CADTH

CADTH Post-Market Drug Evaluation Proposal

Program Overview

January 2022

CADTH

Table of Contents

CADTH

Abbreviations

CIHR	Canadian Institutes of Health Research
DSEN	Drug Safety and Effectiveness Network
FPT	federal, provincial, and territorial
ISKM	Implementation Support and Knowledge Mobilization
PCHO	pan-Canadian health organization
PMDE	post-marketing (or post-market) drug evaluation
RFP	request for proposal
SO	Standing Offer

1. Background

The Drug Safety and Effectiveness Network (DSEN) was established by the Canadian Institutes of Health Research (CIHR) and Health Canada in 2009 for federal, provincial, and territorial (FPT) decision-makers to fill gaps in information on the safety and effectiveness of drugs used in real-world settings, and to increase Canada's capacity to undertake high-quality post-market research. As the pharmaceutical landscape continues to evolve rapidly, the importance of this work continues to grow.

Following an independent evaluation of DSEN in 2019, Health Canada and CIHR announced their intentions to move forward with transitioning DSEN's functions from CIHR to CADTH given its ongoing work with FPT decision-makers, CADTH's ability to support work through contracts and grants, and its integration with the pharmaceutical system in Canada.

In September 2022, CADTH will launch the Post-Market Drug Evaluation (PMDE) Program, creating a network that will leverage Canada's expert applied researchers, methodologists, and data analysts to help meet the PMDE needs of decision-makers. This PMDE Program Overview will provide the guidelines for building this innovative and dynamic network.

Building upon the successes and foundational work of the previous DSEN program and all its research teams, collaborators, and partners, CADTH will lean on its deep knowledge of the pharmaceutical life cycle and its longstanding relationships with FPT decision-makers to reimagine the program.

1.1 Purpose

The PMDE Program's purpose is to respond, with credible and timely evidence, to queries from senior health care decision-makers situated within the FPT governments related to post-market drug safety and effectiveness.

As the health care needs of Canada's population continue to evolve, the requirement for appropriate access to safe, effective, and clinically relevant drugs has become an increasingly important goal for health systems. In addition, the regulatory review system continues to be more agile, clinical development has been accelerated, and the resultant data and evidence provided are progressively more complex. With this innovation and advancement, products may be introduced to market with greater uncertainty of long-term and real-world effectiveness. This new reality requires a more responsive and systemic approach to ensuring the safety and effectiveness of drug products. These are but some of the demands on Canada's current health care system and illustrate the need for a robust, coordinated PMDE system.

The program outlined within this overview will be responsive and collaborative in its approach to PMDE in order to address some of the many health care needs of Canada's population.

1.2 Goals

With this in mind, the goals of the new PMDE Program are to:

1. enhance the pan-Canadian, post-marketing query response capability and capacity by creating an efficient and responsive network of applied researchers, methodologists, and data analysts able to meet the needs of decision-makers using approaches that are appropriate and provide the right balance of methodological rigour and timeliness
2. coordinate access to post-market drug information and data by facilitating communication, awareness, and linkages between applied researchers, methodologists, data analysts, data holders, stakeholders, and decision-makers
3. enable the uptake and utilization (knowledge mobilization and implementation) of post-market evidence and information to inform decision-making through a centralized approach
4. create a culture of continuous quality improvement of the query process and timeliness
5. foster national and international PMDE partnerships to identify and streamline processes for improved post-market evaluation.

CADTH acknowledges that meeting these goals will require a willingness to learn and adapt. These learnings and a commitment to being responsive and transformative will ensure the PMDE Program is a trusted and valued service.

1.3 Principles

The following are the principles upon which the program and the network will operate:

- customer-needs focus (see Section 2.1 for a list of PMDE customers)
- timeliness
- relevance
- quality and rigour of evidence
- collaboration.

1.4 Priorities

As the pace of change in health care continues to accelerate, the need for a more timely, informed, and integrated PMDE Program has become even greater. As an integral part of the drug life cycle, CADTH is well-positioned for developing such a program as it is well-informed (through various channels; see Appendix A for more information) on the current health care climate, as well as the evidence and information needs of the system. The PMDE Program, like CADTH, is also designed to respond to rapidly changing expectations, shifting jurisdictional priorities, and ongoing unmet evidentiary needs. The PMDE Operations Centre will act as a coordination hub that will continuously collect input from decision-makers and will continually adapt the priorities of the program.

The PMDE Program's priorities have been informed through key informant interviews and dialogue with a broad range of experts, health partners, and FPT decision-makers. Through these valued exchanges, the following were identified as areas of importance:

- development of an easy to use, responsive, and timely query response process

- targeted rapid analyses and evidence reviews to provide insight on utilization and uptake of therapies across therapeutic areas, and by indication, by jurisdiction, and across the country
- support for formulary management and harmonization across Canada, including guidance and insight from other jurisdictions
- more integrated and accessible data to generate evidence to support decision-making
- prospective observational studies to support, reinforce, and, if necessary, reassess reimbursement decisions based on real-world data
- improved, sustained, and targeted knowledge translation and mobilization efforts to better use the evidence produced through the network, and to expand its potential impact and benefit
- monitoring and reporting on the pharmaceutical pipeline and changes to the pharmaceutical landscape to better position jurisdictions to proactively address impending health system issues
- relevant appraisal of the evolving pharmaceutical landscape, including the emergence of new therapies and methods.

