CADTH

# Consultation Questions for the Proposed Alignment of CADTH Drug Reimbursement Review Processes

## COMMUNICATIONS FOR DRUG REIMBURSEMENT REVIEWS

Does your organization agree with the proposal to streamline communications for CADTH's drug reimbursement reviews?

## PREAMBLE

It is important to note from the outset the proposed alignment of CADTH process does not address the most critical imminent issue and that is the impact and implications of the PMPRB regulatory changes and guidelines, namely, the usurping of the role of setting maximum reimbursed prices by the PMPRB based on pharmacoeconomic factors, drawing primarily on CADTH reviews of incremental cost effectiveness ratios ($/QALY) and cost-utility ratio (relative to other healthcare expenditures).

How will this aligned process (with Health Canada regulatory reviews) also align with PMPRB price-setting process?

The Canadian Organization for Rare Disorders (CORD), as the umbrella organization for 100-plus rare disease organizations in Canada, we are extremely distressed that the first time we heard about the proposed changes was at the time of the public announcement and we received the document of the proposed processes at the same time as the general public. This represents a big step backwards in the consultative relationship between CADTH and key patient stakeholders. In a previous lifetime, key patient stakeholder organizations participated in a two-way consultative process through the CADTH Community Liaison Forum. We had not only more timely communications but also the opportunity to influence content, presentation, process, and timing communications to assure the needs of the patient community were addressed.

The newly formed Patient and Community Advisory Committee "c*omprises of individuals with lived experience with the Canadian health care system and who are familiar with issues in health care in Canada."* Most of the members do not have experience in soliciting submitting patient input and indeed are not deemed to represent a broader constituency. Each may draw upon his/her personal experience to advise CADTH but as a committee cannot fulfil the role of informed, transparent mutually valuable exchange between the agency and the patient community, especially with respect to input to submissions and beyond. .

With respect to streamlined communications, this is going in the wrong direction for us as a customer/consumer community. CORD serves a large number and variety of patient groups and diseases; what would we really need is early, targeted communications rather than bundled nonspecific communications. We do not have dedicated personnel for CADTH activities nor do we have in-house (or easy access to external) expertise across the many conditions and therapies. For many of our patient groups, making a submission to CADTH will be a new experience. There has not been any training or orientation support from CADTH for years, so often it has fallen to CORD to take groups through the process, often with very limited time to prepare. We do not have the capacity to monitor and read through all CADTH communications to determine if there may be something that is relevant to our extensive patient community.

With highly sophisticated technology available, it would be very easy to tag items with key words and to push the appropriate information to the appropriate users. It may be easier for CADTH to push out a single email and to have everything on one portal (though that may be a good idea) but it is not a good user experience to have to search through the entire document for items of

relevance. Think of us as valued customers. Set up user-friendly services like “Google feeds” or even better have built in AI so the information pushed out is based on our user history.

Do you or your organization have any suggestions for improving CADTH’s drug reimbursement reviews communications?

In terms of improvement in communications, the patient community needs to be notified about a potential application as early as possible. Preferably, we (patient groups) should be informed when CADTH receives the 30-day advance notification in order to prepare to participate, as discussed above.

**CADTH REPORTS AND RECOMMENDATIONS**

Does your organization have any suggestions for improving the clarity and consistency of CADTH clinical and pharmacoeconomic reports?

The clinical and pharmacoeconomic reports should contain all of the necessary data and detailed assessment, evaluation, and analyses for the patient (public) to conduct independent review to replicate or validate the CADTH results and to return an evidence-based assessment as to agreement or deviation from the CADTH conclusions and recommendations. There should be minimal or no redactions

Does your organization have any suggestions for improving the clarity and consistency of CADTH recommendations?

There should be as much transparency as possible as to how the submitted information was reviewed. What information was considered as especially important by the committee? What information was challenged or has less weight? How did deliberations take place and were there key points of agreement and contention? The public should be confident that the deliberation took into consideration all of the relevant information, was fair, balanced and unbiased, all perspectives were equitably considered, and the process for deliberation and arriving at a final recommendation followed a systematic process. The best way of achieving this is to have open meetings where all stakeholders can view the deliberations, albeit the voting on recommendations may be confidential. Any documentations or presentations made to the review committee along with a transcript or video recording of proceedings should be made available the public (similar to NICE or ICER).

