Towards a framework for biosimilar evidence and knowledge exchange

Summary report of the IHE Biosimilars Forum

April 23, 2017

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

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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.

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Executive Summary

Introduction

This report follows from the Institute of Health Economics (IHE) Biosimilars Forum that was held on April 23, 2017 in Ottawa, Ontario. This meeting was a satellite to the 2017 Annual Canadian Agency for Drugs and Technologies in Health (CADTH) Symposium. This is the third IHE Forum on biologics/biosimilars that has been conducted, with the first held on May 29, 2014, and the second on October 6, 2016.

The purpose of this third event was to gather key stakeholders from the public and private sectors, as well as clinicians, academics, and patient and provider associations, in order to:

1. review the experience of NHS Scotland with the development and utilization of a National Biosimilars Prescribing Framework in order to understand options to categorize and consider biosimilars, as well as a process to engage stakeholders to identify place in therapy and further evidence development that may be required; and
2. identify an approach to knowledge exchange that will enable a common view and shared agreement amongst patients and clinicians regarding appropriate and intended use of biosimilars.

Learnings from the Scottish Experience

A keynote presentation shared that Scotland has achieved considerable success in promoting appropriate utilization of biosimilars following the development of a National Biosimilar Prescribing Framework and subsequent additional stakeholder engagement and interventions. A key lesson from this experience is that the opportunity with the introduction of biosimilars is broader than just the cost savings these agents may represent, and is best understood and framed as an opportunity to improve the quality of patient care and appropriate use of all biologic medicines. The Scottish experience suggests that a specialty-specific approach to biosimilar strategy development is required, involving a mix of interventions, with engagement by and leadership from providers in a clinically-led model. Additionally, therapeutic monitoring of outcomes achieved with biologic agents was suggested to be key to physician prescribing confidence and a driver for acceptance and utilization of biosimilars, as well as for better and more appropriate utilization of biologics in general.

Contributions from Canadian clinicians during this meeting emphasized the importance of this work for Canada. Clinicians agreed that we should pursue opportunities with biosimilars, but emphasized that the revolution that some biologics have brought about in patient care is the result of a complex package of the biologic and the clinical model of care in which it is used. It is therefore important to proceed with caution and to be evidence-based, and to consider the similarity of models of care as well as of the biologic agents themselves.

Key Conclusions from the Meeting

The participants in this meeting felt that all stakeholders have responsibility to optimize how medications are used in order to achieve quality care and promote long-term health system sustainability. It was highlighted that the cost-savings potential with biosimilars may represent an opportunity to invest in other areas in order to bring other innovations to patients, and it will be important to articulate how the value of biosimilars will lead to opportunities to increase access to innovation and improve patient care. However, given that biologics have revolutionized care, the

group emphasized that we should proceed cautiously, and with an evidence-driven approach. A number of conclusions emerged from the meeting:

- **A therapeutic area-specific approach is required**: The group concluded that there is a need to consider disease or therapeutic areas separately and to develop approaches tailored to each. Although there are likely common principles, the group felt that a blanket strategy that considers all patients, conditions, and molecules the same is not appropriate or helpful. The importance of robust stakeholder engagement for this effort was emphasized. It was felt that it would be helpful if an overall framework could be developed, within which area-specific work streams could operate, learn from each other, and create "peer pressure" to develop momentum. The group recognized that key therapeutic areas anticipating significant biosimilar entry are at different starting points, may have different objectives, and may have access to different resources and previous work in the area of biosimilars.
- **There is a need for defined leadership and process**: The group noted that there are a number of initiatives to bring stakeholders together to discuss biosimilars. It was felt there would be benefit from developing one structured, predictable, defined process with identified leadership, to promote a coordinated, disease-specific, strategic approach to biosimilars for Canada. This process should describe and provide structure to stakeholders who can then organize and provide transparent and meaningful input. Leadership was emphasized to be best assigned to an organization that is seen to be neutral, and that is able and trusted to bring all stakeholders together and to present and interpret evidence in a clear and unbiased way.
- **The "product" is more than the molecule**: The group agreed that the "product" offered to patients is more than just the biologic molecule. Manufacturers and providers have worked together to significantly improve the management of disease by providing key enabling infrastructure elements such as clinic and product delivery supports, access to medications, education, adherence resources, and outcomes monitoring and reporting. The group felt that it is important to better understand current infrastructure supports provided by industry and providers as a baseline, and policy approaches should, by design, encourage and provide incentives for all manufacturers to work with providers to ensure that appropriate packages of care are offered and delivered to patients.
- **We should strive for healthy biologic agent co-existence and competition**: Competition was highlighted as an important element to bring down the price of molecules. Additionally and importantly, competition was also emphasized as a means to provide incentives for manufacturers to provide a robust "product" beyond just the molecule, including many of the enabling infrastructure elements that have contributed to the success experienced by clinicians and patients to date with biologics. A well-performing competitive market to achieve continued product innovation was noted as one where there is a healthy co-existence of competitors. Given the Canadian experience thus far and the limited uptake of the first anti-tumor necrosis factor biosimilar, it was felt that further discussion was needed in order to determine how we may reduce time to market for biosimilars, as well as how to best foster competition and achieve sustainable cost-savings, including whether we need mechanisms to manage the adoption/utilization of biosimilars in order to achieve this. If such mechanisms are considered to be required, it was felt that there is a need to better understand the implications of any approaches to managing utilization on manufacturers'

incentive to develop robust product offerings, as well as implications for patient and prescriber decision-making.