2. PMDE Program

PMDE is a new CADTH program that offers query-based services to its customers: health care decision-makers situated within the FPT governments and select arm's length organizations. The program will be a core service offered by CADTH and, as with all other CADTH activities, will report to the Conference of Deputy Ministers of Health through its Board of Directors.

2.1 Customers

PMDE customers will submit queries through the PMDE Program, which will then use a network of experts to provide evidence to support customers in their decision-making.

PMDE customers include:

- Health Canada
- federal drug programs
- the Public Health Agency of Canada (or PHAC)
- provincial and territorial decision-makers
- Institute national d'excellence en santé et en services sociaux (or INESSS)
- the pan-Canadian Pharmaceutical Alliance (or pCPA)
- the Patented Medicine Prices Review Board (or PMPRB)

Additionally, given CADTH's existing position in the drug review and approval system, it may have knowledge and foresight of drug products being submitted for regulatory and health technology assessment. In some instances, CADTH may be able to anticipate evidence needs of FPT decision-makers, consult them, and submit queries to the PMDE Program on their behalf.

CADTH will regularly evaluate the PMDE Program and may consider adding new customers who would also be eligible to submit queries to the program.

2.2 PMDE Operations Centre

The PMDE Operations Centre is dedicated team situated within CADTH. The responsibilities of the Operations Centre include:

- query intake and initial refinement with the customer
- identification and selection of the ideal query response team and coordinating collaboration of partners and contractors within the network
- conducting a feasibility assessment of the query to ensure the required data, systems, and expertise are available, and identifying additional expert advice and guidance as needed
- facilitating the scoping and refinement of queries with the customer and the query response team, connecting both for discussions as often as needed
- overseeing the query response process and adjusting the process as required
- ensuring timely dissemination of query reports and all findings to submitters and all other FPT decision-makers

- facilitating connections to additional support, including CIHR's Strategy for Patient Oriented Research and Health Data Research Network, and CADTH's in-house expertise such as its patient engagement, Implementation Support and Knowledge Mobilization (ISKM), Real-World Evidence, Scientific Advice, and Pharmaceutical Review teams.

The PMDE Operations Centre will not generate evidence itself to support queries, nor will it access or hold data. It will act as a hub, connecting people and processes, and will work collaboratively to maximize the efficiency of the network, including, for example, working with health partners to identify and access relevant evidence.

2.2.1 CADTH PMDE Operations Team

The CADTH PMDE team is led by the director and together this team is responsible for the design and implementation of the program, conducting feasibility assessments, managing the scoping and refinement of incoming queries, providing oversight of the network and its partners and collaborators, and reporting on the network's performance and outputs. The team members will be an important point of connection with CADTH's many programs, services, and people.

During the transition period, additional resources will be added to the team to ensure operational readiness before launch and full capacity at the time of launch in September 2022.

2.2.2 PMDE Advisory Panel

The PMDE Advisory Panel is a multi-disciplinary group that will provide advice regarding the PMDE Program, such as guidance and interpretation of pharmaceutical trends and impacts on the PMDE Program, including current and emerging methods; identification of specialized expertise to fill methodological or subject matter gaps; and assisting with the assessment of proposed responses to complex, likely atypical, types of queries.

The membership of the Advisory Panel will include decision-makers, senior applied researchers, methodologists and/or analysts, patients and/or caregivers, and PMDE Operations Centre staff. Its size and composition will reflect the program's commitment to be nimble, to be operationally responsive to changes in the pharmaceutical environment, and to position CADTH to enable future-ready health care by responding to the evidence needs of decision-makers. PMDE Core Network Partners and contractors will be invited as needed to discuss queries.

For more information on the Advisory Panel, refer to the *PMDE Advisory Panel Terms of Reference* (available March 2022).

2.3 PMDE Network

The network will consist of both Core Network Partners and Standing Offer (SO) Contractors. These will be identified and selected through a Request for Proposal (RFP) to create a robust and complementary group of teams and experts who bring diverse methodological expertise, data management capabilities, and both willingness and capacity to work within the parameters of the PMDE Program. Core Network Partners will be selected through a competitive process that will include review of proposals by an ad hoc review panel. For more information on eligibility and the process for submitting proposals for a PMDE Core Network Grant or SO Contract, refer to the *PMDE RFP document* (available for

grants on February 1, 2022, and for SO Contractors on March 1, 2022). All unsuccessful applicants will be eligible to resubmit in subsequent RFPs.

2.3.1 Core Network Partners and Standing Offer Contractors

Researchers, data analysts, methodologists, and other experts interested in PMDE and wanting to become a Core Network Partner or SO Contractor for the PMDE network will be required to submit a proposal. The proposals received will be reviewed by an ad hoc selection panel.

Applicants to the PMDE Program may apply as either:

- a Core Network Partner
- an SO Contractor.

Core Network Partners are teams of applied researchers, methodologists, and/or data analysts who are an established existing or newly created team (see more on expertise in the following section). Core Network Partners will be awarded a 3-year grant and will make up the foundational components of the PMDE network. These teams will be working either individually or collaboratively with other Core Network Partners and/or contractors to use the most appropriate methods and provide evidence to decision-makers. Appropriate teams will be identified by the PMDE Operations Centre to respond to each query, and at times the Operations Centre staff may bring several Core Network Partners together to discuss potential collaboration on a specific query. Core Network Partners will be responsible for ensuring their teams have the capacity and the appropriate methodological expertise to respond to incoming queries throughout the granting period. The number of queries each Core Network Partner will respond to may vary from year to year; however, each grant will identify the minimum requirements, along with the maximum number of queries. If a Core Network Partner has capacity and can respond to additional queries above and beyond the expectations set in the grant agreement, the team may be eligible to receive additional funds in the form of one-time contract(s). Network partner leads (or a designate) will be required to attend PMDE Advisory Panel meetings when the panel is discussing queries for which the network partner is responding to.

