Suzanne McGurn
President and CEO
Canadian Agency for Drugs
and Technologies in Health (CADTH)
865 Carling Ave., Suite 600
Ottawa, ON, Canada, K1S 5S8

August 10, 2020

Dear Ms. McGurn,

On behalf of Innovative Medicines Canada (IMC) and BIOTECanada, please see below our joint response regarding the current CADTH process consultation. This consultation marks the culmination of several years of engagement with CADTH staff on important process and policy items including transparency, integration of pCODR and the Cancer Drug Implementation Advisory Committee into CADTH, and many past discussions on CADTH review processes and how stakeholder input can be optimally incorporated into reviews. The present consultation also includes new items regarding review alignment, ethics, oncology algorithms, as well as some general questions to inform possible future consultations. The industry appreciates the opportunity to provide input and values the constructive approach CADTH staff have taken to engage manufacturers early on this important consultation.

IMC and BIOTECanada's commentary is presented in the detailed document below. Our key positions can be summarized as follows:

- The stakes for HTA within a quasi-judicial regulatory process will be much higher for all stakeholders. HTA quality and objectivity will increasingly be the industry's top priority.
    - CADTH should enhance formal opportunities for engagement and dispute resolution within the review process.
    - Direct engagement with reviewers can help to proactively address analytical issues.
    - Current templates and page counts can limit a manufacturers ability to provide full perspective and identify all relevant clinical and pharmacoeconomic issues. Feedback processes should be amended as described below.
    - For the purposes of sufficient assessment and comment, the timeframe for manufacturers to comment on clinical and pharmacoeconomic reports should be flexible at the manufacturer's discretion.
- There are ongoing concerns regarding CADTH's proposed redaction policies and validation processes.
- The current pre-NOC process should be maintained with aligned reviews continuing to be optional. Information sharing policies and disclosure forms require amendment and further consultation.
- There are opportunities to improve the proposed oncology algorithm process as well as clarify and enhance the role of stakeholders.

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IMC and BIOTECanada welcome the opportunity to provide this initial feedback in response to changes proposed by CADTH. The dialogue is appreciated and the industry looks forward to collaborating with CADTH to enhance the HTA review process. As a priority, further discussions are required to collaboratively manage current system challenges posed by changes to the Patented Medicine Prices Review Board (PMPRB) and related feasibility issues.

Thank you for your consideration and openness to having such a broader system-level discussion.

Sincerely,

Andrew Casey
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Declan Hamill
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Response Outline

IMC and BIOTECanada's feedback is organized as follows:

1. CADTH Within the Broader Medicines Review System
2. Transparency of CADTH's Review Reports and Recommendations
3. Mandatory aligned reviews with Health Canada for all CADTH pre-NOC submissions
4. CADTH Drug Programs Alignment – CDR, pCODR, and Interim Plasma Protein Process
5. Oncology Algorithms
6. Stakeholder Input
7. Incorporation of Ethics
8. Future Items including Deliberative Framework

CADTH Within the Broader Medicines Review System

Recent changes to the *Patented Medicines Regulations* and pending changes to the PMPRB's Guidelines entail a major shift in the Canadian landscape for Health Technology Assessment (HTA) review. Notwithstanding industry's ongoing opposition to these changes, the entrenchment of HTA reviews into price ceiling regulation would have considerable implications for CADTH's role within the broader pricing and reimbursement system. In this context, CADTH reviews will face increased scrutiny and future process policy changes and will be viewed through the lens of their implications for price ceiling regulation.

The industry appreciates that process efficiency is central to many of the changes currently proposed by CADTH. We also view these changes from a holistic system perspective in which HTA quality and objectivity will increasingly be our top priority. Proactive and frequent dialogue to manage analytical disagreements will be of key importance to the effective functioning of the review system. As such, our core suggestion to CADTH for this consultation is to enhance formal opportunities for engagement and dispute resolution mechanisms within the review process wherever possible.

