# CORD Open Letter to Health Ministers

Canadian Organization for Rare Disorders

***VIA EMAIL TO CANADA'S PROVINCIAL AND TERRITORIAL HEALTH MINISTERS***

November 1, 2022

**Subject: Urgent provincial/territorial action needed to address the crisis in rare disease in Canada**

Dear Provincial and Territorial Ministers of Health,

Please put Rare Disease at the very TOP of your agenda as you convene for your annual Health Ministers meeting. I believe you will understand why upon reading this letter.

As all health ministries struggle with the impact that COVID had on healthcare resources, it may be tempting to put rare diseases on the back burner… again… until other issues are resolved. That would be a costly mistake.

About 3.2 million Canadians have a rare disease, more than the number with diabetes, cardiovascular disease or all cancers combined. More than two-thirds affected are children. More than a third of those children will die before their fifth birthday. In Canada, every 39 minutes, a child dies of a rare disease.

The data from developed countries across Europe, the UK, USA, and Australia, as well as our own Canadian data, demonstrate the inordinate impact of rare disease on health resources, a crisis that has only worsened post-COVID.

- In the USA, genetic (mostly rare) diseases account for up to approximately 50% of paediatric hospital inpatient costs
- In the USA, just a subset of <379 of the 7,000 RD, accounted for nearly $US966M direct and indirect cost in 2019
- This cost is greater than many other common conditions, e.g., cancer, diabetes, heart disease and stroke, Alzheimer's dementia and arthritis.

- Two new studies in 2021 confirm these figures and also demonstrate that nationally RD account for 1.5 times ($US 105 Billion) the paediatric inpatient costs compared to all common diseases ($US 150 Billion versus $US70 Billion), and have a proportionately greater impact on children and youth versus adult costs
- In Ireland, 6 in 10 deaths in children and 9 in 10 hospital bed days for death are attributed to RD
- In Canada, 60% or more of ER admissions in major pediatric hospitals are children with rare conditions, some diagnosed and some undiagnosed

The previous patient survey conducted by the Canadian Organization for Rare Disorders documented the long delay to diagnosis (up to seven years), the numerous misdiagnoses resulting in missed opportunities to prevent serious symptoms or death as well as delayed or harmful wrong treatments. We expect that our new survey which is currently in the field will confirm these sobering statistics, because little has changed in how we treat rare disease.

Clearly, doing nothing to address the rare disease crisis is costly… in terms of dollars and lives.

You may know that the Chinese word for crisis is made up of two words: danger and opportunity. Luckily, we have the opportunity RIGHT NOW to do something EXTRAORDINARY.

As you know, in 2019, the federal government committed $1 billion to set up a national Rare Disease Drug Strategy, with an additional $500 million annually. After 3 years of CORD-led multi-stakeholder discussions, there appears to be broad agreement that optimal benefits of a rare drug program can only be achieved if we have a rare disease infrastructure, built on a national network of Rare Disease Centres of Excellence. When fully implemented, this “hub and spoke” network would assure that rare disease patients will get timely and accurate diagnosis, referral to the right specialist, a personal care plan managed by healthcare professionals close to home, and active participation in on-going monitoring.

The second and related major issue is a modern Rare Disease Drug Strategy that is “fit for purpose” of assuring timely access to innovative medicines. Given that only 5% of rare diseases have an approved therapy, CORD calls for investment in academic and non-profit R&D, incentives to encourage commercially developed therapies and sustainable financing models for both types of therapies to assure that Canadian patients have access as soon as possible.

The crisis in rare disease constitutes a clear and present danger not only to the patients and families affected but to the whole healthcare system and to society. But there is an unprecedented opportunity to invest wisely the $1 billion start-up fund and the $500 million annual federal contribution to establishing a “state of the art” Rare Disease Strategy to support a Rare Disease Drug Strategy that optimizes benefits to patients and their families and to all of society.

