Canada's Drug and
Health Technology Agency

CADTH Drugs for Rare Diseases Registry Funding

Request for Proposal (RFP) — Rare Disease Registry Funding

RFP number: C-2401280

March 27, 2024

1. Introduction

CADTH is seeking proposals from qualified rare disease registry holders to enhance the infrastructure, data quality, and utility of rare disease registries in Canada.

1.1 CADTH Overview

CADTH is Canada's drug and health technology agency. It was established by Canada's federal, provincial, and territorial governments to be a trusted source of independent information and advice for the country's publicly funded health care systems. Health administrators and policy experts rely on CADTH to help inform their decisions about the life cycle management of drugs, devices, and services used to prevent, diagnose, and treat medical conditions. CADTH receives funding from Canada's federal, provincial, and territorial governments, except Quebec.

1.2 Drugs for Rare Diseases Registry Funding Overview

In 2023, the federal government announced up to $1.5 billion over 3 years to support the National Strategy for Drugs for Rare Diseases (DRD Strategy). This funding aims to help increase the affordability and accessibility of drugs for rare diseases. There is increasing awareness and recognition that, especially for rare diseases, for which traditional clinical trials can be limited in answering certain questions, there is a need for innovative approaches to evidence generation that can help inform regulatory, reimbursement, and health technology assessment (HTA) needs. If equipped to produce high-quality evidence, registries have substantial potential to help address evidence gaps and guide health care decision-making.

To this end, CADTH is leading several initiatives to improve the collection and use of evidence to inform health care decision-making related to drugs for rare diseases. In particular, we are undertaking a series of activities to help lay the foundation for improving generation and access to real-world data from rare disease–based registries. This work aims to generate fit-for-purpose, decision-grade, real-world evidence to better address regulatory, HTA, and payer evidence gaps throughout the drug life cycle.

CADTH's scope of activities within the registries portfolio includes:

- **Understanding the rare disease registry landscape.**
  Developing an inventory of existing rare disease registries, reviewing the quality and comprehensiveness of data they collect, and assessing their infrastructure and readiness for regulatory decision-making, HTA, and supporting the life cycle management of drugs.
- **Developing and implementing standards and best practices for registries.**
  Developing standards and reviewing guidelines for rare disease registries to ensure they are fit-for-purpose and can generate high-quality evidence in line with leading best practices. These standards and guidelines will cover the breadth of registry development, including data collection, storage, analysis, governance, and data policies.

- **Facilitating quality improvement initiatives to enhance RWE generation.** Supporting rare disease registries in Canada to enhance their existing infrastructure and capabilities to generate high-quality real-world evidence that can be fit-for-purpose. CADTH is aiming to support a range of rare diseases registries at different stages of maturity and to equip registries to complement existing frameworks for evaluating new and emerging therapies for rare diseases.

2. Request for Proposal Overview

2.1 Funding Opportunity for Registry Quality Improvements

As part of the third activity, facilitating quality improvement initiatives to enhance RWE generation, CADTH is launching an **open call for funding via a Request for Proposals (RFP)** for interested **rare disease registry** applicants.

This time-limited funding opportunity (until March 2025) aims to support rare disease registries to increase capacity to generate higher-quality data. This funding is intended to enhance existing rare disease registries and provide an opportunity to demonstrate their readiness for using registry data to answer anticipatory decision-making questions.

CADTH recognizes that the landscape of rare disease registries is diverse, as registries collect a wide range of data from various participants and diseases. Registries in Canada are also at varying levels of maturity in their development, and we recognize it is not practical to apply a one-size-fits-all approach. Therefore, this funding opportunity is not prescriptive of specific improvements that registries should pursue. Instead, it aims to provide an opportunity for rare disease registries to evaluate their current state and propose targeted and measurable quality improvement initiatives that can accelerate their growth and development. Funding is available to cover 3 improvement domains that reflect the maturity and readiness of registries to support decision-making needs. These domains are not mutually exclusive and were adapted from the European Medicines Agency's Data Quality Framework. They include:

- **Foundational registry developments:** These are quality improvement initiatives aimed at developing and enhancing registry infrastructure to collect, generate, and use data. These foundational elements may include improving and/or developing registry governance, data policies and procedures, and legal policies to support data linkage, among other initiatives. Additionally, it may include assessing the existing gaps or limitations and working toward aligning the registry infrastructure with leading best practices.
- **Data quality enhancements:** These initiatives aim at increasing data quality, such as coverage, reliability, and completeness, and making registry data applicable or relevant to decision-making

needs. These initiatives could include assessing and addressing missing data, errors, or outliers, or mapping data to a common standard.

