# Addressing gaps and challenges with the integration of precision health technologies into the Canadian health system

## Summary report of an IHE/CAPT Precision Health Workshop

## October 22, 2017

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The IHE/CAPT workshop was held October 22, 2017 in Toronto, Ontario.

The workshop was supported by unrestricted grants from Merck Canada and Hoffmann-La Roche Limited.

The views expressed herein do not necessarily represent the official policy of these organizations.

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The views expressed in this report are of the Institute of Health Economics.

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## Declared Competing Interest of Authors

Competing interest is considered to be financial interest or non-financial interest, either direct or indirect, that would affect the research contained in this report or create a situation in which a person's judgement could be unduly influenced by a secondary interest, such as personal advancement.

The authors of this publication claim no competing interest.

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## Web Address

# Executive Summary

## Introduction

This report follows from the Institute of Health Economics (IHE, *www.ihe.ca*)/Canadian Association for Population Therapeutics (CAPT, *www.capt-actp.com*) Precision Health Workshop that was held on October 22, 2017 in Toronto, Ontario. This meeting was a satellite to the 2017 Annual CAPT Conference.

A total of 40 individuals registered for the workshop, including three speakers and three panellists. Participants reflected the perspectives of public payers, clinician/providers, academia, regulators, health technology assessment (HTA) agencies, laboratory services, patient advocates, and industry. The format for the day was a number of presentations from invited speakers, followed by a case study exercise and table discussion, and finally a panel discussion.

The objectives of the workshop were to:

1. review the concept of Precision Health and outline its potential impact on patient care and timely access to innovative medicines;
2. share examples/case studies and lessons learned from Precision Health innovations and how they have been introduced into various health systems; and
3. obtain insights from stakeholders on the gaps/challenges, implications, and potential solutions to enable the integration of Precision Health innovations into the Canadian health system.

## The Promise of Precision Health & Lessons Learned

The promise of Precision Health is significant. The Personalized Medicine Coalition in the United States has identified a number of key benefits, notably the improved ability to:

- direct targeted therapy, and reduce trial-and-error prescribing;
- reduce adverse drug reactions;
- reveal new uses for medicines and drug candidates;
- shift emphasis in medicine from reaction to prevention; and
- inform healthcare spending.

However, Canada faces a number of challenges in implementing Precision Health; literature that captures Canadian stakeholder opinions on policy or operational problems related to evaluation, funding, and delivery of companion diagnostic (CDx) testing indicates significant challenges related to:

- HTA;
- funding;
- health system adoption pathways;
- implementation into the healthcare delivery system;
- laboratory oversight and operations; and
- regulatory authorization.

There is some urgency to address these challenges. We are at the tip of the iceberg in terms of Precision Health innovations expected to come to market. Currently, 42% of all new molecular entities in development are associated with a biomarker. This percentage climbs to 73% when just considering oncology candidates.

We have the opportunity to look to other countries for guidance. A recent scan of the implemented approach to reimbursement decision-making for CDx in France, the United Kingdom, Australia, and the United States has revealed that there is:

- typically a standard protocol for assessment;
- criteria outlining information requirements that include clinical effectiveness (analytical and clinical validity, clinical utility), economic implications (cost-effectiveness and budget impact analysis), and system implications (laboratory capacity);
- an integrated approach whereby both the drug and test are reviewed as one package;
- involvement of multidisciplinary advisory committees; and
- assessment performed by either independent groups, sponsors of technology, or staff within the review commissioning organization.

An Alberta structure and framework for provincial evaluation of CDx under consideration for public reimbursement, incorporating learnings from these international approaches, was presented. It is a potential model for other provinces to examine and learn from.

## Reimbursement of Companion Diagnostics

A case study review and table discussion followed the keynote presentations. The objective of this exercise was to obtain insights from stakeholders on the gaps/challenges, implications, and potential solutions to enable the integration of Precision Health innovations into the Canadian health system. There was a particular focus on the reimbursement of CDx in oncology at the provincial level. A number of key ***barriers*** were identified, including:

- lack of alignment in funding review processes between pharmaceuticals and their CDx, due to different budget holders at the provincial level for these benefits/services;
- laboratory services budgets that do not reflective of the expenditure growth required to support new diagnostic testing innovations;
- lack of defined provincial processes to evaluate CDx;
- challenges with how to assess the value of a CDx; and
- provincial differences in terms of implementation, including standardization of test validation, thresholds to be utilized, and results interpretation.

A number of ***solutions*** to the identified barriers for consideration and further discussion were identified, including:

- CDx review at the pan-Canadian Pharmaceutical Alliance (pCPA) or Cancer Drug Implementation Advisory Committee (CDIAC) level in order support alignment of decision-making and funding processes, that would include discussions beyond price negotiation such as advice on test validity and utility, as well as guidance on innovative reimbursement approaches such as pay-for-performance;

- a more global view of budget silos in order to integrate the planning and resource allocation for services and benefits that touch separate areas of the health system;
- improved multi-year laboratory services budget planning, informed by the pipeline of anticipated new innovations with a CDx;
- increased evidence-based dis-investment in laboratory testing in order to create headroom for new innovations;
- creation of a "R&D budget" for laboratory services that permits the development and validation of laboratory-derived tests in order to reduce costs;
- creation of multidisciplinary provincial working groups, and mechanisms for the provinces to learn from each other, to develop standard protocols/business cases to guide CDx assessment;
- provision of greater analysis from a pan-Canadian body, such as the Canadian Agency for Drugs and Technologies in Health (CADTH), to support the provinces with an understating of the utility and validity of a CDx, as well as a framework to assess value that includes decision-making considerations and criteria that provide clear expectations for what is acceptable/unacceptable evidence of value;
- centralized national laboratory testing; and
- development of a harmonized framework for laboratory testing implementation.

## Concluding Comments & Next Steps

It is clear that the Precision Health era has arrived, and will become increasingly meaningful for patients and providers, particularly in the oncology space. Overall, a sense of urgency to address the issue of CDx review and funding was expressed. Ensuring that we have processes in place that can efficiently and effectively evaluate new technologies and make decisions on funding was highlighted as critical to creating appropriate access to new technologies for patients. Provincial partnership was highlighted as key, both with pan-Canadian organizations such as CADTH to understand the future innovation landscape to support proper planning as well as their analysis and view on a particular CDx, and with other provinces and vendors to share resources and achieve efficiencies (for example, to validate tests).

This meeting represented an important conversation on how Canada can prepare for and better integrate innovations in Precision Health into the Canadian healthcare system. A number of key barriers and solutions were identified as a starting point for additional discussion. Importantly, stakeholders expressed interest in continuing to be engaged in the dialogue, and supporting discussions intended to lead to better and more timely and appropriate patient access to new innovations.

# Abbreviations

All abbreviations that have been used in this report are listed here unless the abbreviation is well known, has been used only once, or has been used only in tables or appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

| | |
|---|---|
| **CADTH** | Canadian Agency for Drugs and Technologies in Health |
| **CDIAC** | Cancer Drug Implementation Advisory Committee |
| **CDR** | Common Drug Review |
| **CDx** | companion diagnostic |
| **FDA** | Food and Drug Administration |
| **HTA** | health technology assessment |
| **NDS** | New Drug Submission |
| **NICE** | National Institute for Health and Care Excellence |
| **NoC** | Notice of Compliance |
| **pCODR** | pan-Canadian Oncology Drug Review |
| **pCPA** | pan-Canadian Pharmaceutical Alliance |

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# 1. Introduction

## 1.1 Workshop Overview

This report follows from the Institute of Health Economics (IHE, *www.ihe.ca*)/Canadian Association for Population Therapeutics (CAPT, *www.capt-actp.com/*) Precision Health Workshop that was held on October 22, 2017 in Toronto, Ontario. This meeting was a satellite to the 2017 Annual CAPT Conference.

