Canada's Drug and Health Technology Agency

PMDE Industry Task Force (ITF) Meeting

Meeting Summary and Action Items

November 28, 2023, 8am - 4pm EDT

Facilitator

Don Husereau

Industry Representatives

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1. Welcome

The CADTH President and CEO welcomed everyone. The Facilitator convened the meeting. The Facilitator outlined the meeting agenda, and the meeting schedule.

2. Topic Area 2 – Transparency Recap

Overview of Findings

The Facilitator reviewed the summary highlights from Meeting 2 and the post-Meeting 2 survey findings. The summary highlights are as follows:

- There is a willingness to share data, however there are limits to what sponsors can share, and this will vary on a case-by-case basis.
- Clear objectives, scope, and intended use of data will be critical for sponsors to share data with PMDE.
- Maintaining confidentiality and competitiveness are a concern for unpublished data.
- PMDE should be transparent about industry data, including when data is not shared provided that the rationale is included.

The post-meeting survey findings are as follows:

- There is a willingness to be transparent about industry data sharing and inability to share, rationale included.
- Common limitations to data sharing: data owned by external party, data not helpful (collection not designed for PMDE query), not enough data, PMDE timelines, internal policies/processes, confidentiality/privacy, competitivity/intellectual property/patent.
- Types of data that would be shareable: RWE, CSRs, safety reports, local PSPs, protocols (approved by global
- Other feedback: requestor will need to be transparent about the request, a well-defined process with clear objectives, templates agreed upon, pilot projects.

Discussion

The PMDE query process timeline can vary significantly, from 3 months to 18 months, depending on the needs of the query. The delivery timelines are not self-imposed by the PMDE program, they are requested by the query customers so that they can make decisions in a timely manner. Members indicated there may be challenges to sharing industry data within the query process timeline.

It was asked if there is an opportunity for industry to renegotiate with external data owners about data transfer (aggregate level data), and how difficult this would be to implement moving forward. As Patient Support Program (PSP) data vary significantly between manufacturers, it is difficult to discuss PSP development and standards. For PSPs, at a local level the data may be owned by the manufacturers, however patient consent is still required which is challenging when its retrospective. How the data is captured and the "mineability" of data is also a challenge, this includes data format, the data capture system, data ethics approval, and global approval. However, there is an opportunity to harness this type of data if the conversation is proactive at the onset of data collection; this would mean having conversations now to have data available in years to come. Even with a proactive approach, there will still be challenges gaining approvals and patient consent, but industry is keen to be able to do utilize this data. It was also suggested CADTH have a direct discussion with data registry owners, as industry is generally hands-off these 3rd party data sources. Some manufacturers have attempted to engage PSP registries to collect data for research but received a lot of pushback due to the fact that they may already provide data for another

registry. For PMDE it may be helpful to work with those other registries as they could be better suited for research purposes.

CADTH is currently building an inventory of all data registries and looking at the usability of PSPs. A common sentiment from patients is that they are not interested in being approached multiple times and so CADTH is looking to registries instead. CADTH has been mandated to support registries to ensure registry quality, to go back for patient consent to do research, etc. Being proactive is top of mind to improve the quality of registry data, develop registry standards and infrastructure, and to tie registry data to the drug product pipeline. These conversations must take place before Health Canada authorization, perhaps at the early scientific advice stage. Industry and CADTH need to be mindful of the resources and time required to collect data for research purposes; additional funding is likely required.

There are two possible categories of data: retrospective and prospective. If CADTH approaches industry for retrospective data, it's straightforward in that the data requested will exist or it won't. When it comes to proactive data generation, some thought and discussion is required to determine where in the PMDE process this can occur.

3. PMDE Process

Overview of Current Process

The mandate of the PMDE program is to provide evidence to the Canadian decision-makers and regulators through commissioned Canadian research partners.

CoLab is made up of core network partners (granted) and collaborators (contracts), all teams were selected through a request for proposal (RFP) process and selected by a peer review panel. CoLab teams are Canada based, cannot be for profit entities, typically hosted by an academic institution or research hospital. Industry would not be eligible to be part of CoLab. Currently CoLab is comprised of 4 core network partners, 2 network collaborators and 3 specialty collaborators (additional information available on the CoLab website).

While some CoLab teams have their own data or have their own direct access to data such as jurisdictional administrative data, PMDE has additional data partners such as CIHI, Merative MarketScan, Clinical Practice Research Datalink (CPRD).