When and where CADTH’s interpretation and/or conclusions based on clinical data (from original or subsequent clinical trials and/or real-world data), there should be sufficient justification of the differences to support CADTH’s position. Collaborating evidence or expert opinion based on experience should be provided to allow the public to decide as to the merit. Where evidence from clinical trials or other sources are deemed by CADTH as insufficient (for example, based on clinical trial design), these judgements should be substantiated (by other references) or justified (based on other experience).

There should be clear documentation as to the “frame of reference” used by the review committee in performing the cost-effectiveness and cost-utility analyses, e.g., public healthcare system, public drug plan) and the assumptions made in determine cost-effectiveness or cost utility (alternative therapy, short-term benefits, long-term expected benefits, use in a managed care program). There should be clear delimitation as to the appropriate use of the CEA/CUA (e.g., application to a private drug plan without the offsets of a public health benefit).

The CEA/CUA should include confidence levels. How certain were all of the estimates that were used in the assessments and analyses. What is the certainty that the estimates of measures, specifically patient outcomes, reflect all of the measures relevant to patients and are a reliable estimate of the benefits and risks? In many situations with high uncertainty, a sensitivity analysis should be conducted and the information provided for potential re-assessment. An ICER with a high uncertainty may have very different utility from one that is highly certain. It would also be

important to include enough data to justify pharmacoeconomic analyses conducted by CADTH that differed materially from the PE submitted by the company? Were there differences in the evidence used, the extent to the benefits were calculate, the estimated costs, or other factors. How do all of these affect the PE?

How could the final recommendation document be improved? Is there content that should be added, removed, or presented in a different way?

The overall report should be intelligible to a lay audience while also including all of the technical information (in separate sections) for validation of the recommendations. A meeting with all stakeholders to discuss the draft recommendations would be extremely useful and at the very least sharing of the feedback from all stakeholders prior to the final recommendation.

**HANDLING OF CONFIDENTIAL INFORMATION**

Does your organization support increased transparency in CADTH's reports and recommendations?

This was answered in previous section. Increased transparency is very important; indeed, the rule of thumb should be as much as possible, including open sessions leading up to the reports and recommendations.

Does your organization have any comments or concerns related to CADTH's proposal for information that would be considered disclosable by CADTH?

All of the proposed information should be available.

Does your organization have any comments or concerns related to CADTH's proposed process for redacting confidential information from CADTH documents?

Redacting should be minimal, especially since CADTH is not subject to "Access to Information" as are other public serving agencies.

**PROCEDURAL REVIEW**

Are there any areas within the proposed procedural review process for drug reimbursement reviews that CADTH should address in order to strengthen the proposal?

Please identify and comment on any ambiguities in the proposed procedural review process steps and conditions.

**ELIGIBILITY FOR DRUG REIMBURSEMENT REVIEW PROGRAMS**

Does your organization have any comments related to the proposed alignment of eligibility criteria for CADTH's drug reimbursement review processes?

We have no comment with regard to consistency of eligibility requirement. However, CORD has consistently called for a separate review process for drugs for rare diseases, and this is even more apparent as we recognize non-oncology, oncology, and cell and gene therapies as separate reviews. This differentiation becomes more urgent as we recognize that more of these therapies are submitted for what "ultra-rare" conditions, that is, affecting fewer than 1 in 100,000 persons where a traditional HTA has even less relevance.

Given the leading role of CADTH in international HTA bodies, we are sure you are fully aware of alternative pathways for rare disease drugs used in other countries and, as importantly, the enhanced role of the patient community, organizations, and individual patients and families in the review process? We point you, for example, to patient input in scoping and evidence review in countries such as Australia and France. Patients have participated in model development to transform the review and access for rare disease drugs in countries such as Germany and Scotland. And one only needs to look at NICE to appreciate the importance of modifications to the process for end of life or advanced cancer therapies, and, importantly, the Highly Specialised

Therapies assessment for drugs for ultra-orphan diseases.

As importantly, developments in pricing regulations in Canada raise the stakes for a unique HTA pathway for rare disease drugs. To date, the CADTH economic assessment of the “incremental cost effectiveness ratio” (ICER) and the cost-utility ratio (CUA) were used as estimates for negotiation between the public drug plans and the pharmaceutic companies.

Now, as we consider the imminent implementation of the PMPRB guidelines incorporating pharmacoeconomic factors in the setting of “maximum reimbursed prices” based on the regulatory changes. Unless there are substantial differences in the evaluation of rare disease drugs (as compared to common drugs), the PMPRB formula-driven prices that will be based on the CADTH ICER values will set reimbursed pricing at levels that are unrealistic and therefore will preclude most of these drugs being submitted to Canada.