A total of 40 individuals registered for the event, including three speakers and three panellists. Participants reflected the perspectives of public payers, clinician/providers, academia, regulators, health technology assessment (HTA) agencies, laboratory services, patient advocates, and industry. The format for the day was a number of presentations from invited speakers, followed by a case study exercise and table discussion, and finally a panel discussion.

For a copy of the program, including the agenda and biographies of the speakers and panelists, please see Appendix A; for a list of registrant affiliations, please see Appendix B.

## 1.2 Objectives & Agenda

The objectives of the workshop were to:

1. review the concept of Precision Health and outline its potential impact on patient care and timely access to innovative medicines;
2. share examples/case studies and lessons learned from Precision Health innovations and how they have been introduced into various health systems; and
3. obtain insights from stakeholders on the gaps/challenges, implications, and potential solutions to enable the integration of Precision Health innovations into the Canadian health system.

The agenda for the workshop is below.

| Timing | Item | Presenter/Panellist |
|---|---|---|
| 13:00-13:15 | Introduction & Welcome | Dan Palfrey – IHE |
| 13:15-14:00 | The Potential Contribution of Precision Health to Patient Care and the Canadian Experience Thus Far | Katherine Bonter – Clementia Pharmaceuticals |
| 14:00-14:45 | Regulatory Experiences with Precision Health Technology Introduction | Kelly Robinson – Health Canada |
| 14:45-15:15 | An Alberta Framework for Evaluation of Companion Diagnostics | Jennifer Pillay – University of Alberta |
| 15:15-15:30 | *Break* | |
| 15:30-16:15 | Table Discussion – Gaps and Solutions to Improve Alignment and Access to Innovations in Oncology (focus on Companion Diagnostics) | |

| Timing | Item | Presenter/Panellist |
|---|---|---|
| 16:15-17:00 | Panel Discussion | Judith Glennie – CAPT (Moderator)<br>Judy McPhee – Consultant/Formerly Nova Scotia Dep't of Health & Wellness<br>Louise Binder – Consultant/Save Your Skin Foundation<br>Jim Slater – Diagnostic Services Manitoba |
| 17:00 | Wrap-Up and Adjourn | Dan Palfrey – IHE |

# 2. Summary of Presentations

The following provides a summary of the three keynote presentations.

## 2.1 The Potential Contribution of Precision Health to Patient Care and the Canadian Experience Thus Far

*Katherine Bonter – Clementia Pharmaceuticals*

Canada and other countries face an ongoing challenge in policy and operational reform related to healthcare system adoption of Precision Health: effectively implementing innovations that are ready for use while sustaining long-term improvement and transformation of health care.

The Personalized Medicine Coalition in the United States has recently published a paper[1] that helps to identify the key benefits and promise of Precision Health, notably the improved ability to:

- direct targeted therapy, and reduce trial-and-error prescribing;
- reduce adverse drug reactions;
- reveal new uses for medicines and drug candidates;
- shift emphasis in medicine from reaction to prevention; and
- inform healthcare spending.

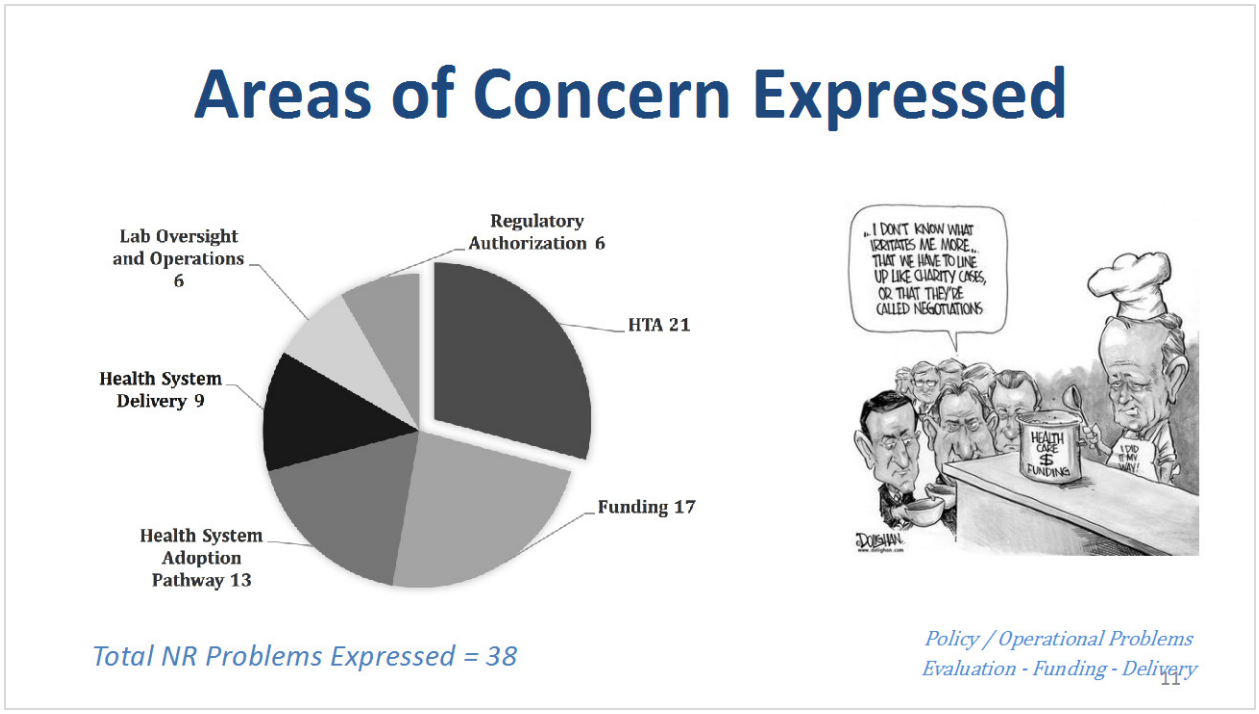
We are currently at the tip of the iceberg in terms of Precision Health innovations expected to come to market. Currently, 42% of all new molecular entities in development are associated with a biomarker. This percentage climbs to 73% when just considering oncology candidates. This suggests some urgency to address the challenges we face today, and to prepare for anticipated challenges in the future.

The productivity of discussion on this topic is hindered by a lack of a common understanding of definitions of the various terms used to describe a Precision Health approach (e.g., personalized medicine, stratified medicine, genomic medicine). There is opportunity to obtain clarity on definitions in order to enhance our ability to have meaningful conversations. The Canadian Agency for Drugs and Technologies in Health (CADTH) has provided some guidance on terminology, as

[1] *http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The-Personalized-Medicine-Report1.pdf*

well as on clinical utility regarding how this approach can support more targeted drug therapy.[2] To develop policy and operational practices that support effective and efficient adoption of innovations and realize the promise of Precision Health, we must recognize the complexity and consequences of decision-making over the short- and long-term.

