Canadian Organization for Rare Disorders

2019 Webinar Series

Jul. 11, 2019

Health Canada's regulatory approach to drugs for rare diseases and accelerated review of human drug submissions

12pm – 1pm

Today's speakers:

PANELISTS:

Durhane Wong-Rieger	President & CEO, Canadian Organization for Rare Disorders (CORD)
Fiona Frappier	Senior Policy Analyst, Office of Policy and International Collaboration, Health Canada
Megan Bettle	Director, Centre for Regulatory Excellence, Statistics and Trials, Health Canada

MODERATOR:

Bill Dempster – CEO, 3Sixty Public Affairs

Context: Canada's Rare Disease Strategy

Five goals:

1. Early detection / prevention
2. Timely, equitable, evidence informed care
3. Enhanced community support
4. **Sustainable access to promising therapies**
5. Promoting innovative research

Called on Health Canada to modernize its approaches regarding drug approval, access to treatments and international collaboration

Context: National pharmacare, budget and federal election

2019-20 Budget and the Hoskins Council Report

- Canadian Drug Agency Transition Office
- Consolidating evaluation functions
- National formulary
- National strategy for high-cost drugs for rare diseases" – with funding of $500 M / yr starting in 2022/23

Federal election October 2019

- Webinar series is part of CORD's non-partisan engagement to help Canadians be informed about the election and issues impacting rare diseases