The PMDE query process can be broken down into the following steps:

- Query submission (reactive or proactive)
- Scoping and refinement with a topic brief – *2 to 6 weeks.*
- Query response team engagement and feasibility assessment – *2 to 4 weeks.*
- Delivery of draft protocols and plans with a query protocol and statistical analysis plan – *2 to 6 weeks.*
- Evidence generation and analysis – *1 to 18 months depending on study type.*
- Interpretation of evidence and findings with a scientific report – *1 to 2 months.*
- Knowledge dissemination with knowledge mobilization tools
- Follow-up for impact

There are two streams of PMDE queries: proactive and reactive. Where reactive would be where customers organically submit a query to the program and proactive is where PMDE through pipeline evaluation and

horizon scanning would identify potential topics and bring these to the customers to prioritize and identify potential topics.

Discussion

Currently, PMDE is looking to build strategic partnerships with industry to expand the breadth of evidence it is able to deliver in its query reports and to its customers.

It was asked if there are any data partners outside of Canada, and the PMDE program currently has data partners in the US and the UK. There is an openness and willingness from the jurisdictions to look outside of Canadian data to fulfill the needs of the queries when Canadian data is insufficient.

It was asked if reactive queries were aligned with the areas of uncertainty identified through CADTH's reimbursement review and if there would be an opportunity to have a post-reimbursement review meeting to align any data generation plans or registry support plans for future PMDE needs. This would allow industry to be prepared for the queries that will come in future years. CADTH sees this opportunity to have the reimbursement review process include a way to highlight any uncertainties or gaps and flag these for future post-market evaluation. Given that the PMDE program is still in its infancy, there hasn't been an opportunity to pilot this process yet. PMDE keeps track of the highlights from reimbursement reviews, horizon scans, and current drug policy issues to develop proactive queries.

The types of questions of queries submitted to PMDE vary greatly but can include questions around utilization (better understanding of uptake), formulary management, health economics or budget impact analysis, evidence reviews. Jurisdictional customers had become disengaged with the former DSEN program (PMDE predecessor) and so these customers are slowly getting to know and understand the products and services PMDE can deliver. Year 1 of the program was a proof-of-concept period and as query reports are completed and shared, this will hopefully drive up the demand.

PMDE reports are published depending on the confidentiality of the query, with the intent to be as transparent as possible.

The impact of the queries is of great importance to manufacturers, understanding that the program is still in its infancy, and we are waiting to see the impact, having a better understanding of the outcomes will dictate industry's willingness to participate and partner. From the PMDE perspective, when queries come to the program, the questions are typically around a health policy issue and a request for CoLab to find evidence to support this policy decision, the impact for the program would be centered around if the evidence product provided to the customer aided them in making their policy decision, what that decision is would be outside of PMDE; PMDE does not make recommendations. The program does have a performance measurement framework in place to collect data on impact once more queries are completed and used to make decisions.

4. Topic Area 3 – Operational Requirements

How have databases been structured and who has access and ownership?

In Canada, databases are mostly industry sponsored and the manufacturer will have ownership or co-ownership of the protocol. Governance and stewardship typically would be managed by the data holder with the manufacturer providing peer review. Since data holders have limited funding, they will partner with industry but are careful not to appear biased and so they may engage with multiple manufacturers, government, etc. This will also vary for different drugs; different agreements will be in place based on the drug. Internationally, this will differ country by country, in some countries industry ownership is more

common. Industry typically owns the clinical trial results, however there may be challenges to access this data. There is significant variability with the structure of the databases on a case-by-case basis and it will also largely depend on the agreement in place as this will contain clauses around shareability.

When thinking about merging industry data with other data, who would own this data? A collaborative agreement where there's co-ownership would be required but there is willingness to work together for proactive data generation.

In terms of timeliness of accessibility, it can differ greatly, for example, chronic diseases data can be accessed in 1 to 2 weeks and rare disease data can take 1 to 2 years. Larger registries tend to have a lot of governance and procedures in place, while smaller registries can be accessed quicker. It is also anticipated that data access issues will continue to improve in the months and years to come.

In the future, the PMDE program could proactively and collaboratively generate data with industry. Presently, the PMDE program has just undergone a new cycle of proactive queries and would like to engage with industry to know what relevant industry data exists.

How will evidence be shared or transferred between collaborators? Where will the evidence be stored? What are the minimal security and firewall requirements?

The CADTH platform used for drug submission Clinical Study Reports (CSRs) is already vetted from the industry side and would be an obvious and easy way to share data with CADTH. However, CADTH is not a data holder but would be a facilitator for CoLab and industry to be able to share evidence, unless it is easier to share directly with CoLab. For some manufacturers, having CADTH facilitate will not make a difference and CoLab will still need to go through the same level of approvals and vetting. For other manufacturers, if CADTH shares industry provided evidence, CADTH would be responsible, and the manufacturer is not responsible for vetting. The vetting process for most manufacturers is quite onerous and would likely not be possible in PMDE query timelines.