SO Contractors have specific technical, methodological, or related expertise (generally from the methods described in the following section), and will be awarded 1-year contracts with the potential for up to 2 1-year renewals. SO Contractors will also be part of the PMDE Network and will be kept appraised of incoming queries within their expertise by the PMDE Operations Centre. SO Contracts will draw down available funding in their contract similar to a retainer and will be invited to respond to a minimum number of queries during the contract period. SO Contractors but may be called upon to attend PMDE Advisory Panel meetings to discuss queries they are responding to.

The methodological and content expertise being asked of Core Network Partners and SO Contractors may evolve over time. The PMDE Operations Centre will continually monitor relevant therapeutic trends and innovative methods and seek out experts in those fields. The PMDE Program will also leverage early learnings through CADTH's access to pharmaceutical pipeline trends and clinical development programs to identify new incoming methodologies.

As Canada's health system continues to evolve, so does the Core Network Partner methodological expertise required to respond to the needs of decision-makers. Applied research teams should be multi-disciplinary with resources and capacity in conducting rapid analyses and reviews across multiple data sources. Some teams should have the capacity to conduct both meta-analysis and network meta-analysis for safety and effectiveness outcome measures. As formulary management is a priority, expertise in real-world drug safety and effectiveness analyses, and drug utilization and statistical analyses is preferred. There will be continued emphasis on the future needs of the health system and entry of new drugs so there will be need for expertise in establishing and conducting prospective cohort studies of drug safety and effectiveness, and experience in current and novel analytic methods to study these data. Given that the PMDE Program is focused on both safety and effectiveness, capacity and expertise in both areas will be required. Specifically, with respect to effectiveness, teams may be asked to evaluate and validate clinical end points, and to assess and report on broad effectiveness topics. For example, where utilization of a drug is intended to reduce broader health care utilization and/or hospitalizations, teams may be asked to validate whether these system savings and patient experience improvements can be demonstrated in real-world settings. Prospective Core Network Partners will have the opportunity to expand on these topics and propose areas of activity beyond those described in this document that will help the PMDE Program meet its objectives.

No single team is expected to have methodological expertise in all these areas, but collectively, the network will include a varied and rich source of skill and capability to allow both safety and effectiveness queries to be answered in a timely, robust, and scientifically rigorous manner.

For more information on grant and contract duration, refer to the RFP (for grants, available February 1, 2022; for SO Contracts, available March 1, 2022). Partners will be eligible to reapply for funding at the end of their funding cycles when RFPs are launched, and interested potential new partners and contractors are also encouraged to apply.