Health Canada Santé Canada

Canada

Health Canada's Regulatory Approach to Drugs for Rare Diseases

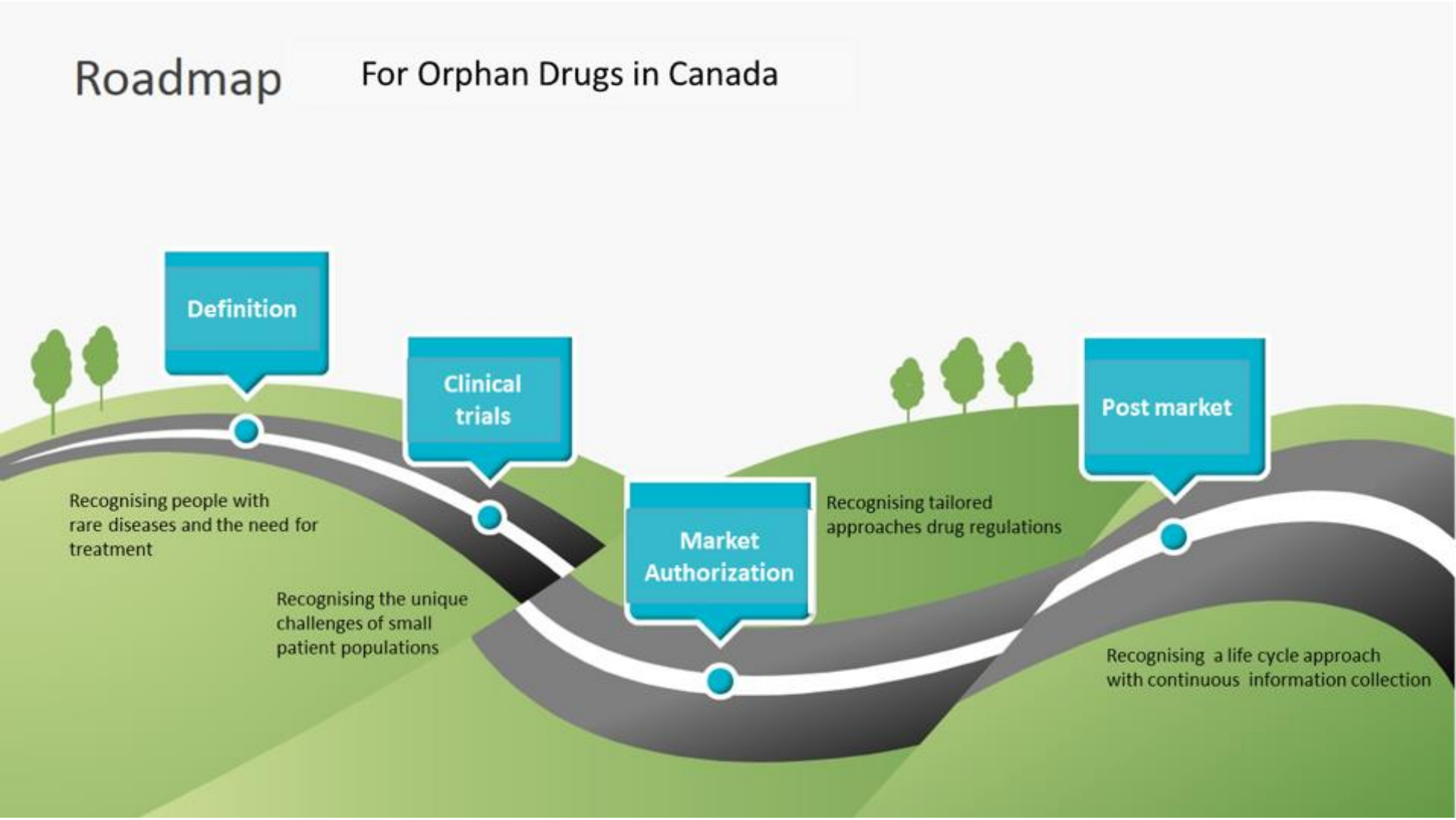
Fiona Frappier

July 11th 2019

CORD Webinar

YOUR HEALTH AND SAFETY... OUR PRIORITY.

Health Canada's Regulatory Approach



To Support Access to Orphan Drugs, Health Canada Currently Offers:

- Shortened review times if conditions are met (Priority Review of Drug Submissions Policy or the Notice of Compliance with Conditions Policy)
- Scientific advice to sponsors on the design of clinical trials in small populations and to support companies' tailored drug development programs
- Access to non-marketed drugs through the Special Access Programme (SAP)
- Data protection in Canada gives 8 years of market exclusivity for innovative drugs. A six-month pediatric extension to the 8-year term of market exclusivity is available. Certificates of supplementary protection can extend patent or data protection by an additional up to 2 years.
- Fee mitigation or fee deferral are possible to reduce the potential negative impact of paying the associated regulatory fees

Orphan Drugs – Canadian Approvals

Each year, Health Canada publishes its New Drug Authorizations: Highlights (Highlights Report).

For the last five years :

- 30 to 40% of new active substances we authorized in Canada are classified as orphan drugs in Europe or the United States
- of these, most were reviewed using accelerated processes

Regulatory Review of Drugs and Devices
Key Projects Impacting Drugs for Rare Diseases

Project/tools	Potential for access to/availability of drugs for rare diseases
Expansion of Priority Review Pathways	Consideration of healthcare system needs in the criteria for priority review pathways
Early Parallel Advice	Opportunity to provide advice to sponsors on supporting data requirements and clinical trial designs at an early stage in development either alone or with health technology assessment organizations
Alignment of Health Canada Review with Health Technology Assessment Body Review	A mechanism to reduce time between regulatory approval and reimbursement recommendations
Use of Foreign Decisions	Use of foreign decisions would allow drugs that would not otherwise be filed in Canada to rely on a decision made by a trusted foreign regulator to issue a Health Canada authorization
Special Access Programme (SAP) Renewal	Modernize to reduce administrative burden for prescribers and bring needed products in via regulated pathways
Strengthening the Use of Real World Evidence	Exploring how and where real world evidence can be used to support regulatory decision-making across the drug life cycle