Moreover, the CADTH process should be compatible with the 2018 proposal from the Provincial/Territorial Expensive Drugs for Rare Diseases” for a distinct “supplemental process” for drugs for rare diseases what will be based on a “managed access” program. Finally, the federal government in its 2019 budget provided $1 billion to set up a Canada’s Rare Disease Drug Strategy which will undoubtedly require distinct assessment and evaluation to get to a national program that will include pricing and access recommendations.

Does your organization have any comments or suggested improvements related to CADTH’s processes for determining the eligibility of resubmissions and reassessments?

Does your organization have any comments or suggested improvements related to CADTH’s processes for communicating situations where a manufacturer declines to file a submission with CADTH for an eligible drug?

We are aware of many situations where it has been impractical or, indeed, impossible to make a submission because the evidence would not fit into the traditional CADTH process for conducting health technology assessment. Even though the drug had received a NOC or sometimes a NOC-C from Health Canada, the clinical trial evidence, including, size, scope, and length would make it very difficult for CADTH to provide a favourable recommendation, one that would be limited to a small subset of the indicated population, and/or one that would require substantial price reduction. It is rather a “fool’s errand” or a conundrum where one is dammed if you do and dammed if you don’t. There needs to be a different pathway that is more conducive to an appropriate, legitimate or useful value-based assessment. Other jurisdictions have waived the cost-effectiveness assessment altogether for these therapies or have a much more flexible process for negotiation and access (than pCPA and in the future PMRPB).

## PRE-SUBMISSION MEETINGS

Does your organization have any suggestions for improving pre-submission meetings with CADTH?

## ADVANCE NOTIFICATION PROCEDURE

Does your organization have any comments or concerns related to CADTH's proposal to align the timing of advance notification to a minimum of 30 business days?

We have addressed this in the previous section. Patients/public should be informed at the same time as the advance notification is provided to CADTH.

Does your organization have any comments related to the type of information required by CADTH when providing advance notification?

Do you or your organization have any comments or concerns related to the new Proposed Place in Therapy template?

## APPLICATION AND SCREENING PROCEDURES

Does your organization have any suggested improvements for the application filing process?

Does your organization have any suggested improvements related to CADTH's processes for screening applications for the drug reimbursement review process?

## SUBMISSION REQUIREMENTS (NON-ECONOMIC)

Does your organization have any comments or concerns related to the proposed alignment of required documentation for CADTH drug reimbursement reviews?

Do you or your organization have any suggestions for improving CADTH's procedural instructions for required documentation? Please focus on non-economic requirements in this section.

If your organization has experience with CADTH's drug reimbursement review process, did you find that CADTH's procedures were clear when describing the documentation that is required in order to accept a file for review through the drug reimbursement review processes? Please focus on non-economic requirements in this section.

The proposed templates for required documentation have been provided in the appendices of the consultation document. Please provide any commentary and/or suggested improvements for these templates.

## SUBMISSION REQUIREMENTS (ECONOMIC)

If your organization has experience with CADTH's drug reimbursement review process, do you find that the CADTH's pharmacoeconomic requirements are clear when describing the information that is required in order to accept a file for review?

Do you or your organization have any suggestions for improving the clarity of CADTH's pharmacoeconomic requirements?

Do you or your organization agree with CADTH's proposal to accept cost-minimization analyses for certain drugs?

Do you or your organization agree with CADTH's proposed eligibility criteria for accepting cost-minimization analyses?

## INDUSTRY ENGAGEMENT

Does your organization agree with the proposal to allow the sponsor to review and comment on the draft CADTH reports before the expert review committee meeting?

If your organization has experience with CADTH's Common Drug Review process, do you have any suggestions for improving the process under which the sponsor can review and comment on the draft reports?

Please provide other commentary regarding your organization's perspective on engagement with the sponsor throughout the review process.

## PATIENT ENGAGEMENT

As a patient group, is it useful to have the opportunity to review CADTH's summary of patient group input?

The opportunity to review CADTH's summary is useful but is a poor substitute for the ideal process and that is to assure that all members of the drug review committees have copies of the full patient submission. Indeed, the summary provides only the most high-level comments that do not fully convey the patient experience.

Do you or your organization have any suggested improvements for CADTH's patient engagement processes?

The essence of patient input is not just the survey responses and summary of "evidence." The goal is not an emotional appeal but conveyance of the experience and impact in the patients' own words, the same as a clinician needs to hear directly from the patient or the patient's carer.

