This Q&A should be read in conjunction with the current published Operational procedures and are intended to provide additional details regarding the Promise procedure.

Question followed by Access Consortium response
1. **An Advanced Therapy Medicinal Products (ATMPs) Working Group was established in 2023, where one of the main goals is to explore potential synergies and opportunities for work-sharing, reliance, and providing joint scientific advice. Would a cell, tissue, and gene therapy product (CTGTP) be considered under the Access work-sharing and/or Promise Pathway (should the eligibility criteria be met)?**
Response: The Access partners welcome the opportunity to collaborate on ATMPs. Initially, it is likely that information-sharing (as opposed to work-sharing) would be a more suitable approach to allow agencies to become familiar with how other agencies review these products. A similar information-sharing approach was taken in the early days of the New Active Substances Work Sharing Initiative (NASWSI). Review teams that are not yet experienced with work-sharing would also likely be involved in the review of such products and a collaborative review leveraging interagency information-sharing would provide an opportunity to build that experience.
2. **Would the promise pathway be considered for drugs seeking provisional or conditional market authorization? In areas of unmet medical need, surrogate endpoints/early data are often used to secure approvals for treatments for serious, life-threatening, or severely debilitating diseases.**
Response: For the time being, market authorization applications (MAAs) for provisional/conditional approvals are out of scope for Access submissions due to significant differences in national criteria. Accordingly, the Promise pathway is also excluded. However, expanding the scope to include provisional/conditional approvals may be considered in the future as the NASWSI evolves. Applicants may contact each agency to discuss their national criteria for provisional or conditional approvals
3. **If an application for the NASWSI Promise Pathway and/or priority review is not accepted and the applicant wishes to proceed with NASWSI under standard review timelines, will the Expression of Interest form (EOI) be automatically reconsidered for review under the standard NASWSI pathway? Or would the applicant need to resubmit the EOI to apply for a standard timeline? Can the filing date for the MAA remain the same?**
Response: In the EOI form, the applicant should indicate their wish for a standard procedure if Promise Pathway entry and/or Priority Review designation is not accepted. If this information is provided in the EOI form then a new EOI would not need to be submitted. A future version of the EOI template will include updates to make this clearer for the applicant. It is not expected that a change in the review timeline from priority review to standard review would have an impact on the MAA filing date.
4. **Could applicants receive status updates on EOI and priority review request assessments to improve predictability of EOI and priority review acceptance?**
Response: Access agencies aim to provide regular status updates to applicants on the status of their EOI and priority review request. Applicants are also welcome to contact their national agency representatives to request status updates at any time.
5. **If the agencies make different decisions about whether an application qualifies for priority review through the Promise Pathway, will the applicant be informed of the decision from each**

agency?

Response:
Step 1: The applicant will be informed of each agency's decision regarding eligibility for the Access Promise Pathway. If the eligibility criteria are met in certain jurisdictions but not others, detailed information will be provided to help the applicant determine the most appropriate submission strategy moving forward.

Step 2: If the EOI is determined to be eligible by all jurisdictions, a differentiated evaluation of the priority review request will follow. Agencies will then aim to reach a consensus decision regarding priority review designation. However, if the agencies cannot reach a consensus, the divergent views of the agencies will be shared with the applicant to help them determine their submission strategy.

6. **Could the recommended timeframe for submitting an EOI that contains a Promise Pathway request be reduced from 6 months to 3-4 months prior to to the market authorization submission? This adjustment could help to ensure better planning, alignment of global dossiers, and mitigate potential risks.**

   Could the evaluation of eligibility for worksharing , determination of the agencies' roles, and creation of the evaluation plan be conducted in parallel with the evaluation of the Promise Pathway priority review request?

Response:
The consortium would like to emphasise that these are recommended timelines.
As stated in the Operational Procedures document: "*The Access agencies understand that an applicant may not know until closer to submission that their application is suitable for priority. Where this is the case, applicants are encouraged to discuss the timelines with the proposed agencies and/or to submit an EOI 6 months before filing and note that they may withdraw their interest in the Promise Pilot pathway pending the outcome of ongoing clinical trials.*"

The Operational Procedures document has also been updated to revise the timeline for the technical pre-submission meeting to 1-3 months before submission of the MAA. This change is intended to ensure that pivotal data are available at the time of the pre-submission meeting.

If the applicant does not yet know whether their application is likely to be suitable for priority review (e.g. because pivotal data are not yet available), they should state this uncertainty in the EOI. In this case – if the pivotal data are not yet available – the timelines for priority review should be discussed with the lead agency to ensure that the proposed filing date is possible.