- **Therapeutic outcomes monitoring is essential**: The group recommended that we be very deliberate about monitoring outcomes achieved with therapies, and that provider and patient confidence in biosimilars will positively correlate with outcomes monitoring and reporting. It was suggested that monitoring should be considered and implemented as part of routine care and not approached as research with all the costs and challenges that go along with this. The group recognized a need to define the essential data to collect (throughout the life cycle of an illness and not just at the start of biologic therapy), and to identify the mechanisms through which it can be captured and coordinated in order to inform decision-making with real-world evidence. It was noted that there are a number of existing databases currently gathering information in key areas that may be leveraged for this purpose.

Next Steps

Going forward, the group recommended that a broad group of stakeholders be engaged in strategy development, including Health Canada, HTA agencies (for example, CADTH, Institut national d'excellence en santé et en services sociaux [INESSS]), the pan-Canadian Pharmaceutical Alliance (pCPA), provincial Ministries of Health, private payers, clinicians (including professional associations), patient groups, industry, health IT/data managers, and researchers.

There was a recommendation that a specific organization or coalition of organizations that has the necessary skills and experience and can be seen to be impartial should be empowered to lead a single, transparent, and inclusive process to develop strategy for biosimilars in Canada. This should include the development of both an overall framework for strategy development and, within that, the development of disease-/therapeutic-specific strategies in a coordinated manner that promotes a common general approach and sharing of learning across streams. Each disease/therapeutic area should begin by agreeing to the scope of the strategy for that area, and, in particular, the extent to which it will focus on overall management of the disease, the role of biologics in that management, and the specific role of biosimilars relative to originator biologics.

It was recommended that a mandate for this work be provided from an appropriate organization (for example, pCPA) to give it authority and credibility and to encourage participation of all stakeholders. There was a call for accountability, both in terms of a commitment by all stakeholders to the process, and for each group to organize and prepare themselves to provide input when requested.

Concluding Comments

This meeting represented an important continuation of ongoing discussions of a "Made-in-Canada" approach to biosimilar introduction. Importantly, stakeholders continued to express interest in engaging in the dialogue and supporting discussions intended to lead to improved cost and care outcomes achieved by the health system, as well as opportunities to invest savings from biosimilars to enable improved patient access to other innovations. Encouragingly, stakeholders at this meeting highlighted strong interest in a formal, defined, single process to develop Canadian biosimilar strategy in order to make decisions and achieve appropriate utilization of biosimilars.

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
CRA	Canadian Rheumatology Association
HTA	health technology assessment
IBD	inflammatory bowel disease
INESSS	Institut national d'excellence en santé et en services sociaux
pCPA	pan-Canadian Pharmaceutical Alliance
TNF	tumor necrosis factor

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1. Introduction

1.1. IHE Biosimilars Forum overview

This report follows from the Institute of Health Economics (IHE) Biosimilars Forum that was held on April 23, 2017 in Ottawa, Ontario. This meeting was a satellite to the 2017 Annual Canadian Agency for Drugs and Technologies in Health (CADTH) Symposium. This is the third IHE forum on biologics/biosimilars that has been conducted, with the first held on May 29, 2014, and the second on October 6, 2016. More information on the previous events can be found at: *www.ihe.ca/research-programs/knowledge-transfer-dissemination/conferences/biologics/bios-about* and *www.ihe.ca/research-programs/knowledge-transfer-dissemination/roundtables/ihebf/about-ihebf*.

The purpose of this third event was to gather key stakeholders from the public and private sectors, as well as clinicians, academics, and patient and provider associations, in order to:

1. review the experience of NHS Scotland with the development and utilization of a National Biosimilars Prescribing Framework in order to understand options to categorize and consider biosimilars, as well as a process to engage stakeholders to identify place in therapy and further evidence development that may be required; and
2. identify an approach to knowledge exchange that will enable a common view and shared agreement amongst patients and clinicians regarding appropriate and intended use of biosimilars.

A total of 73 individuals participated in the event, including a Chair, three speakers, and four additional panelists. Participants reflected the perspectives of public and private payers, clinician/providers, regulators, health technology assessment (HTA) agencies, patient advocates, and originator and biosimilar industry. The format for the day was a number of presentations from invited speakers, followed by panel discussion, a table reflection exercise, and group 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 registrants, please see Appendix B.

1.2 Objectives

The objectives of the forum were to identify: options to categorize and consider biosimilars; a process to engage stakeholders to identify biosimilar place in therapy and further evidence development that may be required; and an approach to knowledge exchange that will enable a common view and shared agreement amongst stakeholders regarding appropriate and intended use of biosimilars.

The half-day forum was divided into two sections as noted below:

- **Session 1: A Framework for Biosimilar Evidence**
    - Introduction & welcome: Dr. Chris Henshall/Dan Palfrey
    - *A Scottish framework for biosimilar prescribing – Experience and lessons for Canada*: Ms. Laura McIver, Chief Pharmacist, Healthcare Improvement Scotland
    - *Interpretation of the evidence and guiding framework in the Canadian context*:
        - Dr. Thomas Walters, Co-Director, SickKids Paediatric Inflammatory Bowel Diseases Programme

        - Dr. Carter Thorne, Assistant Professor, University of Toronto
    - Panel discussion
- **Session 2: A Framework for Knowledge Exchange**
    - Table reflection and group discussion

2. Summary of Presentations

The following provides a summary of the three keynote presentations. Videos of each presentation and accompanying slides prepared by the invited speakers can be found at: *www.ihe.ca/research-programs/knowledge-transfer-dissemination/roundtables/ihe-bif/bif-about*.