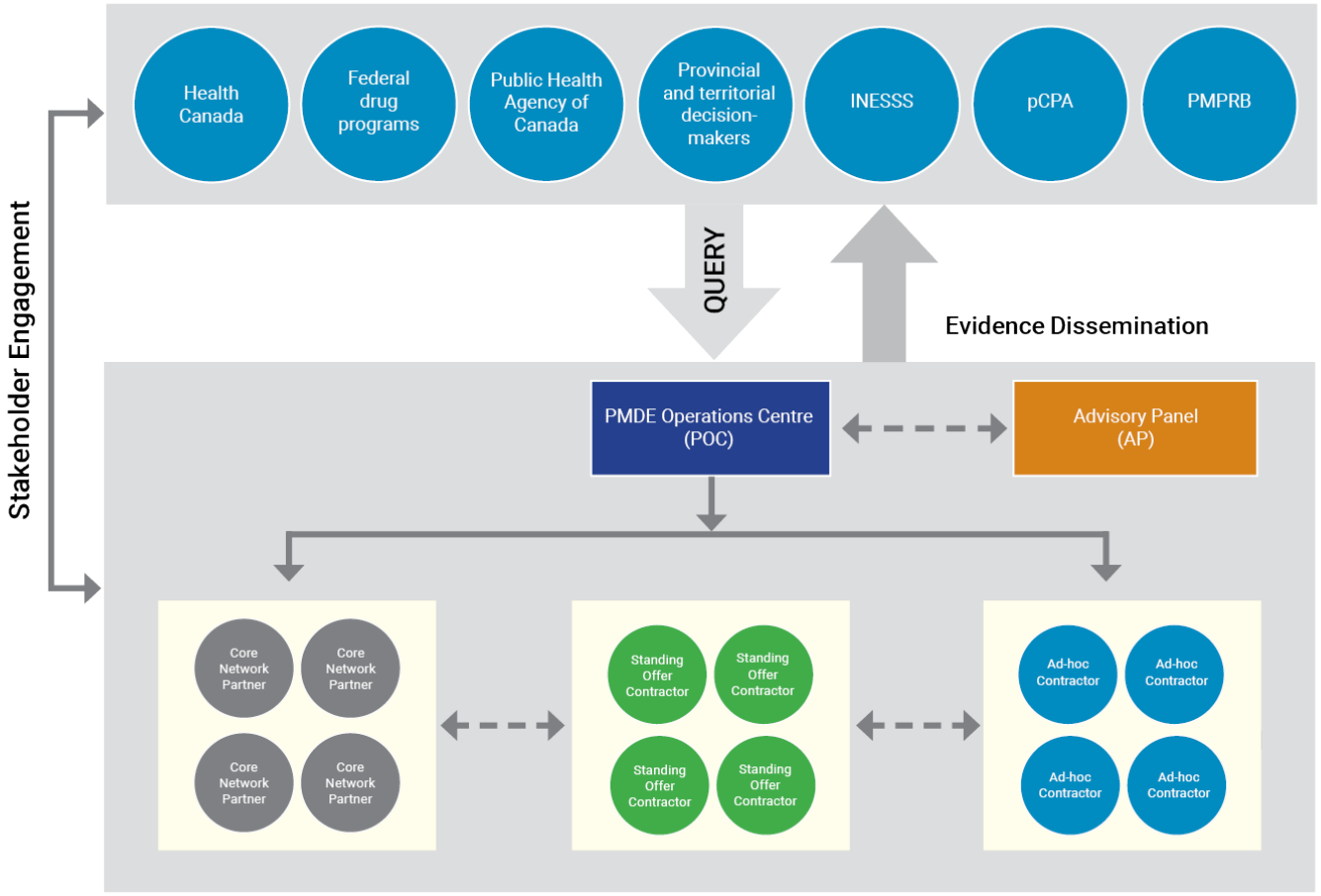
2.3.2 Ad Hoc Contracts

If complex queries or queries requiring additional expertise outside of the network, the Operations Centre, with input from PMDE Advisory Panel as needed, may elect to retain ad hoc contractors. Also, when evidence demands are high, the Operations Centre may issue additional ad hoc contracts to augment existing network capacity. The program will specifically consider leveraging early career researchers, including those that are granted by CIHR's Health Research Training Grant to continue developing capacity in the post-market evaluation space. The ad hoc contractors needed will be identified from the network of applied researchers, methodologists, and analysts established by CADTH, as well as those referenced by the Core Network Partners.

Ad hoc contractors are encouraged to consider responding to future RFPs for Core Network Partners or SO Contractors as they continue to gain experience and familiarity, and interest in the PMDE network.

2.4 Network Structure

Figure 1: Post-Marketing Drug Evaluation Network Structure



INESSS = Institute national d'excellence en santé et en services sociaux; pCPA = pan-Canadian Pharmaceutical Alliance; PMDE = Post-Market Drug Evaluation; PMRB = Patented Medicine Prices Review Board.

2.5 Partnerships and Collaboration

With support from the PMDE Operations Centre, the Core Network Partners and contractors will be encouraged to leverage existing pan-Canadian relationships and other Canadian data and real-world evidence organizations. The PMDE Program within CADTH will work to become a coordination hub that identifies data needs for queries coming from decision-makers and collaborates with groups aware of data sources (e.g., Health Data Research Network Canada) and those that hold data (e.g., Canadian Institute for Health Information, Statistics Canada, research groups, PMDE network teams).

Data partners will facilitate access to data and improve connectivity to data networks. Data partners may include:

- the Canadian Institute for Health Information
- Statistics Canada
- the Health Data Research Network Canada
- provincially funded research groups.

Other partnerships that may bring additional expertise and perspective may include:

- Institute national d'excellence en santé et en services sociaux
- clinicians and clinical societies or networks
- patient, caregiver, or community organizations
- other relevant partners and collaborators.

The PMDE Program strives to leverage CADTH's existing relationships with pan-Canadian Health Organizations (PCHOs), when possible, to improve the efficiency of existing data resources and capabilities. CADTH's reach within this network of PCHOs will also extend the range and potential uptake for dissemination of findings produced by the PMDE network. Many decision-makers within the health care system will have similar policy issue priorities and improved access to evidence between PCHOs will benefit many.

The PMDE Network Partners and SO Contractors should also strive to engage with CIHR's Health Research Training Grant Program and its grantees to continue building capacity in PMDE and developing early career researchers and analysts. Additionally, the PMDE network and CIHR's Health Research Training Platform (HRTP) program will meet at the annual PMDE meeting, held in conjunction with the CADTH Symposium, to discuss emerging trends, methods, or other related issues within the pharmaceutical sector.

Where possible, collaboration between the network and industry (pharmaceutical and private insurers) will be encouraged to allow for more coordinated generation and dissemination of PMDE used to inform reimbursement, reassessment, and decision-making.

2.5.1 International Partnerships and Collaborations

When appropriate, PMDE work may benefit from leveraging international relationships. International partnerships and collaborations may expand data access, methodological expertise, and so forth. International partners may include, but are not limited to:

- ENCePP, the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance, in France
- the SIGMA Consortium in Europe
- Sentinel in the US
- OHDSI, Observational Health Data Sciences and Informatics, in the US.

International collaborators are not eligible to receive funding from the PMDE Program and any collaborative activities will follow the terms and conditions outlined by Health Canada and CADTH.

2.6 Stakeholder Engagement

2.6.1 Patient and Caregiver Engagement

As CADTH is dedicated to including the patient lived experience in its work, Core Network Partners and SO Contractors will be asked to indicate their experience and ability to engage patient and/or caregiver participation in requests routinely and/or as needed. Examples may include patients on project steering committees and working groups, as members of research teams providing expert review or consultation, or as knowledge brokers, providing insights on and connections with specific, affected communities. Patients might be involved in identifying research questions, outcomes of relevance, analyses of findings, report reviews, and as conference co-presenters. Teams may also incorporate existing evidence regarding the patient experience on a specific issue related to a query, or consider patient priorities as identified by patient-facing organizations. For additional insights into CADTH's approach to patient engagement, please refer to the patient engagement framework. Integrating relevant guidance from other organizations — including, notably, CIHR's Strategy for Patient Oriented Research — is recommended.