The Consortium aims to determine the agencies' roles and plan the assessment procedure as early as possible after receiving the EOI. When feasible, this may be done in parallel with other planning and evaluation activities.

7. **What would happen if the confirmatory data are not available within 6 months, does eligibility lapse and/or applicants need to resubmit an EOI and wait another 6 months?**

Response:
As stated in the Operational Procedures document, interested applicants are advised to submit their Promise Pathway EOI at least 6 months before filing their application for marketing authorization. The EOI does not lapse if submitted >6 months prior to submission, or >6 months prior to confirmatory data becoming available. In cases where confirmatory data is delayed, we ask that applicants update their agency representatives on the anticipated timelines and the agencies will work with the applicant on a case-by-case basis. Please also see the response to question 6.

8. **Once you indicate in your EOI that you'd like to be considered for the Promise Pathway, do applicants still need to prepare national requests for priority review in each country or is it possible to submit only one priority review request? If only one request needs to be submitted, can the submission format from any of the Access countries be used?**

Response:
Once the participating agencies have sent confirmation to the applicant that the Promise Pathway eligibility criteria have been met and clarified which agency will lead the review of the priority review determination, one scientific data package should be filed to address the priority review criteria required by Canada, Australia, Switzerland or Singapore legislation and/or guidance documents. Preferably, the format and criteria from the lead agency should be addressed. While a single scientific data package can be used, a copy of the package should be filed to each jurisdiction where priority review is being sought.

9. The Operational Procedures document indicates: *"However, those national criteria are very similar and allow the applicant to prepare 1 data package, which is submitted to all jurisdictions."*

a) Is this referring to the Promise Pathway priority review request package?

b) If the Promise Pathway request is denied and the applicant has already prepared a single Promise Pathway priority review request package, can this package be re-used by each national authority to determine eligibility for national priority review designation? Or would the package have to be reformatted into the national template and resubmitted?

Response:

a) Yes, this is referring to the priority review request. The national criteria for priority review requests/Fast Track requests at HC, TGA, HSA and Swissmedic are very similar. In addition to the Promise Pathway eligibility criteria:

- *diagnoses, treats or prevents a condition that is serious, life-threatening or severely debilitating;*

AND

- *for which no other treatment is currently registered and marketed in participating jurisdictions for the proposed indication,*

The access agencies will also assess the evidence of a significant therapeutic benefit using the information provided by the applicant in the scientific data package.

b) The applicant would need to review the national criteria and submit data packages that meet those national criteria, including all national forms requested. Applicants may consult with national agency representatives to determine whether a Promise Pathway priority review data package contains sufficient information to address their agency's requirements for national priority review designation.

10. Page 5 of the Operational Procedure indicates:

"*If the Access agencies cannot agree, the applicant may continue to submit the application using the:*

- ***Promise Pilot pathway for those agencies that accepted the request or***
- ***standard Access procedure to all requested agencies.***

If priority review status is not granted, an applicant cannot use the Promise Pilot pathway. An applicant may still submit a national priority/fast-track request or a national reconsideration application, where applicable."

- What process should the applicant follow in a scenario where entry into the Promise Pathway is denied but the applicant believes the criteria for national priority review/Fast-Track are met?

- If an applicant wishes to be considered for national priority review/Fast-Track designation in the event that their application for the Promise Pathway is not accepted, would a separate national priority review/Fast-Track application need to be submitted in parallel with the Promise Pathway request?

- In a situation where some agencies accept a Promise Pathway application but others do not, could the agencies who accepted the Promise Pathway request proceed with priority review timelines without the applicant needing to file a subsequent application for national priority review designation in those countries?

Response:
If entry into the Promise Pathway is not granted then the applicant may choose to submit individual national priority review/Fast-Track requests to the relevant agencies as per each agency's legislation/requirements. As noted in the response to Q11, it is recommended that the applicant awaits the outcome of the Promise Pathway assessment before filing an application package via the national priority review pathways.

If separate national priority/fast-track requests are accepted, priority review of a subsequent NASWSI work-sharing MAA would still be possible with all Access partners who have accepted the national priority review/Fast-Track requests.

Ultimately, there are multiple options for the applicant, including:
• NASWSI Promise Pathway for agencies that accepted entry into the Promise Pathway
• NASWSI with priority review timelines for agencies that granted national priority review designation
• NASWSI with standard timelines for all implicated agencies (see also Q15)
• National (i.e., non-NASWSI) MAA procedures, including potential for national priority review where eligible (see also Q12).

As indicated in the Operational Procedures document: *"If the Access agencies cannot agree on the Promise priority review request, the applicant may continue to submit the application using the Promise Pilot pathway for those agencies that accepted the request."* In these cases, it would not be necessary to apply for national priority review designation again for those agencies that accepted entry into the Promise Pathway.