In the past, HTA review was largely used to inform payer negotiations. Manufacturers and CADTH would not always agree on incremental cost-effectiveness ratios (ICERs), comparators, and the range of analytical assumptions, but files could advance under manageable uncertainty due to the downstream flexibility and opportunity for dialogue provided by reimbursement negotiations. Now that HTA reviews will be used by PMPRB in a more arithmetic fashion to set binding regulatory price ceilings, the stakes for all parties will be much higher. HTA is inappropriate for regulatory purposes because it involves subjective analytical assumptions. Enhanced analytical precision will therefore be required for HTA within the PMPRB's quasi-judicial and subsequent Federal Court judicial contexts.

Industry appreciates CADTH staff efforts to meet on its review process and acknowledges that some drug system factors are beyond their control. Nevertheless, we have concerns regarding the general lack of progress in articulating how this system might function. CADTH has asked for input on how to improve the clarity and consistency of clinical and pharmacoeconomic reports. Information on point estimates and the proposed pharmacoeconomic price (PEP) calculation is our industry's most immediate priority.

It should be noted that HTA files submitted in the next few months will be published under the new PMPRB regime which is scheduled to take effect on January 1, 2021. We have asked PMPRB on numerous occasions for greater clarity regarding the PEP and its confidentiality but answers have not been forthcoming to date. PMPRB is deferring to CADTH to provide much of the analysis needed to implement PMPRB's new economic factors. If CADTH is not yet in a position to provide answers to implementation and review-related questions that will have material business impacts in a few short months, we encourage CADTH appeal to the federal government and PMPRB for a delay in the scheduled effective date of the PMPRB changes, particularly regarding the implementation of the new economic factors.

Ultimately, if CADTH is to provide a single point estimate to inform a PEP as suggested during our discussion on July 29, 2020, then the responsibility and liability for publishing this information, including rationale for analytical choices and any disclosure of confidential information, will rest with CADTH. The use of a point estimate is concerning since it involves subjective analytical choices and may misrepresent treatment value due to inherent limitations. Clarification is required regarding the deliberative process, and how decisions regarding reanalysis, data, and reporting of pharmacoeconomic results will be made. We would propose to build on the previous discussions initiated March 2, 2020 with additional technical discussions on a priority basis.

Another area that requires a more system-based discussion is the incorporation of real-world evidence into reimbursement and review pathways. The analytical framework for innovative payer agreements, risk-sharing, and coverage with evidence development remains undeveloped in Canada. Discussions on how such frameworks can be developed and advanced in light of PMPRB Guideline changes would also be timely. A flexible approach to conditional HTA recommendations may be needed. Please refer to IMC and BIOTECanada's recent joint submissions to CanREValue (previously provided) for further perspectives on this topic in the context of CDR and pCODR reviews. Further discussion on HTA assessment of drugs for rare diseases is also needed.

Transparency

The innovative medicines industry remains supportive of enhancing transparency of regulatory and HTA processes to the extent that there remain opportunities for the protection of sensitive confidential information. IMC and BIOTECanada greatly appreciate the opportunities provided by CADTH staff to discuss these important issues and CADTH staff's recognition that some material will remain redactable. Our main ongoing challenge relates to the final decision-making process for redactable information. The suggestion made on July 20, 2020 that CADTH staff will be the authority and make the final decision on what constitutes redactable confidential business information (CBI) is problematic. In no other realm of

business to business contracts, including public private partnership agreements (example: infrastructure) would a private entity relinquish their rights to maintain the confidentiality of business information.

The current pCODR process is notable for its high level of engagement and consensus building on redactable content. However, our industry is concerned that moving all CADTH programs to a paper-only "accept or reject" process for redaction decision making, well after all confidential material has already been submitted to CADTH, and with no appeal mechanism, will provide manufacturers with no recourse to protect their trade secrets or CBI. It is also recommended that timelines for sponsors to identify confidential information should be extended (e.g. by at least two additional business days, consistent with the current pCODR process) to allow for sufficient time for industry to carefully consider and reduce the volume of redacted material.

