Canada's Drug Agency
L'Agence des médicaments du Canada
Drugs. Health Technologies and Systems. Médicaments, technologies de la santé et systèmes.

Assessment Framework

Planning for a Coordinated Assessment Framework for Biomarkers Used in Cancer Care: A Report from the Biomarker Advisory Panel

Draft for Feedback

About the Consultation

Canada's Drug Agency, on behalf of this time limited advisory panel (the advisory panel), is inviting interested parties to provide input on a draft consensus-based framework intended to inform adoption or funding decisions on molecular, genetic, and genomic biomarker testing in cancer care. Your input is both needed and highly valuable. Your comments will be used to inform a final report that will be shared with provincial and territorial governments, and made publicly available. The advisory panel prepared this document to promote dialogue around this work.

This document outlines how the advisory panel's work was approached and captures the collaborative efforts undertaken by CDA-AMC and the advisory panel to develop the draft consensus-based assessment framework. The report progresses from context-setting to the development of guiding principles, a proposed assessment framework, and future considerations. The structure of the report reflects the logical flow of the panel's work and includes actionable, non-binding recommendations to support implementation of the framework and achieve the intended goals.

Please submit your responses and comments using the online form available at the following links:

- English form
- French form

You are welcome to respond to some or all questions. The consultation period will close on September 30, 2025. If you have any questions about this consultation, please email us.

Public Posting for Input

To promote transparency and encourage meaningful dialogue, Canada's Drug Agency will publicly post the feedback received through this consultation process. By submitting written comments, individuals and organizations acknowledge and agree that their submissions may be published in full. Submissions will not be edited for content, accuracy, or completeness, and any references or links included will not be verified. Organizations and groups that submit feedback will be named publicly; however, individual names will not be published.

As part of the submission process, Canada's Drug Agency will collect personal information, including name, contact details, and organizational affiliation. While respondents are encouraged to self-identify to support follow-up and engagement, anonymous submissions will also be accepted. However, please note that anonymous submissions may limit our ability to respond to specific questions or provide updates related to the feedback provided. All feedback received will be reviewed and incorporated, as appropriate, into the final report.

Advisory Panel's Recommendations

The advisory panel developed the following non-binding recommendations to guide health system decision makers for the short-term (1 to 2 years) and medium-term (2 to 3 years) to help support the implementation of this biomarker assessment framework. These recommendations are presented without any assigned priority.

Guiding Principles

Short-Term Recommendation (1 to 2 Years)

1. Encourage responsible partners within jurisdictions to apply the guiding principles to inform all stages of the biomarker assessment process.

Medium-Term to Long-Term Recommendation (2 to 3 Years)

2. Adopt the guiding principles to support the development and implementation of a coordinated approach to biomarker assessment in Canada. This model should be built collaboratively across jurisdictions to ensure alignment with existing structures and minimize disruption.

Overall Biomarker Assessment Framework

Short-Term Recommendations (1 to 2 Years)

3. Promote awareness of this advisory panel's biomarker assessment framework and recommendations among responsible partners within jurisdictions to encourage adoption. Engage partners early and continuously to ensure the model supports rather than duplicates or disrupts existing processes.

4. Contribute to the development and implementation of a formal mechanism (e.g., pan-Canadian community of practice, working group, or committee) for jurisdictions to share biomarker assessment activities and outputs, enabling cross-jurisdictional learning and alignment.

Medium-Term Recommendations (2 to 3 Years)

5. Contribute to the development and implementation of a governance structure to support a transparent, inclusive, and coordinated approach to biomarker assessment across jurisdictions in Canada. This model should be built collaboratively across jurisdictions to ensure alignment with existing structures and minimize disruption.

6. Establish a structured process to involve and engage patients, caregivers, clinicians, laboratory professionals, jurisdictional representatives, and other key interested and impacted parties in the design and implementation of a coordinated model.

Topic Identification and Intake Process

Short-Term Recommendations (1 to 2 Years)

7. Encourage responsible partners within jurisdictions to adopt the proposed topic identification and intake model to complement existing practices, as an initial step. This approach would allow for flexibility and respects jurisdictional autonomy, while laying the groundwork for potential future transition to a coordinated pan-Canadian model.

8. Encourage responsible partners within jurisdictions to provide guidance, tools, and a process to allow patients and patient groups to contribute to topic identification at the jurisdictional level, if not already available.

9. Provide input into an assessment of the need for, feasibility of, and methods for a pan-Canadian inventory of biomarkers in cancer care that are being or have been assessed, as well as the outcomes (e.g., funded, not funded, de-funded). Such an

inventory could help promote transparency, clarity, and equity. It could be maintained by an existing pan-Canadian health organization such as CDA-AMC and be made publicly available online with a search feature.

Medium-Term Recommendations (2 to 3 Years)

10. Contribute to the development of a central intake committee, convened by an existing pan-Canadian health organization, such as CDA-AMC. The committee should include diverse perspectives and expertise and have a mandate to review submissions, triage topics, and help prioritize biomarker assessments based on system needs, evidence readiness, and potential impact on patient care and outcomes. The committee should be built collaboratively across jurisdictions to ensure alignment with existing structures and minimize disruption. A proof of concept exercise with interested jurisdictions would help evaluate feasibility and refine processes before pan-Canadian rollout.

11. Encourage coordination among various interested and impacted parties within jurisdictions to help ensure that both therapeutic and diagnostic components are assessed, funded and implemented when appropriate in a coordinated, timely and equitable manner.

Evidence Criteria and Assessment

Short-Term Recommendation (1 to 2 Years)

12. Encourage responsible partners within jurisdictions to adopt the proposed evidence criteria independently to complement existing practices as an initial step, emphasizing the benefits of a standardized approach across Canada to improve equality. While standardization may not fully address equity on its own, it can promote greater consistency and transparency, helping to identify and address disparities more effectively. This approach allows for flexibility and respects jurisdictional autonomy, while laying the groundwork for future potential transition to a coordinated pan-Canadian model.

Medium-Term Recommendation (2 to 3 years)

13. Contribute to the development and implementation of a centrally coordinated biomarker evidence assessment process that leverages existing jurisdictional review infrastructure and an existing pan-Canadian health organization, such as CDA-AMC. This could involve a rapid and standardized approach to help facilitate timely decision-making. Such a process should be built collaboratively across jurisdictions to ensure alignment with existing structures and minimize disruption.

14. Contribute to a pilot of a centrally coordinated assessment model with interested jurisdictions while prioritizing collaboration with patients, patient groups, clinicians, and clinical societies. A proof of concept exercise would help evaluate feasibility and refine processes before pan-Canadian rollout.

Question 1: Do you agree with the proposed recommendations? Please provide your reason(s) and suggested changes, if any.

Definitions

Analytical validity: The accuracy with which a test identifies the biomarker of interest

Biomarker: A biological molecule found in blood, other body fluids or tissues that is a sign of a normal or abnormal process, or of a condition of disease.[1] Within the context of this report, cancer biomarkers are defined as those produced during tumorigenesis and progression of cancers and have value in cancer diagnosis, prognosis prediction, recurrence detection, or monitoring of therapeutic efficacy. Changes in these biomarkers can be due to genetic mutations, changes in gene activity, or modifications after protein formation. Biomarkers include proteins, DNA/RNA, antibodies, peptides, and patterns in gene expression, and metabolites.[2,3]

Clinical utility: The balance of benefits and harms of using knowledge of biomarker status on how it affects or informs health outcomes and its value in guiding clinical decisions using test results.

Clinical validity: The accuracy with which biomarker status (through its test) identifies the condition of interest .

Companion diagnostic biomarker: A biomarker that is required for the initiation, monitoring (response or safety), or discontinuation of a specific companion drug or biological treatment.

Complementary diagnostic biomarker: A biomarker that provides additional insights to support treatment decisions and is not mandatory to determine treatment eligibility. A complementary diagnostic biomarker is recommended and can, for example, identify patients who are more likely to benefit from treatment or help inform dosing adjustments.

Health equity is achieved when everyone has an equal chance to attain their maximum health potential. It involves eliminating unnecessary and avoidable disparities that are unfair and unjust.

Setting the Context

The rise of precision medicine that includes biomarker testing to help guide diagnosis, treatment selection, and disease monitoring, is transforming patient care, currently most prominently within oncology.[4] However, rapid advancements in biomarker testing capabilities and other targeted, or precision, health technologies also create new challenges for health care decision-makers in Canada and around the world. Decision-makers must assess how these innovative therapies will affect health systems and patient care[5] to support delivery of care that is clinically effective, equitable, and cost-effective.[6-8] New assessment approaches may be required, as the evidence base evolves to include more real-world data, new clinical trial designs, and studies with smaller patient populations.