- **"Fit-for-Purpose" for HTA, regulatory, or payer decision-making:** This domain refers to quality improvement initiatives that aim to enhance skills and systems to answer specific decision-making questions for evaluating drugs for rare diseases. The initiatives may allow registries to test their existing platforms for question-specific needs, demonstrating that they have the readiness, appropriate and relevant data, and established systems to support anticipated evidence needs for decision-making (i.e., being fit-for-purpose). These data outputs or demonstrations should be related to assessing new and emerging therapies in the development pipeline, particularly those nearing immediate or near-term market entry, with a high likelihood of entering Canada in the next 2 to 5 years. This also applies to existing therapies with conditional approval or limited coverage due to uncertain outcomes.

Applicants should note that in parallel to this funding opportunity, CADTH is working with academic collaborators to develop comprehensive rare disease registry standards through a consensus building approach. Although the specific components of the standard (including data and reporting elements) are not likely to change, the relative importance of specific components in the final standards could influence the prioritization of quality metrics and improvement initiatives. CADTH is committed to funding quality and improvement initiatives that are aligned with the future landscape of rare disease registries and real-world evidence needs. We reserve the right to adapt our guidance and funding expectations in response to these developments. This includes the possibility of revising the prioritization of quality metrics and reporting elements and ensuring our approach remains aligned with the evolving landscape of rare disease registries and real-world evidence needs. Our commitment is to enhance registry operations and facilitate greater adoption of registries to inform health care decision-making in Canada.

2.2 Applicant Eligibility

This opportunity is open to both active registries (i.e., those that are currently enrolling and collecting data) and newly established registries (i.e., those that are beginning to build their infrastructure). Priority will be given to active registries; however, new registries that are just beginning to build may apply, should they demonstrate alignment with the RFP objectives, particularly regarding feasibility and showing readiness for impact by the conclusion of the project.

2.2.1 What Is a Rare Disease?

For eligibility, this RFP aligns with the rare disease definitions set out by the European Medicines Agency or the FDA. In recognition of the fact that Canada does not have an official rare disease definition, we will consider registries that address diseases with significant unmet needs beyond these definitions, even if they do not strictly adhere to these international definitions.

2.2.2 What Is a Patient Registry?

As there are multiple definitions and evolving characterizations of registries, for the purposes of this funding opportunity, CADTH will consider the definition of a patient registry by the Agency for Healthcare Research and Quality. According to this definition, a patient registry is "an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves one or more predetermined scientific, clinical, or policy purposes."

2.2.3 Data Collection Requirements

To qualify, registries must collect comprehensive data, including clinical information, health outcomes, treatment information, health resource utilization, and other relevant data from patients and caregivers. Only registries focused on gathering clinical information will be considered. Those aimed at only listing patients for awareness or advocacy purposes do not meet eligibility criteria at this time.

Should a registry be uncertain about its eligibility, please contact registries@cadth.ca.

3. Proposal Submission Guidelines

The application process for the rare disease registry funding is structured as a 2-stage process. Applicants are first required to submit a Letter of Intent, and then, if appropriate, will be invited to submit a full proposal. The full proposal contains 2 separate documents that must be submitted in searchable PDF format. All submissions should be sent to contracts@cadth.ca, with "Registries RFP" in the subject line. Please note that the maximum email size is 20 MB (inclusive of all attachments).