All levels of data need to be stored in a similar manner, with security and firewall requirements. Once the evidence is shared with CADTH, it would be re-shared with the CoLab research team and approvals would need to be in place. While it would be more efficient for there to be coordination between the CoLab research team and the manufacturer for evidence sharing, privacy and security may be challenging. From the industry standpoint, it seemed to be preferrable for CADTH to store industry evidence and provide access to CoLab research teams.

The risk of patient reidentification is a particular challenge in oncology and rare diseases where there aren't many patients. There will always need to be assessment to determine the level of risk.

What would also be helpful to the PMDE program at times is understanding what data/evidence is available and what are the challenges of accessing this data. This information is very helpful when PMDE is conducting a feasibility assessment of the query so that they can go back to the customer to determine if the topic is feasible and may influence the customer's decision to pursue it or not.

In the rare disease space, identification is more probable given the inherent nature of the disease, however some governments are requiring patients to submit data for safety, regulatory or policy making (not academic research). CADTH is looking at drafting consent forms and ways in which it could function as a proxy for the provinces and territories to be able to access data for policy making. Research in this space would also preclude Research Ethics Board (REB) approvals.

Patient consent is an important consideration for evidence sharing. There may be limitations to sharing evidence beyond one research partner. Manufacturers will need to clarify if this is concern for aggregate tables, where the analysis is already completed. There are different considerations of patient consent for different forms of evidence and different therapeutic areas (e.g., rare disease). Receiving any evidence will be beneficial for the PMDE program as it will allow greater understanding to address the needs of a query and share information with the policymaker.

How can the evidence be accessed? Who can access the evidence?

Confidentiality agreements need to be in place with any teams who will be accessing the evidence. If CADTH takes responsibility for evidence sharing, then the process is simplified from the industry side, but CADTH would be responsible for vetting. From the CADTH side, it will take deep thinking to set up a sub-contract to share data with the CoLab research teams, however this may not be required for aggregate data tables. A deeper dive would be necessary for patient level data; however, it is unlikely that CADTH would be looking for this type of data. If an agreement is required for each query, this may not be possible given timelines. However, if CADTH had existing agreements in place that may allow for quick access to aggregate tables.

The CoLab research teams conduct analyses based on the multiple sources of evidence available to answer a query so in many instances, industry data/evidence would be analyzed in conjunction with other data/evidence. All queries are anchored to a health policy question.

How long will it take to establish access to the evidence?

The intent would be to create efficiencies and to be strategic in the PMDE query process. CADTH may be aware of upcoming drug policy questions in certain therapeutic areas, and there could be sufficient time to put in place an agreement to access certain data registries. Legal implications will need to be considered for the agreements being put in place. The query process timeline may create limitations in being able to access the evidence from industry, including aggregate tables. As PMDE query needs and timelines can be quite variable, the process to create an agreement can vary as well. Earlier industry engagement will assist in creating efficiencies in this process.

5. Topic Area 4 – Integrating into the PMDE Process

When in the post-market evaluation process is it possible for industry to be involved? What role would they play?

Industry can be engaged as early as the scoping and refinement process. It would be useful for PMDE to understand what published work exists to prevent duplication of work and industry often does their own data landscaping which they could potentially share with CADTH to reduce duplication. If PMDE flags the query to the relevant manufacturers, it would be beneficial for collaboration between those companies to send joint feedback and any existing published work for the drug. In CADTH's recent RWE pilot project, manufacturers did come together to contribute to this pilot. In order for this to happen, CADTH would need to be the facilitator. There was a suggestion to leverage industry associations such as IMC and BIOTECanada, however not all manufacturers are affiliated with associations, so there could be an issue of competitive advantage. If PMDE queries are drug agnostic, it would make a lot of sense to work collaboratively, and manufacturers seem willing to do so.

CADTH indicated that there may be an opportunity for the ITF to continue on in different iterations to address different issues/questions.

It was suggested that engaging industry about post-market evidence needs at the pre-submission stage for reimbursement reviews would be likely allow for better opportunities to collect evidence of relevance, however industry may have concerns about the impact on the reimbursement process. The purpose of these conversations is to identify data gaps and the needs for real-world evidence for the drug(s). Another suggestion was made to have these conversations post-reimbursement review and it was recommended to include the payors.

Industry also does surveillance work as a part of their process, and this work could be shared since it is publicly available information.

It was asked about identifying uncertainties and data needs at the pre-submission phase, but manufacturers felt that this was a difficult time to have these discussions as the payor is not a part of that meeting. For manufacturers, when investing in pipelines the price tag is quite high, and this can be a challenge to get approval for.

Having a multi-stakeholder forum and being clear about each stakeholder's role is an important aspect of this work. CADTH is working on creating this type of forum within the activities of the Drug Data Services and Analytics team. Of note, CADTH considers patient reported and caregiver reported outcomes for all products and services.