We urge the provincial and territorial Ministers of Health to ACT NOW to adopt a consensual approach in meeting with the federal Minister of Health to accept and invest smartly the $500 million annual allocation for rare diseases.

Over 3 million Canadians are counting on you and we know you will not let us down.

**MAKE A RARE DISEASE STRATEGY YOUR HEALTHCARE LEGACY TO CANADIANS!!!**

Sincerely,

Durhane Wong-Rieger
President & CEO
Canadian Organization for Rare Disorders
151 Bloor Street West, Suite 600
Toronto, Ontario M5S 1S4

Encl. **CORD Proposal for Canada’s Rare Disease Drug Program within a Canadian Rare Disease System, including Rare Disease Centres of Excellence**

**CORD Proposal for Canada's Rare Disease Drug Program**
**within a Canadian Rare Disease System, including Rare Disease Centres of Excellence**

## *CORD's June 2022 Conference: Getting It Right!*

In 2019, the federal government announced the commitment of $1 billion over two years (2022-2023) to implement a national Rare Disease Drug Strategy with on-going investment of $500 million annually. The purpose of the CORD June conference was to develop a blueprint for a "made-by-Canadians-for-Canadians" national Rare Disease Drug Program by bringing together the many voices representing all stakeholders who had engaged with CORD in a series of 25 educational forums and deliberations over the past 20 months. We recognized there was much to be learned from international experts and approaches but there was no single "best practice" that Canada could adopt or even just adapt. Importantly, we had come to agreement on three core building blocks for implementing a Canadian rare drug system that would be "fit for purpose" for today's and tomorrow's innovative therapies.

1. **Invest in a rare disease infrastructure built around a Network of Rare Disease Centres of Excellence,** that can serve as the "hubs" for other sites to assure every rare disease patient has access to timely diagnosis, specialist care, individualized best drug access, comprehensive care close to home, enrollment in patient registry, and participation in real world data collection.
2. **Invest in alternative pathways for drug access** that can be customized to the specific requirements of each rare condition and therapeutic option to provide affordable, consistent and sustainable access for all patients regardless of where they live in Canada. Overall, the drug system must meet the triple goal of:
    a. patients receiving affordable and timely access to individualized best therapy;
    b. healthcare systems and public and private drug plans are able to reasonably predict and manage health and drug budgets to achieve an optimal return on health resources while meeting the needs of the population and individuals.
    c. Researchers and manufacturers must experience adequate incentives to invest in rare disease drug research and achieve also return on investment through the distribution of therapies to patients. The ROI must be sufficient to sustain the developers but also motivate new R&D.
3. **Patients must be fully engaged as partners throughout the drug program**, including the level of individual decision making on therapeutic options, design and delivery of healthcare and drug-related services, regulatory and health technology assessment, pathways for access (criteria for managed access plans), and patient information management (including patient registries and real-world data collection and use).

To these ends, the June conference participants worked with the concepts of **SMART systems** that built on existing infrastructure and expertise but were designed as agile, continuous learning models using SMART technology that could adapt to different circumstances and evolving health technologies. and deliberated on each of these core elements separately and their integration.

**What Health Canada Got Right … and Not**

**Proposed Draft Framework for National Strategy**

In April 2022, Health Canada released a proposed draft framework which opened with a restatement of "what was heard" and proposed investment in four strategic pillars

1. Improve access to rare disease treatments and make it consistent across Canada
2. Optimize, collect, and use evidence that meets the needs of decision-makers along the pharmaceutical management continuum and across the lifecycle of the drug
3. Support optimal patient outcomes and sustainability of the Canadian health care system by ensuring spending on drugs for rare diseases brings value for money
4. Strengthen alignment of research and innovation systems with drugs for rare diseases access objectives

Health Canada proposed an iterative approach to implementation that specified several elements, the first of which was unforeseen and not included in any previous consultations. Please see **Appendix C for a summary of the federal government's proposal** including drug coverage, governance, evidence generation infrastructure.