The PMDE Operations Centre and CADTH's existing patient engagement team are available to the network to support and facilitate patient engagement throughout the query process. The PMDE Program acknowledges that some urgent rapid queries may not allow sufficient time to engage with patients; however, the program will strive for a centralized process of patient engagement activities for queries with longer timelines.

Additionally, the PMDE Advisory Panel membership includes patient and/or caregiver members who will bring the patients' perspective to the program and specific queries as they are discussed. Patient involvement on PMDE Advisory Panel supports public accountability and transparency and helps ensure that the queries undertaken are relevant to patients concerns. Patient members can champion participant-friendly research networks and grow connections with peer networks and difficult-to-reach patient communities.

2.6.2 Clinician Engagement

Core Network Partners and contractors will also be asked to describe the feasibility of and their ability to engage with clinicians in carrying out query work and also to report back on any specific clinician engagement that occurs in the course of responding to any given query.

The CADTH PMDE team may assist network partners and contractors in leveraging its existing network of clinicians for large or complex queries.

3. Queries

3.1 Prioritization

The Operations Centre will maintain a dynamic list of priorities based on FPT requests identified through CADTH's ISKM function, its various committees, and its Horizon Scanning program, reflective of novel therapeutics and disruptive technologies, new methods, and evolving pharmaceutical needs (see Appendix A for more information). These priorities will be conveyed to the PMDE network and will allow for proactive approaches and inform prioritization of queries if the volume of queries is beyond the capacity of the network at any given time.

In addition, PMDE will leverage CADTH's existing position in the health care system and its relationships with Health Canada to work toward a more systematic approach to signalling potential safety and effectiveness issues flagged at the time of issuing a Notice of Compliance or reassessing Notice of Compliances with conditions to inform proactive short- or long-term queries. Collaborative relationships with pharmaceutical manufacturers will also inform the network of incoming therapeutics, methodologies, and potential health policy priorities.

To respond to decision-making needs throughout the drug life cycle, the PMDE Operations Centre will collaborate with FPT partners and the pan-Canadian Pharmaceutical Alliance to facilitate bringing forward relevant queries. The FPTs may benefit from both reactive and proactive queries as they relate to more urgent developing policy issues, as well as more strategic, proactive queries to improve formulary management. Decision-makers, either individually or collectively, may benefit from more rapid analysis to support reimbursement conditions and/or decisions, and may also look to longer-term queries as one of the potential sources of evidence used to support their actions.

In the early stages of the program, a prioritization process will be developed and conveyed to the network and to health partners, including decision-makers, with their prior input and guidance. Prioritization will be employed to effectively manage incoming queries and the capacity of the network. CADTH will aim to balance the volume of rapid requests and larger systemic requests to ensure that the most relevant topics can be addressed.

The program will also strive to achieve a balance between queries that are primarily focused on safety and those that are focused on effectiveness. Ultimately, the balance will be dictated by the needs of decision-makers and may be adjusted in response to prioritized needs as they arise, particularly when it comes to safety issues that require timely action.

3.2 Process

The query process can be summarized by the following steps (as displayed in Figure 2):

1. **Query submission** — Decision-makers will be able to submit queries through the CADTH website. Queries may also come through ongoing dialogue within CADTH committees or through the ISKM network. (PMDE customers are listed in Section 2.1.) The PMDE Operations Centre will acknowledge and confirm receipt of queries within 2 working days.
2. **Feasibility assessment** — The PMDE Operations Centre will initiate a feasibility assessment and identify the appropriate network team(s) of applied researchers, methodologists, and data analysts, as well as access to the required data or potential data gaps.
   For complex queries, the Operations Centre may call upon an assessment team with methodological, applied research, and health policy expertise for additional input.
3. **Assembling the query response team** — The Operations Centre will identify a fit-for-purpose network response team for the submitted query. All decisions will be communicated across the PMDE network before calling a meeting of the selected and willing members of the response team, and before work begins to issue contract(s), if needed.
   As the PMDE Program will focus on collaboration, the ideal research team for any given query may be a combination of Core Network Partners and contractors. Individuals and teams will be selected and connected through the Operations Centre to make up a query-specific team based on methodological expertise and data needs. All deliverables and specific accountabilities will be established at the preliminary meeting of the query response team.
   The identified query response team will be given access to a shared folder in CADTH's SharePoint to facilitate sharing of information, templates, reports, and so forth.
4. **Scoping and refinement** — The PMDE Operations Centre will oversee a scoping and refinement process to ensure there is consensus among the query response team and the customer(s) on the following elements:
   - research question(s)
   - intended use of the evidence product
   - timelines, including the query submitters required deadline for the evidence product
   - scope of work
   - capacity of the responding team
   - type of evidence package required
   - research ethics board approval (where needed)
   - confidentiality requirements and level of transparency
   - dissemination and communication plans, and any other relevant information
   - potential follow-up queries
   - publishing.

   Additionally, the responding team will be required to submit a query protocol (Deliverable 1), which will be shared with the query submitter before commencing the following step.

5. **Evidence generation and analysis** — The responding team will generate evidence and analyze existing evidence with the objective to support the decision-making process. The Operations Centre will track progress regularly throughout this stage to ensure query outputs are on schedule. Query submitters will be provided regular updates throughout this step, including sharing of preliminary findings, when possible.