From an industry perspective, what are some of the perceived challenges and potential risks or biases? How can these be mitigated?

There may be perceived challenges from industry entities outside of Canada, such as "global", who may not recognize or be familiar with CADTH. Industry's financial investment in data structure is seen as a risk if it does not yield high-quality real-world data and will also depend on the impact and outcomes of the query. Clear agreed-upon outcomes will be important for this kind of engagement between industry and CADTH.

There was consensus that manufacturers have the right to refuse to participate in CADTH projects for a multitude of reasons, however CADTH will share the refusal and the rationale of the refusal in its reports. It was asked if a manufacturer would be perceived poorly if they refuse to participate and this would depend on the reason for refusing or lack of transparency around the rationale, however there are no repercussions.

It was proposed for the PMDE program be more flexible with the query process timelines as it may impact the manufacturer's ability to participate. The timelines are dictated by the policymakers, however from experience there can be some flexibility if additional data could be available. Manufacturers may also know other entities with published work in the specific therapeutic area and could point CADTH to these sources. It would be helpful for manufacturers to know what the historical challenges are for reimbursement reviews or drug pricing negotiations as the challenges may be similar to the PMDE program. Industry will need to better understand the outcomes and impacts of PMDE work so they can better gauge the risks of engagement.

Can decision-makers post-market data needs be considered during evidence generation processes by industry?

This question was answered during the earlier discussions (above questions).

For the impact of the PMDE program and its queries, a few projects have recently been completed and follow-up with policymakers will take place in the coming months. The PMDE program specifically serves Canadian jurisdictions, however the published reports are on a public platform (CADTH website) and therefore can be used by international entities.

6. Topic Area 5 – Privacy and Intellectual Property

What are the privacy issues to be considered for data sharing and/or using data for purposes outside of the original intent?

Currently, industry may be unable to share PSP data (patient level or aggregate) due to patient consent and global approval issues. For other types of data, the intended use by PMDE must align with what was prespecified at the time of PSP establishment to receive internal approval for data sharing. The internal approval is protocol driven and peer reviewed, and the timeline of this may not fit the PMDE query process. The approvals would also depend on if the data is being analyzed by the CoLab research network, what the data analysis entails, and how critical the PMDE query is for the drug(s) of interest. The methodology of the data analysis would be shared with the manufacturer, or industry data analysts may be involved with the analysis with consultation from the PMDE Scientific Advisor. If the evidence is within the public domain, there are no privacy issues. If industry hires a vendor to do a landscape or horizon analysis, then industry either owns this data or has approval to share this data. Ultimately, the privacy issues would depend on the data source being potentially shared to address the purpose of the PMDE query.

Consideration of patients' rights?

Historically, PSPs have specific statements asking for patient consent, mainly for drug utilization purposes. However, for the future, PSPs may be able to ask for broader patient consent to include for policy research or post-market drug surveillance. For data registries, the patient's rights need to be addressed on a case-by-case basis. Thus far, there has been significant variability in the use of data registries for PMDE queries, depending on the needs of the jurisdictions.

Who holds the IP for the RWE produced? (i.e., co-owned, vs. license to use)

As previously mentioned, there are different circumstances depending on the data source. For co-ownership, all involved parties would have to sign for the ownership including the PMDE program, the manufacturer, and the CoLab research team.

Consideration of publication of findings

As per the PMDE query process, the priority is to produce a scientific report for the policymaker, that is made publicly available on the CADTH website. Once policymakers have used the report, the CoLab teams can publish their work in academic journals. If there is a partnership, such as between PMDE and INESSS, the scientific report is published on both websites at the same time. The goal is to prevent any delay in providing the report to decision makers.

It was asked if the manufacturer would be listed as an author in the PMDE scientific report. If yes, the manufacturer would have a review process of the report. PMDE would acknowledge any authors contributing to the content of the scientific report. If the policymaker indicates not to publish the report, as the evidence provided is confidential, the CoLab research team would adhere to this.

7. Closing Remarks

Members were asked for their feedback about the meeting. It was suggested to prepare for the January meeting Topic Area 6: Collaborative Data Generation for post-market evaluation and decision-making.

Any additional input can be sent to Nadine and all documents can be accessed by ITF members through the SharePoint site.

The PMDE team is considering another in-person meeting in March 2024 to finalize the summary report.

Action item: PMDE staff to share the Meeting 3 Summary and Meeting 4 pre-meeting questions.
Action Item: Members are to fill out Meeting 3 Survey ahead of meeting 4.

Adjournment

Meeting was adjourned at 4:00pm EDT. Next meeting will be January 16, 2024 (virtual).