Orphan Drug Resources

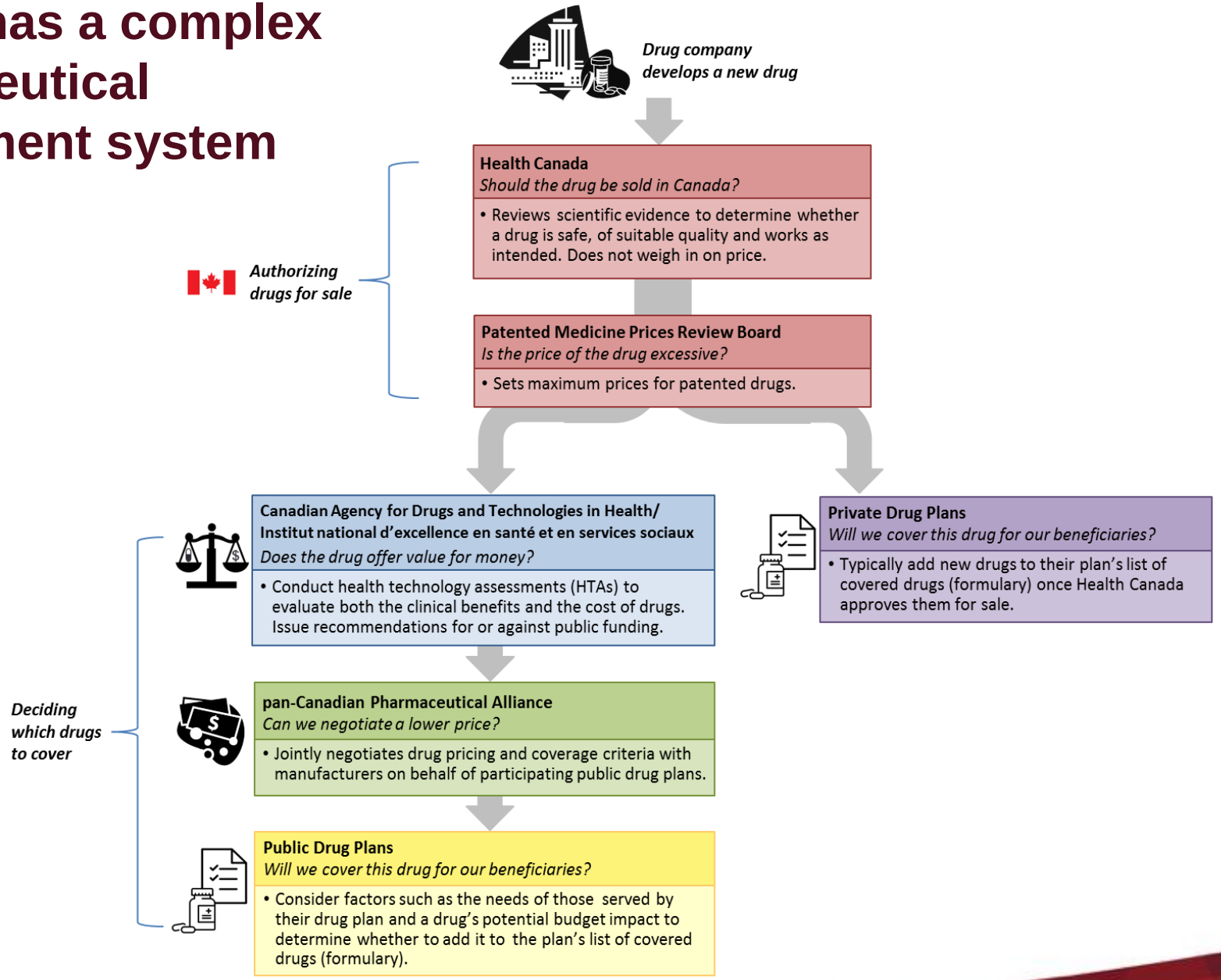
- A number of tools are available to provide information on orphan drugs available in Canada and to support informed decision-making:
  - Drug Product Database,
  - Regulatory Decision Summaries,
  - Summary Basis of Decisions
  - Clinical trial search and Clinical Trials.gov
  - Special Access Program
  - Submissions Under Review

- Orphan drugs are now identified in the annual Health Canada New Drug Authorizations report.
- Program developments for the Regulatory Review of Drugs and Devices
- Through Canadian Institute of Health Research, the Government of Canada is an active member of Orphanet, an online resource that offers a directory of specialized information for people with rare diseases and health service providers.