Preceding these presentations, the IHE provided a brief summary of the previous 2016 IHE Biosimilars Forum in order to set the stage and provide continuity between events. The report from this event can be found at: *www.ihe.ca/research-programs/knowledge-transfer-dissemination/roundtables/ihebf/ihebf-docs*.

2.1 A Scottish framework for biosimilar prescribing: Experience and lessons for Canada

Ms. Laura McIver, Chief Pharmacist, Healthcare Improvement Scotland

Scotland has achieved considerable success in promoting appropriate utilization of biosimilars following the development of a National Biosimilar Prescribing Framework in 2015, as well as subsequent additional stakeholder engagement and interventions. There were three main drivers for change that started the work on biosimilars in Scotland. These included:

1. significant spending on biologic medicines, with these agents accounting for 9 out of the top 20 medicines by expenditure, and many expected to lose patent protection in the next 5 years;
2. pressure to replicate the significant biosimilar utilization observed in other countries such as Norway; and
3. considerable budget challenges as a result of an economic downturn, resulting in a transformation change initiative that included a focus on effective prescribing with priority placed on biosimilars.

Two key enablers to biosimilar utilization in Scotland preceded the development of the Prescribing Framework. The first was removal of the requirement for biosimilars to go through the HTA process. The Scottish Medicines Consortium (SMC) requires all new medicines that receive a license to go through its HTA process; however, based upon the HTA experience of 11 biosimilars where it was felt there was little value in this exercise, a decision was made in 2015 to not require HTA review for a biosimilar if an originator had already been through the process. The second enabler was the removal of a decision step by Health Board Area Drug and Therapeutics Committees, where it was decided that, once a biosimilar was licensed for use, it would become available for physicians to prescribe.

With these two enablers in place, the bulk of efforts in Scotland have focused on biosimilar prescribing for individual patients and the shared decision-making with their provider that this entails. In 2015, a decision was made that the development of an approach to increased biosimilar utilization was to initiate and be clinically-led, as opposed to a procurement- or finance-driven

approach as in other countries. This was felt to provide significant benefit in alleviating stakeholder concern with the driver for the initiative. A clinically-led approach, involving provider groups representing different disciplines that prescribe biologic medicines, was initiated to develop the National Biosimilars Prescribing Framework.

The Prescribing Framework developed recommends biosimilars as an alternative to originator biologics, recognizes that clinical experience is still emerging and there is a need to create comfort despite a recommendation of no efficacy or safety concerns, indicates that biosimilars are suitable for new patients, and acknowledges that switching is a decision to be made by clinicians together with their patients. The Framework does not support interchangeability at the point of dispensing. Since publication of the Prescribing Framework, some provider groups have evolved their public positions and have become much more open to the use of biosimilars, including switching patients from originator to biosimilar biologics.

The Prescribing Framework developed represents a high-level approach across therapeutic areas, and it became clear that a one-size-fits-all approach was not appropriate across all specialties or medicines, and that there are unique differences that have to be considered. The follow-on work to the 2015 Prescribing Framework has taken a very specialty-specific approach. A multi-disciplinary Biosimilars Project Team was formed to support this work. It was realized that the broad opportunity was in the financial savings with biosimilars, but also with improving the quality of care for patients more generally. Engagement of clinicians was identified as a key success factor, and it was felt that their involvement would be limited if the driver of the initiative was just about saving money. A broader agenda to improve the use of biologic medicines, not just biosimilars, with a focus on shared decision-making and personalized care was communicated, and permitted the achievement of the goals of both managers and clinicians. The biosimilars workstream was redefined as a biologic medicines workstream, with the goal to drive improvement in the use of biological medicines (including biosimilars) to deliver quality improvements and financial savings (that is, do more with less resources). Multiple interventions with an invest-to-save approach have been put into place by this group, including the following:

- Establishment of a framework pricing agreement
- Identification of biologics leads in each health board
- Identification of national clinical leads in gastroenterology and rheumatology
- Specialty-specific engagement events
- Sharing of good practice
- Identification of targets for uptake
- Creation of peer pressure between health boards to share uptake data