Further, definitions are important. While industry is supportive of alignment with Health Canada and notes that its definitions of CBI may be sufficient for clinical information at the regulatory level, those definitions do not contemplate economic information and other reimbursement-related analyses. Therefore, provincial laws and regulations must also be consulted when defining permissible bounds for confidential information as well as Federal Access to Information legislation. [1]

The transparency issue can be grouped into four categories of information:

- **Confidential Economic Information** – including confidential company assessments of budget impacts and market size and share assumptions.
- **CADTH-Specific Analyses** - information such as sub-population analyses provided only to CADTH on a by-request basis for the purposes of Canada-specific decision making.
- **Academic-in-Confidence (AiC)** – Typically unpublished clinical information developed internationally as part of trial programs and subject to international confidentiality restrictions.
- **Submission Intentions** – For example, the publication of information related to 'non-submissions.'

Regarding confidential economic information, we greatly appreciate that CADTH understands the ongoing need to redact select information and will continue to provide redaction opportunities. Industry is committed to working with CADTH to make the redaction process as administratively simple as

[1] The delivery of health care and the administration of the public drug plans is the responsibility of the provinces. CADTH has been established to assist with certain functions but acts under the direction of provincial Ministries of Health when it performs these functions. CADTH is also partially funded by the provinces and, the provinces will usually not consider a product for listing unless a manufacturer has filed a submission with CADTH. The provinces have effectively delegated responsibility to CADTH to determine the pharmacoeconomic value of a drug. If a manufacturer is compelled by provincial or federal drug plans to make a submission to CADTH as a prerequisite for listing, then CADTH's procedures should align with the obligations and responsibilities of provincial and federal governments. Because CADTH functions within the machinery of government, it should respect and protect confidential information in a similar manner.

possible and to keep redactions to an absolute minimum. We are particularly encouraged there will be ongoing protections for elements of budget impact analyses, confidential market-share and market size estimates, and other confidential economic information. When it comes to the treatment of a manufacturer's confidential information, particularly as it relates to pharmacoeconomics, a manufacturer must be certain that this highly sensitive information will be protected.

Regarding CADTH-specific analyses, IMC and BIOTECanada appreciate CADTH's stated challenges regarding the need to be able to justify its funding recommendations. The industry also recognizes CADTH's efforts to provide draft "disclaimer" language regarding the publication of certain types of information. However, the proposed disclaimer (indented on page 3 of CADTH's letter March 25, 2020) does not address concerns regarding international permissions to disclose data and Canada-specific analysis requested by CADTH (e.g. sub-population analyses).

The industry remains of the view that the publication of certain *ad hoc* or Canada-specific analyses can have international implications, and that mandatory disclosure, even with qualifiers, could ultimately impact what information and analyses are disclosed to CADTH, and thus the breadth of information available to inform quality HTA and decision-making.

If moving forward, CADTH should engage manufacturers directly in review-specific adaptations to its proposed disclaimer for inclusion in reviews, and should also retain the flexibility for case-by-case redaction discussions for particularly sensitive CADTH-specific analyses or information. In other words, CADTH should adopt a flexible disclaimer, in addition to some redaction opportunities.

It should be noted that Health Canada has allowed as many back-and-forth engagements on redactions as needed to come to a mutual agreement. Ultimately, CADTH and the manufacturer must agree before confidential information is disclosed. CADTH should also consider the implications of sharing information, against a manufacturer's wishes, with other government agencies which are subject to access to information regimes.

Regarding AiC information, CADTH and industry seem to have reached an impasse regarding impacts to international trial publications. Industry has provided a notional draft process outline to initiate a discussion with CADTH on a compromise process to address some of CADTH's concerns through time-limited redactions, where the burden of work and onus would be transferred to industry. CADTH recently requested evidence of potential harms, however, at this time industry is not sure exactly what type of prospective or counterfactual proof could be provided. We will continue to consider this request into the Fall 2020. Many within the Canadian industry have consulted with global counterparts and the view is that in many cases, permissions to disclose sensitive unpublished clinical information will simply not be granted if it is not protected until the time of academic publication. This is especially true where companies have research collaborations (i.e., they do not own the publishable content), as was noted in our September 27, 2019 submission.