To support this, BioCanRx has supported efforts to systematically identify and characterize problems related to Canadian healthcare system adoption of companion diagnostics (CDx), as well as proposed solutions to these problems. A thorough review of the literature was completed to systematically capture Canadian stakeholder opinions on policy or operational problems related to evaluation, funding, and delivery of CDx testing. Twenty-one articles were identified in the search and included in the analysis, with the opinions of 112 different stakeholders represented. The most predominate areas of concern identified are presented in the slide below.




Top **HTA** problems that were expressed include (in order of most mentions):

- No formal process for evaluating CDx
- Inconsistent practices and criteria
- Separate evaluation of drugs and the CDx
- Gaps in evidence to demonstrate clinical utility of CDx
- Inter-provincial differences in HTA
- Lack of a dynamic mechanism to deal with new evidence

[2] *https://www.cadth.ca/sites/default/files/pdf/CADTH%20Personalized%20Medicine%20Typology%20Briefing_FINAL.pdf*

Key solutions to address some of these challenges identified include the establishment of a national common review, increased transparency of process and criteria, and increased stakeholder engagement.

Top **funding** problems that were expressed include (in order of most mentions):

- No link between drug approvals and CDx funding
- Requirement for pharmaceutical company subsidy of CDx implementation
- Limited or static funding for CDx given budget considerations

Recommended solutions to these issues include the creation of a link between HTA and CDx funding, the elimination of budget silos, funding for multi-centre standardization of each CDx, and the creation of an oversight body.

Top **health system adoption pathway** problems that were expressed include (in order of most mentions):

- Lack of a coordinated/harmonized pathway nationally
- Duplication of effort
- Lack of predictability and transparency of pathways
- Separate approval pathway for drugs and their CDx

The solutions recommended are to create more stakeholder engagement opportunity, de-implementation of tests not demonstrating sufficient value, and alignment of HTA and regulatory processes.

Top **health system delivery** problems that were expressed include (in order of most mentions):

- Lack of coordination between labs
- Use of lab-developed alternatives to approved proprietary devices
- Duplication of efforts and expertise
- Lack of stakeholder engagement
- Limited guidance for ordering of tests

Solutions recommended include centralization of specialized laboratory services, development of more guidelines for laboratory services, and coordination of implementation.

Top **regulatory authorization** problems that were expressed include (in order of most mentions):

- Lab-developed tests not being subject to Health Canada authorization
- Regulatory authorization of drugs and CDx are separate processes
- Lack of standard language regarding CDx on product labelling

Two solutions were recommended and include a requirement for specification of the CDx used in clinical development in a new drug submission and inclusion in the product labelling, and more emphasis on the clinical utility of the CDx in the review process and guidance from the regulator.

Overall, many problems have identified by Canadian stakeholders, however there remains a gap in terms of good solutions to these problems. Good solutions require well-defined, prioritized

problems, and this requires the perspective, experience, and knowledge of all stakeholders. Other jurisdictions, including the Food and Drug Administration (FDA) in the United States, have provided a significant amount of guidance on Precision Health and CDx. An important next step is to review what other jurisdictions have done and translate them into the Canadian context in support of identifying an appropriate path forward for Canada.

## 2.2 Regulatory Experiences with Precision Health Technology Introduction

*Kelly Robinson – Health Canada*

Precision Health has an important role to play to help target medications for the right patient, at the right dose. It has other valuable utility, such as surveillance or monitoring to determine disease stage and whether therapeutic intervention has an effect on disease progression, as well as for the investigation of the genetic basis of adverse drug reactions. However, there is need to have validated tests with an established link to clinical outcomes.

The scope and mandate of Health Canada is very well-defined by the legislative framework, notably the *Food and Drugs Act*. Health Canada is primarily concerned with the evaluation of pharmaceuticals and medical devices from the perspective of efficacy, safety and quality. Cost is not a consideration, and decisions are made solely on the science. Health Canada will issue a Notice of Compliance (NoC) for drugs approved to be marketed and sold in Canada. In some cases when the evidence is promising but not yet substantiated, a NoC with conditions is provided. The drug is made available to Canadians, with a requirement for the manufacturer to provide further clinical trial evidence. The majority of NoCs with conditions are issued for oncology drugs. A future opportunity may be to additionally inform on drug efficacy and safety using data captured in clinical practice outside of the clinical trial context.

All devices intended to be used for pharmacogenomic testing are classified as Class III medical devices. Health Canada has guidance for submission of pharmacogenomics information,[3] and also utilizes the International Council on Harmonization guidance to support in review decisions. Biomarkers are not defined in the *Food and Drugs Act*, and Health Canada has some flexibility in approval. Laboratory-developed tests, as well as direct-to-consumer genetic testing, are outside of the scope of Health Canada under the *Food and Drugs Act* and Regulations, and oversight is a provincial responsibility.

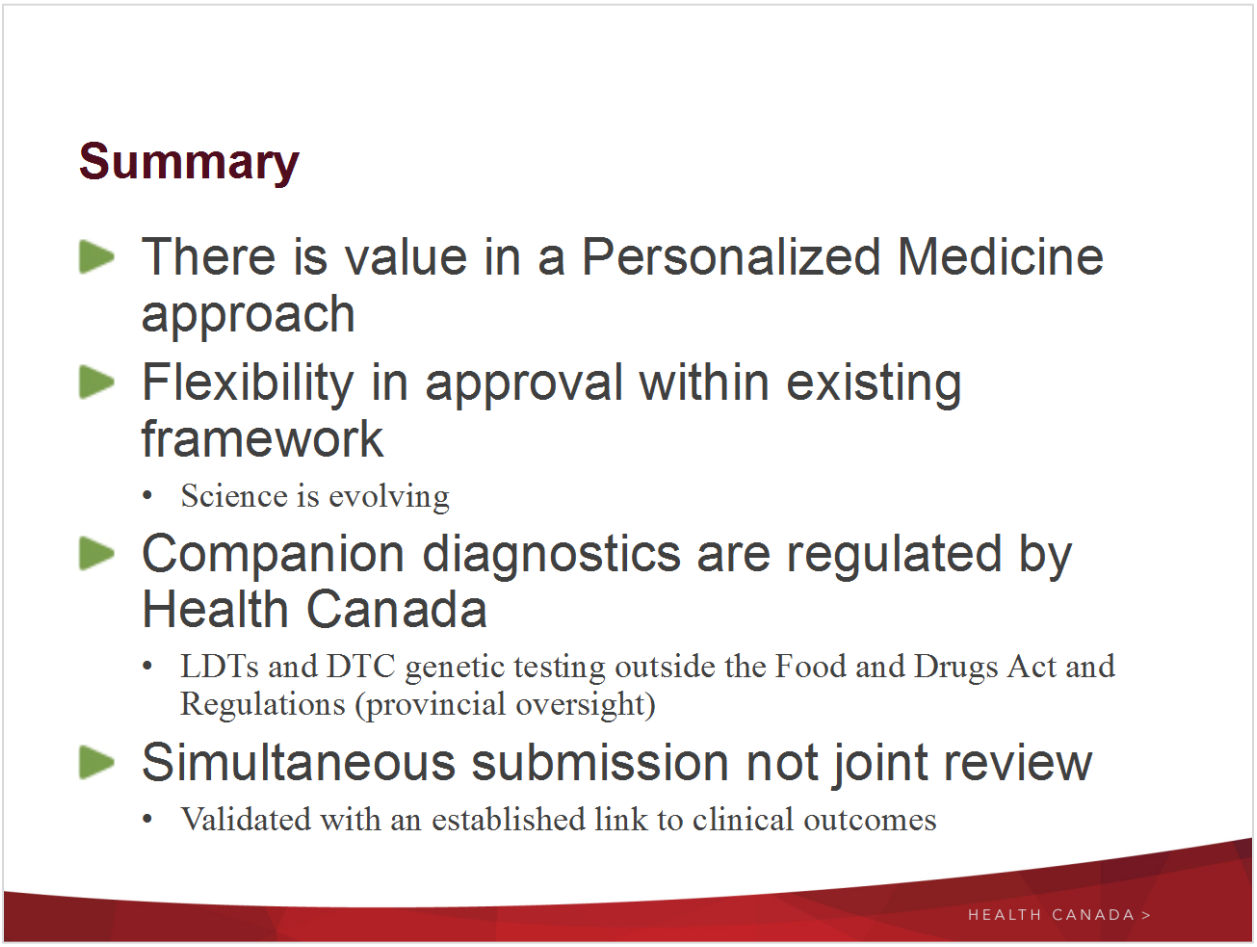
New Drug Submissions (NDS) for NoC and medical device license submission are to two different groups in Health Canada (Therapeutic Products Directorate, and Medical Devices Bureau, respectively), and the timelines for approval are quite different (300 days for an NDS, and 75 days for a Class III device license submission). Health Canada NDS or supplemental NDS application review will examine the sensitivity and specificity of a CDx to determine how well it identifies the appropriate patients in order to determine the appropriateness of the test.