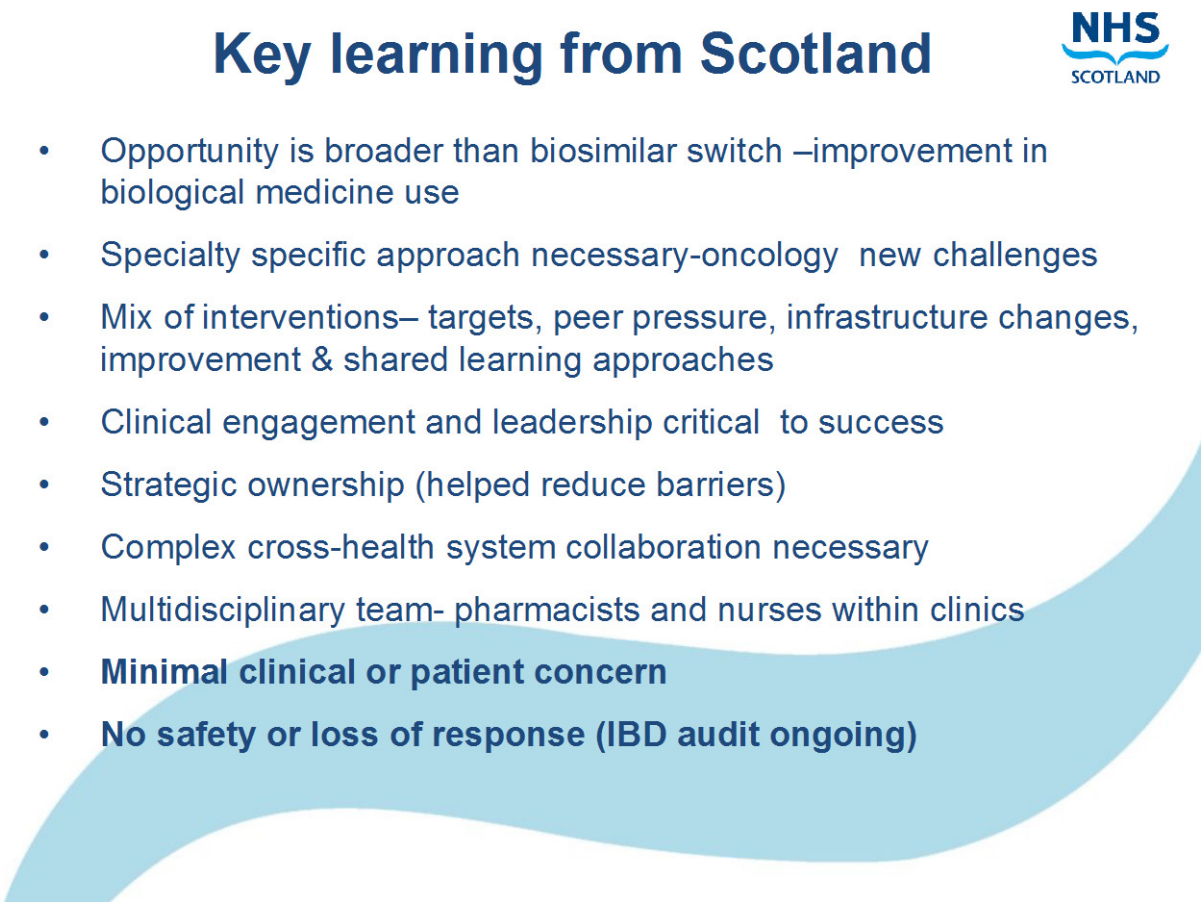
Clinical leads have focused on the following four key areas:

1. Evidence gathering regarding current delivery – engaging with NHS Boards on current use of biologics, potential for improved effectiveness at the local level, and any additional support required (for example, capacity impact)
2. Development of best practices – protocols for prescribing, monitoring, and testing of biologics, identification of improved care pathways, identification of core elements of best practice, and patient engagement

3. Establishment of infrastructure – development of a Scottish solution to therapeutic monitoring, and definition of a minimum dataset and recommended IT solutions for data capture (with focus on gastroenterology and rheumatology)
4. Preparation for new biosimilars

Targets were set for biosimilar uptake for each Health Board, and monthly comparative uptake data is shared. The targets were realistic, and have been achieved earlier than anticipated. Significant utilization of biosimilars has been realized; 85% for infliximab, and 53% for etanercept.

The key learning from the Scottish experience is that the opportunity for care and cost improvement is broader than just biosimilars, and is best understood and framed as an opportunity to improve use of all biologic medicines. The Scottish experience suggests that a specialty-specific approach is required, involving a mix of interventions, with engagement by and leadership from providers in a clinically-led model. Additionally, therapeutic monitoring of outcomes achieved with biologic agents was suggested to be key to physician prescribing confidence and a driver to acceptance and utilization of biosimilars, as well as for better and more appropriate utilization of biologics in general.



2.2 Interpretation of the evidence and guiding framework in the Canadian context

Dr. Thomas Walters, Co-Director, SickKids Paediatric Inflammatory Bowel Diseases Programme

Biological therapies, in particular the anti-tumor necrosis factor agents (anti-TNFs), have made a significant impact on the management of inflammatory bowel disease (IBD) and have changed the treatment paradigm. There is now a treat-to-target approach that has shifted from the goal of patients feeling better to actual mucosal healing. Canadian gastroenterologists are very sophisticated with their use of anti-TNFs, which they have become accustomed to using over the last two decades, and consider them the most effective drugs that they work with.

Anti-TNFs were initially used as induction agents, and were prescribed as required when patients relapsed in an episodic maintenance model. As the time to use the medications became increasingly shorter, physicians came to realize that these agents can stop working and, when they do, they stop working permanently. Gastroenterologists have had to think like immunologists, and understand that continuous presentation of antigen leads to tolerance, and that intermittent presentation leads to immune responsiveness and neutralizes the medication. Gastroenterologists have now adopted a regular maintenance model of use of these agents, which has improved tolerance, reduced the chance of neutralizing antibody development, and markedly improved the durability of response to the agents. In doing this, gastroenterologists have also had to think like pharmacologists, utilizing two simple rules: if the medication is not there, it cannot help, and if it keeps coming and going, it will not be tolerated.

Gastroenterologists not only now treat to target, but encourage the targeting of treatment. A key consideration is timing of agent introduction. The Australian concept of "king hit" is helpful when thinking about the use of anti-TNFs in IBD; it is the most effective punch or strike that can be delivered, and sends the aggressor off-balance even if it does not hit the intended target. Early use of anti-TNF has been demonstrated to be superior versus step-up therapy, including a marked difference in irreversible damage.