### *Building on Canadian Infrastructure and Expertise: SMART Rare Disease Program*

On March 9-10, 2020 (just before the COVID shut down) participants at CORD's annual Rare Disease Day Conference laid out the pillars for a Rare Disease System built around **(1) Centres of Excellence to assure timely diagnosis and comprehensive care and (2) a Rare Disease Drug System built around "managed access" programs** to facilitate earliest possible access to innovative therapies.

**Working SMART together:** The mostly in-person conference with extended participation through a virtual platform brought together 150 participants providing perspectives and expertise from all sectors. The sessions were designed to gain consensus on a Canadian Rare Disease infrastructure and Rare Disease Drug access strategies and specifically to:

- **Share Canadian expertise and best practices toward building Canada's Rare Disease Centres of Excellence, including:**
  - Newborn screening and next-generation testing toward timely diagnosis
  - Rare disease specialty centres and networks
  - Patient registries
  - MICYRN Pediatric network for collaboration on research and clinical trials
  - Children's Healthcare Canada network of children's hospitals and service providers
  - Additional topics:
- **Learn from International Rare Disease Centres of Excellence**
  - WHO-RDI Global Rare Disease Networks
  - USA Rare Disease Research Institute
  - USA NORD Rare Disease Centers of Excellence
- **Consider Essential Role of Rare Disease Centres for Drug Management**
- **Opportunities and challenges for Canadian patient access to rare disease drugs**

- **How to build on momentum to meeting goal of Canadian government commitment to improving access by investment in Canada's Rare Disease Drug Program**
  - National vision
  - Opportunities from research community
  - Opportunities from industry
  - Quebec Rare Disease Drug Strategy
  - Role of Centres of Excellence in advancing rare disease research

## *Why a SMART Rare Disease System for SMART Rare Disease Drug Program*

Based on the consultations to date, CORD is proposing the following to set up a SMART RD Drug Program. (Please **see Appendix D for a detailed summary of the SMART essential elements)**

- **SMART Goal:** Every patient gets a diagnosis and specialist referral in as short a time as possible and is prescribed a course of treatment based on best practice guidelines specific to the individual patient profile
- **SMART Infrastructure:** Rare Disease Centres of Excellence
- SMART design and functioning with Interconnected centralized specialty hubs for diagnosis, consultation, and training and spokes for comprehensive care, allied services, and localized patient management
- **SMART technology** for real-time connection of sites, health (patient) data sharing, and analyses, and practice guidelines
- **SMART learning**: Real-time analytics, feedback for individual patient management, updating of practice guidelines, and revision to access criteria
- **SMART patient/public engagement:** Engagement, education, training, and support of patients, families, patient associations throughout the patient journey and healthcare system
- **SMART adaptive pathways for access:**
  - Multiple pathways that are adaptable and "fit for purpose" to specific disease and drug scenarios, models and templates with access and monitoring criteria, integration of patient outcome measures, and review process
  - Overarching and disease-specific steering and advisory groups including healthcare professionals and patient representatives to design pathways, monitor pathways, and update pathways
  - Capacity to collect and analyze real-world data to generate useful real-world evidence for real-time improvements in access

## *Solutions to Optimal Drug Access Require Optimal Rare Disease Health Care Delivery System*

A rare disease drug program that meets the three goals of:

1) **individual patient-centred access to the best medicine;**
2) **optimal health and drug system resource allocation; and**

3) **industry return on current and future innovation research** must be premised on a system of comprehensive integrated health and social services coordinated through Rare Disease Centres of Excellence and Speciality Networks.

The financing of rare diseases must be optimized to meet needs and take advantage of opportunities. These must be available through appropriate public investments, financing mechanisms to pool all sources of funding (federal, provincial/territorial funders, private providers, and industry), innovative financing schemes matched to patient needs, and drug potential for outcomes and cost effectiveness.

The governance structure must include all stakeholders, including patients and patient groups.