Technological Advancements Introduce Complex System-level Needs

Although assessing individual therapies and drugs remains a central focus of health technology assessment, there is also increasing attention paid to associated testing technologies, in particular for precision-based therapies. Emerging genetic and molecular testing technologies, including but not limited to companion diagnostics that inform the eligibility and suitability of targeted therapies, are transforming the testing landscape and bringing complex decision-making to the forefront of jurisdictions.[9,10] Integrating and implementing these new testing technologies into routine care can be affected by a complex range of system level costs and issues including health care workforce, laboratory infrastructure, and testing capacity among others.[11] In 2024, Canada's Drug Agency enhanced the drug reimbursement review process to incorporate more information about associating testing technologies and their potential implementation within drug reviews, to better equip federal, provincial, and territorial decision-makers.[12]

Building upon this work and with recognition that testing technologies are advancing at a rapid pace, including to provide a growing capability to assess multiple biomarkers through panel testing, next-generation sequencing, and other assays at a broader scale, there is a need to further support jurisdictions to assess biomarkers as a distinct health technology.[4] That is, a need to assess the value, place, and considerations of specific biomarkers by synthesizing evidence that can guide decisions about which biomarkers can be recommended for testing as part of system-level adoption.[10] Tailoring and centering assessments specifically on biomarkers

brings the potential towards a targeted assessment approach that can help address system-level needs of health care decision-makers amidst the rapidly evolving testing and treatment landscape.

Opportunity to Coordinate and Consolidate Efforts Across Canada

There are several frameworks used in Canada and internationally for assessing testing technologies, many of which are based on the ACCE[13] (**A**nalytical validity, **C**linical validity, **C**linical utility, **E**thical, legal, and social implications) model that provide a strong foundation to inform the assessment of biomarkers.[14]CDA -AMC's recent environmental scan about the landscape of biomarker testing frameworks[15] highlighted that most provincial and territorial jurisdictions in Canada have processes in place to guide testing decisions, some based on an ACCE model or some of the components. However, both within and across jurisdictions there are differences and inconsistencies in terms of specific assessment methods and processes, and perhaps relatedly what tests are covered by health systems. These inconsistencies have been observed to lead to disparities in equitable access, and timely access, to testing, and variability in laboratory capacity to conduct certain tests.[15-17] As new health technologies continue to be introduced, these disparities could hamper efforts to realize the full potential and promise of precision medicine.[16] Therefore, to help ensure equitable and consistent access to promising innovative therapies, there is a need and opportunity for health systems in Canada to better align, coordinate, and harmonize biomarker assessments.[18]

Within this context, CDA-AMC brought together an expert advisory panel that developed a consensus-based framework for assessing oncology biomarkers. This framework lays a foundation to ensure health systems are equipped for the ongoing growth and expansion of precision oncology. Assessing the value of biomarkers as distinct health technologies, albeit highly related to testing technologies and drug therapies, will play an integral role in informing health care decision-makers about wider issues related to future implementation and funding considerations. Moreover, the framework offers the opportunity to coordinate and consolidate efforts across jurisdictions, ensuring patients across jurisdictions in Canada receive high quality, effective, equitable, and consistent access to innovative therapies.

Approach

An advisory panel was convened to develop a consensus-based framework to inform adoption or funding decisions on molecular, genetic, and genomic biomarker testing in cancer care. Specifically, they developed consensus-based recommendations for:

1. Guiding Principles that reflect the goals and values health systems aim to achieve relevant to biomarker assessment
2. Key components of a Biomarker Assessment Framework including
    a. Topic identification and Intake: To identify and prioritize biomarkers for assessment by allowing eligible interested parties to make assessment requests.
    b. Evidence criteria and assessment: To evaluate and appraise the evidence supporting biomarkers by using a standardized list of evidence criteria.

As part of the discussions, the panel shared insights about best practices as well as existing opportunities to improve across jurisdictions. They also emphasized actionable non-binding recommendations to support health system decision makers across Canada to implement the framework.

The panel consisted of 15 members, including a chair, representing diverse roles, experiences and perspectives across various regions in Canada. The panel met 4 times between February and June 2025. More information on the advisory panel can be found in Appendix 1.

The advisory panel was informed by a CDA-AMC led environmental scan[15] that included a literature review and consultations with experts and senior leaders from organizations across jurisdictions involved in assessment, implementation, and funding decisions for cancer biomarkers. Building from the environmental scan, and through structured discussions and deliberations, the panel sought to build consensus on evidence-based, equitable, and system-ready approaches for biomarker assessment. The approach was rooted

in the recognition that diverse jurisdictional needs and existing practices must be acknowledged while working toward harmonized processes that enable efficient, transparent, and patient-centered decision-making.

Engagement

To gather the perspectives of diverse interested parties on the draft assessment framework, we posted an open call inviting people with personal or professional experience with molecular, genetic and genomic testing for biomarkers in cancer care in Canada to connect so they could be informed of any updates or opportunities to be involved, including providing feedback on draft documents and attending future webinars. Targeted groups were patients, families, and caregivers; patient group representatives; clinical groups, associations, or representatives; industry partners; clinicians; geneticists; pathologists; health system payers; and other health system decision-makers. Three information sessions were held in May 2025, each tailored for industry representatives, the patient community, and clinicians and clinical societies. During the sessions, information was provided about the development of the assessment framework and the status of the work, with the goal to help ensure interested parties are prepared to contribute to an extended feedback period on the proposed framework. Feedback from all interested parties is being requested for August and September 2025. All feedback received will be shared with the advisory panel, and considered and incorporated as appropriate before finalizing the framework.

Scope of the Assessment Framework

The scope of the assessment framework is outlined in Table 1 and includes biomarkers used for a wide range of purposes. It is intended to support a range of decisions, including whether to introduce, continue, or discontinue testing for specific biomarkers.

Importantly, the framework is limited to cancer-related assessments, given the majority of biomarker testing to inform care are currently in the field of oncology. The focus is on decisions at the biomarker level and intentionally excludes decisions regarding how to implement testing, for example based on specific testing platforms, given this might vary across jurisdictions depending on local context, needs, and infrastructure.

The panel identified 4 stages to a comprehensive biomarker assessment process: topic identification and intake; evidence criteria and assessment; deliberation and consensus-based recommendation development; and implementation, monitoring and continuous evaluation. The scope of this time limited advisory panel included the first two stages. Later stages of an assessment process were outside the scope of work, although may be addressed by this advisory panel or another similar group in the future.

Table 1: Assessment Framework Scope

Dimension	In scope	Out of scope
Purpose of the biomarker	Any type of biomarker, including those intended to support • Drug eligibility assessment (e.g., companion diagnostic) • Diagnosis • Prognosis • Recurrence detection • Monitoring and treatment response	• Biomarkers intended to support screening
Type of variant	• Any type of variant, including somatic and germline variants	
Approach to testing	• Reflex testing or not, and in what circumstances or patient populations • Recommendations including guidelines on testing combinations, i.e., biomarkers to test together or sequentially	• Type of testing platform • Single gene test or multi-gene panel

Type of decision	• Funding a new biomarker not currently tested for as part of standard care, including
	  • Tests that are available through clinical trials only
	  • Tests that are available through compassionate access, or patient support programs[1], only
		• Location of testing (e.g., within jurisdiction or out of jurisdiction)

	• Tests that are approved for one indication but may be used for another • Tests that are approved by Health Canada but not funded in a jurisdiction • Continue or discontinue funding of a biomarker currently being tested for	
Assessment stage	• Topic identification and intake • Evidence criteria and assessment	• Deliberation and consensus-based recommendation development; • Implementation, monitoring and continuous evaluation
Assessment criteria	• Criteria to support decision-making on adoption or funding at the biomarker level in cancer care	• Criteria to support decision-making at the test platform level • Criteria to support decision-making for conditions other than cancer
Implementation	• Implementation considerations or recommendations	• Implementation of rules or requirements
Type of testing sample	• Any type of sample, including blood-based (e.g. ctDNA), tissue-based (e.g. EGFR, HER2), and other liquid-based (urine, cerebrospinal fluid, saliva) samples	