3.1 Proposal Components

Applicants must provide their proposal in 3 separate documents, as follows:

1. **Initial submission of Letter of Intent:** The Letter of Intent serves as a notification to CADTH of the applicant's intention to submit a proposal for funding under the rare disease registry funding program. The Letter of Intent should be submitted by the team lead, and it should be no more than 2 pages. The letter should provide us with a concise summary of the rare disease registry, the main objectives of the work proposed, and an outline of the primary objectives and anticipated quality improvements.
2. Detailed proposal submission:
    a) The **technical proposal** must comply with the following proposal instructions and the evaluation criteria detailed in this RFP. Applicants are instructed to address each requirement in sufficient depth to permit a complete analysis and assessment by the review panel.

b) The **financial proposal** will be assessed to determine its compliance with the proposal instructions and the evaluation criteria detailed in this RFP.

CADTH will provide a Financial Proposal Form (in Excel) to be used by the applicant; refer to the Request for Proposal webpage for more information.

The technical and financial proposals must be completed according to the following specifications.

3.2 Proposal Preparation Instructions

3.2.1 Technical Proposal Preparation Instructions

Each interested applicant is expected to prepare a Proposal and Statement of Work that describes:

- **Registry information:** Include the legal name of the registry, the host institution (if applicable), and the name of the organization that will execute the contract.
- **Overview of the registry:** provide a brief description of the registry, including its purpose, scope, diseases it covers, and the sources of funding used to operate the registry. Briefly outline the technical and organizational infrastructure supporting the registry (e.g., data management systems, software).
- **Team information:** Include details about the lead and coapplicants (i.e., full names, positions, departments, institutions, contact details, weekly hours allocated, roles, and affiliations).
- **Proposed objectives and work plan:** Describe the project scope, objectives, and project management.
- **Alignment with the RFP objectives:** The proposal should clearly demonstrate how its goals and planned activities directly support and contribute to the overarching aims outlined in this RFP.
- **Risk and mitigation strategies:** The proposal should identify the risks associated with the project and proposed mitigation strategies to address the identified risks.
- **Deliverables and schedules:** The applicant should include a table in the proposal that summarizes all project deliverables. This table should include the list of deliverables, expected completion date, and associated costs. Funding recipients are expected to submit a midyear and an end-of-funding performance and financial reporting update. Financial reports may be subject to audit by CADTH or CADTH-appointed auditors.

Format requirements: Please submit your technical proposal in a Word document or PDF using the following format:

- Page size: letter size (21.59 cm x 27.94 cm)
- Font: Arial, 11 pts (no condensed type)
- Numbering included in the bottom right corner of every page
- Graphs, tables, and illustrations may be included, but will count as part of the set page limits

- Format must be a searchable PDF or Word file (prints, photocopies, scans, and faxes will **not** be accepted)
- Maximum of 12 pages

3.2.2 Financial Proposal Instructions

- **Validity**: Proposals submitted in response to this RFP must remain valid for acceptance for 155 calendar days following the proposal submission deadline, as listed in Appendix 4.
- **Updates:** Applicants are advised to check the Request for Proposal webpage regularly for updates. Updates may contain questions and answers, provide additional clarity to the content, revisions to the schedule, or other pertinent information.
- **Language:** Unless stated otherwise, all work and deliverables are to be done in English; CADTH will be responsible should any translation be required.
- **Location:** All work is expected to be performed at the funding awardees' facilities or, as described in the applicant's proposal, **in Canada**.
- **Costs:** No costs incurred in the preparation and submission of the proposal will be paid by CADTH. Refer to Appendix 2 for a list of eligible and ineligible expenses.
- **Term and budget:** Specific funding terms will be provided, with a total budget of approximately $3.3 million until **March 31, 2025**. The budget will not necessarily be distributed equally among all funding recipients. CADTH reserves the right to negotiate technical and financial proposals to ensure an optimal balance of competencies and alignment with priorities.