In terms of labelling, the approach used by the FDA in the United States is to typically indicate that a drug is to be used with a specific test. The approach of Health Canada, in contrast, is to indicate that an agent is to be prescribed following a validated test as opposed to a requirement for a specific test kit. This flexibility in labelling is to recognize that there may be evolution of the CDx during the life cycle of the product on market, as well as laboratory-developed tests that may be used. When a CDx

[3] *http://hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/brgtherap/pharmaco_guid_ld-eng.pdf*

has been used in the pivotal trials for an agent, it will be detailed and described in the clinical trials section of the product monograph. Health Canada will also consider labelling of additional pharmacogenomics test information when:

- subgroups of patients experience higher or lower clinical efficacy
- subgroups of patients are at higher risk for adverse drug reactions
- subgroups require special dosing considerations
- testing is recommended to optimize the use of the drug




## 2.3 An Alberta Framework for Evaluation of Companion Diagnostics

*Jennifer Pillay – University of Alberta*

Alberta has been developing its approach to evaluation and decision-making for CDx for several years, beginning in 2013 following a pan-Canadian Oncology Drug Review (pCODR) recommendation to fund crizotinib as second-line therapy for patients with ALK-positive advanced non-small-cell lung cancer. The focus over time has shifted from understanding how to review a CDx for a drug recently approved and recommended for reimbursement, to an understanding of the process Alberta should follow to ensure that there is adequate information collected on a CDx at the

time a recommendation on the accompanying drug is made through pCODR or Common Drug Review (CDR) (to ensure patients have access to recommended testing in a timely manner).

To inform the Alberta framework, an environmental scan of international approaches was completed, and an Alberta Working Group on CDx was established. The environmental scan reviewed the implemented approaches in France, the United Kingdom, Australia, and the United States. This exercise revealed that there is:

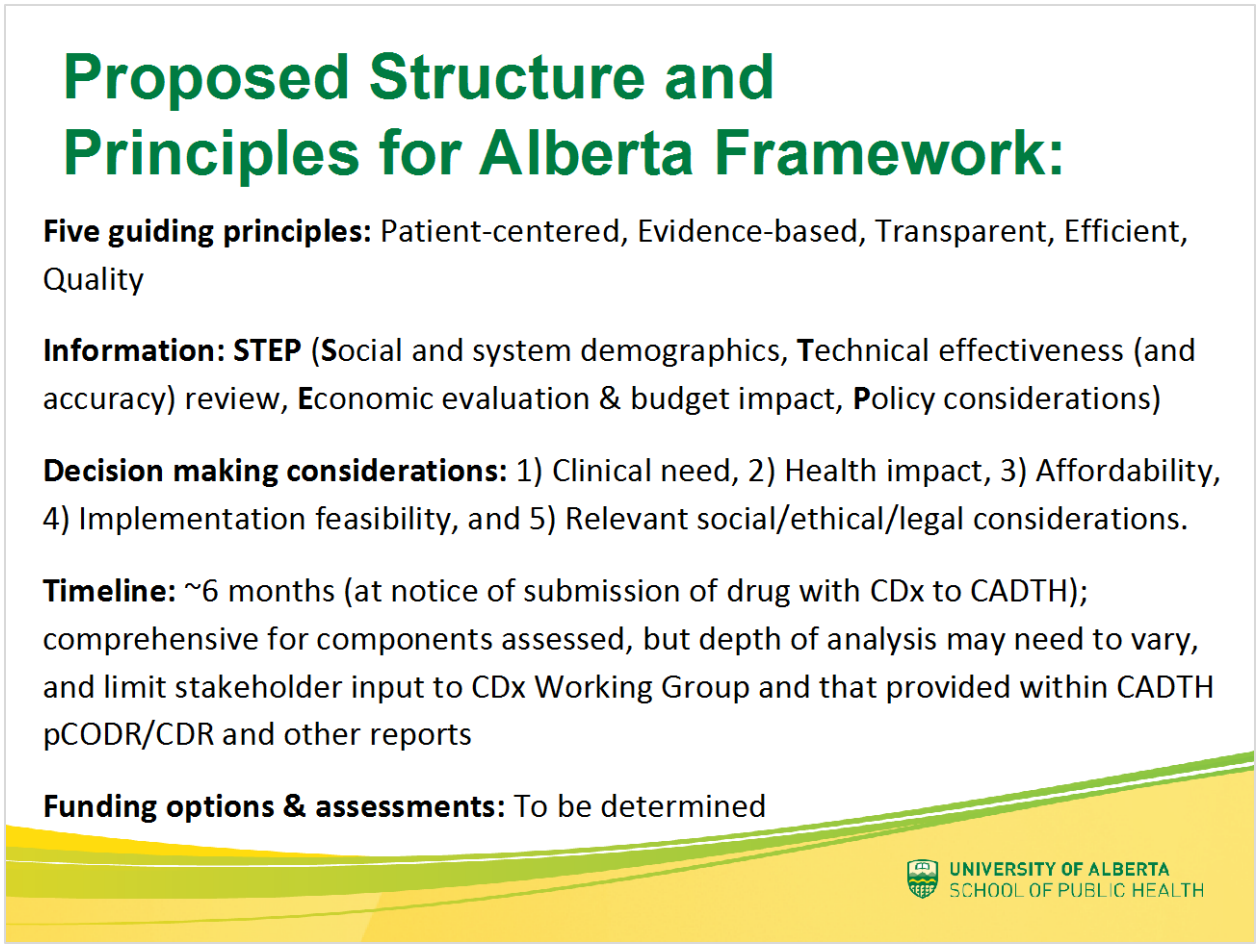
- typically a standard protocol for assessment, with criteria outlining information requirements (in some cases regarding analytical validity);
- involvement of multidisciplinary advisory committees (in some cases with input from patients, caregivers, and the diagnostics industry);
- variation in who conducts the assessments (e.g., independent groups, sponsors of technology, or staff within the review commissioning organization); and
- variation in duration from less than 6 months to greater than 12 months.