Study on the Improving Access to Drugs for Rare Diseases

- The Standing Committee on Health (HESA) adopted a motion in April 2018 to study barriers Canadians face accessing treatments for rare diseases.
- The committee held 5 meetings, hearing from 24 witnesses, and assessed 10 written submissions from stakeholders.
- Four themes were identified as barriers Canadians face when accessing treatment of rare diseases:
  - regulatory approval of drugs for rare diseases;
  - pricing;
  - reimbursement for drug costs through PT drug plans; and
  - research on diagnosis for rare diseases and real world evidence.
- HESA's final report – Canadians Affected by rare Diseases and Disorders: Improving Access to Treatment - was released on February 28, 2019.
- The Government Response (GR) was tabled June 11th in the House of Commons.

Canada has a complex pharmaceutical management system



Canadian Federal Government Programs Supporting Research and Development

- Key research and development programs through both the Canadian Institutes of Health Research and Genome Canada
- Provide support for research and development through the Canada Revenue Agency's Scientific Research and Experimental Development (SR&ED) Program
- Small and medium sized enterprises receive guidance through the National Research Council's Concierge service
- Further industry support comes through Innovation, Science and Economic Development

The Spectrum of Patient Involvement

- Patients, including patient advocates or representatives, currently provide advice to Health Canada through varying means:

During regulatory framework and guidance development

E.g. Publication of draft regulations in CGI, consultation on draft guidance documents

Scientific Advisory Committees and Panels

E.g. - Scientific Advisory Committee on Respiratory and Allergy Therapies (SAC-RAT)- Scientific Advisory Committee for Oncology Therapies

Pilot Project(s)

E.g. Orphan Drugs Patient Involvement Pilot Project

Stakeholder Meetings and Consultations

E.g. –online What was heard reports, National roadshows, bilateral meetings

On-Line Questionnaires

E.g. Protecting Canadians from Unsafe Drugs Act Transparency Needs-based Assessment

During preparation of reports concerning health products, including adverse reaction reporting

E.g. Patient reports are considered with all sources as adverse event reports by Health Canada

CIOMS Working Group XI- Patient Involvement in the Development and Safe Use of Medicines

Working Group XI

- Launched in April 2018
- Members represent perspectives from patients industry, regulators, & CIOMS academia
- Working together to formulate pragmatic *Points to Consider* in patient involvement and develop guidance.

Open Meeting with Patients (30 Apr 2019)

- Presented CIOMS WG XI work to date in 4 sessions w/accompanying panel discussions
- Obtained input from patient organizations and other stakeholders
- Feedback informed WG meeting discussions & its approach going forward

CIOMS Guidance - Patient involvement in the development and safe use of medicines

- History
- Lifecycle approach
- Best practice
- Challenges & opportunities
- Into the Future…

International Regulatory Collaboration

Health Canada is a member of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH).ICH's mission is to achieve greater harmonization worldwide. Its intention is to ensure that safe, effective, and high quality medicines are developed and registered in the most resource-efficient manner. Some key examples include:

- ✓ ICH topic E6 - Good Clinical Practice
- ✓ ICH Topic E9 - Statistical Principles for Clinical Trials
- ✓ ICH E10 - Choice of Control Group and Related Issues in Clinical Trials
- ✓ E16 Biomarkers Related to Drug or Biotechnology Product Development: Context, Structure and Format of Qualification Submissions
- ✓ ICH E17 – General Principles for the planning and design of multi-regional clinical trials (MRCTs)
- ✓ ICH E18 - Genomic Sampling and Management of Genomic Data
- ✓ ICH E11 - Clinical Investigation of Medicinal Products in the Pediatric Population