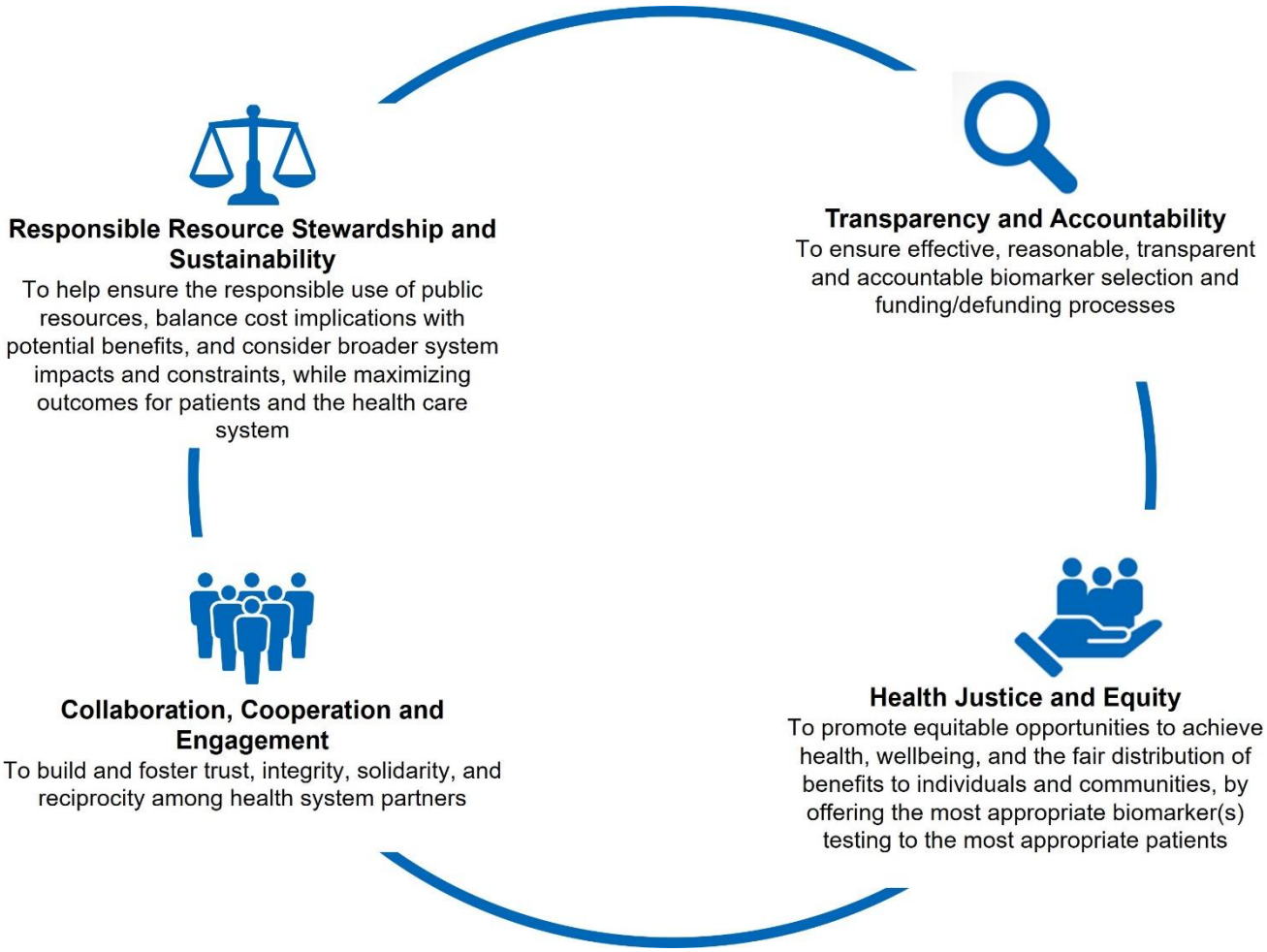
ctDNA: Circulating Tumor DNA; EGFR: Epidermal Growth Factor Receptor; HER2: Human Epidermal Growth Factor Receptor 2; CSF: Cerebrospinal Fluid
[1] In some instances, companion diagnostic biomarker testing is made available to patients through patient support programs which are usually sponsored by pharmaceutical or diagnostic companies and are designed to provide early access to therapies and related testing at no cost to patients while funding decisions are pending.

Biomarker Assessment Framework

1. Guiding Principles for the Assessment Framework

The advisory panel identified 4 guiding principles (Figure 1) that reflect the goals and values health systems aim to achieve relevant to biomarker assessment. The panel drafted these principles based on findings in the CDA-AMC Environmental Scan,[15] and through discussion and consensus-building. The panel used these principles to inform and shape the development of the overall biomarker assessment framework and recommendations for its future implementation. The guiding principles are intended to be considered collectively, as they influence, balance, support, and, in some cases, build on one another.

Figure 1: Guiding Principles



Advisory Panel Recommendations on Guiding Principles

The advisory panel recommends that decision makers use these guiding principles when refining or implementing processes for biomarker assessment in cancer care.

Short-Term Recommendation (1 to 2 Years)

1. Encourage responsible partners within jurisdictions to apply the guiding principles to inform all stages of the biomarker assessment process.

Medium-Term to Long-Term Recommendation (2 to 3 Years)

2. Adopt the guiding principles to support the development and implementation of a coordinated approach to biomarker assessment in Canada. This model should be built collaboratively across jurisdictions to ensure alignment with existing structures and minimize disruption

Question 2: Do you agree with the proposed guiding principles and definitions? Please provide your reason(s) and suggested changes, if any.

2. Biomarker Assessment Framework

There is currently no centralized governance structure for biomarker assessment in Canada. As the administration and delivery of health care is a provincial and territorial responsibility, each province and territory has its own governance structure. This decentralized model means that each jurisdiction is independently responsible for identifying biomarkers to assess, identifying and assessing evidence related to the use of biomarkers, developing recommendations, and implementing and monitoring biomarker testing and outcomes. While this approach allows for regional autonomy and responsiveness to local needs, it has also been observed to lead to variability in decision-making processes, timelines, and access to biomarker testing across the country. Depending on the jurisdiction, there may or may not be a transparent or defined pathway for biomarker assessment.

The process and related recommendations from the advisory panel are intended to complement each jurisdiction's existing practices. The advisory panel, however, identified additional opportunities for efficiency and transparency if a pan-Canadian approach, for some or all stages of the biomarker assessment process, were to be adopted. Such a future state could support more consistent decision-making, reduce unnecessary duplication of effort, and help ensure that all people living in Canada benefit from timely and evidence-based access to biomarker innovations, regardless of where they live.

Advisory Panel Recommendations on Overall Biomarker Assessment Process

The advisory panel provides the following general short-term and medium-term recommendations to guide jurisdictions in adopting and operationalizing the proposed biomarker assessment framework while fostering collaboration, alignment, and stakeholder engagement.

Short-Term Recommendations (1 to 2 Years)

3. Promote awareness of this advisory panel's biomarker assessment framework and recommendations among responsible partners within jurisdictions to encourage adoption. Engage partners early and continuously to ensure the model supports rather than duplicates or disrupts existing processes.
4. Contribute to the development and implementation of a formal mechanism (e.g., pan-Canadian community of practice, working group, or committee) for jurisdictions to share biomarker assessment activities and outputs, enabling cross-jurisdictional learning and alignment.

Medium-Term Recommendations (2 to 3 Years)

5. Contribute to the development and implementation of a governance structure to support a transparent, inclusive, and coordinated approach to biomarker assessment across jurisdictions in Canada. This model should be built collaboratively across jurisdictions to ensure alignment with existing structures and minimize disruption.
6. Establish a structured process to involve and engage patients, caregivers, clinicians, laboratory professionals, jurisdictional representatives, and other key interested and impacted parties in the design and implementation of a coordinated model.

Question 3: Do you have any specific changes that you would recommend for the proposed recommendations on the overall biomarker assessment process?