In Australia, the pharmaceutical and medical services advisory committees have an integrated approach whereby both the drug and test are reviewed as one package. Decisions made may be different for the drug and the test. In the United Kingdom, the National Institute for Health and Care Excellence (NICE) assesses drugs and the CDx via the Technology Appraisal Programme in most cases. Recently, NICE created a Diagnostics Assessment Programme for more complicated assessment, including when a drug has already been assessed, or when multiple test options are in use.

Typical information requirements for countries with an implemented approach include the following:

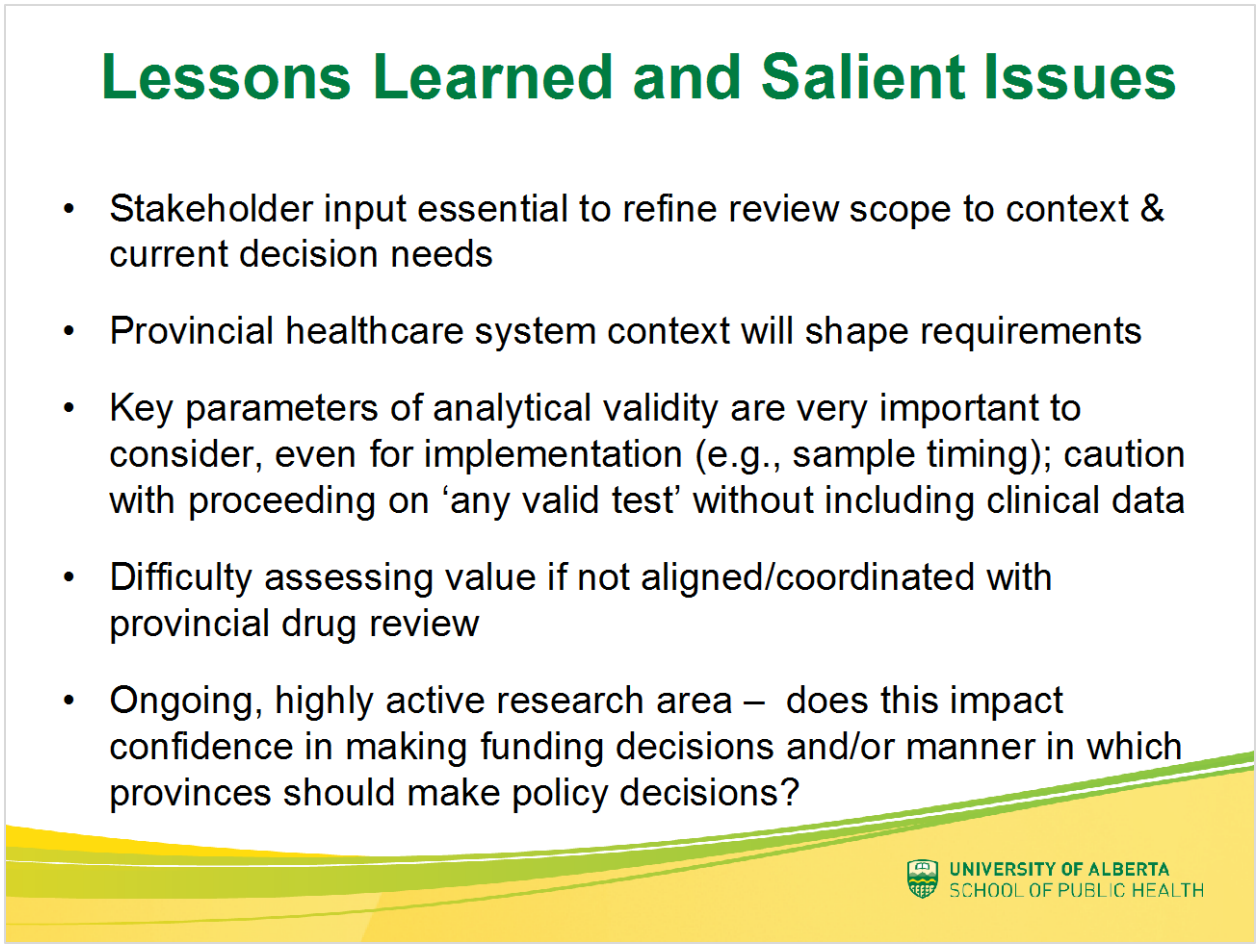
- Clinical effectiveness
    - Analytical validity (which may include agreement between multiple tests)
    - Clinical validity
    - Clinical utility (i.e., impact of test results on clinical decision-making that leads to improved health outcomes)
    - Local practice (e.g., testing strategies currently used, number of tests performed, and external quality assessment schemes in place)
- Economic implications
    - Cost-effectiveness of different testing strategies
    - Budget impact analysis
- System implications
    - Capacity of local laboratories to perform the testing strategy identified as the most clinically and cost-effective

A proposed structure and framework for Alberta has been developed that is aligned with current assessment criteria and principles for HTAs and is presented in the slide below.




Alberta is currently piloting the framework using PD-L1 biomarker testing for advanced non-small cell lung cancer, and the "S" and "T" steps noted above have been completed. This project was chosen due to the number of agents currently or soon to be available that utilize this biomarker to guide treatment decision, the significance of this form of cancer, the complexity of the assessment, as well as an immediate need for a funding decision in the province. CADTH is expected to increasingly inform the work in Alberta following a June 2017 announcement that they will "investigate factors relevant to testing that would inform the implementation of associated drugs under review by CADTH."

Key lessons learned from the Alberta experience are presented in the slide below.




# 3. Table Discussion

## 3.1 Overview

A case study review and table discussion followed the keynote presentations. The objective of this exercise was to obtain insights from stakeholders on the gaps/challenges, implications, and potential solutions to enable the integration of Precision Health innovations into the Canadian health system, with a particular focus on the reimbursement of CDx in oncology. Individuals were assigned seating at the tables in order to deliberately encourage conversation amongst stakeholders with different perspectives. To review the hypothetical case study, please refer to Appendix C.

The following questions were posed to the group to guide the facilitated discussion:

1. What do you see as the key barriers to reimbursement decision-making for medications whose appropriate use is tied to a biomarker?
2. What are some potential solutions to address these barriers; and, who should be responsible for moving forward with these solutions?

## 3.2 Key Barriers & Solutions

The following represent the key barriers and solutions identified by the participants. Each group was asked to report back on the single top barrier and solution identified. For the complete notes from the discussion, please refer to Appendix D.

### Barrier 1 – Funding review alignment and silo budgeting

A key barrier identified by the group discussion is the lack of alignment in funding review process between pharmaceuticals and their CDx. This barrier is relevant at a number of levels of the healthcare system (e.g., regulatory, HTA, provincial), and the group focused on the provincial level given the challenge posed in the case study. This observation in many respects stems from the fact that there are different budget holders at the provincial level for these two benefits/services, and they effectively operate independently without strong communication and information sharing to initiate and inform their work. This barrier leads to delays in decision-making and lack of coordinated patient access to pharmaceuticals and their CDx.