The Innovation Project

1
Methods of Horizon Scanning

Lead: MHLW/PMDA

Participants: AIFA (Italy), DKMA (Denmark), EMA (EU), FDA (US), Health Canada (Canada), HPRA (Ireland), MFDS (Korea), MHRA (UK), MPA (Sweden), and Swissmedic (Switzerland)

2
Horizon Scanning Outcomes & Capacity Building

Leads: EMA, HPRA

Participants: AEMPS (Spain), AIFA (Italy), DKMA (Denmark), Health Canada (Canada), HSA (Singapore), MFDS (Korea), MHLW/PMDA (Japan), MHRA (UK), MPA (Sweden), PEI (Germany) and Swissmedic (Switzerland)

3
Novel Approaches to Drug Licensing

Lead: Health Canada

TGA (Australia), ANVISA (Brazil), EMA (EU), AIFA (Italy), MHLW/PMDA (Japan), COFEPRIS (Mexico), MedSafe (New Zealand), SAHPRA (South Africa), Swissmedic (Switzerland), MHRA (UK).

Collaboration in International Regulations

- Identifying and prioritising new product innovations: policy work, consultation
- Identifying regulatory approaches: scientific advice, legislation, review pathways
- Leveraging expertise: internal and external, expert advisory Meetings, regulatory cluster meetings,
- Regulatory networks and establishing common principles: ICH, ICMRA
- Building on stakeholder networks and approaches: academic, patient, industry

Health Canada Santé Canada

Canada

Draft Guidance - *Accelerated Review of Human Drug Submissions*

Regulatory Review of Drugs and Devices

Megan Bettle
July 11th 2019
CORD Webinar

YOUR HEALTH AND SAFETY... OUR PRIORITY.

Drug Submission Review

- In order to market a drug in Canada, a submission must be filed to Health Canada

- Sponsors must provide sufficient evidence of the product's safety, effectiveness and quality for assessment, including
  - Manufacturing details and controls to ensure consistent quality
  - Pre-clinical data to establish safety
  - Clinical data to support proposed indication, including “substantial evidence of effectiveness”
  - Proposed labels – claims, instructions for use
  - Assessment of possibility for name confusion

- Health Canada then reviews the evidence and decides whether the benefits of the product outweigh the risks, and whether the risks can be managed, before issuing a Notice of Compliance

- Standard review time for a New Drug Submission is **300 days**

Current accelerated review pathways

Priority Review

- Requested by sponsor before submission
- 180 day review time for qualifying submissions
  - Serious, life-threatening or severely debilitating where no current treatment, or where new product offers improvement in benefit-risk profile
- "Substantial" evidence provided in submission - no requirements for additional studies after NOC

Notice of Compliance with Conditions

- Requested by sponsor before submission, or decision made by Health Canada during review
- 200 day review time for qualifying submissions
  - Serious, life-threatening or severely debilitating where no current treatment, or where new product offers improvement in benefit-risk profile
- "Promising" evidence - sponsor commits to conducting confirmatory studies after NOC (not currently legally-binding)

**Pathways are mutually-exclusive, a submission cannot be both priority review and NOC/c*

HPFB Regulatory Review of Drugs and Devices (R2D2)

Objective: An agile regulatory system that supports better access to therapeutic products based on health care system needs

Expanded collaboration with health partners

- Alignment of the Health Technology Assessment (CADTH) Review with Health Canada Review
- Implementing a Mechanism for Early Parallel Scientific Advice
- Use of Foreign Reviews/Decisions
- International Collaboration and Work Sharing in Reviews

More timely access to drugs and devices

- Expansion of Priority Review Pathways
- Improving Access to Biosimilars and Biologics
- Improving Access to Generic Drugs
- Building Better Access to Digital Health Technologies
- Pre-Submission Scientific Advice for Medical Devices
- Special Access Programme (SAP) Renewal