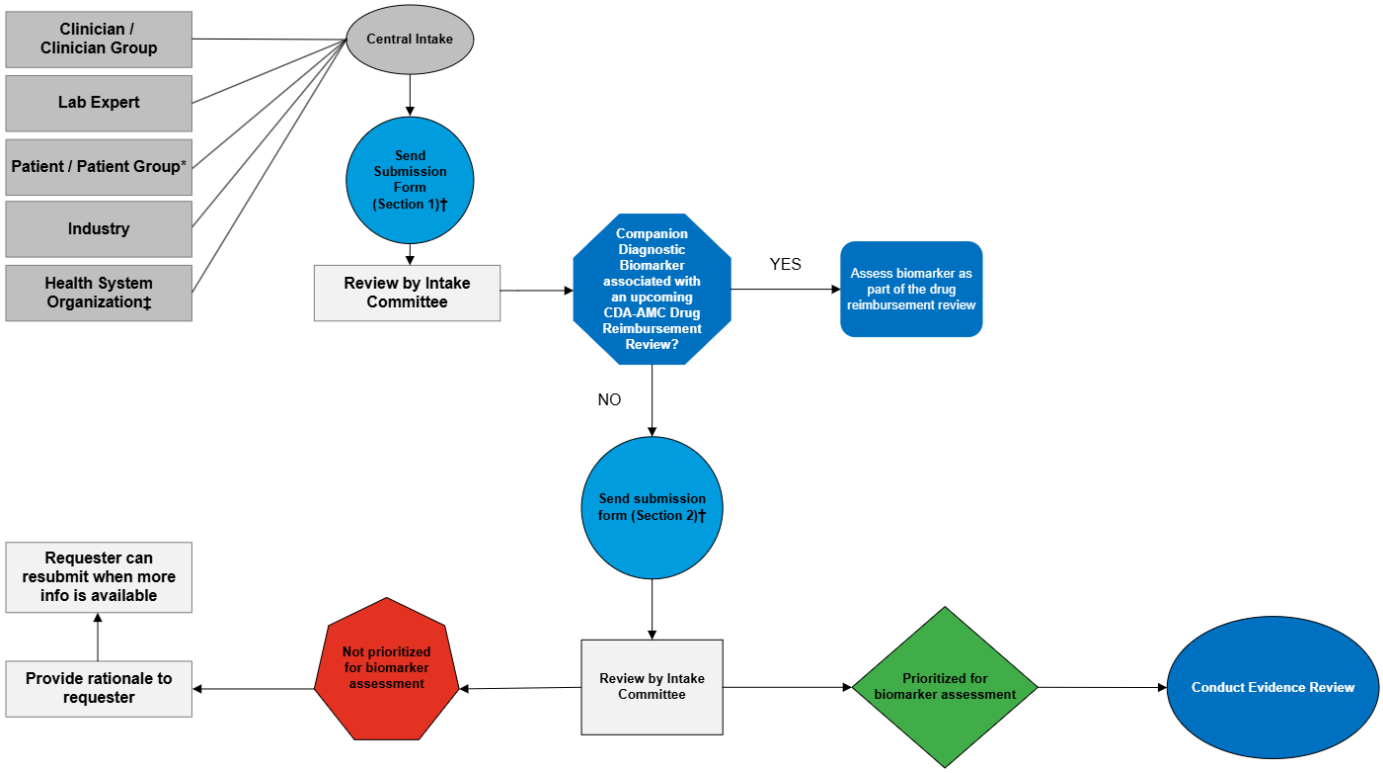
a. Topic Identification and Intake

The advisory panel recommends that jurisdictions adopt a standardized and clearly defined approach for the identification and intake of submissions for biomarkers to potentially undergo assessment. As a first step, this standardized approach could be implemented within each province and territory by leveraging existing jurisdictional practices. When and if appropriate, the advisory panel recommends transitioning to a pan-Canadian coordinated model (see Recommendations).

A topic identification and intake process could allow multiple health system partners to identify biomarkers for assessment (e.g., as is currently done in some provinces such as Alberta and Quebec), use standardized intake or submission forms to gather consistent information, and follow a structured process to prioritize and guide intake decisions. Most jurisdictions currently have distinct processes for companion diagnostics and companion diagnostic biomarker tests (e.g., AB, BC, MB, ON, QC, SK), and the advisory panel recommends continuing this distinction moving forward.

Suggested components for a standardized topic identification and intake process are outlined in Figure 2.

Figure 2: Topic Identification and Intake Process



*Additional submission support may be provided to patients/patient groups on a case-by-case basis
‡Health system organization includes health ministries or authorities, and cancer agencies or other specialty health agencies
†A complete submission form, with sections 1 and 2 completed, can be submitted at once (see guidance document)

i. A Central Intake Mechanism

The panel recommends jurisdictions adopt an open and centralized intake mechanism for the identification and nomination of biomarkers for potential assessment. This process would promote a coordinated, equitable, consistent, and transparent process to initiate appropriate assessments by providing a clear and inclusive pathway. Eligible biomarkers would be new biomarkers that are not currently tested for as part of standard care, or existing biomarkers with expanded indications.

Importantly, the panel is not prescribing a one-size-fits-all solution. A central intake mechanism could be adapted to fit each jurisdiction's capacity and infrastructure with a common goal to ensure there is one clearly identified point of contact where all biomarker assessment requests are directed. For example, this might involve designating a specific individual or office to receive submissions, setting up a shared email inbox, or creating a web-based form or portal.

While a central intake mechanism can be implemented independently by each province or territory as a first step if one does not already exist, the panel recommends that jurisdictions work toward a coordinated pan-Canadian intake model over time. A pan-

Canadian approach would help streamline efforts, reduce unnecessary duplication, and help promote more consistent access to biomarker testing across the country.

ii. Broad Eligibility for Requesters

The panel suggests that a wide range of health system partners be eligible to submit biomarker assessment requests, including clinicians and clinician groups, lab experts, patients and patient groups, industry representatives, and health system organizations including health ministries or authorities, cancer agencies and other specialty health agencies. Collective submissions by multiple groups are encouraged over individual submissions to increase efficiency, help avoid siloed efforts and to promote system-level alignment. Other groups not listed here could contact an intake committee or other designated individual for eligibility consideration on a case-by-case basis.

iii. Enhanced Support and Requirements for Specific Requesters

The panel suggests that on a case-by-case basis patients and patient groups be provided with enhanced support, such as help in gathering data elements for the Submission Form requested at the second step of the submission process. Furthermore, an intake committee or similar designate could help identify a clinician champion or other support to help advance patient and patient group-led submissions upon request.

To help promote implementation readiness, the panel suggests that biomarker assessment requests originating from industry partners (i.e., pharmaceutical and diagnostic companies) be supported by at least one clinician or clinician group, likely from the field of oncology, as well as a lab expert when available. The name, role, affiliations and contact information of the individual(s) or group(s) that was consulted should be provided during the submission process.

iv. An Intake Committee, or Designate, to Prioritize Assessments

To support a fair, transparent, and well-informed intake process, the panel recommends that jurisdictions consider establishing an intake committee, or similar function, to review submissions, triage topics, and help prioritize biomarker assessments based on system needs, evidence readiness, and potential impact on patient care and outcomes. The advisory panel developed example guiding questions for each evidence criterion (Appendix 2, Table 3) that may be used by an intake committee or similar designate to support prioritization decisions. Submissions that are deemed to have complete or sufficient information could proceed for evidence review.

The committee could also play a brokering role, linking eligible requesters with relevant clinical, lab, or jurisdictional partners to help advance submissions through the submission and intake process. This may take the form of a newly established intake committee, adapting an existing committee with a similar mandate, or designating a responsible individual to ensure that all submissions are reviewed consistently and equitably, while also bringing together diverse perspectives to inform prioritization decisions.

An intake committee could include diverse representation including for example health care professionals, lab professionals, administrators, patient and caregiver representatives, and jurisdictional health system representatives. Clinical expertise could include clinical oncology, anatomical pathology, molecular pathology, immunohistochemistry, hematopathology, genetics, and/or other specialities where appropriate.

v. Submission Process and Intake Form

The panel recommends that jurisdictions adopt a submission process that is flexible and responsive to the different levels of readiness among requesters. To support collection of consistent information, the panel created a sample intake form with 2 main sections (Appendix 3). The 2 sections are intended to help guide requesters in their submission preparation, and accommodate varying availability of supporting evidence at the time of request.

Section 1 collects essential information about the requester and the biomarker (e.g., biomarker description, target population, current use). This allows for early engagement between a requester and a submission process and the opportunity to seek clarification if needed. Section 2 gathers more detailed information (e.g., clinical utility, analytical and clinical validity, estimated costs). Requesters

may take a phased approach (i.e., first submit Section 1 and then Section 2 when prompted by the intake committee or a similar designate) or a one-step approach (i.e., submit both Section 1 and 2 at the same time). The advisory panel recommends that all requesters be required to declare any conflicts of interest at the time of submission.

Complete submission packages would be reviewed by an intake committee, or a similar designate, and the requester would be provided with a decision on whether an assessment of the biomarker would proceed based on system needs, evidence readiness, and potential impact on patient care and outcomes. If there is insufficient information from the submission package, the intake committee or designate may ask the requester for additional information or clarification. A clear rationale would be provided to the requester if the decision is not to proceed with a biomarker assessment. The requester could resubmit when more information is available. A public-facing repository of submissions is recommended, with status indicators (e.g., under review, deferred, approved).

vi. Companion vs Non-Companion Diagnostic Biomarkers

The advisory panel recommends a submission process that distinguishes between companion diagnostic and non-companion diagnostic biomarkers. Requesters could identify a biomarker as a companion diagnostic, or not, during the submission process, which would be validated by an intake committee or similar designate. The advisory panel recommends that companion diagnostic biomarkers are assessed at the same time as the companion drug or biological treatment. In instances where a companion diagnostic biomarker has been submitted for assessment, the intake committee or designate would inform the CDA-AMC and verify whether there is an existing or anticipated related CDA-AMC Drug Reimbursement Review, and whether the biomarker assessment would proceed as part of that review. By integrating the companion diagnostic biomarker assessment in the Drug Reimbursement Review process, the timing for funding recommendations addressing both the drug and associated companion diagnostic biomarker could be aligned. For the purposes of this biomarker assessment framework, complementary diagnostic tests would be assessed through the non-companion diagnostic biomarker review stream.