The group suggested that there may be opportunity to address this barrier via discussions at the pan-Canadian Pharmaceutical Alliance (pCPA) or the Cancer Drug Implementation Advisory Committee (CDIAC) level in order to bring laboratory services into the conversation and support alignment of decision-making and funding processes. This implies a focus of the discussions beyond price negotiation, including direction on validity and utility, as well as potentially innovative reimbursement approaches such as pay-for-performance.

### Barrier 2 – Laboratory services affordability

A second key barrier identified is the observation that the annual budget for laboratory services is typically static, and may not reflect the expenditure growth that may be required (holding baseline spending constant) with new diagnostic testing opportunities. This creates an affordability challenge for new CDx that represent incremental costs for laboratory services. It was noted that pharmaceutical budgets are typically subject to multi-year forecasting exercises to a greater extent, with visibility to new agents coming to market, and drug plan managers may be better able to properly plan for required budget increases than their counterparts in laboratory services. The group also noted that provincial pharmaceutical benefits planning, in contrast to laboratory services planning, also typically includes initiatives to review existing benefits and dis-invest or reduce costs as appropriate. The group felt that laboratory services budget holders likely struggle to keep up with the pace of innovation, and may not have the visibility to future service requests as they are not made aware of innovation pipelines to the extent that pharmaceutical budget holders are.

A number of solutions were posed to address this barrier. The group highlighted a need for a more global view of budgets in order to integrate the planning and budgeting for services and benefits that touch separate areas of the health system. The group felt there was opportunity for laboratory services to conduct multi-year budget planning exercises, informed by the pipeline of anticipated new innovations with a CDx (achieved, for example, by inclusion of laboratory services representatives in manufacturer pipeline meetings with drug plan managers, or from information contained in environmental scanning documentation provided an organization like CADTH). It was noted that there is a need, potentially involving external support with data liberation and analysis, for laboratory services to make informed dis-investment decisions, to the extent possible, in order to create headroom for new innovations. Additionally, it was suggested that laboratory services be

provided a "R&D budget" that permits the development and validation of laboratory-derived tests in order to reduce costs.

### Barrier 3 – Provincial process for CDx review

A third key barrier identified during the discussion is that there is typically a lack of defined provincial process to evaluate CDx. It was also noted that where provincial reviews are completed, there is duplication amongst the provinces. This is considered a barrier as it prevents timely decision-making regarding CDx funding, and delays patient access to required testing.

To help reduce this barrier, the group recommended the creation of multidisciplinary provincial working groups, and mechanisms for the provinces to learn from each other, to develop standard protocols/business cases to guide assessments. This intent is to ensure that assessments are prepared in a consistent way, and present similar types of information for reviewers to consider, regardless of the specific CDx under review.

### Barrier 4 – Assessment of the value of CDx

A fourth key barrier identified is the challenge provinces face in terms of how to assess the value of a CDx. It was noted that the provinces struggle to understand the validity and utility of tests, as well as their economic value and budget impact (across all patients, and for those at various thresholds of test results). This is particularly challenging when multiple different tests have been utilized in the trials for agents within a class, all with different methodologies and thresholds for guidance from test results. Without a standardized framework to assess value, the provinces are challenged to make informed decisions.

To address this barrier, the groups suggested that a pan-Canadian body, such as CADTH, could provide the provinces with more analysis regarding the utility and validity of the CDx, as well as a framework to assess value that includes decision-making considerations and criteria that provide clear expectations for what is acceptable/unacceptable evidence of value.

It should be noted that CADTH, following a late 2016 consultation, has recently indicated that they will "explicitly and consistently investigate factors relevant to any required biomarker testing that would inform the implementation of associated drugs under review through the CADTH CDR and pCODR programs."[4] Evidence on the analytic validity, clinical validity, and clinical utility of the CDx must be provided by applicants, and CADTH reviewers will critically appraise this clinical evidence and produce a rapid response report, which will be incorporated into the clinical review report for the drug. CDx must also be included in applicants' economic analyses, including budget impact assessments for the drug and CDx (in combination and separately) for critical appraisal by the CADTH economic reviewers.[5]

### Barrier 5 – Provincial implementation of CDx

A fifth key barrier identified is provincial differences in terms of implementation, which is particularly pronounced when there are multiple drugs with multiple tests in the same indication, as well as multiple versions of the same tests available. Implementation includes standardization of test validation, thresholds to be utilized, and results interpretation.

[4] *https://www.cadth.ca/sites/default/files/cdr/cdr-pdf/CDx_Process.pdf*
[5] *https://www.cadth.ca/sites/default/files/pdf/CADTH_Consult_Proposed_Process_Companion_Diagnostics.pdf*

A solution for consideration highlighted was centralized testing for the country. Additionally, it was suggested that the development of a harmonized framework for laboratory testing implementation would be helpful.

# 4. Panel Discussion

Each of the three panellists was provided the opportunity to reflect upon what they heard during the workshop, and provide their insights. A sense of urgency to address the issue of CDx review and funding was expressed, and one panellist noted: "*We have been dealing with this issue for a number of years, and CDx in some cases have just been absorbed into the system. With the significant number of CDx coming to market in the near term the time is now to effectively address the issue.*"

The panellists underscored that we have a profoundly complex and rapidly moving research and innovation environment. One panellist suggested that "*process is the new content, and we need to ensure that our evaluation and decision-making processes are fluid and able to rapidly react.*" Ensuring that we have processes in place that can efficiently and effectively evaluate new technologies and make decisions on funding was highlighted as critical to creating appropriate access to new technologies for patients.

It was noted that laboratory services has opportunity to utilize a similar planning process as that typically utilized to manage pharmaceutical budgets. It was highlighted that drug plan managers tend to have a 5-year forecasting time horizon to plan for anticipated expenditures, and when expenditure growth is anticipated to be larger than budget growth they conduct class or other review in order to identify opportunities for dis-investment and other avenues for cost reduction. It was suggested that laboratory services has the same opportunity to conduct this exercise. For more short-term budget planning exercises, as previously noted CADTH has revised their review process and will now include reference to and analysis of CDx in their reports, which will provide useful information, and amongst other initiatives to integrate planning could serve as a signal for drug plan managers to communicate with laboratory services and ensure awareness of anticipated service requests to support their planning.

Hope was expressed that in some provinces we are close to solving some of the key barriers. Personalized Medicine Manitoba was cited as an example. This organization has the support of Cancer Care Manitoba and the Provincial Clinical Genetics Program, and is guided by a multidisciplinary advisory committee. With this structure comes opportunity to make the horizontal connections required to align drug funding and approval mechanisms with that of laboratory services. Partnership was highlighted as key, both with pan-Canadian organizations such as CADTH to understand the future innovation landscape to support proper planning as well as their analysis and view on a particular CDx, as well as with other provinces and vendors to share resources and achieve efficiencies (for example, to validate tests).

# 5. Concluding Comments & Next Steps

It is clear that the Precision Health era has arrived, and will become increasingly meaningful for patients and providers, particularly in the oncology space. This meeting represented an important conversation on how Canada can prepare for and better integrate innovations in Precision Health into the Canadian healthcare system. A number of key barriers and solutions were identified and are described in this report. Importantly, stakeholders expressed interest in continuing to be engaged in the dialogue, and supporting discussions intended to lead to better and more timely and appropriate patient access to new innovations.