From an ethical perspective, industry is unwilling to take any risk that would put publication of such information in jeopardy. The publication of scientific information obtained from patient volunteers is an ethical duty of those conducting the research. We cannot accept verbal assurances that scientific journals will publish research that has already been published by CADTH, because many journals have policies specifically prohibiting the acceptance for publication of research that has previously been published in any form. Industry has provided CADTH examples of such policies, and believes that the onus is on CADTH to provide evidence that its proposed policy will not jeopardize researchers' and industry's ethical duty to publish scientific data obtained from patient volunteers. Despite the current impasse, we remain open to further discussions on this issue.

Regarding non-submissions, industry previously noted that information regarding whether or not a manufacturer is planning to file a submission, as well as anticipated timelines of potential future filings, constitutes confidential business information. Manufacturers believe it is inappropriate for CADTH to publicly post this information. Further clarification regarding these publications is needed to address questions raised in the industry submission dated September 10, 2018, and the follow-up submission dated September 27, 2019.

Mandatory Aligned Reviews for all CADTH pre-NOC Submissions

The industry remains concerned about making the aligned review and information-sharing process mandatory for all pre-NOC submissions. There are many reasons for low uptake of the program, including modest benefits that are far outweighed by the uncertainty of the pending PMPRB changes. If manufacturers are not choosing to participate in aligned review, this may suggest they either only see modest benefits or have concerns about information sharing provisions and would prefer to leverage the existing CADTH pre-NOC process.

It is anticipated that the proposed policy change may result in lower uptake of pre-NOC reviews. This outcome would be counter to the general purpose of aligned reviews to accelerate reimbursement recommendations where possible. Consequently, the aligned process and its information sharing requirements should remain voluntary.

Manufacturers also have particular concerns about proposals to share information with almost any public federal or provincial body, including entities that have not been specifically identified. All parties subject to information sharing should be identified and agreed to beforehand by the manufacturer on a file-specific basis.

The industry is also strongly opposed to any direct file-related information sharing between CADTH and the PMPRB, which is a quasi-judicial tribunal independent of government, or its staff.

We remain open to a broader discussion with Health Canada, INESSS, CADTH, and other system stakeholders on potential improvements to the aligned review process. At a minimum, the proposed changes should be delayed until such a broader discussion can take place. As an immediate step, the

consent template should be revised to be explicit about confidentiality provisions, specific agency and HTA body information sharing authorizations (e.g. for manufacturers to opt in/opt out by entity), and to confirm that all chemistry, manufacturing, and control information is excluded for release. The revised template should also be subject to additional consultation prior to any implementation.

Further discussion is also required on collaborative workspaces, access to collaborative workspaces, security measures, and related permissions issues. Some members have noted that due to the sensitivity of information it is important that file-level access permissions, including access for pre-specified personnel, are needed, and should be discussed further.

It would be helpful if Health Canada and CADTH could hold an information/update session to discuss the aligned reviews program key learnings to date, performance metrics, and provide more information on how information sharing may be benefitting the process. It would also be helpful to understand the broader vision associated with info sharing and aligned reviews, given the ultimate benefit of initiating pre-NOC HTA reviews has not always translated into earlier time to listing by jurisdictions and the program has not worked to offset the negative impacts and uncertainty associated with the pending changes to the PMPRB's regulatory framework.

CADTH Drug Programs Alignment – CDR, pCODR, and the Interim Plasma Protein Process

The industry greatly appreciates CADTH's perspective and commitment it will remain open to more direct engagement throughout the review process, including the flexibility to engage in sponsor with written email questions throughout the review. However, we remain disappointed that pCODR-style checkpoint meetings will not be adopted, and that there will be fewer formal opportunities for engagement. As discussed on July 29, 2020, the industry is most interested in ensuring robust opportunities for dialogue as a driver of quality HTA, and for proactive alignment on information and assumptions. While CADTH's general openness to engagement is appreciated, it is important to reflect this in the formal process document. The formal process document should reflect at least two optional touch points of up to one hour each at the manufacturers request, with timing to be agreed with CADTH on a case-by-case basis. Both clinical and pharmacoeconomic reviewers should be present for these meetings and should engage directly with manufacturers. External reviewers can also participate in these meetings on an anonymized basis, similar to the pCODR checkpoint meetings, and should be able to pose questions to the sponsor.