The question to answer is not whether anti-TNF agents will work for patients, but rather will they continue to work and demonstrate a durable response. Early trial data showed a loss of response of 20 to 30% within 12 months, with higher drug levels associated with better durability. In terms of real-world experience, when examining response rates at the SickKids hospital in Toronto after the first decade of experience with anti-TNFs, it was observed that 90% of patients were primary responders, with 80% still responding at 5 years. Overall, a 4% loss of response was observed. Most patients lose response due to the development of antibodies. More than a third of patients get dose-optimized within the first 12 months. This Canadian experience is similar to that observed in European adults, where 90% of patients are primary responders, with about 10% loss thereafter.

The therapeutic paradigm in Canadian gastroenterology is as follows:

- Selection of initial therapy based upon the estimate of disease outcome risk
- Regular review of outcomes and if not meeting target change therapy
- When using anti-TNFs, aim for dose optimization and try to avoid the risk of exposure/ re-exposure, which creates irreversible sensitization

When considering the evidence for biosimilars, the questions to ask are: do they work, will they keep working, and is it okay to switch? There are weak observational studies with significant variability between them that suggest that immunogenicity and clinical outcomes are affected by previous use of the originator biologic. The NOR-SWITCH trial (on switching from innovator to biosimilar infliximab; see *clinicaltrials.gov/ct2/show/NCT02148640*) is randomized, however the power assumes 30% loss or response, which is not reflective of actual experience (which is much less), and a non-inferiority margin of 15%, which is not adequate. The largest sub-set of patients in the study had Crohn's disease and did the poorest, and appears to be an outlier.

There are non-molecule concerns regarding biosimilars that physicians have, including the following:

- Any additional administrative requirements to start, review, or monitor biologics with the introduction of biosimilars
- Continued access to current supports that are provided by originator manufacturers
- Organization and funding of therapeutic monitoring

In Canada, we have resources that facilitate timely therapy starts, early optimization of exposure (including access to medications), and improved adherence. Almost all of these resources are paid for by pharmaceutical companies. When considering biologics, it is important to understand that it is about more than just the molecule, and there are a wide range of tools and services available from manufacturers of originator biologic agents. Together with the molecule, this package has resulted in marked, durable health care improvement for the majority of patients. To maintain patient-centred outcomes at their current levels, there is a need for a "product" similar to that provided by originators that is beyond just the molecule. There is a need for cost containment, but we need to approach this in a manner that does not reduce the healthcare outcomes that we have already achieved.

Dr. Carter Thorne, Assistant Professor, University of Toronto

Patients with inflammatory joint disease have been the trial area for most biologics. There has been a significant change in care pathways over time as a result of new therapies, but also due to a change in the therapeutic approach. The Canadian Rheumatology Association (CRA) first engaged on the topic of biosimilars in 2011, at both the provincial and federal level. The CRA appreciates that the utilization and acceptance of biosimilar use will continue to evolve based on evidence and experience. In 2013, the CRA developed a position statement that is to be reviewed biannually. This statement is not to guide members as is intended with a therapeutic guideline, but rather to inform stakeholders. The position statement has seven points:

1. In an individual naïve to a specific molecule, choice and/or interchangeability between a biosimilar and an innovator molecule might be considered.
2. Administrative switch/interchangeability for patients on established therapy is not supported at the present time.
3. Substitutions from one biologic to another, including a biosimilar or an innovator molecule, by someone other than the treating physician must be avoided.
4. There should be establishment of post-marketing surveillance for all for new-entry products, including biosimilars and new innovative biologics, in order to determine uncommon side effects and durability of response (there are a number of established registries across the country, with four large databases in place, that can be readily developed for this purpose).

5. All biologic molecules should be identified by an appropriate naming system (for example, molecular name-suffix) in order to ensure correct attribution of adverse events.
6. Biosimilars and innovator molecules (those currently available and new-entry agents) should have indications only where data is sufficient from well-conducted clinical studies and approved by Health Canada.
7. Approval and access to biosimilars and innovator molecules must acknowledge the clinical needs of the patients and respect the context of the therapeutic interaction of patient and physician.

Regarding surveillance, the CRA suggests that results of activities should be made available for external review, and all acquired data should be collated for comparative purposes. The CRA supports the use of third party research-based groups, independent of the pharmaceutical industry, to ensure transparency and validity, with involvement by all stakeholders including patient groups, industry, private payers, and governments. The recommended defined observational period is 3 to 5 years. An initiative has been developed by the CRA to encourage collection of clinical data elements in a standardized fashion and to support routine clinical care and best practices; a minimal data set and encounter sheet for extraction from electronic medical records has been identified (Canadian Rheumatoid Arthritis Core Clinical Dataset [CAN-RACCD]), and the goal is to regularly extract this data and integrate it into a database to monitor patient outcomes.

The CRA is committed to ensuring best outcomes by advocating for evidence-based care and best practices (reducing variability in strategy and outcomes), and is committed to taking a proactive lead, as "Experts in Arthritis Care". A model of success includes an initiative completed by the Ontario Rheumatology Association, with the support of the CRA, to work with the Canadian Life and Health Insurance Association to develop a new standard for biologic use criteria amongst private payers.

The CRA believes it is not the molecule but rather the product that is important; it is the model of care with a view to the cost relative to the outcomes achieved. The CRA endorses a collaborative approach involving members, those with arthritis, and payers both public and private.

