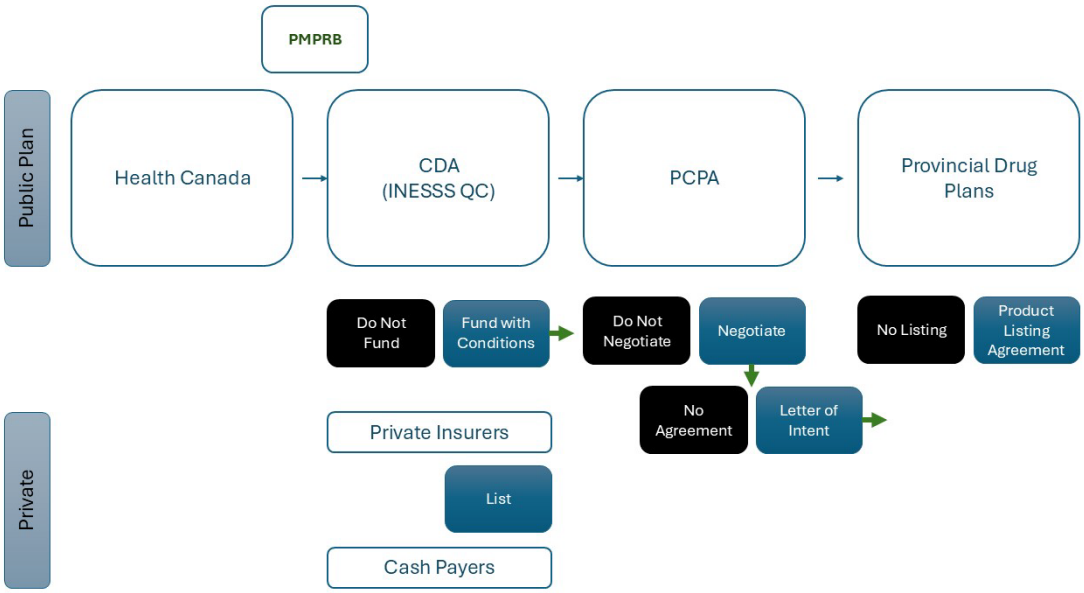
Summary of Drug Access in Canada

Background reading about the drug access system in Canada, prepared by Keith McIntosh. The panel will include presentations by Keith McIntosh, Avram Denburg, and Paul Gibson, followed by a panel discussion moderated by Ross Wallace.

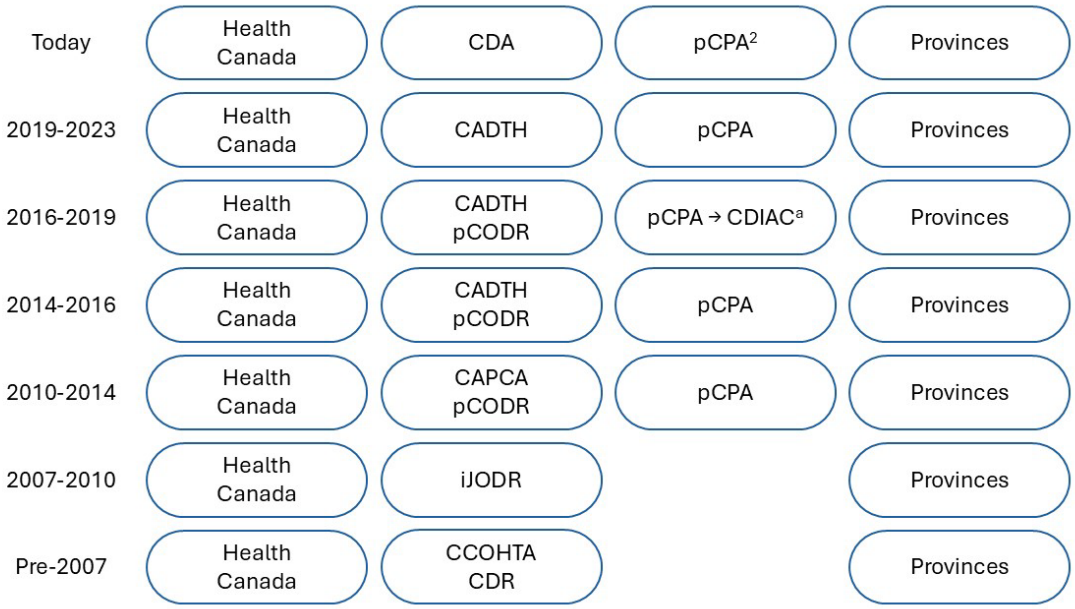
Purpose of the Drug Access System



Canadian Drug Review and Evaluation



Evolution of Canadian Cancer Drug Access



Why is the history important?