It is also recommended that page limits for manufacturers comments be increased from 10 (which in actuality is closer to 5 pages given CADTH's template) to 15 pages, unless more is warranted under specific circumstances. CADTH should discontinue the template approach and should not restrict manufacturers' commentary. This approach will balance the need for manufacturers to address all relevant issues, reduce downstream disputes regarding methodology and assumptions, while also provided some target parameters. Given the ongoing shift to HTA in a regulatory context noted above, fixed page-count limits prevent manufacturers from fully identifying and explaining potential file issues. Future complications may also be avoided through flexibility for increased page-count 'guidance' rather

than 'limits'. Manufacturers should also have the option to comment directly on review documents, for example, through the PDF comment function or Microsoft the Word comment function.

Similarly, the seven-day limit for manufacturers to provide comments on both clinical and pharmacoeconomic reviews is generally insufficient for HTA within a regulatory context and given that manufacturers will increasingly need to coordinate comments with their international colleagues. This is particularly the case for smaller companies operating with limited staff. Seven days could continue to be the target but the review process documents should clarify that more time can be taken when needed by the manufacturer. In such cases, CADTH could account for these files in its performance reporting under a separate category where manufacturer deemed the time insufficient to comment on detailed reports.

To help with efficiency, accuracy, and mutual understanding, the economic reviewers should state how the results of any re-analyses they conducted were validated and provide the models themselves used for any re-analyses back to the sponsor to verify numerical accuracy.

The CADTH proposal notes that "the identities of the clinical experts who participate in the panels will remain confidential." CADTH should be transparent about the policies that underlie how these individuals are selected and/or ruled out. The selection policies should be transparent to the public.

While flexibility for cost-minimization analysis is helpful, CADTH should note the significant automatic penalization of products with a cost-minimization analysis under the PMPRB's proposed Guidelines (See 2020 Draft Guidelines, section 62). CADTH's support in opposing this automatic and significant penalization would be welcomed. At a minimum, it should be a sponsor's choice as to what model to submit to CADTH.

Regarding the proposed review protocol for new formulations of existing drugs eligible for review. this should be case-by-case and optional depending on current funding across the country.

Industry is generally supportive of the "major/minor revisions" approach to reconsiderations, but no fees should apply for "minor" revisions. For "major" revisions, CADTH should explore options for reconsiderations with a different third-party expert committee than that which considered the original file. With respect to reconsideration process, it is recommended that patient and clinicians have opportunity for input and feedback in reconsideration deliberation. Manufacturers also support the ongoing possibility for file applications from clinician groups.

There have been some questions raised within the industry as to the proposed place in therapy template which seems to require considerable information prior to a submission. The industry is supportive of early opportunities to discuss place in therapy. However, this proposal is being reviewed in more detail and we would like to engage with CADTH staff further, including on issues of timing within the review process and scope of information requirements.

Finally, products under the CADTH Interim Plasma Protein Product process are subject to RFP processes, where the product price is confidential, and subject to change between RFPs. For these products, a price agnostic to pharmacoeconomic analysis would be most useful for decision makers.

Oncology Algorithms

The industry is supportive of CADTH's general intention to limit the frequency for the development of oncology algorithms and keep the production of these to a minimum, on an as needed basis. However, specific criteria could be established to help enhance predictability for when algorithm process can be expected. To the extent possible, the need for a review-plus-algorithm versus a standard drug review only should be identified at the initiation of the review.

Similar to previous industry comments regarding consensus for reassessments, clear criteria should be established and any oncology algorithms should only move forward with high provincial payer/cancer agency consensus on the need for an algorithm (e.g. 90%+). Where there is no such consensus (e.g. a one-off request), other options to provide individual jurisdictions with decision support could be explored.