11. Provide clarity whether parallel submissions to Access Promise Pathway and national priority review pathways (where relevant) are permitted

Response:
The Promise Pathway is the preferred and recommended pathway for priority review via the NASWSI as it streamlines the assessment of the request for priority review for all parties. However, it does not prevent applicants from pursuing priority review through national frameworks at individual agencies. In general, it is recommended that the applicant await the outcome of the Promise Pathway assessment before filing an application package via the national priority review pathways. Such an approach streamlines the assessment of the request for priority review, thus maximizing the benefits and efficiencies of the Promise Pathway for all parties. Furthermore, noting that not all agencies have formal national priority review pathways, it allows the request for priority review to be considered by the Consortium as a whole.

12. In the event that one agency accepts entry into the Promise Pathway but the other agencies do not, can the applicant then submit their MAA to this agency under their national priority review/Fast-Track procedure? Or would the applicant need to file a subsequent application for national priority review/Fast-Track in order to receive an accelerated timeline for their MAA?

Response:
The applicant will be informed of each agency's decision regarding the Promise Pathway request to support the applicant in determining their MAA filing strategy.

In cases where one agency grants Promise Pathway entry but the others do not, the company may consult with that agency to discuss their national submission strategy and review timelines.

13. The Operational Procedure document makes reference to a national reconsideration application, can you clarify what this is?

Response:
The reconsideration application referred to is specific to Health Canada's reconsideration process. For additional information, please see Health Canada's *Guidance Document: Reconsideration of Decisions Issued for Human Drug Submissions and Natural Health Products*. Please note that decisions related to Promise

Pathway acceptance are not eligible for Health Canada's reconsideration process.

14. Applications for Promise Pathway entry may involve applicants receiving clarification questions from the agencies with only a 2 calendar day response time, can this be extended to allow applicants additional time to respond?

Response:
It would be difficult to extend this 2 day response time and still assess the Promise Pathway request within the 30 calendar day performance standard. Should an applicant require more time to respond to questions, they can request an extension and the relevant agencies will assess that request on a case-by-case basis.

15. When are evaluation plans shared with the applicant for standard and Promise applications? .

Response: For NASWSI procedures with standard timelines, the evaluation plan for the MAA is shared with the applicant prior to the MAA submission.

For Promise Pathway procedures, upon initial acceptance into the Promise Pathway, the applicant will be informed that their application is eligible for the pathway, which agency will lead the assessment of the priority review data package, and the timeline for issuing a final decision on whether Promise Pathway entry is granted. Once Promise Pathway entry is granted and prior to the applicant filing their MAA, the evaluation plan for the Promise Pathway MAA will be shared. The evaluation plan includes expected timelines and also specifies module distribution amongst participating agencies.

16. Can you provide clarity on the determination of lead agency?

Response:
The Access agencies distribute responsibilities for conducting the assessment of Modules 3, 4, and/or 5 according to expertise and the resources available during the expected review timeline. The lead agency for each module will be communicated to the applicant in the evaluation plan for the MAA.

17. Can you provide clarity on when the sovereign decision steps start?

Response:
National or sovereign decision steps begin once all responses to common questions are evaluated and final review reports are shared amongst the participating agencies.

18. Can you provide updates to the applicant once the sovereign decision steps start?

Response:
The Access agencies acknowledge that applicants wish to be informed once the sovereign/national steps begin. In most cases the milestone dates are included in the evaluation plan that is shared with the applicant, which includes the date on which national steps are expected to begin. Applicants may also contact their national agency representative for status updates at any time.

19. For a situation where a filing through the NASWSI pathway may include two indications for the same drug product and one of the indications qualifies for entry into thePromise Pathway while the other indication does not:

a) Would the two indications need to be filed as separate MAAs?
b) Can two NASWSI submissions (one with a priority review timeline and the other with a standard timeline) be submitted in parallel?

Response:
If only one indication qualifies for the Promise Pathway, two separate MAAs should be submitted as they will have different timelines. If the applicant wishes to file two parallel MAAs for the same drug product simultaneously, it is recommended that the applicant first consult with the national agencies regarding their filing strategy. In some jurisdictions there may be complications regarding administrative items, such as submission classification and evaluation fees.

If the applicant decides to seek Promise Pathway acceptance for multiple indications in parallel, there must be separate priority review data packages to support each indication.