3. Reflection of the Discussion

3.1. Panel discussion

A panel discussion followed the presentations. General comments from the panelists and participants emphasized that all stakeholders have responsibility to optimize how medications are used in order to contribute to long-term health system sustainability. It was highlighted that the cost-savings potential with biosimilars may represent an opportunity to invest in other areas in order to bring new innovations to patients, and it will be important to articulate how the value of biosimilars will lead to opportunities to increase access to innovation and improve patient care. However, given that biologics have revolutionized care, the group emphasized that we should be cautious and evidence-based, very clear about how we define and communicate similarity of both biologic agents and models of care and service delivery, and be very deliberate in providing stakeholders with a meaningful opportunity to contribute to the discussion and debate. A number of conclusions emerged from the meeting, and are presented below.

3.1.1. A therapeutic area-specific approach is required

The group concluded that there is a need to look at each disease or therapeutic area separately and develop approaches tailored to each. Although there are likely common principles, the group felt that a blanket strategy that considers all patients, conditions, and molecules the same is not appropriate or helpful. It was felt that it would be helpful if an overall framework could be developed, within which area-specific work streams could operate, learn from each other, and create "peer pressure" to develop momentum.

The group recognized that key therapeutic areas anticipating significant biosimilar entry are at different starting points, may have different objectives, and may have access to different resources and previous work in the area of biosimilars. It was suggested that, similar to the Scottish experience, rheumatology may be in the best position to consider biosimilars within the broader context of good management of inflammatory joint disease, taking advantage of the significant work and data infrastructure available. Gastroenterology was felt to have early opportunity to consider good use of biological medicines and, within this, the role for biosimilars. The most narrow starting point objective was suggested for oncology, where little previous work has been completed, with an exercise to examine the role of biosimilars versus originators as part of the regimen of care.

3.1.2. There is a need for defined leadership and process

The group acknowledged that there are many stakeholders getting together to discuss biosimilars, but felt there is significant rationale and benefit from developing one structured, predictable, defined process with identified leadership, in order to develop a disease-specific strategic approach to biosimilars for Canada. This process should describe and provide structure to stakeholders who can then organize and provide transparent and meaningful input. Leadership was emphasized to be best assigned to an organization that is seen to be neutral, and that is able and trusted to bring all stakeholders together and to present and interpret evidence in a clear and unbiased way.

3.1.3. The "product" is more than the molecule

The group understood that the "product" offered to patients is more than just the biologic molecule. Manufacturers and providers have worked together to significantly improve the management of disease by providing key enabling infrastructure elements such as clinic and product delivery supports, access to medications, education, adherence resources, and outcomes monitoring and reporting. The group felt that it is important to better understand current infrastructure supports provided by industry as a baseline, and policy approaches should, by design, encourage and provide incentives for all manufacturers to work with providers to ensure that appropriate packages of care are offered and delivered to patients. As an example, it was felt that a tendering approach with a winner-take-all model might not achieve this goal, given the potential for emphasis on the price of the molecule as opposed to establishing market conditions for continuous product innovation.

3.1.4. We should strive for healthy biologic agent co-existence and competition

Competition was highlighted as an important element to bring down the price of molecules. Additionally and importantly, competition was also emphasized as a means to provide incentive for manufacturers to provide a robust "product" beyond just the molecule, including many of the enabling infrastructure elements that have contributed to the success experienced by clinicians and patients to date with biologics, as noted above. Competition amongst the originator anti-TNFs were observed as a driver to the current high quality products available, and biosimilars were highlighted

to represent an opportunity for further competition to improve upon this, and perhaps even drive better patient care and outcomes.

A well-performing market in which we can realize cost savings and achieve continued product innovation was noted as one where there is healthy co-existence of competitors. Limited uptake of the biosimilar to infliximab in Canada after three years on the market may indicate that we have not yet achieved this. Further discussion may be needed in order to determine how we may reduce time to market for biosimilars, as well as how to best foster competition and achieve sustainable cost-savings, including whether we need mechanisms to manage adoption/utilization of biosimilars in order to achieve this. If such mechanisms are considered to be required, it was felt that there is a need to better understand the implications of any approaches to managing utilization on manufacturer incentive to develop a robust product offering, as well as implications for patient and prescriber decision-making.

3.1.5. Therapeutic outcomes monitoring is essential

The group recommended that we be very deliberate about monitoring outcomes achieved with therapies, including biosimilars. As observed in Scotland, provider and patient confidence was felt to positively correlate with monitoring and reporting of outcomes achieved with biosimilars. It was suggested that monitoring should be considered and implemented as part of routine care and not approached as research with all the costs and challenges that go along with this. The group recognized a need to define the essential data to collect (throughout the life cycle of an illness and not just at the start of biologic therapy), and to identify the mechanisms through which it can be captured and coordinated in order to inform decision-making with real-world evidence. It was noted that there are a number of existing databases currently gathering information in key areas that may be leveraged for this purpose.

3.2 Table reflection

Given the conversation during the panel discussion, a decision was made to refocus the last portion of the meeting on an approach to therapeutic area-specific strategy development, as opposed to a discussion on knowledge exchange.

A brief table exercise followed the panel discussion with a focus on answering the following questions:

- Who needs to be involved in developing biosimilar strategy for identified therapeutic areas?
- What needs to happen to bring this group together and who should have leadership responsibility?
- What are the key elements within each strategy that must be considered?

The group reported that a broad group of stakeholders should be engaged, including Health Canada, HTA agencies (for example, CADTH, Institut national d'excellence en santé et en services sociaux [INESSS]), the pan-Canadian Pharmaceutical Alliance (pCPA), provincial Ministries of Health, private payers, clinicians (including professional associations), patient groups, industry, health IT/data managers, and researchers.