The intent of this workshop was for it to provide information to inform the discussion, and in many respects is a starting point for subsequent conversations. There is opportunity to drill down into more specific definitions of both the barriers and opportunities to strengthen the introduction of Precision Health approaches in Canada. To support this effort, in the coming months the IHE Open Innovation Platform™ (a partnership between the IHE and CAPT), which is an online "ideasourcing" or "crowdsourcing" tool, will be utilized to reach out to a broad set of healthcare stakeholders to continue to explore this challenging area and move the discussion forward. Further information on this online opportunity to contribute can be found at *iheinnovation.ideascale.com/a/register*.

# Appendix A: Precision Health Workshop Program

# INSTITUTE OF HEALTH ECONOMICS/ CANADIAN ASSOCIATION FOR POPULATION THERAPEUTICS

# Precision Health Workshop

## Sunday, October 22nd, 2017
## Chelsea Hotel, Rossetti Room
## Toronto, Ontario

| | |
|---|---|
| 13:00 – 13:15 | Introduction & Welcome<br>**Dan Palfrey**, Senior Consultant, IHE |
| 13:15 – 14:00 | *The Potential Contribution of Precision Health to Patient Care and the Canadian Experience Thus Far*<br>**Katherine Bonter**, Director of Intellectual Property, Clementia Pharmaceuticals Inc. |
| 14:00 – 14:45 | *Regulatory Experiences with Precision Health Technology Introduction*<br>**Kelly Robinson**, Director, Health Products and Food Branch, Health Canada |
| 14:45 – 15:15 | *An Alberta Framework for Evaluation of Companion Diagnostics*<br>**Jennifer Pillay**, MSc Student, University of Alberta |
| 15:15 – 15:30 | Break |
| 15:30 – 16:15 | Table Discussion: *Gaps and Solutions to Improve Alignment and Access to Innovations in Oncology* (focus on Companion Diagnostics) |
| 16:15 – 17:00 | Panel Discussion<br>**Judith Glennie**, CAPT (Moderator)<br>**Judy McPhee**, Consultant, Formerly Nova Scotia Department of Health and Wellness<br>**Louise Binder**, Consultant, Save Your Skin Foundation<br>**Jim Slater**, Chief Executive Officer, Diagnostic Services Manitoba |
| 17:00 | Wrap-Up and Adjourn |

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Supporting Health Policy and Practice

CAPT ACTP

## Louise Binder

### Health Policy Consultant, Save Your Skin Foundation

Louise is a lawyer and health advocate who has been involved in informing the development of health policy and systemic treatment access practices from a patient perspective for more than 20 years. She started her work in this area in the HIV community in the early 1990s after her own diagnosis and before effective treatments were available for HIV. She co-founded the Canadian Treatment Action Council (CTAC) in 1996, which successfully ensured access to treatments and quality care for people living with HIV by working with the federal and provincial governments and other relevant stakeholders to enhance drug review and approval systems, pricing policies and access to liver transplants for this community. She wrote a paper on universal drug coverage a decade ago while chair of CTAC. She had a special interest in women's issues, chairing the Ontario women's organization Voice of Positive Women for more than a decade, and has been involved in these issues internationally as well. Two years ago, Louise began similar work in the cancer area and is presently health policy consultant for the Canadian Cancer Survivor Network. She has been recognized by many organizations for her work, including receiving an Honorary Doctorate of Laws from her alma mater, Queen's Law School; the Order of Ontario from the Province of Ontario; and two Queen Elizabeth II medals.

## Katherine Bonter

### Director of Intellectual Property, Clementia Pharmaceuticals Inc.

Katherine has more than 15 years' experience in intellectual property (IP) management and corporate development in the biopharmaceutical domain both in the private- and public-sector. Between 2009 and 2016, she worked for a National Centre of Excellence mandated with enabling personalized medicine innovation. This role included research and promotional activities as well as developing and managing the IP interests of the host institution as well as projects funded by the Centre. Starting in 2013, she was involved in Genome Canada funded academic research projects with a focus on patenting and clinical development trends. Her main research interest is the relationship between public policy and innovation. She is currently completing a PhD on this topic at McGill University. She is also currently Director of Intellectual Property for Clementia Pharmaceuticals, a Canadian Biopharma company repurposing small molecule therapies for rare diseases. Together with BioCanRx, an Ottawa-based Centre of Excellence, as well as other public- and private-sector partners, Katherine is involved in creating a stakeholder alliance, Alliance for Innovation in Molecular Diagnostics (AIMD). The main objective of the alliance is to enable improved market access and clinical implementation of molecular diagnostics in Canada by informing and advocating for policy reform.

## Judy McPhee

### Consultant, McPh2 Consulting

Judy recently retired from government, where she held the position of Executive Director of Pharmaceutical Services and Extended Health Benefits with the Nova Scotia Department of Health and Wellness. In this role, she was responsible for advising and setting the strategic direction for the funding and use of medications in Nova Scotia. Judy is a pharmacist and, in addition to having experience in formulary management and the development of policy and legislation, she has experience in different facets of pharmacy. Before joining government in 2004, she worked for many years as a pharmacy manager in a large tertiary care hospital. She has also worked in community practice and in the pharmaceutical industry, and has been very active in many jurisdictional and professional committees at both the national and provincial level including having been Chair of the Drug Policy Advisory Committee at CADTH and Co-Chair of the pan-Canadian Pharmaceutical Alliance for both brand and generic. She is currently a member of the National Drug Scheduling Advisory Committee.

## Jennifer Pillay

### MSc Student, University of Alberta

Jennifer has been working in research with the University of Alberta since 2005, and joined the Alberta Research Centre for Health Evidence in 2013. At ARCHE, she leads and contributes to all aspects of various forms of evidence synthesis and methods projects, within the University of Alberta Evidence-based Practice Center, commissioned by the U.S. Agency of Healthcare Research and Quality, and an Evidence Review Synthesis Centre, funded by the Public Health Agency of Canada and informing recommendations of the Canadian Task Force on Preventive Health Care. She has been working towards her MSc in the School of Public Health, specializing in Health Technology Assessment, for which she is conducting a thesis on the topic of assessment of companion diagnostics to help inform reimbursement decisions in Alberta.

## Kelly Robinson

### Director, Health Products and Food Branch, Health Canada

Kelly joined Health Canada in 2001. After 10 years with Health Canada's Marketed Health Products Directorate, Kelly joined the Therapeutic Products Directorate in 2011. She is currently the Director of the Bureau of Metabolism, Oncology and Reproductive Sciences. In this role she leads a team of Scientists who are responsible for reviewing pharmaceutical drug submissions and recommending drugs for authorization in Canada.

## JIM SLATER

### CHIEF EXECUTIVE OFFICER, DIAGNOSTIC SERVICES MANITOBA

Jim began his career as a Medical Laboratory Technologist (MLT) and completed his advanced certification in Transfusion Medicine (ART) at Vancouver General Hospital. He furthered his education by completing his Bachelor of Science (BSc) and Masters of Business Administration (MBA). Jim held leadership positions at the Regina Qu'Appelle Health Region where he was Executive Director of the Laboratory, Diagnostic Imaging, Nuclear Medicine and Infection Control & Infectious Diseases departments from 2003 to 2008. He became CEO of Diagnostic Services Manitoba in October 2011. Jim is currently Executive Sponsor for Choosing Wisely Manitoba as well as Personalized Medicine Manitoba. He serves on the Board of the Healthcare Reciprocal Insurance of Canada (HIROC), Manitoba Centre for Health Policy (MCHP), Advisory Medical Board for Cancer Care Manitoba and volunteers on the Board of Food Matters Manitoba (FFM). His appointments as Instructor, at the University of Manitoba and as Instructor, at Red River College provide an opportunity to share his passion for teaching leadership concepts and health system transformation to physicians, nurses, and other healthcare professionals.