Patients should be able to be present at the committee meetings, especially those who have provided input; ideally the meetings should be broadcast and taped, as they are with ICER in the USA. Patients should have the opportunity to appear and to make orally presentations, as INESSS is starting to do; or they could provide taped testimony and listen by phone (as do clinicians).

It is still not clear how conflict of interest is used in the CADTH process, as it applies to patients and also to clinicians. Declaration of funding is not meant to be a bias in evaluating the submission but what purpose does it serve? Why are groups required to report monetary sums? Actually, what we really need is funding from CADTH, the public drug plans, Health Canada, and other publicly accountable sources to help us do patient work, including the patient submissions but also other work that is related to optimal use of drugs. Patient groups have asked for this for years and other countries have done better in terms of support.

## CLINICIAN ENGAGEMENT

Is the rationale behind CADTH transitioning to clinician group input as opposed to open clinician input clear?

There are many clinicians who are experts in the treatment and support for patients who do not have the time, training, or support to engage in submissions. We need a process to provide the support to engage these experts, whether as representatives of a group or as key individuals.

For rare diseases, there may not be a so-called group since they are rather few in numbers. For rare diseases, the clinicians with most expertise and experience are excluded because they are also the ones who have been conducting the clinical trials. This is a true disservice because opinion then comes from those who are not experts or are from outside Canada and do not know our context.

Do you or your organization have any suggested improvements for the proposed template for clinician group input?

## DRUG PROGRAM ENGAGEMENT

Do you or your organization agree with CADTH's proposal to align the processes for obtaining and communicating input from the drug programs?

CORD does not have a sense of how this will impact the work of the committee so we would request evaluation after a pilot period to determine how early input from the drug programs affects the deliberation and recommendations. This would require transparency in terms of the committee's processes.

It should be very clearly stated that the CADTH health technology assessments and the recommendations on cost-utility or place in therapy are performed within the context of and for use by a public health system. Therefore, the outputs should not be extended automatically to the private drug programs which operate within a very different cost-benefits or cost-utility environment. The private drug program environment is very different from that in the USA or in other countries where private insurance also covers other healthcare benefits and therefore, are considered in the offset. The environment is quite different from those in which ICER in the USA or the Agency for Care Effectiveness in Singapore conduct their assessments.

## REVIEW PROCEDURES

Do you or your organization have any suggestions for improving CADTH's processes for reviewing clinical evidence?

Can we assume that CADTH and Health Canada will now be aligned in terms of their reviews of the clinical evidence?

Do you or your organization have any suggestions for improving CADTH's processes for reviewing economic evidence?

We have already called for transparency to assure that any interested stakeholder could compare CADTH's process with those of other jurisdictions (inside and outside of Canada) or could reasonably validate or replicate.

## DELIBERATIVE PROCESS AND FRAMEWORK

Are the criteria used in the deliberative frameworks for CADTH's pharmaceutical review committees (the Canadian Drug Expert Committee [CDEC] and the pan-Canadian Oncology Drug Review Expert Review Committee [pERC]) transparent and explicit?

We can see the criteria in pERC's deliberative framework but there is no transparency as to how these are applied. That requires documentation of process and detailing of the deliberation with accountability (to a public audience, for example). Are there specific elements in each of these criteria or does each apply as he/she chooses? In addition, it is not clear how these factors are weighted, if at all. Are they all equivalent?

Are you or your organization familiar with any criteria used in deliberative frameworks in other jurisdictions that you think CDEC and pERC should consider adopting?

In some frameworks, criteria specific to the drug under review are developed and appropriate weights are attached to these to assure that the most appropriate criteria are applied. In some frameworks, criteria are premised on the principles for drug assessment and reimbursement. These are best when based on assessed societal values.

Are there aspects of the deliberative processes of CDEC and pERC meetings that you would like to understand in greater detail?

We really know next to nothing about this process. There are so many ways of doing this and it would be important to understand what takes place in the committee discussions.

~~Are you or your organization familiar with any deliberative processes used in other jurisdictions that~~

you think CADTH committees should consider adopting?

In some frameworks, criteria specific to the drug under review are developed and appropriate weights are attached to these to assure that the most appropriate criteria are applied. In some frameworks, criteria are premised on the principles for drug assessment and reimbursement. These are best when based on assessed societal values.

Are you or your organization familiar with any deliberative processes used in other jurisdictions that you think CADTH committees should consider adopting?