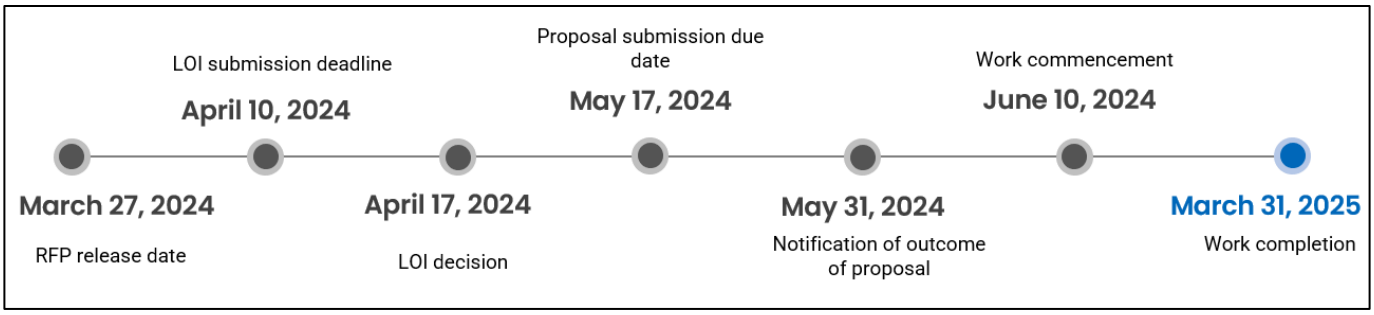
3.2.3 Performance Measures and Reporting

Performance measurement and evaluation are crucial for tracking the project's effectiveness and contributing to CADTH's goals. The applicant must include a plan to provide timely, quarterly performance metrics and data to report on the progress and impact of the registry improvements. Examples of metrics to be considered can be found in Appendix 3.

In addition to providing the performance metrics, registries are required to demonstrate that they have adequate time and resources to meet the stated objectives and deliverables. Registries should also identify potential risks to the project's success and propose appropriate mitigation strategies to address the identified risks, to ensure project objectives can be completed.

4. Application and Funding Process

Figure 1: Key Dates



LOI = Letter of Intent; RFP = Request for Proposals.

For a detailed list of schedules and timelines refer to Appendix 4.

4.1 Submitting Your Application

4.1.1 Submit a Letter of Intent

- **Deadline**: Submit by April 10, 2024.
- **Submission**: All Letters of Intent to be submitted to contracts@cadth.ca.
- **Feedback**: CADTH will review your Letter of Intent, provide acknowledgement, and may request further information, extend an invitation to submit a full proposal, or provide notice of nonconsideration with reasons.
- **Decision**: Provided by April 17, 2024.
- Please note that the maximum email size is 20 MB (inclusive of all attachments).

4.1.2 Enquiries

- **Deadline:** Submit enquiries by April 23, 2024.
- **Submission:** All enquiries can be submitted to contracts@cadth.ca.
- **Bulletins:** CADTH will respond to all enquires and 1 bulletin (collated responses to enquiries) will be posted on the Request for Proposal webpage on April 25, 2024.

4.1.3 Full Proposal Submission

- **Deadline**: Submit by May 17, 2024, for those invited to submit a full proposal.
- **Requirements**: Applicants who are invited to proceed to a full proposal submission must follow the RFP instructions. The following documents will need to be submitted with the full proposal:
  - Technical proposal in searchable PDF format (instead of a scanned PDF)
  - Financial proposal in searchable PDF format (instead of a scanned PDF)

- **Review process**: Proposals will be assessed for compliance with application requirements, relevance to funding priorities and criteria, and overall merit. CADTH will confirm receipt, conduct a review, recommend approval where appropriate, and proceed with the funding agreement.
- **Notification of the outcome of the proposal**: By May 31, 2024.

4.2 After Approval and Signing of Funding Agreement

4.2.1 Implementation and Monitoring

Once a funding agreement has been reached, all deliverables will be specified in the contract.

5. Proposal Evaluation and Selection

CADTH is committed to fostering significant advancements in rare disease registries by supporting initiatives that enhance data quality and ensure the data is fit-for-purpose. Our goal is to prioritize projects that can demonstrate meaningful progress within a 10 month time frame, which aligns with the strategic importance of data quality and applicability.