Industry also acknowledges CADTH's responsiveness regarding the idea of other impacted manufacturers to have some awareness and visibility to the process. As discussed on July 29, 2020, there is some ongoing lack of clarity regarding when other stakeholders such as patients and clinicians would have an opportunity to comment on an algorithm, independent of their input on an individual file review. It appears that CADTH will not be consulting with patients when developing algorithms.[2] At this point in the review process, patients have not been asked for input on matters related to an actual algorithm that could help to determine a drug's place in therapy. What if there is a perspective that a patient could contribute? CADTH should clarify that all stakeholders will be permitted to comment on the algorithm itself and identify the process for this to take place.

A policy could also be put in place to ensure that competing patient perspectives are not used to slow down the process by, for example, requiring that patients are engaged if it is reasonable to believe that they might have a new perspective to offer. The panel that advises on implementation and the creation of the provisional algorithm could include a patient as a member.

It would also be helpful for CADTH to provide additional clarity on how the oncology algorithm fits within pERC file review meetings, pERC algorithm meetings, and timing vis-à-vis pCPA. This new approach has the potential to cause some new medicines to be delayed in getting to market by at least 2-3 months.[3] As noted in the industry webinar, CADTH's experience with oncology algorithms to date suggests that algorithms will be completed 2-3 months after pERC or CDEC share their final recommendations. It is unclear how this sequencing will impact preparation for pCPA discussions which

[2] *CADTH Proposal* at p 52 (see 11.2.2).
[3] *CADTH Proposal* at p 51.

is a concern. The consultation documents leave our members with some timing and sequencing questions that require further clarification.

If moving forward with the algorithm sequencing at the end of the process, rather than the outset, CADTH should review performance and stakeholder views after some time and experience with the changes. An early identification mechanism so that the manufacturer can have a sense of whether its submitted product will be subject to a review only, or a review-plus-algorithm process, is also recommended. Given that CADTH asks sponsors to fill out a "proposed place in therapy" at the outset of a submission, CADTH should also be open to input and information from manufacturers about their drug's optimal role/place in therapy when there is a better sense of whether a reimbursement recommendation will be made.

Stakeholder Input

There have been several positive developments with respect to the role of patients and patient groups. It was noted during the webinars that patient groups do not need to be incorporated or recognized in any official way in order to qualify as patient groups for the purpose of making submissions to CADTH. Specifically, it was noted that a patient group can simply be a Facebook group or a group that has formed on a social media platform. It is important that the definition of a patient group remains flexible to facilitate the inclusion of these important stakeholders.

We understand that all draft recommendations will be posted publicly for stakeholder feedback and that the drafts will be posted approximately two weeks after the relevant committee has made a decision. However, it remains unclear who is defined as a stakeholder. We note that patient groups who miss the original deadline to make a submission are excluded from providing feedback on draft recommendations. Given the resource limitations of many groups, CADTH should allow even those who did not make a submission to comment on the draft recommendations. It would be unfortunate if patient groups or clinicians who could provide valuable perspectives were prevented from doing so for administrative reasons.

Beyond being able to make an initial submission and then commenting on the committee's draft recommendation, the role of patient input remains unclear and could often be better explained within the review. For transparency purposes, CADTH should make all patient submissions public, including comments on draft recommendations (unless the patient/group has a valid reason to request confidentiality or redaction). Review committees should also be empowered to ask patient groups to provide additional information if they feel it would be useful.

Industry is also concerned about the proposal to diminish the role of clinicians on the HTA review within the pCODR process. The Clinical Guidance Panel (CGP) is an integral component of the review to support the recommendation-making of the expert review committee. We do not understand how

engaging fewer clinicians and reducing their contribution supports best practices in a multidisciplinary HTA process. This will limit the understanding of practice variation across provinces, will limit the clinical interpretation of evidence, and may also result in reduced acceptance by clinician experts. Most importantly, the CGP's expertise is intended to support pERC's decision making because they do not have experience in all disease areas.

We would also encourage CADTH to continue to include tailored questions for clinician input similar to the current pCODR process. When pCODR introduced the clinician input pilot program in 2016, there was a standard template used for clinician input. Upon evaluation of the pilot in 2018, the process was refined to include tailored questions based on feedback from registered clinicians, pERC and PAG. We would welcome a discussion on the rationale for moving away from this refinement.