Innovative drug access pathways to match the opportunities of innovative therapies and the challenges of small patient populations must be core components of the Canadian Rare Disease Drug Program. Please see Appendix E for a summary of the recommended Innovative approaches for building a RD Program.

### *Patients as Partners*

To meet the triple goals for patient timely access to best medicines, optimal resource allocation for health systems, and innovation incentives for industry, patients must be meaningfully engaged as partners throughout Canada's Rare Disease System and Canada's Rare Disease Drug Program. The SMART way forward in designing and operating the Rare Disease Drug Program is to empower all public, private and patient stakeholders to be engaged as partners, each with responsibility for appropriate use, management, and resource allocation. To those ends, the patients must be appropriately trained and resourced to assume meaningful roles at every level, from individual use to top-level governance and decision-making. The National Organization for Rare Disorders (NORD) in the United States and the European Organization for Rare Diseases (EURORDIS) n Europe, are recognized and resourced to participate as effective and vital partners that not only ensure patient expertise at every level from the individual and family to the European Rare Disease Reference Networks Centres and the Centres of Excellence in the USA. Similarly, Rare Diseases International work as important partners with the World Health Organization and the United Nations in advancing policies and best practices at the global level.

The Canadian Organization for Rare Disorders should be engaged and resourced to serve as partners in the Rare Disease System and the Rare Disease Drug Program, representing but also engaging the entire patient community, including the disease-specific patient organizations and Centres of Excellence.

### *Next Steps for the Rare Disease Community*

CORD will engage all stakeholders in another series of collaborative consultations with the objectives of developing specific proposals for the implementation of Canada's Rare Disease Drug Strategy. These will be presented in iterative stages to Health Canada and the provincial governments for feedback and refinement.

## APPENDIX A – Work to date

Over the past two years, even as Health Canada has focused on the pandemic, we have been heartened by the government's repeated reinforced of its commitment to the rare disease drug strategy. However, we were stressed by the lack of visible action. To ensure we are ready for 2022, in October 2020, the Canadian Organization for Rare Disorders launched a nation-wide multi-stakeholder consultation that grew to consist of 25 strategic dialogues and two virtual conferences and culminated on June 8-9, 2022 with a two-day "face-to-face" conference to reinforce the consensus that had developed over the 20 months of meetings.

The sense that we were achieving multi-stakeholder alignment was reinforced by Health Canada's feedback in the July 2021 "What We Heard from Canadians", which picked up on the key themes:

- What we heard . . . about improving access to rare-disease treatments and making it consistent across Canada: Where someone lives should not make a difference in their access to treatment.
- What we heard . . . about getting the best possible evidence for decisions on drugs for rare diseases: Because of the small numbers of people with rare diseases, meeting the usual standard of evidence for drug approvals is rarely possible. Many participants said rare-disease drugs need to be assessed differently than drugs for common diseases.
- What we heard . . . about balancing spending on drugs for rare diseases and keeping Canadian health care sustainable overall: Many people felt the emphasis on the high-cost of drugs overlooked their value for patients, the health system and society as a whole…In considering options, most people felt better cost-sharing and pooling of risks was the best approach….Some felt the federal government could reinsure drug plans, by paying costs for drugs over a specified dollar threshold….Other ideas raised included pay for performance (where governments fund drugs based on how well the product works),…
- What we heard . . . from Indigenous partners: What impact the national strategy would have on Indigenous health programs in place now was a concern for participants, as there are agreements between Indigenous and other governments on funding and delivering health services.

**Next steps identified that were important to participants included:**

- Working closely with provinces, territories, Indigenous partners and stakeholders to develop a coordinated strategy that get patients the effective treatments they need.
- Establishing common definitions of "rare diseases" and "high-cost drugs" and better guidelines for what constitute "benefits" and "improvements" for assessing rare-disease treatments.
- Researching best practices in other jurisdictions including France, Germany, the U.K. and Australia.
- Ensuring Canada's regulatory approach, drug pricing landscape, and research and innovation capacity are conducive for rare-disease drugs.
- Considering how to support patients more holistically, including screening, testing and diagnostics.