5.1 Proposal Evaluation Process

CADTH will conduct an administrative review to ensure each submission meets the RFP's section 4 requirements. Submissions that meet these requirements will then be evaluated by a multidisciplinary review panel. This panel may include internal and external experts in rare diseases, real-world evidence, registries, and data standards, and will assess the technical merits of each application.

The review panel will review and score applications based on priorities and technical criteria, with scores being compiled with and discussed at a panel meeting scheduled about 1 week after the applications are distributed to panel members.

CADTH reserves the right to award in its best interest. Submissions with the lowest cost, or any submission, need not necessarily be accepted. CADTH, at its sole discretion, reserves the right not to award this to any applicants. All decisions are final.

5.2 Selection Methodology

Section 2 of this document describes the priority areas for funding. For a more detailed list of possible funding activities, please refer to Appendix 1.

Proposals will be evaluated based on specific criteria, which may be subject to change. Applicants who are shortlisted may be requested to present specific components of their proposal via a video conference meeting with a subset or full review panel as part of the selection process.

- **Feasibility:** The project should demonstrate a clear and realistic plan for initiating the project and achieving measurable progress within a 1-year time frame. This includes a well-defined scope, a detailed work plan with milestones, and a realistic budget that aligns with the project's objectives.
- **Immediate impact:** The proposed initiative should have the potential to quickly improve data quality or make the registry data more applicable and useful for HTA and regulatory decision-making. Proposals should provide evidence or a solid rationale for how the project will achieve immediate improvements.
- **Strategic importance:** The project should align with the strategic goals of advancing rare disease research and improving patient care, particularly in areas where there is an urgent need or significant potential for impact. This could involve filling critical gaps in knowledge, improving data interoperability, enhancing patient outcomes, or supporting the development of innovative treatments. The project's strategic relevance should be well-articulated, demonstrating its contribution to the broader goal of enhancing rare disease research infrastructure.

While we have outlined our primary focus areas and evaluation criteria, we recognize the dynamic nature of rare disease research and the unique challenges and opportunities presented by different registries. Therefore, we remain open to considering innovative proposals that may fall outside these specified areas but demonstrate a strong potential for impact. The final prioritization of funding will depend on the quality and potential of the submissions received.

We encourage applicants to clearly articulate how their project aligns with the priority areas, RFP objectives, and evaluation criteria specified, providing specific examples where possible.

Appendix 1: Examples of Registry Improvement Initiatives for Funding Consideration

The following table outlines the potential applications of funding for rare disease registry improvements. Each domain includes several categories with potential funding uses, designed to support comprehensive registry development and maintenance. Funding activities will vary based on the existing maturity and infrastructure of your registry.

Table 1: Examples of Potential Registry Improvement Initiatives

Foundational registry developments	Data quality enhancements and/or improvements	Ensuring the registry is "fit-for-purpose" for health technology assessments, regulatory decision-making, or payer outcomes evaluations
Description		
Initiatives to improve the procedures and systems for generating, collecting, storing, processing, standardizing, and providing access to data	Initiatives to improve the overall quality of the data in the registry	Initiatives to enhance the ability to answer specific questions to evaluate new and emerging therapies
Examples of objectives or activities that might be considered for funding		
• Enhance registry governance structure • Develop or enhance data governance policies • Improve representativity to ensure the registry reflects the full spectrum of disease characteristics • Develop or enhance standard operating procedures • Develop or enhance standardized consent and data collection forms • Develop or enhance training for registry staff, data providers, and new users • Develop or enhance the data quality assurance plan • Develop or enhance secure data sharing and access policies for research and nonresearch (e.g.,	• Ensure adherence to standardized national and/or international terminologies and classifications for diseases, symptoms, interventions, and outcomes in the registry • Enhance completeness (e.g., missing values) and coverage of data • Enhance coherence (e.g., allowable values) of data • Enhance processes for data validation and cleaning to identify and address errors and inconsistencies • Develop or enhance comprehensive data dictionaries • Establish or enhance a core dataset based on justified common data elements,	For new and emerging therapies in the development pipeline or those with a high likelihood of entering Canada in the next 2 to 5 years, or for existing therapies with conditional approval or limited coverage because of high uncertainty of outcomes: • Develop or enhance longitudinal data collection to enhance understanding of disease progression and treatment outcomes • Enhance relevance and alignment of registry data elements with evidence from clinical trials to assess the real-world safety and effectiveness of health technologies • Enhance interoperability to facilitate sharing and/or linkage to data from other sources (e.g., clinical trials, electronic health records, administrative databases) to generate comprehensive evidence for pre- and postmarket decision-making