# Appendix B: Workshop Registrant Affiliations

| No. | Registrant Affiliation | No. | Registrant Affiliation |
|---|---|---|---|
| 1 | University of Waterloo | 21 | Shire |
| 2 | University of Manitoba | 22 | Roche |
| 3 | Memorial University | 23 | Novartis |
| 4 | UCB | 24 | Health Quality Ontario |
| 5 | Canadian Association of Population Therapeutics | 25 | McMaster University |
| 6 | QuintilesIMS | 26 | CADTH |
| 7 | Health Quality Ontario | 27 | Canadian Cancer Survivor Network |
| 8 | Roche | 28 | Roche |
| 9 | GlaxoSmithKline | 29 | Innomar Strategies |
| 10 | Bayer | 30 | Merck |
| 11 | Canadian Cancer Survivor Network | 31 | Roche |
| 12 | McGill University | 32 | Canadian Association of Population Therapeutics |
| 13 | Alberta Health Services | 33 | Institute of Health Economics |
| 14 | Health Quality Ontario | 34 | Clementia Pharmaceuticals |
| 15 | University of Toronto | 35 | Health Canada |
| 16 | PharmKARe consulting | 36 | Diagnostic Services Manitoba |
| 17 | Merck | 37 | Save Your Skin Foundation |
| 18 | Canadian Organization for Rare Disorders | 38 | MCPH2 Consulting |
| 19 | University of Toronto | 39 | University of Alberta |
| 20 | University of Calgary | 40 | Dalhousie University |

# Appendix C: Table Discussion Case Study

## Case study for xyzmab and its companion diagnostic test for biomarker AB-C3 in colorectal cancer

Preamble/Instructions

- The following case is hypothetical, and a general representation of the scope of information available and some of the issues encountered in dealing with Precision Health products.
- It is not possible to address all possible challenges in this area, but we hope that this session will help us begin the dialogue and help identify additional topics that require further discussion.
- Please take 5 minutes to review the following case study.
- Thereafter, your facilitator will guide your group through the discussion questions.

Situation

Colorectal cancer (CRC) is the second most common cancer, accounting for 13% of all cancers. In Canada, it is the 2nd leading cause of death from cancer in men (1 in 14 will develop CRC, 1 in 29 will die of it), and the 3rd leading cause of death from cancer in women (1 in 16 will develop CRC, 1 in 32 will die of it).

A company has recently received Health Canada approval for its drug xyzmab for use in advanced CRC. The indication is for CRC patients with expression of biomarker AB-C3. The immunohistochemistry companion diagnostic test for AB-C3 has been validated both analytically and scientifically to predict patients most likely to respond to treatment with xyzmab.

The clinical utility is high, as patients expressing AB-C3 treated with xyzmab have an increased overall survival (OS) of 35% compared to current standard of care (SOC). Patients that do not express AB-C3 have a response rate with xyzmab comparable to current SOC, with no difference in OS. In addition, there are 2 other companies that are close to bringing medications to market in the same therapeutic class as xyzmab, for various cancer types, and using the same biomarker.

The Notice of Compliance (NoC) for xyzmab stipulates that any validated test similar to the one used in its clinical trials can be used. pCODR released a positive recommendation for xyzmab and related biomarker testing, stating that jurisdictions should have a biomarker test available to help select patients and support optimal use of healthcare resources. The company has already undertaken a validation and quality control exercise with provincial labs for AB-C3 mutation testing across Canada in anticipation of launching xyzmab. However, the medication reimbursement decision may not be finalized at provincial levels until an appropriate funding system is in place for biomarker AB-C3 testing.

Key Questions

1. What do you see as the key barriers to reimbursement decision making for medications whose appropriate use is tied to a biomarker?
2. What are some potential solutions to address these barriers; and, who should be responsible for moving forward with these solutions?

# Appendix D: Table Discussion Notes

| Barriers | Solutions |
|---|---|
| • Lack of CDx process and/or lack of alignment with drug process<br>  ○ Lack of process on how to evaluate CDx at provincial level – OR, duplication of work if done province by province to evaluate CDx<br>  ○ Systems are disconnected<br>  ○ Lack of communication<br>  ○ Different payers for drug and CDx | • **NOTE:** Onus is on provinces (and/or their delegates) to solve this problem! External stakeholders are not the key drivers of solutions for this issue<br>• Integrated process informed by pan-Canadian inputs<br>  ○ National process or provincial NICE?<br>• Can this be addressed during the pCPA or CDIAC process?<br>  ○ pCPA/CDIAC could bring lab people to the table, to get alignment of funding processes<br>  ○ CADTH CDx process needs to add value for this to work |
| • Silo budgets<br>  ○ Drugs vs. diagnostics<br>  ○ Lab budgets static<br>  ○ Drug budgets only pay for drug<br>  ○ provincial variability in how these budgets are managed (i.e., cancer agency vs. provincial drug plan + provincial lab services) | • Need for a more global view of funding (vs. current divided drug vs. test approach)<br>• Set aside R&D budget in lab to support development of new CDx |
| • Lack of holistic view of value of CDx to the use of the drug | • Need a single value proposition that captures the value of the drug and includes the contribution of the CDx to the use of the drug |
| • Planning and forecasting<br>  ○ Finite resources and planning cycles that don't match<br>  ○ Provinces need more information re: what is coming in the future | • Need a business case to get through the budget process<br>  ○ Include patient numbers, capacity, number of different kits<br>  ○ Operational impact needs to be assessed<br>  ○ Typical economic evaluations stop at operations, and don't take into consideration the operational impact |
| • Pace of change<br>  ○ Can't keep up, but need to make decisions with imperfect information<br>  ○ Uncertainty – health technology management, formulary management, new entrants<br>  ○ Challenge to payers re: multiple drugs with multiple tests in the same indication | • Earlier cross-functional involvement (get lab into pharma pipeline meetings) |
| • Patient needs and perspectives<br>  ○ Average patients don't understand access processes, organizations, decisions<br>  ○ Patients will still want access even if negative | |
| • Lack of disinvestment | • Review current technologies to flag wastage (need more data) |

| Barriers | Solutions |
|---|---|
| • Operational implementation challenges<br>  ○ Provincial differences in CDx implementation<br>  ○ Importance of standards re: validation, thresholds, results interpretation<br>  ○ No controls on testing<br>  ○ Lack of post-approval monitoring | • Centralized testing for the country?<br>• Harmonized framework for operation of labs?<br>• Review pre- and post-adoption |
| • Cost of diagnostic<br>  ○ Prevalence<br>  ○ Budget impact | |
| • Value of targeted treatment to patients is lost in the discussion<br>  ○ In terms of targeted treatments offering more predictable efficacy and/or improved safety vs. not targeting the use of the agent | |
| • Not feasible for health system to have multiple versions of the same test<br>  ○ How to choose? | |
| • Need for streamlined approaches to tests to ensure efficiency | |
| • Education/implementation | |

This report provides a summary of the IHE/CAPT Precision Health workshop that took place on October 22, 2017 in Toronto, Ontario. The intent of the workshop was to identify gaps and opportunities in implementing precision health technologies into the Canadian health system.


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