Enhanced Use of real world evidence

- Leveraging Data for Assessing Drug Safety and Effectiveness
- Strengthening the use of real world evidence and regulations for medical devices

Modern and flexible operations

Updated System Infrastructure

Appropriate cost recovery framework

Public Release of Clinical Information

Regulatory Review of Drugs and Devices (R2D2): Expansion of Priority Review Pathways

- **Under the "More timely access to drugs and devices" pillar**

- **Policy Intent:**

  - To expand the scope of the current Priority Review of drugs for human use so that health care system needs can be considered in the decision-making during the regulatory review process, allowing Canadians to have more timely access to those drugs needed most

  - Since the Priority Review pathway is already an accelerated pathway, this project was not intended to create additional time savings

What have we heard?

- Early consultation included an online questionnaire targeted to stakeholders across health care system including patients, health professionals, industry and drug plans, as well as HC staff
  - consultation open from March 27- April 27, 2018
  - ***1,131*** external responses / ***69*** internal responses

- Dominant response themes included:
  - improving **access to affordable drugs,** including through prioritization of competitor products
  - supporting medications for **special populations** (especially seniors and pediatrics)
  - enabling **faster access**
  - including medications that **improve quality of life** (and would contribute to system savings)

- External stakeholders also suggested prioritization of new products for specific conditions (e.g., cancers, dementia), for pain management, and for products which have already been approved by other regulators

The Proposal – Accelerated Review of Human Drug Submissions

1. **Expand product eligibility criteria for accelerated review**
   - Provides greater clarity around the types of products which are eligible for faster review

2. **Create conditions that support availability of alternative treatments**
   - Allows some additional products to be accelerated

3. **Create a single accelerated review pathway, merging priority review and the NOC/c pathway**
   - Simplifies the process for Health Canada and industry
   - Consulting on technical workflow options

The Guidance – Scope and Application

"The …guidance document applies to a New Drug Submission (NDS) or Supplement to a New Drug Submission (SNDS) in support of a prescription pharmaceutical, biologic (excluding biosimilars) or radiopharmaceutical drug product for human use for a **serious**, **life-threatening** or **severely debilitating disease or condition** for which:

1. there is evidence of clinical effectiveness that the drug provides treatment, prevention or diagnosis of a disease or condition for which there is no available therapy or drug marketed in Canada; **or**

2. there is evidence of clinical effectiveness that the drug provides a significant increase in efficacy and/or significant decrease in risk such that the overall benefit/risk profile is improved over existing therapies, preventatives or diagnostic agents for a disease or condition that is not adequately managed by an available therapy or drug marketed in Canada; **or**

The Guidance – Scope and Application (cont'd)

…**or**…

3. there is evidence of clinical effectiveness that the drug provides treatment, prevention or diagnosis of a disease or condition for which an existing drug for the same indication has been on the Canadian market for 12 months or less; (NEW) **or**,

4. there is evidence that the drug addresses a health care system need by delivering high clinical benefit for public health or high clinical benefit for patients. (NEW)

   - Examples provided here for public health needs include opioid crisis, antimicrobial resistance
   - Examples provided for patient benefit include significant reduction in treatment burden, pediatric formulations, drugs for rare diseases

Anticipated impacts of proposed changes

- Could allow additional drugs to receive an accelerated review that may not currently qualify
- Would simplify review processes
- Would still allow conditional authorizations for promising products, with commitments for submission of confirmatory data

- Would not lower Health Canada's requirements for safety, efficacy and quality
- Would not affect how payers make funding decisions

How to provide input/ What's next?

- Guidance document is open for public consultation until July 21, 2019
- Guidance can be requested from, and comments can be provided to:
  hc.regulatory_review-examen_reglementaire.sc@canada.ca
- All comments will be reviewed and considered in order to revise the proposal
- A final guidance document is planned to be released and implemented in 2020

Discussion / Q&A

Thank you!

For more information on CORD, please visit:

www.raredisorders.ca

Canadian Organization for Rare Disorders