   Deliverables may include:

   - Deliverable 2: Statistical analysis plan to the data partner (if external)
   - Deliverable 3: Statistical analysis report, from the responding team or data partner
   - Deliverable 4: Study report prepared by the responding team (and the data partner, if engaged)

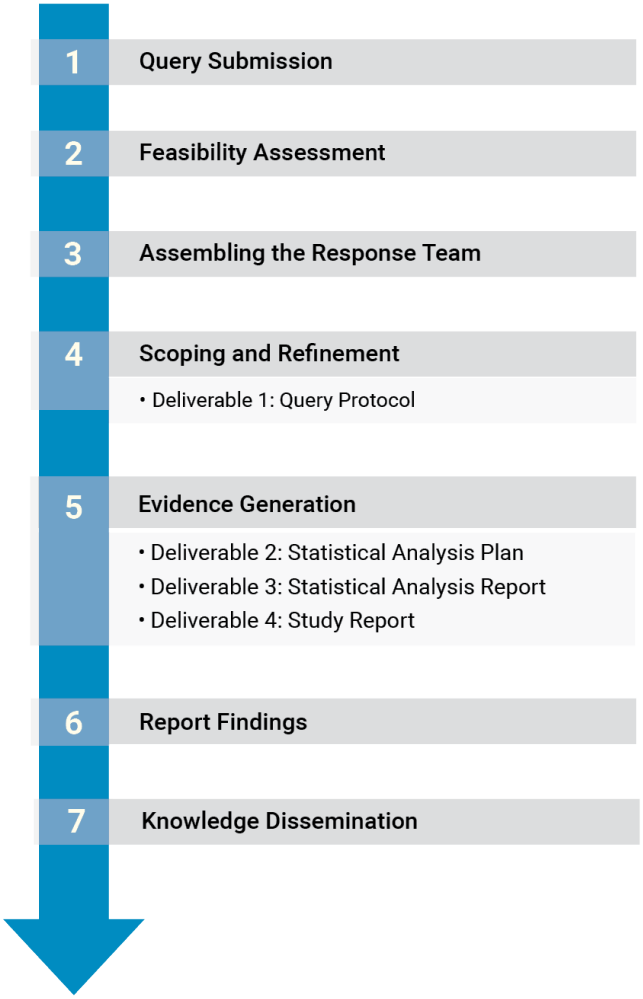
6. **Report Findings** — The responding team will submit a study report to the PMDE team, using PMDE product templates for the various product types. The PMDE Operations Centre will then review and submit the report to the query submitter. Post-query meetings may be held to discuss the submitter's needs in terms of follow-up queries, knowledge dissemination, and so forth.

   With agreement from the query submitter and at CADTH's discretion, PMDE will share reports with other FPT decision-makers.

   6.1 Subsequent queries — At the time of reporting, should additional queries emerge, the PMDE team will work with the responding team and determine if additional resources are needed to respond to the subsequent query. Each new query would be subject to the same feasibility assessment and scoping and refinement process. If found to be necessary, documentation will reflect these considerations to ensure the responding team, Operations team, and query submitter are clear with regards to expectations.

7. **Knowledge dissemination** — Once a report is prepared and validated by the PMDE Operations Centre, the Operations Centre will submit it to the customer and coordinate any follow-up discussions or actions with the query response team, including further dissemination to decision-makers to support decision-making or generation of knowledge translation tools by CADTH's ISKM team. Upon completion of the query report, network partners and contractors are encouraged to publish in peer-reviewed journals and conference proceedings. (For more information, refer to Section 3.4.)

Figure 2: Post-Marketing Drug Evaluation Network Structure Query Process



3.3 Data Management

The PMDE Program is dedicated to fostering a collaborative network focused on ensuring that decision-makers have access to the appropriate information required to make evidence-informed decisions in a timely manner.

As CADTH is not a data holder but acknowledges that data access is a critical success factor in meeting the PMDE Program objectives, the PMDE Operation Centre's mandate will be to support and coordinate the needs of the network by leveraging its relationships with data partners, as well as the data that network researchers bring to it.

Data access management, retention, and sharing will primarily be the responsibility of the network partners and they will be requested to clearly describe their data management plans when responding to the RFP, while upholding any privacy requirements that they must

adhere to. The PMDE network strives to have open access to data but acknowledges that pre-existing privacy barriers may sometimes limit sharing of data. Core Network Partners and contractors shall act in a collaborative manner and will work toward providing access to data for other network partners for the purposes of responding to queries, when possible. The PMDE Operations Centre should be given insight into monitoring and progress of any data collection related to any given query. Data should be retained after query submission to ensure that any follow-up evidence or additional queries can make use of this data. The PMDE team will work collaboratively with the applied research teams and contractors across the entire network to ensure that quality standards and outcomes captured are consistent and harmonized.

While CADTH is not a data holder, nor is it envisioned to become a data holder, it will continue to stay informed of data management and support the alignment work being undertaken toward a pan-Canadian health data strategy.

3.4 Further Dissemination of Findings

The PMDE Program is focused on the needs of the decision-maker and will prioritize query reports and the dissemination of query findings to decision-makers as quickly as possible. Reports must be submitted by the agreed-upon deadline and will be written with customer needs at the forefront, using decision-maker–appropriate language. The Operations Centre will offer templated query protocol, statistical analysis plan, and reports based on the type of query for network researchers to present their findings. While the intent is to always make both the query and query response public through publication or, if warranted, by other means, there may be a delay between sharing the information with decision-makers and making it publicly available, but only under exceptional circumstances. Publishing in an academic journal will not be sufficient justification to delay the public release of findings from a PMDE query.