Foundational registry developments	Data quality enhancements and/or improvements	Ensuring the registry is "fit-for-purpose" for health technology assessments, regulatory decision-making, or payer outcomes evaluations
regulatory, health technology assessment) purposes • Develop or enhance policies and procedures to support data linkage	aligning with national and/or international standards	

Appendix 2: Expenses

Eligible

1. Stipends, honorariums, salaries, and benefits.
2. General office and administration, including institution overhead, to a maximum of 25%. Please note that institution overhead above 25% must be justified in the proposal, will be considered during the proposal review process, and may be subject to negotiation as the agreement is finalized. This expense category includes, but is not limited to:

    a) equipment, IT, support services, data retention, and software licenses beyond what is typically provided by the host institution

    b) costs for equipment maintenance and service contracts, training of staff operating equipment and/or software, and extended warranty for equipment limited to the life of the agreement.

Ineligible

1. Discretionary severance or separation packages.
2. Benefits for trainees.
3. Any project costs that are funded, will be funded, or will be reimbursed by any third party, ministry agency, or organization of a federal, provincial, or territorial government.
4. Travel costs other than on an exception basis and with pre-approval by CADTH.

Appendix 3: Performance Measures

Performance measurement and evaluation are crucial for tracking the project's effectiveness and contributing to CADTH's goals. The applicant must include a plan to provide timely, quarterly performance metrics and data to report on the progress and impact of the registry improvements. To facilitate a standardized reporting process, we will provide a form for the submission of these metrics and data.

To guide applicants, the following metrics are provided as **examples** for consideration. Please note that these are not exhaustive, and we reserve the right to update or refine these metrics as necessary.

Table 2: Performance Measure Examples

Foundational registry developments	Data quality enhancements and/or improvements	Ensuring the registry is "fit-for-purpose" for health technology assessments, regulatory decision-making, or payer outcomes evaluations
• Improvement in the consent rate and time to patient consent • Reduction of the consent withdrawal rate • Expansion of the number of patients included in the registry • Increase in collaborations with health care providers, patients, and other stakeholders in registry activities • Creation of new or updated policies (e.g., governance, data privacy, security, data sharing)	• Number of engagement initiatives to improve completeness and coverage of data • Percentage increase in completeness of data elements • Reduction in inconsistencies or discrepancies in data values; track the percentage of data entries flagged before and after the implementation of enhanced validation and cleaning procedures • Increase in collaborations with key stakeholders to inform the establishment or revision of the core dataset	• Number of new or revised data elements to enhance relevance and alignment of registry data elements with evidence from clinical trials • Number of data linkages established: the total number of successful linkages made between the registry data and other data sources • Number of analyses or reports generated from registry data contributing to regulatory or health technology assessment submissions

Appendix 4: Request for Proposal Schedule and Timelines

Table 3: Timelines and Key Milestones

Item	Description	Date
1	RFP information session	March 14, 2024
2	RFP release	March 27, 2024
3	Letter of Intent deadline; send to contracts@cadth.ca	April 10, 2024
4	CADTH's feedback to Letters of Intent	April 17, 2024
5	Enquiry submissions deadline (i.e., questions related to the RFP)	April 23, 2024
6	CADTH to issue bulletin (collated responses to enquiries)	April 25, 2024
7	Proposal submission due date	May 17, 2024
8	Notification of outcome of proposal	May 31, 2024
9	Work commencement	June 10, 2024
10	Work completion	March 31, 2025

RFP = request for proposal.