There was a recommendation that a specific organization or coalition of organizations that has the necessary skills and experience and can be seen to be impartial should be empowered to lead a single, transparent, and inclusive process to develop strategy for biosimilars in Canada. This should

include the development of both an overall framework for strategy development and, within that, the development of disease/therapeutic-specific strategies in a coordinated manner that promotes a common general approach and sharing of learning across streams. Each disease/therapeutic area should begin by agreeing to the scope of the strategy for that area, and, in particular, the extent to which it will focus on overall management of the disease, the role of biologics in that management, and the specific role of biosimilars relative to originator biologics. As noted above, the group felt that work could begin in more mature areas with respect to biosimilars such as rheumatology, and that the learnings be applied to support other areas that may be less advanced (for example, oncology).

It was recommended that a mandate for this work be provided from an appropriate organization (for example, pCPA) to give it authority and credibility, and to encourage participation of all stakeholders. There was a call for accountability, both in terms of a commitment by all stakeholders to the process, and for each group to organize and prepare themselves to provide input when requested.

Key elements that were considered critical to address within each strategy include the following:

- Guiding principles
- Scope of strategy development
- Criteria to evaluate options
- Stakeholder accountability
- Documentation of current care pathways and outcomes achieved
- Current biologic product (beyond the molecule) definition and delivery model reflective of minimum standards
- Originator and biosimilar molecule recommendations by patient segment (naïve, switch)
- Approach to gain-sharing and reinvestment
- Approach to outcomes monitoring and reporting, including methodology and targets/indicators

4. Concluding Comments

This meeting represented an important continuation of ongoing discussions of a "Made-in-Canada" approach to biosimilar introduction. A number of key conclusions and opportunities were identified and are described in this report. Importantly, stakeholders continued to express interest in engaging in the dialogue and supporting discussions intended to lead to improved cost and care outcomes achieved by the health system, as well as opportunities to invest savings from biosimilars to enable improved access to new innovations for patients. Encouragingly, stakeholders at this meeting highlighted strong interest in a formal, defined, single process to develop Canadian biosimilar strategy in order to make decisions and achieve appropriate utilization of biosimilars.

Appendix A: Forum Program

INSTITUTE OF HEALTH ECONOMICS
ALBERTA CANADA

Towards a Framework for Biosimilar Evidence & Knowledge Exchange

SUNDAY, APRIL 23, 2017
WESTIN HOTEL, OTTAWA
BC/MANITOBA ROOM

12:30 – 1:00 p.m. Lunch & Opening Remarks

- **Dr. Chris Henshall, Professor, Health Economics Research Group, Brunel University**

1:00 – 1:15 p.m. Setting the Stage: Enabling Elements to Achieve Biosimilar Objectives

- **Mr. Dan Palfrey, Senior Consultant, Institute of Health Economics**

1:15 – 2:15 p.m. A Scottish Framework for Biosimilar Prescribing: Experience and Lessons for Canada; Interpretation of the Evidence and Guiding Framework in the Canadian Context

- **Ms. Laura McIver, Chief Pharmacist, Healthcare Improvement Scotland**
- **Dr. Thomas Walters, Co-Director, SickKids Paediatric Inflammatory Bowel Diseases Programme, Toronto, Ontario**
- **Dr. Carter Thorne, Assistant Professor, University of Toronto**

2:15 – 3:15 p.m. Panel Discussion

- **Ms. Laura McIver, Chief Pharmacist, Healthcare Improvement Scotland**
- **Dr. Thomas Walters, Co-Director, SickKids Paediatric Inflammatory Bowel Diseases Programme, Toronto, Ontario**
- **Dr. Carter Thorne, Assistant Professor, University of Toronto**
- **Mr. Eric Lun, Executive Director, Drug Intelligence & Optimization, Medical Beneficiary & Pharmaceutical Services Division, B.C. Ministry of Health**
- **Ms. Dawn Richards, Vice President of the Canadian Arthritis Patient Alliance**
- **Mr. Frédéric Lavoie, Vice President of Access & Government Relations, Pfizer**
- **Ms. Julia Brown, Vice President, Government Affairs & Market Access, Janssen Inc.**
- **Dr. Sandy Sehdev, Oncologist, The Ottawa Hospital Cancer Centre**

3:15 – 3:30 p.m. Break

3:30 – 4:30 p.m. Knowledge Exchange Workshop

4:30 p.m. Adjourn

Dr. Chris Henshall

Dr. Henshall is a Professor in the Health Economics Research Group at Brunel University and works as an independent consultant in health, research, and innovation policy. Previous appointments in Canada include Board Director of the Alberta Research and Innovation Authority (ARIA) from 2010 to 2015, and Board Director of Alberta Innovates Health Solutions from 2015 to 2016.

Dr. Henshall has held senior positions in the British Government and university systems. From 2005 to 2010, he was Pro Vice Chancellor at the University of York with responsibility for enterprise and innovation and links between the University, regional and national government, and industry. Prior to that he was Director of the Science and Engineering Base Group in the Office of Science and Technology in the Department of Trade and Industry in London, where he was responsible for around $5 billion US annually of government support for research and innovation.

Earlier in his career, Dr. Henshall served as Deputy Director of Research and Development in the Department of Health and the National Health Service (NHS), where he led the creation of an NHS R&D budget and was closely involved in establishing the NHS Health Technology Assessment (HTA) Program and the National Institute for Clinical Excellence (NICE). Dr. Henshall was the founding President of Edmonton-based Health Technology Assessment International (HTAi) and the founder and Chair from 2004 to 2007 and 2010 to 2016 of its HTA Policy Forum, which brings together senior figures from life sciences companies and public health systems from around the world.