When appropriate, CADTH will leverage its other programs to offer tools to support the needs of PMDE customers (see Appendix A).

Once customers have received a query report, network partners wanting to publish or present their findings through academic channels may do so, and it may be supported in part by funding received by the PMDE Program. Funding for these types of publications will be established with the PMDE Operations Centre. Priority and emphasis will be placed on publicly facing query reports; however, peer-reviewed publications and the sharing of knowledge at scientific conferences and other venues will be supported, when appropriate. These publications will need to follow the *CADTH PMDE Publication Guide* (available March 2022), which will be discussed in the scoping and refinement stages; they may also be revisited after submitting a report to the customers.

Network-applied researchers, methodologists, and data analysts may wish to publish in the CADTH's journal, the *Canadian Journal of Health Technologies*, to expedite its dissemination and for a more integrated approach.

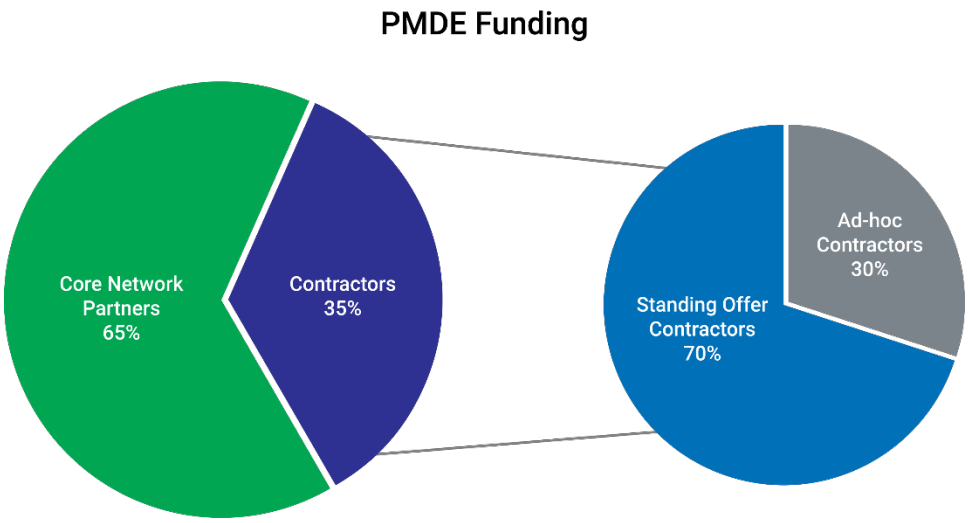
4. Funding Model

To ensure a solid network foundation that is both responsive and dynamic, funding through the PMDE Program will be allocated, as follows:

- 65% to its network partners through grants
- 35% through contracts (70% to SO contractors; 30% to ad hoc contractors).

This allocation takes into consideration the findings of an independent evaluation of the current DSEN model, which determined that contracts would allow the network to be nimbler in accessing expertise outside of the Core Network Partners, as needed, while also maintaining stability with Core Network Partners. This funding distribution is suggested and may be adjusted based on a future evaluation of the funding model, and contingent on the number of proposals received during the RFP process.

Figure 3: Post-Marketing Drug Evaluation Network Funding Model



PMDE = Post-Market Drug Evaluation.

All funds will be issued through CADTH. For more information, please refer to the PMDE RFP documents.

4.1 Core Network Partner Funding

A significant portion (65%) of PMDE funds will be distributed through multi-year grants to Core Network Partners. This funding structure will ensure that Core Network Partners are able to retain analysts, methodologists, and applied researchers and have them at the ready. Funding will also help these partners maintain existing data structures and systems, while simultaneously being responsive to queries, particularly when rapid analysis is needed.

The process by which grants are awarded, and the grantees selected, will be made publicly available.

4.2 Contracts

A portion (35%) of PMDE funds will be distributed through contracts. PMDE will offer 2 types of contracts: SO contracts (70% of contract funds) and ad hoc contracts (30% of contract funds) for queries requiring additional expertise or capacity.

The process by which contracts are awarded, and the contractors selected, will be made publicly available.

5. Network Management

5.1 Network Communication

The PMDE Operations Centre will keep the PMDE network informed of new methodological and data needs, other initiatives in the pharmaceutical environment that may impact work, as well as new or evolving priorities. CADTH and its PMDE Operations Centre may also flag potentially disruptive technologies and changes in the drug approval pipeline to ensure that data collection may be designed accordingly. The PMDE team will work to bring teams together into a collaborative environment to catalyze and foster network collaboration and support innovation through the network. The PMDE Operations Centre will work to accomplish this with regular network communication and is planning to conduct annual network meeting in conjunction with the CADTH Symposium where teams can discuss methods, innovation, and ways to improve collaboration.

5.2 Implementation Support and Knowledge Mobilization

CADTH's ISKM team is embedded in and supports the needs of most provinces and territories, as well as the federal government, and offers a wide range of tailored products and services to support bridging the evidence-to-action gap. The PMDE Program will leverage the experience and expertise of this team, as well as the direct linkages between the decision-makers, to share knowledge across its pan-Canadian customers. The network will continue to use and lead with the knowledge mobilization expertise that it brings and use the dissemination networks at its disposal; however, the CADTH ISKM function may be used as an adjunct or additional resource and can be accessed, as required. The functionality of this knowledge mobilization approach will result in a more comprehensive and strategic dissemination of evidence generated through queries when needed and appropriate.