A conflict of interest policy for members of the committees is undergoing review and will soon be updated. This process should include patients/patient groups given the recent decision to require those groups to publicly disclose all conflicts of interest. Patient groups will be able to contribute a timely and meaningful perspective to discussions about determining the appropriate COI policies for committee members.

Incorporation of Ethics

There was relatively limited emphasis placed on the role of ethics and/or ethical analysis in the CADTH Proposal document or during the two webinars. We do know that CADTH has made some movement to ensure that ethical analysis will be part of all reviews going forward. A dedicated ethicist will be added to both the CDEC and pERC, but practical role of these ethicists is deserving of some scrutiny.

At the beginning of every review, "CADTH develops a review plan to ensure that the review will capture pertinent ethical considerations."[4] The ethics review, as it has been described by CADTH, requires the ethicist to prepare a summary but does not seem to permit the expert to offer any synthesis or analysis of the literature they have reviewed. Industry is concerned about this limitation and believes that the ethicist must be treated as having an integral and independent role. The limited role of the ethicist becomes problematic when the type of product under review has not already been well-scrutinized in the literature.[5]

[4] It is not clear who is included in this process and how much weight is given to the dedicated ethicist's opinion. These ethicist is expected to prepare a literature review that merely describes the literature that the ethicist deems to be relevant (again, given the confines of the "review plan" that has been developed by CADTH) and provide a narrative summary of ethical considerations that have been identified within that relevant literature.

[5] "[w]here the scope of the ethics review includes broader technology or condition topics than the specific product and indication under assessment, CADTH ethics reviewers will work with the economic and clinical reviewers to scrutinize the proposed broader topics for their relevance." *CADTH Proposal* at p 36.

As a result, not only is the responsibility to analyze the ethics literature left to non-ethicist, but so too are the questions about what related literature might be helpful. This is problematic because a great deal of academic literature relevant to science and technology is theoretical, or motivated by theory, but can still contribute a great deal to grounded analysis about specific issues related to individual products. The ethicist must be an expert who is given the freedom to explore the literature without having to worry that the committee might limit the parameters of the literature review. If the review plan that CADTH has set out for a specific product is not framed with sufficient breadth and the intellectual freedom of the ethicists is not guaranteed, there is a risk of valid viewpoints being left off the table. This will be especially important when considering issues of health inequity.

CADTH's ethicists must be able to contribute something more meaningful than a descriptive literature review. They must be treated as ethics advisers and be empowered to ask ethics-related questions of the review committees, while also being permitted to assist those committees with addressing otherwise unanticipated ethics-related questions that may arise in the course of a review. Finally, it is not clear whether and to what extent the CADTH pharmacoeconomic analysis integrates a robust ethical analysis.

Future Items including Deliberative Framework

The industry supports addressing the Deliberative Framework at a later date, and appreciates that CADTH will remain open to receiving comments through the Fall of 2020, and will hold additional formal consultations on any specific proposals. We understand CADTH's reasons for wanting to postpone consideration of the Deliberative Framework until after the current consultation. However, a related task that should not be delayed is a careful examination of the potential impact on the perception of integrity of CADTH's deliberative process from its new role in calculating cost-effectiveness for the PMPRB to be used in setting regulatory price ceilings.

This task appears to be inconsistent with CADTH's primary role up to date, which has been to inform the reimbursement decisions of public drug plans through, multifaceted assessment that includes, for example, clinical opinion, social factors, ethics, and stakeholder engagement. There are international HTA processes with open and cooperative deliberative process between the sponsor, stakeholders and HTA. It would be useful to consider alternative models to examine their potential applicability to the Canadian context.

It is recommended these issues be placed on the agenda for a fall Industry Liaison Forum (ILF) meeting. The industry appreciates the many detailed future-focused questions provided by CADTH and may comment on those issues at a later date. Our comments above may not be exhaustive of all member perspectives on these issues, but IMC and BIOTECanada have tried to comment on those that are the highest common priorities to the industry. We look forward to further conversations with CADTH on these topics.