## APPENDIX B - Background and Need for the RD Strategy

### What We Need to Get Right

**Case Example 1:** Michael, diagnosed with atypical hemolytic uremic syndrome (aHUS), a rare disorder that destroys red blood cells, had suffered failure of two kidney transplants. In 20Health Canada approved the first treatment for aHUS, CADTH recommended "not to reimburse" Soliris, the first approved therapy, citing "insufficient evidence" of clinical and cost effectiveness. Three years later, the public drug plans agreed to provide access but excluded aHUS patients who needed a transplant, which set up Michael's "Catch-22." His surgeon would not transplant unless Michael was stabilized on Soliris, but he could not get Soliris if he needed a transplant. Through assiduous dialysis 40 hours a week, Michael stayed alive and through relentless advocacy, he finally got approved for pre-treatment Soliris. Michael got his transplant 15 years after the first failed attempt. But under the current drug program, his access to Soliris has to be re-approved every six month.

**Case Example 2:** Madi was only 12 years old when she launched her campaign for access to Kalydeco, the first targeted cystic fibrosis therapy that restored lung function and prolonged life for 4% of the patients. But Canadian drug plans were slow to fund, and Madi, who had been waiting for this therapy since she was six-years-old, couldn't wait any longer. She fought, and she succeeded. So, seven years later, when Trikafta, the combination therapy that was effective for 90% of the patients was approved in the USA but not in Canada, she and her mom were back on the front lines.

**Case Example 3:** Ever since her daughter was diagnosed with spinal muscular atrophy, a progressive neuromuscular disorder, Susi had been on the front lines providing awareness and support to other families but all the time keeping one eye on an emerging first-ever drug that could slow or even stop progressive loss of function. She led the families in advocating for access but when the initial reimbursement criteria were released, her own daughter was excluded. Five years later, there was another chance when CADTH accepted a submission for adult SMA patients based on real-world evidence that had been successful in countries. but in the end, CADTH rejected the evidence as insufficient. Today, only Quebec is making Spinraza available to adults with SMA on a case-by-case basis.

## APPENDIX C – Federal Governance Proposal

**Drug Coverage**

Through the strategy, the federal government proposed it could work with partners and payers to improving accessibility of rare disease drugs by supporting coverage for select drugs of common concern. This initial list of drugs could form the basis to work toward a formulary for drugs for rare diseases.

Example activities proposed were:

- Establishing an initial set of drugs for rare diseases
- Adopting common principles and developing a decision-making framework to assess and manage a formulary of Drugs for Rare Diseases
- Conducting horizon scanning and planning for the pipeline of rare disease drugs

**Governance**

To ensure national consistency, decision-making and advisory structures would need to be in place to manage and improve the list of select drugs and evidence generation activities overtime.

Example activities proposed were:

- Building fit-for-purpose advisory committee(s) and working groups that include a range of partners and stakeholder groups (e.g., patients, NGOs, industry, clinicians)
- Exploring the feasibility of sustainable and innovative cost-sharing/risk-sharing models with multiple payers
- Building relationships with international partners and networks, and fostering information sharing among health system partners

**Evidence generation infrastructure**

Invest in infrastructure that could support evidence generation to improve drug coverage decision-making over time and across the drug lifecycle. This could include investment in real-world data and evidence activities (e.g., creation or adaptation of patient registries), support for a data framework / data standards, and where needed data-sharing agreements. Investments could also support improved knowledge of rare diseases and drugs for rare diseases and patient outcomes.