The panel acknowledges the potential for misalignment in timing between drug funding approval and the establishment of biomarker testing infrastructure, potentially delaying timely or equitable access to treatment. Addressing this misalignment may require proactive coordination among various interested and impacted parties such as drug sponsors, diagnostic companies, jurisdictional health systems, and HTA bodies to ensure that both therapeutic and diagnostic components are evaluated and implemented in a timely and equitable manner.

vii. Prioritization for Biomarker Assessment

Biomarkers would be prioritized for assessment based on system needs, evidence readiness, and potential impact on patient care and outcomes. If the intake committee or a similar designate determines that a submitted biomarker has sufficient information to inform an assessment based on the submission package, a recommendation would be made to proceed with an evidence assessment. The focus of an evidence assessment would be to assess and appraise the quality of submitted evidence and information by using available evidence grading frameworks. If there is insufficient information from the submission package, the intake committee or similar designate may ask the requester for additional information or clarification.

Advisory Panel Recommendations on Topic Identification and Intake

The following short- and medium-term recommendations are intended to guide and support jurisdictions in enhancing biomarker topic identification and intake processes in cancer care, while respecting jurisdictional autonomy and existing practices.

Short-Term Recommendations (1 to 2 Years)

7. Encourage responsible partners within jurisdictions to adopt the proposed topic identification and intake model to complement existing practices, as an initial step. This approach would allow for flexibility and respects jurisdictional autonomy, while laying the groundwork for potential future transition to a coordinated pan-Canadian model.

8. Encourage responsible partners within jurisdictions to provide guidance, tools, and a process to allow patients and patient groups to contribute to topic identification at the jurisdictional level, if not already available.

9. Provide input into an assessment of the need for, feasibility of, and methods for a pan-Canadian inventory of biomarkers in cancer care that are being or have been assessed, as well as the outcomes (e.g., funded, not funded, de-funded). Such an inventory could help promote transparency, clarity, and equity. It could be maintained by an existing pan-Canadian health organization such as CDA-AMC and be made publicly available online with a search feature.

Medium-Term Recommendations (2 to 3 Years)

10. Contribute to the development of a central intake committee, convened by an existing pan-Canadian health organization, such as CDA-AMC. The committee should include diverse perspectives and expertise and have a mandate to review submissions, triage topics, and help prioritize biomarker assessments based on system needs, evidence readiness, and potential impact on patient care and outcomes. The committee should be built collaboratively across jurisdictions to ensure alignment with existing structures and minimize disruption. A proof of concept exercise with interested jurisdictions would help evaluate feasibility and refine processes before pan-Canadian rollout.

11. Encourage coordination among various interested and impacted parties within jurisdictions to help ensure that both therapeutic and diagnostic components are assessed, funded and implemented when appropriate in a coordinated, timely and equitable manner.

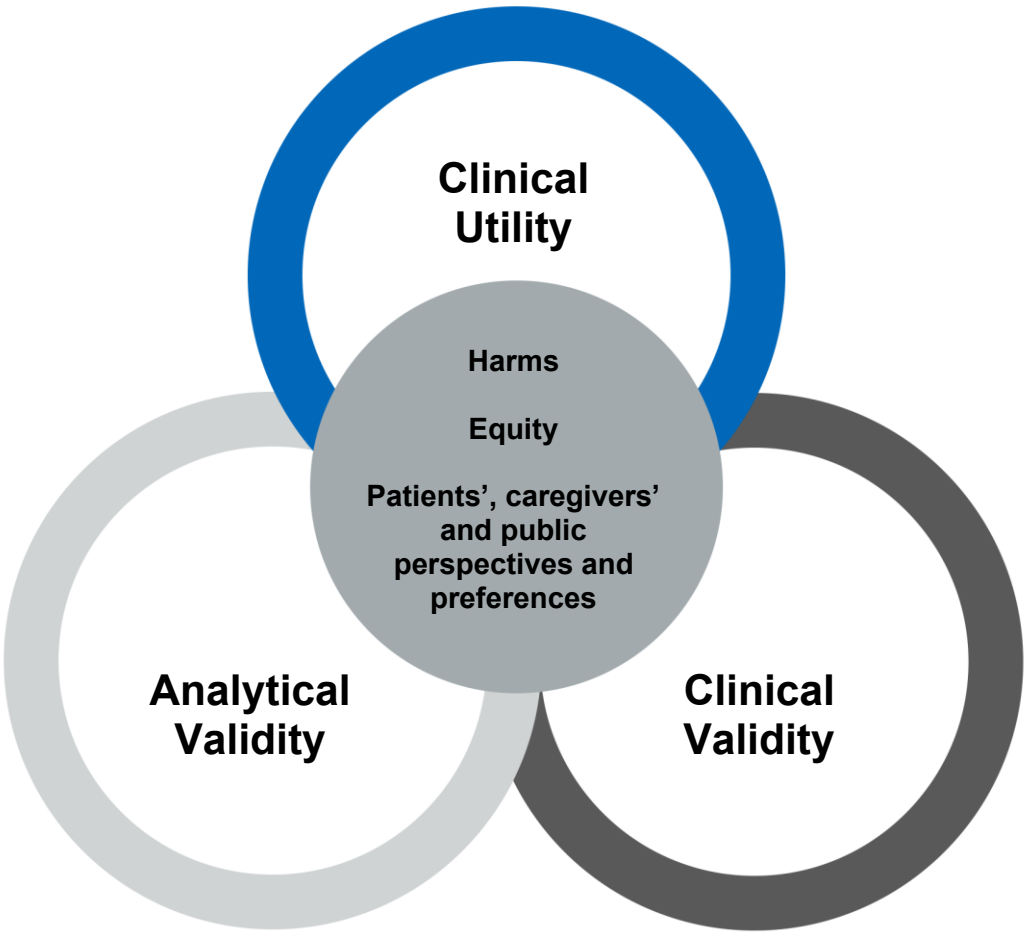
Question 4: Do you agree with the short-term and medium-term recommendations on topic identification and intake? Please provide your reason(s) and suggested changes, if any.

b. Evidence Criteria and Assessment

The advisory panel proposed 3 core (i.e., clinical utility, analytical validity, clinical validity) and 3 cross-cutting (i.e., harms, equity, patients', caregivers', and public perspectives and preferences) evidence criteria to use for the assessment of biomarkers (Figure 3). The identification of these criteria was informed by the CDA-AMC Environmental Scan, review of available jurisdictional process documents, and panel discussions.[15] The core criteria are proposed to assess whether information about biomarker status provides meaningful clinical benefit, is analytically sound, and testing can be implemented equitably. The 3 cross-cutting criteria were identified as important across the 3 core criteria, and as such are embedded within or across each. Of note, the panel discussed that not all relevant equity considerations are embedded within the 3 core criteria, and as such equity is also retained as a standalone criterion. Having equity as a core and a cross-cutting criterion helps ensure that any overarching or cross-cutting equity issues (e.g., access disparities, population-specific impacts, systemic barriers) that may not be fully captured within the core criteria can still be explicitly assessed and addressed.

The advisory panel discussed the inclusion of cost, or cost considerations, as an evidence criterion and ultimately decided against its inclusion. The panel discussed that while cost considerations are relevant, and necessary to uphold the guiding principle of responsible resource stewardship and responsibility, cost is often context-specific and may be more appropriately addressed during jurisdictional deliberation and funding recommendation development, rather than during an evidence assessment process. Nonetheless, the panel acknowledged the importance of understanding potential affordability concerns early in the process. As such, the Submission Form (Appendix 3) includes a field requesting the estimated cost of the biomarker test, if available. This preliminary cost information, in addition to an estimated number of individuals who would be expected to require the biomarker testing, is intended to support early detection of affordability issues and inform downstream planning and decision-making.

Figure 3: Evidence Criteria



The panel recommends that these standardized evidence criteria be implemented within existing jurisdictional processes as a first step. When appropriate, a subsequent step could be to transition to a pan-Canadian coordinated model (see Recommendations).

A description of each criterion, recommended evidence or information requirements, and example evidence or information sources are provided in Table 2.