In the context of the evaluation and reimbursement decisions of pediatric cancer, it is important to understand how the process has evolved over time. Pediatric clinical evidence is rarely available when a new cancer drug is first approved and may take many years to be ready for a regulatory submission to put the pediatric use “on label”. As the process evolves, a new pediatric indication may be put through processes not required for the original drug review and listing.

Organizations in the Canadian Drug Evaluation Landscape

Health Canada

Health Canada’s *Health Products and Food Branch* (HPFB) is the national authority that regulates, evaluates, and monitors therapeutic and diagnostic product safety, efficacy, and quality, and reviews the information submitted in the clinical trial application.

CCOHTA

Canadian Coordinating Office for Health Technology Assessment was established in 1989 to facilitate cross-Canada drug evaluations for public prescription drug programs. Eventually, the Common Drug Review (CDR) process was established.

CADTH
Canadian Agency for Drugs and Technologies in Health was established in 2006 to succeed CCOHTA with a renewed mandate to support standardization and reduce duplication of health technology assessments through the CDR.

CDA
In September 2024 CADTH transitioned into Canada's Drug Agency, with continued responsibility for drug reimbursement reviews and expanded role in the drug system.

iJODR
Oncology drugs were originally in the CDR mandate, but it was felt the perspective and methods at CDR did not suit active cancer treatment. Early in 2007, the *Joint Oncology Drug Review* was created to conduct reviews of these drugs and update methods. This became an interim process, i.e., iJODR, when it was determined that a new organization (pCODR) needed to be formed.

pCODR
The *pan-Canadian Oncology Drug Review* was formally established in 2010 to assess drugs for active cancer treatment only. The pCODR recommendations are largely positive with a focus on a place in therapy approach for the treatment of the type of cancer. In 2014 pCODR was transferred to CADTH to better alignment pCODR and CDR evaluations.

CDIAC
In 2016, CAPCA created the *Cancer Drug Implementation Advisory Committee* (CDIAC) to oversee the Cancer Drug Funding Sustainability Initiative. This Committee supported provinces integrating new drugs into existing treatment plans and creating funding algorithms to help provinces identify and deliver the best cancer treatment. In 2019 this work was transferred to CADTH.

pCPA
The *pan-Canadian Purchasing Alliance* was established in 2010 by 9 provinces to achieve greater value for publicly funded drug programs and patients through the combined negotiating power of participating jurisdictions. Quebec joined the renamed *pan-Canadian Pharmaceutical Alliance* in 2015, with the Government joining in 2016. In 2023, pCPA was created as a stand-alone non-profit corporation controlled by the public drug plans.

CAPCA:
The *Canadian Association of Provincial Cancer Agencies* provides a forum for leaders of Canada's cancer care system to address issues affecting cancer care delivery in Canada. The Board is made up of the most senior leaders responsible for cancer care in each province and the CEO of the Canadian Partnership Against Cancer.

INESSS

In Quebec, *Institut National d'Excellence en Santé et en Services Sociaux* is mandated to evaluate drug listing requests and then make recommendations to the Minister of Health and Social Services as part of the updating of the *List of Medications* (the formulary for the basic drug insurance plan) and the *List of Medications – Institutions*. A key difference between INESSS and CADTH/CDA is that INESSS takes a societal perspective when evaluating a drug whereas CDA, takes a health system perspective when evaluating costs and benefits.

Phases of Drug Development

Discovery	Pre-clinical	Clinical	Regulatory	HTA	Negotiate	List
Finding a specific molecule — a chemical, DNA sequence, protein, etc. — that plays a crucial role in a disease state and can be targeted by a drug to produce beneficial and therapeutic effects.	In vitro (test tube) or in vivo (in an animal) testing to assess whether a compound has the potential to cause serious harm. It also tests what the drug does in the body.	Testing in Humans via clinical trials. Phase I focuses on safety and dosing. Phase II focuses on effect of drug Phase III focuses on comparing to standard treatment.	Evaluates the clinical data for safety and effectiveness. It includes an assessment of benefit/risk. They also ensure high quality manufacturing. Approves labeling.	To recommend reimbursement to public drug plans, the drug under review demonstrates same or better clinical benefit and acceptable cost or cost-effectiveness relative to comparator(s).	Negotiate price and listing conditions between manufacturers and public drug plans based on HTA recommendations. Concludes with Letter of Intent (LoI).	LoI forms basis of individual contracts between public drug plans and manufacturer.
Labs Uni.	Labs, Uni., Pharma	Pharma, Clinicians	Health Canada, Pharma	CDA, INESSS, Pharma	pCPA, Pharma	Provinces, Pharma
3-5 years	1-2 years	6-7 years	1 year	1 year	1 year	2-18 mos

Discovery

The discovery phase of drug development focuses on identifying potential therapeutic compounds and targets. Researchers first study the biology of a disease to pinpoint molecular targets, such as proteins or genes, that play a role in its progression. High-throughput screening, computational modeling, and structure-based drug design are used to identify lead compounds that interact with these targets. Once identified, these compounds are refined for improved efficacy, safety, and drug-like properties through medicinal chemistry. This phase also includes validating the target, conducting initial safety tests, and narrowing down the most promising candidates for preclinical and clinical development. It's a critical step toward innovative treatments.