Example activities proposed were:

- Developing a data governance framework
- Creating a plan for a future national data system, including assessing, piloting, and enhancing existing databases and patient registries
- Engaging with Indigenous Peoples for input and collaboration on governance and infrastructure requirements, including data governance

## APPENDIX D – SMART Program Elements

### Essentials of A SMART Rare Disease Health System

**SMART Patient Outcomes**

- Every person at risk for a rare disease will have access to testing, a timely diagnosis, and timely referral to a specialist in a Centre of Excellence
- Every person with a rare disorder will be provided with on-going knowledge and support to engage as an effective partner in making decisions about and managing his/her health care. Every patient diagnosed will be enrolled in a patient registry, usually through a CoE or specialty program. Each person will partner in developing a comprehensive care and treatment plan based on best practice guidelines that includes access to the best medicines, necessary medical equipment, related health and social services, and connection to a patient support group.
- Patients prescribed a therapy will participate in on-going monitoring and support programs to collect "real-world" data on outcomes measures, including biological, clinical, and quality of life, including benefits and adverse effects. Data shall be collected from various sources including patient experiences, healthcare provider reports, and (digital) technology feedback. Aggregation and transformation of data from all sources on individual, patient cohort, and population basis will be critical to generate evidence that can be summarized, interpreted, and analyzed to learn, among other things, validation of expected findings, long-term impacts, additional uses, future research, and potential value of the interventions. To these ends, AI (artificial intelligence) is a potential powerful and valuable tool to transforming data (for example, clinician notes or electronic health records) into useable evidence.

**SMART Patient Registries**

- Not just a repository of patient information but dynamic data resource serving multiple functions for diverse stakeholders, for example:
- Improve knowledge of natural history of condition
- Enable and support clinical trials by providing patient participants, outcome and performance indicators, post-trial monitoring data, and follow-up experiences.
- Define, support, and evaluate standards of care including appropriate access to treatment
- Track and demonstrate impact of therapies and interventions on patient outcomes and health care utilization
- Functional, flexible and feasible patient registries
    - Canadian Hemophilia Registry, since 1988, is providing data on inherited bleeding disorders community through 40 years of changes in therapies and care management supporting continuous improvement and patient engagement
    - CHEO-led INFORM RARE disease registries, co-created with patient groups, will collect long-term real-world data on impact of therapeutic interventions, currently for three populations: SMA, MPS, PKU.

- NORD's IAMRARE provides a cutting-edge, cloud-based registry platform that is mobile-friendly, secure and easy for patient associations to use to engage members and to promote research and therapeutic development

**SMART Approach to Ending the Diagnostic Odyssey**

- Newborn screening has improved significantly in the past decade but is still not standardized across the country, with no national directives and discretional provincial testing ranging from 18 in BC and Quebec to 22 in the Maritimes and Alberta to over 30 in Ontario and Saskatchewan to 40 in Manitoba. Despite years of advocacy, there is no national process for nominating and approving additional NBS. There are also no standard guidelines for reporting findings to HCPS and patients nor mandated and monitored follow-up procedures for positive tests. Good news: in lieu of federal initiatives and funding, the provincial NBS programs are collaborating toward shared information, best practices, and learning.
- Through six implementation projects across Canada, Genome Canada's "All for One" initiative will increase equitable and timely access to accurate, genomics-enabled clinical diagnosis for Canadians with serious genetic diseases, thus helping to end the diagnostic odyssey for Canadians with rare conditions.

**SMART Approach to Creating Canada's Network of Rare Disease Centres of Excellence: Far Behind and Yet Far Ahead of the Curve**

WHO Global Network of Rare Disease Centres of Excellence is envisioned as a "Network of Networks" that enables people living with a rare disease - no matter where they live - to reach a network of expertise to access appropriate knowledge, diagnosis, and care. Following characteristics have been proposed:

- Designated Single or Multi-Centers as National Hubs, mandated to strengthen health systems competency in RD
- Hubs of Expert Centres & Patient Organisations to connect with healthcare systems under a "hub and spoke" model to support strengthening of local systems in rare diseases.

In the USA, the Children's National Rare Disease Institute at the Research & Innovation Campus provides a new, state-of-the-art home for clinical genetic and specialty services, offering a wide array of services to make top-quality genetic care more convenient and accessible to families in and around the Washington, D.C., metropolitan area.