20. 'The Operational Procedure states *"**The applicant and all agencies proposed for work-sharing may wish to hold a joint pre- submission meeting/teleconference (combined logistical and technical). Applicants should propose possible meeting dates in their EOI form."***

a) Can a scientific meeting be held bilaterally with the respective agencies?
b) Can applicants be informed at the joint pre-submission meeting which agencies will take the lead on assessing each module in the MAA?

Response:

a) Yes. The technical pre-submission meeting will usually be held with the Module 5 lead agency, although bilateral meetings with each jurisdiction may also be possible.
b) Yes. Applicants would usually be informed of module distribution by email. In the vast majority of cases this will be prior to the pre-submission meeting; an exception to this may be if the applicant requests an early pre-submission meeting, and module distribution has not yet been decided.

Annex 2 in the Operational Procedures document indicates that the screening timeline for a Promise Pathway MAA is 25 calendar days, can this be reduced further?

Response:
The overall screening and review timeline is significantly reduced for Promise Pathway applications. At the moment, no further reduction of the screening time is possible.

21. If there are divergencies during the assessment procedure of a MAA with priority review timelines, which will prolong the evaluation of the MAA, can the procedure be continued bilaterally in order to not delay a regulatory decision in a country which may be able to continue adhering to the priority timeline?

Is there a risk that one agency can delay the whole evaluation process or will all partners be committed to an accelerated assessment throughout the procedure?

Response:
Since it is a work-sharing process, final reports for modules, where agencies are aligned, would usually need to be shared between agencies before entering into the national phase. In case of divergencies, agencies may continue nationally.
For Promise Pathway MAA evaluations, all participating agencies are committed to an accelerated assessment timeline which is communicated to the applicant in the evaluation plan.

22. Can you provide information on the fees for applicants and whether they are in addition to the agencies' respective national fees for MAA review)?

Response:
All user/evaluation fees are according to the participating agencies' national legislation. No additional fees apply for NASWSI submissions.

23. The Operational Procedures document indicates:
"For joint review of an application under the priority review pathway, agency questions will be issued as "rolling questions" throughout the evaluation period (i.e. during Phase 2)."
- However, according to the table in Annex 2, it appears a consolidated List of Questions (LoQ) may also be possible. Can you explain whether clarification questions from the agencies would be issued as consolidated questions or rolling questions?

Response:
For a MAA evaluation procedure with priority review timelines, rolling questions with a final round of consolidated questions or a consolidated LoQ are both possible.

24. Can applicants request a schedule for rolling questions to be published to increase predictability and resource planning?

Response: Whenever possible, a schedule for rolling questions will be included in the evaluation plan. Evaluation plans are always discussed with the applicant in advance.
25. Can an extension to the response timeline for agency issued clarification questions be requested?
Response: Yes, extensions to response timelines can be requested and will be assessed by the agencies on a case-by-case basis.
26. Can the agencies eliminate rolling questions for MAA evaluation procedures with priority review timelines and rely solely on a consolidated LoQ for clarification questions?
Response: At this time Access agencies have very little experience with work sharing MAAs with priority review timelines and therefore cannot commit to eliminate rolling questions.
27. Is it possible to waive regional/country specific Chemistry, Manufacturing, Controls (CMC) requirements for those countries not leading the review of module 3? For example, if Australia is leading the module 3 review, would it be possible to forgo any additional items that may typically be required by one of the other participating agencies?
Response: Each agency has their own specific CMC requirements and these need to be fulfilled before market authorisation is granted. As such, waiving regional/country specific CMC requirements is not currently possible. Access Consortium members acknowledge that these differing requirements can create additional complications, and we share industry's commitment to improving alignment of regulatory approaches, as outlined in the recently published Access Strategic Plan 2025-2028.
28. Annex 2 of the Operational Procedure: specific to AU, Delegate Overview (DO) and Advisory Committee on Medicines (ACM) meeting timing. A critical milestone for AU affiliate planning is the availability of the DO, which will determine the reimbursement filing timing. Under current timeline in Annex 2, it is not clear when/whether the DO would be issued. Similarly, it is also not clear whether/when the ACM meeting will take place.
Response: TGA: DO and ACM meeting dates are advised closer to time (depends on Round 2 questions, Access evaluation timeline, and if application meets the TGA priority review target date of 150 WD).
29. Is a final decision really issued by Swissmedic on Day 180 (separate sovereign decision)? i.e. do all labeling discussions with Swissmedic also take place within the 180-day review? Compared to the standard pathway, the "national phase" is missing here.
Response: Swissmedic: This depends on the outstanding issues. If there are no outstanding issues after the evaluation of the responses to the rolling questions and/or consolidated questions, the preliminary decision can be issued before D180. However, there is a possibility that the preliminary decision will be issued on D180.