Pre-clinical

The pre-clinical phase of drug development evaluates a drug candidate's safety, efficacy, and pharmacokinetics and pharmacodynamic before human testing. This stage involves in vitro (test tube) and in vivo (animal) studies to determine the compound's biological activity, toxicity, absorption, distribution, metabolism, and excretion. Researchers aim to identify potential side effects, safe dosage ranges, and the best drug delivery methods. Regulatory agencies, such

as the Health Canada or FDA require detailed preclinical data to approve investigational drug Clinical Trial applications, enabling clinical trials in humans. This phase is critical to minimizing risks, ensuring ethical practices, and establishing a strong foundation for clinical development.

Clinical
The clinical phase of drug development involves testing a drug candidate in humans to evaluate its safety, efficacy, and optimal dosing. It is conducted in three main phases:

- **Phase I**: Focuses on safety, determining tolerable dosage, and understanding pharmacokinetics and pharmacodynamics in a small group of healthy volunteers or patients.
- **Phase II**: Explores efficacy and safety in a larger group of patients with the target condition, refining dosing and identifying side effects.
- **Phase III**: Confirms efficacy and monitors adverse reactions in large, diverse patient populations, comparing the drug to existing treatments or placebos.

Successful trials lead to regulatory submissions for market approval.

Despite the rapid proliferation of approved cancer drugs in the last quarter century, the vast majority of drug development for pediatric cancer use has remained at the clinical stage. Since 2000, U.S. FDA has approved more than 600 agents for cancer use (more indications).

Roughly a dozen agents have received a regulatory approval for use in children in both the US and Canada. US FDA has approved roughly 20 pediatric cancer indications since 2020. The Canadian review and evaluation system needs to be prepared.

Phases of Drug Marketing and Reimbursement

Market Approval (Regulatory)
The regulatory phase of drug development involves submitting a comprehensive application to regulatory agencies, such as Health Canada, of FDA, to obtain approval for public use. In Canada this application is called a New Drug Submission (NDS) and includes pre-clinical and clinical data, manufacturing, and labeling information. Regulatory authorities evaluate the drug's safety, efficacy, and quality to ensure it meets standards and demonstrates the benefits outweigh any risks.

When a regulator approves a label, it specifies the "indication" - the specific medical condition(s) and population(s) for which a drug is approved to be used. It is the legally basis for marketing the drug and is based on clinical trial evidence filed in the application.

Post-Market (Regulatory)
Once an approved drug is on the market, regulators monitor the drug's safety, effectiveness, and long-term impact. Pharmaceutical companies conduct post-marketing surveillance studies

to identify rare or delayed adverse effects, drug interactions, and real-world efficacy in diverse populations. Health Canada and other regulatory agencies require periodic safety reports and may mandate additional studies or risk management plans.

To add a new label indication to an approved drug, (i.e. a new condition, disease, or population) clinical trials are required to provide evidence of the safety, efficacy, and risks for the new use. Once the evidence is available, the drug manufacturer must file a supplemental New Drug Submission that is reviewed by the Regulator using the same standards of review as a new drug. If approved, the drug's labeling is updated to include the new indication, expanding its therapeutic applications. A Health Canada NDS with only clinical data costs $125,000.

Health Technology Assessment

The Health Technology Assessment (HTA) process evaluates the clinical effectiveness, safety, and cost-effectiveness of health technologies. The assessment involves gathering input from the sponsoring manufacturer and other stakeholders, including healthcare professionals, patients, and the provincial drug plans. A detailed report is then created, providing recommendations to guide drug adoption and funding. Provincial health authorities use these assessments to make decisions about which technologies should be publicly funded, ensuring value for money. A CDA reimbursement review filed by a manufacturer cost between $99,000 and $174,000 depending on the level of complexity. An INESSS review costs between $63,000 and $95,000.

Price Negotiation

For branded medicines, pCPA uses the HTA recommendation(s) as a baseline to negotiate with pharmaceutical companies to secure lower drug prices and establish listing criteria. As of October 024, pCPA had successfully concluded 621 negotiations, concluded 101 negotiations without an agreement, and chosen not to negotiate 108 files. A successful negotiation concludes with a Letter of Intent (LOI) is issued and forms the basis for contracts executed by each jurisdiction under each individual legislation, regulations, and contract language. This provincial process varies by provinces, and can take weeks, or up to 18 months.