Table 2: Evidence Criteria

Criteria	Recommended evidence or information requirements	Example sources

Clinical utility
The balance of benefits and harms of using knowledge of biomarker status on how it affects or informs health outcomes and its value in guiding clinical decisions using test results
	• Available studies or information on clinical utility, including patients' perceptions of value and impact, and impact of knowledge of biomarker status on:
	  • Clinical decision-making
	  • Patient outcomes
		• Clinical studies (e.g., RCTs, cohort studies)
		• Real-world evidence
		• Guidelines, position statements, expert opinion
		• Health technology assessments
		• Qualitative studies or other sources of qualitative information describing:
		  • Clinicians' perspectives
		  • Lab experts' perspectives
		  • Patients', caregivers', and public perspectives

Analytical validity
The accuracy with which a test identifies the biomarker of interest
	• Available studies or information on analytical validity, including:
	  • Analytic sensitivity
	  • Analytic specificity
	  • Limit of detection
	  • Accuracy
	  • Precision
	  • Linearity across expected concentration range
	  • Robustness
	  • Limit of quantitation
	  • Biomarker stability under different storage or handling conditions
	  • Validated reportable range
	  • Reference intervals
		• Test validation studies
		• Clinical studies (e.g., RCTs, cohort studies)
		• Real-world evidence
		• Health technology assessments
		• Qualitative studies or other sources of qualitative information describing:
		  • Clinicians' perspectives
		  • Lab experts' perspectives
		  • Patients', caregivers', and public perspectives

Clinical validity
The accuracy with which biomarker status (through its test) identifies the condition of interest
	• Available studies or information on clinical validity, including:
	  • Clinical sensitivity
	  • Clinical specificity
	  • Positive predictive value
	  • Negative predictive value
	  • Prevalence
	  • Ability to identify or predict cancer presence, progression, or treatment response
		• Clinical studies (e.g., RCTs, cohort studies)
		• Real-world evidence
		• Health technology assessments
		• Qualitative studies or other sources of qualitative information describing:
		  • Clinicians' perspectives
		  • Lab experts' perspectives
		  • Patients', caregivers', and public perspectives

Additional equity considerations
Health equity is achieved when everyone has an equal chance to attain their maximum health potential. It involves eliminating unnecessary and avoidable disparities that are unfair and unjust
	• Available studies and information on any additional equity considerations (e.g., access disparities, population-specific impacts, systemic barriers)	• Qualitative studies or reviews
		• Health technology assessments
		• Qualitative studies or other sources of qualitative information describing:
		  • Clinicians' perspectives
		  • Lab experts' perspectives
		  • Patients', caregivers', and public perspectives

Question 5: Do you agree with the proposed evidence criteria? Please provide your reason(s) and suggested changes, if any.

Evidence Submission

The panel has developed a sample Submission Form (Appendix 3) to collect evidence and information that relate to the evidence criteria, and to support a subsequent review and assessment. Most jurisdictions currently use some or most of the identified criteria as part of their existing assessment processes, and several reference the use of guidelines or external reports to supplement or validate submitted evidence and information.

The evidence criteria in Table 2 are ordered without implying any hierarchy or relative importance. The panel acknowledged that the relative importance of each criterion may vary depending on the specific biomarker being assessed. To promote consistency and completeness in submissions, requesters could be asked to refer to such a table for the recommended evidence requirements and example sources of evidence and information relating to each evidence criterion.

The panel acknowledged that the current evidence supporting many biomarkers used in cancer care may be limited in scope and/or quality. The advisory panel recommends that all available evidence for a biomarker should be submitted as part of the submission process to support subsequent review and to help inform decisions about its appropriate use in clinical practice.

Question 6: Do you agree with the proposed process for evidence submission? Please provide your reason(s) and suggested changes, if any.

Evidence Review

The purpose of an evidence review would be to identify, assess, critically appraise and summarize the quality, relevance, and completeness of the submitted evidence and supporting information using established evidence grading frameworks. The advisory panel agreed that the evidence review should be informed by the evidence criteria. This process is intended to result in a report that synthesizes the findings and provides a structured appraisal of all available evidence and information. The report would then be submitted to a deliberative body to inform the development of a recommendation on a specific biomarker. This ensures that decision-making is grounded in a transparent, consistent, and evidence-based approach.

The advisory panel developed example guiding questions for each core evidence criterion (Appendix 2, Table 3) that may be used by to guide an assessment. This list of guiding questions is not intended to be exhaustive; rather, it is designed to illustrate the types of considerations an assessment body could take into account during the evidence review process. It may not be possible to address all of these questions in an evidence review, given the nature and intended use of the biomarker and the state of the body of available evidence. An independent literature search to address any areas of limited knowledge is recommended to support an evidence review.

The advisory panel acknowledged that an evidence review process be inclusive of appropriate experts, and those with lived and living experience, to uphold the guiding principle of collaboration, cooperation and engagement. The scope, detail, and timeline for completion of the evidence review would be contingent upon practical, technical, and methodological considerations; however, the panel agreed that timeliness is an essential consideration and that the time for an evidence review should not unduly postpone recommendations for or access to valuable biomarker testing.

Question 7: Do you agree with the proposed process for evidence review? Please provide your reason(s) and suggested changes, if any.

Advisory Panel Recommendations on Evidence Criteria and Assessment

The following short- and medium-term recommendations are intended to guide jurisdictions in strengthening evidence criteria and assessment processes for biomarkers in cancer care, while supporting alignment and flexibility across Canada.

Short-Term Recommendation (1 to 2 Years)

12. Encourage responsible partners within jurisdictions to adopt the proposed evidence criteria independently to complement existing practices as an initial step, emphasizing the benefits of a standardized approach across Canada to improve equality. While standardization may not fully address equity on its own, it can promote greater consistency and transparency, helping to identify and address disparities more effectively. This approach allows for flexibility and respects jurisdictional autonomy, while laying the groundwork for future potential transition to a coordinated pan-Canadian model.

Medium-Term Recommendation (2 to 3 years)

13. Contribute to the development and implementation of a centrally coordinated biomarker evidence assessment process that leverages existing jurisdictional review infrastructure and an existing pan-Canadian health organization, such as CDA-AMC. This could involve a rapid and standardized approach to help facilitate timely decision-making. Such a process should be built collaboratively across jurisdictions to ensure alignment with existing structures and minimize disruption.

14. Contribute to a pilot of a centrally coordinated assessment model with interested jurisdictions while prioritizing collaboration with patients, patient groups, clinicians, and clinical societies. A proof of concept exercise would help evaluate feasibility and refine processes before pan-Canadian rollout.

Future Considerations

Opportunities in Subsequent Stages of the Biomarker Assessment Process

The panel identified 4 stages to a comprehensive biomarker assessment process, and the scope for this panel's work was on the first 2 stages: topic identification and intake; and evidence criteria and assessment. As a potential future phase of work, the advisory panel or another similar group could focus on the subsequent stages in the biomarker assessment process: deliberation and consensus-based recommendation development; and implementation, monitoring and continuous evaluation. These latter stages are critical as they directly influence how evidence is translated into funding decisions and how biomarkers are integrated or removed from clinical practice. While outside the scope for this time-limited advisory panel, some recommendations were inevitably raised during their conversations and are included below.

Deliberation and Consensus-based Recommendation Development

The panel emphasized the importance of taking a structured, inclusive, and evidence-informed deliberative approach to making recommendations about biomarker funding and implementation. Jurisdictions are encouraged to adopt standardized, well-documented approaches to ensure consistency and transparency in funding or defunding decisions. This could include applying the panel's proposed 4 guiding principles and ensuring that deliberative bodies are broadly representative, while leveraging expertise and experience from professionals in oncology, pathology, genetics, economics, ethics, and patient advocacy. The complexity of interpreting evolving evidence, balancing multiple criteria, and incorporating patients', caregivers', and public perspectives may require a thoughtful engagement strategy. The panel also recommends that jurisdictions consider publishing draft recommendations for broad feedback before implementing or de-implementing testing for a given biomarker into health systems.

Implementation, Monitoring and Continuous Evaluation

A range of operational challenges may need to be addressed to ensure successful biomarker testing implementation. A commonly identified challenge is the misalignment between drug funding approval and the readiness of biomarker testing infrastructure, particularly for companion diagnostic biomarkers. Delays in funding, lab capacity, equipment acquisition, and workforce training can

hinder timely access to testing, and therefore treatment. Additionally, the panel identified that the absence of a centralized body to coordinate pricing and procurement may contribute to fragmentation and inefficiencies.

The panel may consider reconvening to support development of a coordinated pan-Canadian framework to support these later stages and foster further alignment across provinces and territories. To inform this potential future work, a comparative assessment could assess jurisdictional differences, highlight existing strengths, and estimate the effort needed for greater coordination.