Additionally, the National Organization for Rare Disorders (NORD) has designated 31 NORD Rare Disease Centers of Excellence across the United States, establishing a unique network of medical centers, clinics, and institutions to reduce time to diagnosis and improve availability and coordination of multi-specialty clinical care. These Centers of Excellence will collaborate to develop new care guidelines, improve medical and family education, create safe and effective referral pathways, and innovate around new treatments, therapies, and research.

In Canada, Centres of Expertise and National Networks of Excellence provide a framework for creating a network with designated Rare Disease Centres of Excellence. These include the following entities.

Canadian Rare Disease Specialty Programs: specifically,

- Inherited Metabolic Diseases Program and Network -
- Ottawa Pediatric Bone Health Research Group and The Canadian Consortium for Children's Bone Health/Canadian Alliance for Rare Disorders of the Skeleton - Leanne Ward, CHEO
- Canadian Neuromuscular Network, Western University - Craig Campbell, LHSC Ottawa

The **Maternal Infant Child and Youth Research Network** (MICYRN) is a federal not-for-profit, charitable organization founded in 2006 to build capacity for high-quality applied health research. It now links 21 maternal and child health research organizations based at academic health centres in Canada; is affiliated with more than 20 practice-based research networks. MICYRN is unique in the world for this type of collaborative engagement that enables the sharing of innovations and reduces duplication of effort and resource use.

- *MICYRN's Clinical Trials Consortium increases access to high-quality clinical trials supported by an efficient, safe, and family-centered national infrastructure. It is working to develop a collaborative national infrastructure in Canada to support clinical investigations, with an emphasis on multicentre clinical trials. The consortium will identify common processes that could benefit from being harmonized across institutions, and develop tactical approaches to realize shared efficiencies and best practices.*
- *The Quality Improvement and Metrics Initiative can improve timeliness, feasibility, and number of academic- and industry-sponsored pediatric clinical trials in Canada. It can assure high quality data, support negotiation of master agreements for protocol and research ethics approvals, and offer coverage to Canadian sites that were unable to acquire the necessary insurance to participate in international investigator-initiated grant-funded trials.*

Children's Healthcare Canada is a national association including all 15 children's hospitals, as well as community hospitals, rehabilitation/children's development centres, and home care, respite and palliative care organizations. Activities around four strategic priorities:

- Inform the development of **innovative and integrated health systems**
- ***Share evidence and accelerate implementation*** *of high-quality child-, youth-, and family-centred healthcare wherever it is delivered.*
- ***Unite strategic partners*** *to foster excellence in children's health*
- ***Advocate*** *to improve children's health and health systems*

Moreover, pediatric hospitals are already linked and collaborating within a province and in some regions across provinces and territories. Some are specifically linked to adult rare disease programs and community programs of care and support.

**SMART Approach to Real-World Data Management and Evidence Generation**

Canada needs to invest in a data Infrastructure for patient management and real-world evidence generation that incorporates the following elements.

- Data sources: patient registries, electronic health records (physician and hospital), pharmacy, patient support programs, patient self-report)

- Data sharing and analysis
- AI technology for enhancing and transforming data to monitor and manage prescribing, uptake, patient outcomes and system impact.

## How Developing a Rare Disease System is Essential to Optimal Functioning of a Rare Disease Drug Program

**Issue 1:** Determining which diseases to include in rare disease system and drug program

World Health Organization, in collaboration with Rare Diseases International, is expanding on core "definition" of rare disease with context-specific operational "description" of rare diseases specific to challenges arising from rarity, burden of disease, and actions to address unmet patient needs.