Knowledge mobilization and implementation-support strategies can be customized to specific queries based on audience identification, context assessment, and input from decision-makers (knowledge users). CADTH's ISKM team can lead or support the development of knowledge mobilization tools (such as plain language summaries, prescribing tools and decision aids, infographics, publications, online resources, and so forth). The team can also provide customized services to create awareness and support the uptake and use of the evidence in health care policy or practice decision-making (such as presentations, webinars, workshops, other mechanisms for convening stakeholders for facilitated discussion of the evidence).

5.3 Reporting and Performance Measurement

The PMDE Program is a new and integral part of CADTH's overall work and, as such, ultimately reports to CADTH's President and CEO. And as with other areas of CADTH's work, PMDE progress and performance measurement reports will be shared with the CADTH Board of Directors and its funders, as appropriate. While the program will be monitored on an ongoing basis, the progress of the program will be included in CADTH's current reporting system.

To ensure program performance, performance data from each query will be collected to demonstrate the impact of the overall program and to inform future iterations of the program.

The Operations Centre will, at minimum, collect the following quantitative data from its network:

- number of queries completed on time (as established at the time of scoping and refinement), as well as any variance between expected and actual completion timelines
- number of partnerships (names and affiliations of all collaborators to be provided)
- percentage of queries with patient input
- cost of each query by type of query
- cost of accessing data external to the network
- number of queries submitted per fiscal year, per customer
- number of customers referencing a query for decision-making or policy change
- percentage of PMDE reports resulting in demonstrated impact in more than one jurisdiction
- percentage of overhead costs
- number of web visits.

The following qualitative data will be collected through surveys, interviews, and other feedback:

- overall satisfaction of the customer (Did the output meet the customer's needs? Were the findings shared in time? Were the findings decision-grade and relevant to the needs of the decision-maker?)
- reports contributing to a policy change or decision-making (Was the report helpful?)
- feedback and qualitative data on using the PMDE Program and network (Was it easy to use?)
- feedback and suggestions from the research teams and contractors
- success and impact stories.

Core Network Partners and SO contractors will be provided with regular feedback.

At the end of the 3-year funding cycle and at regular intervals thereafter, the program will undergo independent program evaluations.

5.4 Equity, Diversity, and Inclusivity

PMDE Core Network Partners and contractors are expected to adhere to their institution's equity, diversity, and inclusion principles (or, if none exist, principles from an equivalent Canadian organization) for all aspects of their work — from hiring to designing query response protocols and reporting results.

5.4.1 Sex- and Gender-Based Analysis Plus

CADTH is committed to performing Sex- and Gender-Based Analysis Plus (SGBA+) as part of its PMDE Program.

Diversity in pre-market research and clinical trials is a well-documented concern. Given the unequal representation of specific populations in research, there may be a considerable gap

in the full understanding of the safety and effectiveness of new pharmaceuticals products in the real world following market authorization.

PMDE Core Network Partners and contractors will be responsible for collecting and analyzing relevant information to contribute to the overall SGBA+ analysis of the network. Of note, as it pertains to any First Nations, Métis and Inuit data, the PMDE Network is required to adhere to any Indigenous Data Sovereignty protocols. More details will be made available in the reporting templates.

5.5 Transparency and Confidentiality

The PMDE Program will strive to be transparent and accessible to all its customers. Whereas some data and evidence may be confidential in nature for a period of time, the intent is to ensure that all query outputs and reports are made available as soon as possible. In the event that a customer requests the response be kept confidential, it will be determined at the initiation phase and be conveyed to the responding team in advance of any work.

5.6 Conflict of Interest

CADTH is a trusted and credible source of evidence and strives to maintain this standard in all its work, including the PMDE Program. Core Network Partners and all contractors are therefore expected to comply fully with CADTH's Conflict of Interest Policy.

Appendix A: PMDE Channels to Decision-Makers

Note that this appendix has not been copy-edited.

- Pharmaceutical Advisory Committee (PAC)
  - Provide strategic direction and identify system-level queries
- Formulary Working Group (FWG) and FWG-health technology assessment (HTA)
  - Identify pharmaceuticals and therapeutic areas that would benefit from post-marketing drug evaluation
  - Stakeholder to receive evidence generated from PMDE network to allow for potential reimbursement change
- Expert Review Committees — CADTH Canadian Drug Expert Committee (CDEC) and CADTH pan-Canadian Oncology Drug Review (pERC)
  - Identify actively reviewed pharmaceuticals that may benefit from proactive pharmaceutical queries
  - Potential trigger for future evidence generation as it relates to conditional recommendations
- Health Canada (Health Products and Food Branch, or HPFB; and Marketed Health Products Directorate, or MHPD)
  - Identify actively reviewed pharmaceuticals that may benefit from proactive pharmaceutical queries
  - Potential for evidence generation as it relates to Notice of Compliance with conditions (or NOC/c)
- Integrated Implementation Support and Knowledge Mobilization (ISKM)
  - Bi-directional information sharing; awareness of evolving health care landscape needs and trends and dissemination of PMDE network evidence
- Board of Directors
  - Input on system-level needs and evaluation of evolving PMDE Program strategy
- Engagement of Patients and Clinicians
  - Opportunity to include patient voice in queries
  - Identify relevant methodological trends and prioritized therapeutic areas within the clinical community; dissemination of evidence generated through PMDE network