Impact of Real-World Evidence in Decision-Making

The panel recognized the importance of real-world evidence in informing biomarker assessments, particularly in cases where RCTs or large cohort studies are limited or unavailable. Real-world evidence provides insights into how biomarkers perform in routine clinical settings and across diverse patient populations. This is relevant for understanding clinical utility and equity impacts as some demographic groups may be underrepresented in clinical trials. The panel emphasized that collecting demographic-specific data could help inform whether biomarker testing can be equitably implemented and accessible across different demographic groups.

In addition to supporting broader evidence collection, the panel also discussed the potential for a coordinated, pan-Canadian approach to real-world data collection. This could involve building up infrastructure to support data sharing across jurisdictions and harmonizing data elements. These efforts would not only enhance the body of evidence for biomarker assessments but also enable continuous learning and refinement of funding and implementation decisions over time.

Expanding Biomarker Assessments Beyond Cancer

There was interest throughout this panel's discussions and CDA-AMC's information sessions in expanding the biomarker assessment framework beyond cancer care. For example, participants from patient and clinical communities asked whether the assessment framework could be adapted for use in other areas of medicine, such as infectious diseases and chronic illnesses. While the panel's current focus is on cancer-related biomarkers, the panel acknowledged that a future phase of work could explore how to tailor the framework for other clinical areas. This would likely involve refining evidence requirements and engaging subject-matter experts in non-oncology fields. The panel encourages future efforts to consider how this foundational work might serve as a model for broader biomarker assessment across the health care system.

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Appendix 1: About the Advisory Panel Members

The names, biographies, and conflict of interest declarations of the 15 members on the advisory panel, inclusive of 2 observers, are available on the Canada's Drug Agency website.

Panel Members

- **Maureen Trudeau (Chair)** Medical Oncologist at Sunnybrook Health Sciences Centre (Ontario).
- **Angela Hyde** Medical Oncologist at Newfoundland and Labrador Health Services (Newfoundland and Labrador).
- **Darryl Boehm** Director of Oncology Pharmacy Services at Saskatchewan Cancer Agency (Saskatchewan).
- **Eric Hamilton** Health Innovation, Patient Engagement and Advocacy (Alberta).
- **Eshwar Kumar** Medical Officer at New Brunswick Cancer Network (New Brunswick).
- **Harriet Feilotter** Director and Lead of Clinical Implementation at Ontario Molecular Pathology Research Network, Ontario Institute for Cancer Research (Ontario).
- **Helen Anderson** Medical Oncologist and Senior Executive Director, Systemic Therapy and Clinical Programs at BC Cancer–Provincial Health Services Authority (British Columbia).
- **Michael Carter** Medical Director of Molecular Diagnostics at Nova Scotia Health (Nova Scotia).
- **Robby Spring** Health Innovation, Patient Engagement and Advocacy (Ontario).
- **Shantanu Banerji** Director of Precision Oncology and Medical Oncologist at CancerCare Manitoba (Manitoba).
- **Stirling Bryan** Health Economist and Professor at the School of Population and Public Health, University of British Columbia (British Columbia).
- **Tammy Hofer** Chief Operating Officer at Alberta Precision Laboratories (Alberta).
- **Yvonne Bombard**, Canada Research Chair in Genomics Health Services and Policy Professor at the Institute of Health Policy, Management and Evaluation, University of Toronto (Ontario).
- **François Sanschagrin (Observer)**, Medical Biology Advisor at the Laboratory and Medical Imaging Directorate of the Quebec Ministry of Health and Social Services (Quebec).
- **Mélanie Martin (Observer)** Deputy Director in Technology Innovation and Medical Biology and Genomics of the Institut national d'excellence en santé et en services sociaux (INESSS) in Quebec.

Conflict of Interest Statements

- Each panel member and observer have provided a conflict-of-interest statement, detailing any potential conflicts related to their roles and affiliations. (https://www.cda-amc.ca/advisory-panel-framework-assess-cancer-biomarkers)

Appendix 2: Example Guiding Questions for Topic Prioritization and Evidence Review

Table 3: Example Guiding Questions*

Clinical utility

General considerations

- What patient important clinical outcomes (e.g., overall survival, progression-free survival, disease-free survival, quality of life, avoidance of unnecessary/incorrect treatments) are expected to be impacted by knowledge of biomarker status and subsequent treatment decision-making?
- What is the comparative clinical utility of knowing the biomarker status compared to current standard practice or alternative diagnostic approaches? What are the potential implications of not knowing biomarker status on patient important clinical outcomes?
- At what point(s) along the patient care pathway should biomarker testing be implemented to maximize clinical utility, such as at diagnosis, recurrence, prior to first-line therapy, or upon disease progression? How does this timing influence treatment decisions and outcomes?
- Is the estimated change in outcomes clinically meaningful to patients, caregivers, and health care providers?
- Has clinical utility of this biomarker already been evaluated in an existing HTA or assessment in Canada or internationally?

Harms considerations

- Are there potential harms or potential downstream consequences of biomarker testing (e.g., unnecessary follow up procedures, biopsies, or treatments triggered by false positive results)?
- What are the risks that the knowledge of biomarker status could lead to worse outcomes compared to standard care?
- What is the risk that premature adoption of biomarker testing could divert resources or attention from more effective interventions, ultimately harming patient outcomes?
- Could misinterpretation of biomarker status lead to adverse patient outcomes following from delayed diagnosis or missed cases?
- What is the likelihood that reliance on information about biomarker status could result in overtreatment, or incorrect treatment, exposing patients to unnecessary procedures or toxicities?

Equity considerations

- Does knowledge of biomarker status have the potential to impact outcomes and inform clinical decisions equitably across all populations? Which populations may be inequitably impacted and why?
- How might the introduction of testing for the biomarker affect health disparities or access to care?
- Were diverse populations included in the clinical utility studies, and do results generalize to all groups who may need the test?
- Are demographic subgroup data available? What populations were assessed in the supporting evidence?
- Are there differences in how biomarker test results are communicated or acted upon for patients with varying health literacy or language proficiency, potentially impacting outcomes?
- Does the implementation of biomarker testing risk widening disparities in cancer outcomes if certain groups are less likely to receive testing or benefit from resulting therapies?

Patients', caregivers' and public perspectives and preferences

- What are the perceived values and impacts of knowledge of biomarker status in informing their care?
- Do patients feel supported in understanding how biomarker test results will be used in treatment planning?
- What are preferences regarding shared decision-making based on biomarker test results?

Analytical validity**

General considerations

- Which specific analytical metrics for measurement (e.g., sensitivity, specificity, precision, reproducibility, repeatability,) are relevant and necessary to evaluate when measuring a specific biomarker?
- Has the accuracy of the biomarker measurement been evaluated in the context of the assay used for submission?
- Are the mutations or variants of interest clearly defined along with the required sensitivity and specificity for detection?
- What methods were used to evaluate the linearity of the biomarker across its expected concentration range?
- How was the limit of quantitation determined?
- How were the reference intervals determined?
- Has the within-run precision (i.e., repeatability) been evaluated for the biomarker in the context of the assay used for submission?

- Has the between-run precision (i.e., reproducibility) been evaluated for the biomarker in the context of the assay used for submission?
- Has analytical validity already been evaluated in an existing HTA or assessment in Canada or internationally?

Harms considerations

- Does the biomarker test have sufficient analytical validity to outweigh the risk of potentially causing more harm than benefit if the test is inaccurate?
- Could false positives or false negatives due to assay imprecision, sample handling errors, or technical limitations lead to subsequent harm?
- How reproducible and robust are results across different laboratories or platforms? Could this variability result in inconsistent clinical decisions or patient harm?

Equity considerations

- Does the biomarker test reliably and accurately measure the biomarker in all relevant populations?
- Has the biomarker test been validated across diverse demographic groups (e.g., race, ethnicity, age, sex, socioeconomic status) to ensure accuracy and reliability for all patients?
- Are demographic subgroup data available? What populations were assessed in the supporting evidence?

Patients', caregivers' and public perspectives and preferences

- How confident are these groups in the accuracy and consistency of the biomarker test results?
- How is information about analytical validity communicated to these groups?
- What are perspectives about false positives or false negatives from these groups?

Clinical validity**

General considerations

- Does the biomarker status (through its test) predict or measure the relevant clinical condition (e.g., diagnosis, prognosis, treatment response)?
- Does the biomarker accurately and consistently predict or measure the relevant clinical condition (e.g., diagnosis, prognosis, treatment response)?
- How does the clinical validity change as a biomarker is used outside of clinical trials?
- Has clinical validity of this biomarker already been evaluated in an existing HTA or assessment in Canada or internationally?

Harms consideration

- Could misinterpretation of biomarker status lead to delayed diagnosis or missed cases?
- Are there patient subgroups where the biomarker status is less able to predict or measure the relevant clinical condition, which could result in an increased risk of harm for these individuals?