There is a huge literature on this, everything from highly quantitative, validated measures to simply qualitative approaches. It would be valuable to host consultations on these, try some out in various case studies to assess the differences, and also train the patient and public on these.

**DRAFT RECOMMENDATIONS**

Do you or your organization have any comments related to the proposal to post all draft recommendations for stakeholder feedback?

We support posting all draft recommendations for stakeholder feedback but it is critical to send notice directly to those who have provided input. As a patient group with many members, we may not always track each submission.

Do you or your organization have any comments or concerns related to the proposed process for requesting the redaction of confidential information from the draft recommendation document?

Given that there is no Access to Information for CADTH documents, redaction needs to be minimal and justified with the reason for redaction noted.

Do you or your organization have any suggested improvements for the proposed stakeholder feedback form?

**RECONSIDERATION PROCESS**

Do you or your organization support CADTH's proposal to reduce the number of reviews that undergo reconsideration following issuance of the initial recommendation?

Under a more progressive definition of reconsideration, it is likely that reconsiderations of initial assessments and recommendations may need to be built into drug access, as real-world experience will allow for the initial assessment and pharmacoeconomic value to be updated. These reconsiderations would be built into the recommendations.

Do you or your organization support CADTH's proposal to introduce greater flexibility to the reconsideration process (i.e., requests for major revisions, minor revisions, or editorial revisions)?

Yes, greater flexibility (more options) is essential.

Do you or your organization have any suggested improvements for the reconsideration process?

See previous answers.

**FINAL RECOMMENDATIONS**

Do you or your organization have any comments or concerns related to CADTH's proposed timelines for issuing and posting final recommendation documents?

**TEMPORARY SUSPENSION AND WITHDRAWAL PROCEDURES**

Does your organization have any comments or concerns related to CADTH's existing processes for temporarily suspending files due to incomplete information?

Does your organization have any comments or concerns related to CADTH's proposal to establish a firm cut-off point for voluntary withdrawal from the drug reimbursement review processes?

## IMPLEMENTATION ADVICE ON REIMBURSEMENT RECOMMENDATIONS

Do you or your organization have any comments or suggested improvements related to CADTH's processes for issuing implementation advice reports after final recommendations have been issued?

CADTH's role is to provide recommendations on reimbursement. Unfortunately, given the new self-proclaimed role of the PMPRB to set reimbursed prices, it is not clear as to the pathway from CADTH to reimbursement: direct to pCPA (as now) or back to PMPRB and then to pCPA? It is not clear what additional role CADTH could or should play. If implementation advice on reimbursement recommendations will assure more timely and consistent access to therapy, that would be a good thing. If it leads to delays or confusion as to who is accountable, that would be a bad thing.

## PROVISIONAL ALGORITHM

Do you or your organization have any comments or suggested improvements related to CADTH's proposal to revise the provisional algorithm process?

For many drugs for rare diseases, it should be clear from the outset (based on many factors about the disease, clinical trials, and drug experience) as to whether a provisional algorithm will be needed, mostly in the form of a managed access program (aka coverage with evidence developing) as well as place in therapy as more rare disease therapies with different modes of action become available. This should be considered prior to and as part of the HTA process. As discussed in our previous responses, these drugs should trigger a different pathway since much of the data available at time of approval and launch could be highly uncertain and require confirmation or updating with real-world usage.

The provisional algorithm must reflect much more than budget impact (aka willingness to pay) but for durable therapies (aka long-lasting near-cures), the provisional algorithm could be based personal profiles and responses (aka personalized medicines). Indeed, with highly personalized therapeutic regimes already being used, based on factors beyond the patients genetic/genomic characteristics but also other conditions, lifestyle, and personal preferences, provisional algorithms may need to be re-considered as personal algorithms. These are already demonstrated as not only more effective for the patient but also more cost-effective (not wasting money trying out therapies that are not appropriate or not likely to be tolerated).

There are many factors that will need to be considered and Canada should have a different multi-stakeholder "agent" to develop and manage these. In the rare disease space, this will hopefully be developed out of the P/T EDRD Supplemental process and integrated into Canada's Rare Disease Drug Program.

Do you or your organization have any suggestions on how patient groups and clinician groups could provide input into provisional algorithm process?

Based on the previous response, it is clear that patient groups, clinician groups, individual patients and families need to be formally integrated into the development, monitoring, and evaluation of a multi-stakeholder provisional algorithm process and part and parcel of any specific provisional algorithm.