In Canada, there is no official definition of rare disease or orphan drug but there are references to rare disease and orphan drugs in many contexts that accords specific provisions to rare conditions. While Health Canada does not have distinct legislation or regulations for rare disease drugs, it recognizes orphan designations by the US FDA and European Medicines Agency, identifies a rare disease as a "life-threatening, seriously debilitating or serious and chronic condition affecting a fairly small number of patients", and provides tools and resources to drug sponsors including:

- Advice on clinical trials for small populations
- Accelerated (priority) review pathways
- Special access programs
- Fee mitigation options
- Use of foreign reviews and third-party data
- Use of international guidance documents through International Council for Harmonisation of Technical Requirements Pharmaceuticals for Human Use (ICH)
- Option for requests for aligned reviews made to Health Canada and the health technology assessment agencies (CADTH and INESSS)
- Using existing and new real-world evidence to support regulatory decision-making across a drug's life cycle

**Issue 2:** Barriers and potential solutions to access to rare disease drug embedded in patient journey and parallel drug journey

- Barriers along patient journey include lack of awareness of rare disease, screening and diagnosis, access to specialist, comprehensive care and best treatment prescribing, and community care and follow-up.
- Challenges along the drug journey occur in clinical trial execution, regulatory approval, product availability, value assessment and pricing, patient access to specialist for diagnosis and prescribing, process for monitoring and real-world data sharing, outcome/impact assessment, and long-term follow-up and assessment

To address these issues, an optimal drug program must balance three requirements:

- Patient access to individual best therapy
- Health system and drug programs manage resource allocations to optimize societal good
- Industry reimbursement covers current and future R&D investment

## APPENDIX E – Innovative Approaches to setting up a RD Program

**Innovation 1:** Rare drug therapies may have high potential for treating unmet needs of small patient populations but existing data are based on small, short clinical trials creating uncertainty in terms of long-term effectiveness and value. Successful pathways for access are managed entry programs that identify criteria for initial access with biomarker, clinical, and performance indicators for individual continuance and extended population use.

**Innovation 2:** Cell and gene therapies offer the potential of long-term benefits with one-time administration but also a significant one-time price that, in some jurisdictions, have been amortized into periodic payments that can be tied to continued patient response.

**Innovation 3:** Health Canada should renew and enhance Special Access Programs to improve access to products that are currently not authorized for sale in Canada. These should be evaluated on a regular basis and outreach made to manufacturers to encourage regulatory submission for frequently accessed products.

**Innovation 4:** Health Canada with public and private payers should create early or fast-track pathways to allow patients timely access to potentially life-saving or life-altering therapies for patients with rare severe, progressive and/or life-threatening conditions. These therapies should be made available as soon as possible after Notice of Compliance or Notice of Compliance with Conditions.

**Innovation 5:** New therapies that are projected to benefit very small patient numbers and/or with low budget impact (defined) should be made available to the designated patient population without need for health technology assessment. If patient numbers or budget impact exceeds the predefined thresholds, the drug may be reassessed and re-valued.

**Innovation 6:** Patients (and family members if appropriate) should be enrolled in a common. disease-specific patient registry, preferably through a Centre of Excellence or Specialty Network, regardless of where they live or their drug plan provider. Appropriate data regulations and guidelines should be put in place to allow for patient privacy and patient consent/control of data but also sharing of de-identified data as appropriate.

**Innovation 7:** Outcomes relevant to patients should be included as important measures in developing, approving, assessing and monitoring the effectiveness and value of all therapeutic interventions. To that end, patients and patient groups should be meaningfully engaged by all stakeholders in all phases of the drug journey from pre-clinical trials to post-market evaluation.

**Innovation 8:** Rare Disease Drug Program should be governed by an independent transparent board that is inclusive of all stakeholders, including patients and providers. The program shall be evaluated on a regular basis against national and international performance benchmarks to identify best practices and promote continuous improvement.

**Innovation 9:** Canada's Rare Disease Drug Program shall be enshrined in legislation and guaranteed annual funding of a minimum of $500 million, which should be adjusted according to changing needs and new therapies.

**Innovation 10:** Canada's Rare Disease Drug Program should invest in research toward discovery, development, and management of innovative therapies to benefit rare disease patients in Canada and worldwide.