Equity considerations

- Does the biomarker status (through its test) accurately predict or measure the clinical condition across all populations?
- Does the biomarker demonstrate consistent predictive value and clinical correlations across different demographic and socioeconomic groups?
- Were diverse populations included in the clinical validation studies, and do results generalize to all groups who may need the test?
- Are demographic subgroup data available? What populations were assessed in the supporting evidence?

Patients', caregivers' and public perspectives and preferences

- Are these groups aware of the connection between the biomarker and the clinical condition? How important is this connection and why?
- How accepting are these groups of varying levels of inaccuracy?

Additional equity considerations

- Does knowledge of biomarker status and the decisions it is intended to inform uphold society and ethical values such as justice and inclusivity?
- Does knowledge of biomarker status and the decisions it is intended to inform promote fairness in care delivery, or could it unintentionally worsen existing health disparities?
- Are health care providers adequately informed about biomarker tests available through public funding to ensure equitable access for all eligible patients?
- Are there disparities in awareness or understanding of the biomarker among clinicians serving different communities, potentially affecting test ordering, interpretation, or follow up care?
- Is access to biomarker testing and subsequent targeted therapies equitable across all patient populations, regardless of geography or health care setting?
- Are there cost, logistical or other barriers (e.g., sample transport, specialized equipment) that disproportionately affect certain groups or geographic areas that could prevent equitable integration of the biomarker into routine care for all eligible patients?

- Does the laboratory infrastructure and capacity vary across regions or health systems, potentially limiting access to high-quality testing for underserved populations?
- Does the specimen collection process itself pose a barrier to access for some groups (e.g., invasive procedures, travel requirements, or cultural concerns)?
- Could alternative testing approaches (e.g., point-of-care testing in remote regions, ctDNA testing for patients unable to undergo tissue biopsy) help overcome identified access barriers?
- Are there mechanisms in place to collect equity-related data (e.g., demographic, geographic, or socioeconomic indicators) to monitor and address disparities in access and outcomes over time?
- Have equity considerations already been evaluated for this biomarker in an existing HTA or assessment in Canada or internationally?

* This list of guiding questions is not intended to be exhaustive. Furthermore, not all biomarker submission packages may be able to address all these questions depending on the state of the body of available evidence.
** Given the inherent interdependence between the biomarker and its associated testing platform, some guiding questions may be applicable to both components, reflecting their combined influence on a biomarker's clinical utility.

Appendix 3: Biomarker Assessment Submission Form

When making a request to assess a biomarker, eligible requesters can complete Section 1 of this submission form. Submission packages will then be reviewed by an intake committee or similar designate and the requester will be provided with a decision on whether an assessment of the biomarker will proceed. The committee or designate may ask the requester for additional clarification questions, broker connections to help advance submissions to the next step or advance the submission for further consideration and request the completion of Section 2. If sufficient information is available at the outset, requesters may complete and submit both Section 1 and 2 at the same time.

If the submitted biomarker is deemed as a true companion diagnostic biomarker, the intake committee will inform the CDA-AMC and verify whether there is an existing or anticipated related CDA-AMC Drug Reimbursement Review, and whether the biomarker assessment would proceed as part of that review. If so, the recommendation will be to assess the companion diagnostic biomarker at the same time as the related targeted drug therapy, with the drug sponsor requested to submit relevant information as part of that process.

Section 1

1. Contact Information

Required Information	Response
Requestor	<name of the organization, institution, or company>
Date of submission	
Name of submitting consultant (if applicable)	
Primary contact information	Name: Title: Email: Phone number:
Secondary contact for submission (if applicable)	Name: Title: Email: Phone number:
Expert contacts consulted during submission preparation (for industry led applications)	☐ Clinician/clinician group name, role, affiliations and contact details (required): ☐ Lab expert name, role, affiliations and contact details (if applicable):

2. Biomarker Information

Required Information	Response
Biomarker name	
Provide a brief description of the biomarker	
What specific feature(s) or alteration (s) of the biomarker would be measured?	☐ Expression level ☐ Mutation type (e.g., point mutation, indel, deletion), please specify: ☐ Epigenetic modification (e.g., methylation status) ☐ Protein modification ☐ Other (please specify):

Type of specimen required for testing	☐ Tissue ☐ Blood ☐ Saliva ☐ Urine ☐ Other (specify):
Current use	☐ Biomarker not commonly tested for as part of routine care ☐ Biomarker currently tested as part of routine care, but for a different indication. If so, please identify the indication(s) for which the biomarker is currently tested:
Target population (e.g., type of cancer and stage, any subgroups)	
Please explain the purpose of the biomarker	☐ For therapy selection (see question below): ☐ Diagnosis ☐ Staging and prognosis ☐ Risk assessment ☐ Surveillance ☐ Monitoring ☐ Discontinuation ☐ Other (specify):
Is this biomarker a companion or complementary diagnostic to a therapy?	☐ Companion diagnostic: The biomarker test is essential for the safe and effective use of a companion therapy, which cannot be prescribed without the biomarker result. ☐ Complementary diagnostic: The biomarker test helps inform treatment decisions, but is not required for determining patient eligibility for a therapy. ☐ Neither ☐ Unclear / unknown

If this biomarker is a companion or complementary diagnostic to a therapy, please provide a response:	Please provide the name and indication of the drug or biologic treatment, or other therapy: _____ Please indicate the status of the drug or biological treatment in Canada: ☐ Approved by Health Canada ☐ Under Health Canada review ☐ Not approved/ rejected by Health Canada ☐ Available via Special Access Program only ☐ Available for clinical trials only ☐ Other (specify): Please indicate the funding/ reimbursement status in Canada: ☐ Publicly funded ☐ Not publicly funded ☐ Under HTA review (CDA-AMC/ INESSS) ☐ Recommended for public reimbursement ☐ Other (specify):
Has this biomarker been assessed by any Canadian or international HTA organization(s)?	☐ Yes If yes, please specify which organization(s): If yes, please include references. ☐ No ☐ Unclear

Section 2

3. Clinical information

Required Information	Response
What is the intended clinical use or decision supported by assessing this biomarker?	
Provide any other clinical context that might be of interest .	
Provide an overview of the current testing pathway for the indication and where in that pathway the biomarker testing procedure best fits (e.g., reflex during diagnosis, upon disease progression, monitoring during treatment).	
What is the estimated number of individuals in your jurisdiction who would be expected to require the biomarker testing (e.g., per year)? Please provide any references or supporting information to justify the response.	
Is it anticipated that biomarker testing would need to be repeated more than once before, during, or after the course of treatment? Please describe.	
What is the evidence regarding clinical utility[a] of the biomarker?[e]	Please provide any references or supporting information to justify the response.
What is the evidence regarding analytical validity[b, d] of the testing procedure(s) of the biomarker?[e]	Please provide any references or supporting information to justify the response.

What the evidence regarding clinical validity[c] of the biomarker?[e]	Please provide any references or supporting information to justify the response.
What information and evidence exists to support relevant health equity considerations[d] for the biomarker?[e]	Please provide any references or supporting information to justify the response.

[a] Clinical utility: The balance of benefits and harms of using knowledge of biomarker status on how it affects or informs health outcomes and its value in guiding clinical decisions using the test
[b] Analytical validity: The accuracy with which a test identifies the biomarker of interest
[c] Clinical validity: The accuracy with which biomarker status (through its test) identifies the condition of interest.
[d] Health equity is achieved when everyone has an equal chance to attain their maximum health potential. It involves eliminating unnecessary and avoidable disparities that are unfair and unjust.
[e] Please refer to Table 2 and Appendix 2, Table 3 of the Planning for a Coordinated Assessment Framework for Biomarkers Used in Cancer Care: A Report from the Biomarker Advisory Panel for additional details about how to respond to this question.

4. Testing and Cost Information:

Required Information	Response
What testing methods could be used to test for this biomarker? Select all that apply	☐ Immunohistochemistry (IHC) ☐ Polymerase Chain Reaction (PCR) ☐ Next Generation Sequencing (NGS) ☐ Other (please specify): ☐ Unclear/ unknown
Are any of testing strategies/ platforms approved by Health Canada?	☐ Yes. If yes, what is the name of the strategy(s)/platform(s): _____ If yes, what is the date of Health Canada approval: _____ ☐ No. ☐ Under review. Estimated date of approval: _____ ☐ To be confirmed (requested, Health Canada decision pending) ☐ Other, please specify: ☐ Unclear

Has testing for the biomarker been funded in any jurisdictions in Canada?	☐ Yes ☐ No ☐ Not sure If yes, please specify the jurisdictions and what testing strategies are used, where known.
What is the expected cost per test of the biomarker? If there are multiple testing methods, please include available information. If no cost information is available or known, please indicate so.	