Laura McIver

Laura McIver is the Chief Pharmacist for Healthcare Improvement Scotland, the national healthcare improvement organization for Scotland. Healthcare Improvement Scotland was established to advance improvement in healthcare and has a vital role in supporting healthcare providers to deliver safer, more effective, and more person-centered care.

Laura has held a variety of posts in the hospital sector including Chief Pharmacist to an NHS board, which allowed her to redesign the hospital pharmacy service to strengthen its focus on patients and maximize the pharmacy team's contribution to the safe and effective use of medicines.

In 2002, Laura joined the Scottish Government implementation team for the National Pharmacy Strategy. In 2005, Laura was appointed Chief Pharmacist to Scottish Medicines Consortium, providing clinical and cost-effective advice to NHS Scotland for all new medicines and, in 2012, Laura was appointed to her current post.

Dr. Carter Thorne

Dr. Thorne is an Assistant Professor at the University of Toronto, and is on the Consultant Staff at Southlake Regional Health Centre in Newmarket, Ontario, where he is Chief of the Division of Rheumatology and Director of The Arthritis Program; the latter is a unique inter-professional care program established to optimize outcomes for people who have arthritis and other rheumatic disorders. He is sought for his expertise in developing outcome-based clinical Programs, not only in Arthritis Care, but also Shared Care in a Comprehensive Musculoskeletal Program, Wound Management, and NeuroRehab/Stroke Care.

He is active in Clinical Research as Principal Investigator with The Arthritis Program Research Group Inc. As part of a strategic interest in identifying 'Best Practices', he has established an Early Arthritis Clinic, collaborating with a national initiative (CATCH, of which he is Operations Director), and an Osteoporosis Intervention Clinic. He sits on the Steering and Scientific Committee of the Ontario Best Practices Research Initiative, a collaborative attempt among

stakeholders to describe and disseminate outcomes and best practices in the management of Rheumatoid Arthritis. He was an active Investigator and participant in the successful Canadian Rheumatology Research Consortium and served as Secretary-Treasurer, until its conclusion in 2014. He is a founding member of the Ontario Rheumatology Association and Past-President (2006 to 2010). He is past President of the Canadian Rheumatology Association (2012 to 2014). He is past Secretary-Treasurer of PANLAR, and has served on the Steering committee of CARE, a European-based group interested in the non-pharmacologic management of arthritis.

Dr. Thorne recently presented the Canadian Rheumatology Association position statement on Biosimilars at a Health Canada meeting (March 20, 2017).

Dr. Thomas Walters

Dr. Walters graduated from medicine at the University of Western Australia, and completed his training in Paediatric Gastroenterology at the Hospital for Sick Children, University of Toronto, with a fellowship in Paediatric Inflammatory Bowel Disease and post-graduate training in Clinical Epidemiology. He is currently Co-Director of the SickKids Paediatric Inflammatory Bowel Diseases Programme in Toronto. He has a broad range of clinical research interests related to the aetiology, manifestations, and outcomes in children and adolescents with IBD.

He has extensive experience in developing data management systems and collection platforms; and is the founding Director of the Data Co-ordinating Centre for both PRO-KIIDS, a multi-centre Paediatric IBD Research Network fully funded by the Crohns and Colitis Foundation of America, NEOPICS, an international collaborative originating from SickKids Toronto investigating IBD in the very young, and IMAGEKIDS, an international multi-centre study developing standardized reporting tools for MR enterography in Paediatric IBD.

Dr. Walters's clinical research interests are broadly focused around the inflammatory bowel diseases, particularly on projects related to phenotyping, genetics, and longitudinal therapeutic outcomes. He is a recognized expert in the analysis of growth impairment related to IBD. His combined background in clinical epidemiology, biostatistics, database design, and management has resulted in him leading the development of a number of data platforms in North America and internationally that support numerous ongoing multicenter clinical research endeavours in Paediatric IBD. He is the founding and ongoing Director of the Data Co-ordinating Centre for the recently established Canadian Children Inflammatory Bowel Diseases Network, a joint partnership with CIHR and the CHiLD Foundation.

Dan Palfrey

Dan Palfrey is a senior consultant working with the Institute of Health Economics. In previous roles, Dan has held progressive leadership positions with a multinational pharmaceutical organization in Market Research, Sales, Marketing, Product Management, and Government Relations, and most recently was a Vice President with one of Canada's leading Electronic Medical Record (EMR) companies. Dan has Master of Public Health and Bachelor of Science degrees from the University of Alberta, and is a past recipient of the Robert Wood Johnson Award.

Dawn Richards

Dawn Richards, PhD, is the founder of Five02 Labs Inc, a boutique consulting firm that offers clients a range of science- and patient-related services. Principally amongst its service offerings are: writing and communications (grants, manuscripts, corporate materials, lay language), incorporation of the patient perspective, and developing working relationships with patients and patient organizations. Clients include academics, not-for-profit organizations, and pharmaceutical and biotech companies. With a PhD (Analytical Chemistry) from the University of Alberta, Dawn has worked over the past 15 years in roles ranging from bench scientist, to operations manager, to business development manager. Her diagnosis with rheumatoid arthritis ten years ago instigated her career journey to intertwine her passion for science and make the most of her diagnosis.

As a patient advocate and volunteer, Dawn is Vice President of the Canadian Arthritis Patient Alliance, a Research Ambassador for the Institute of Musculoskeletal Health and Arthritis (of the Canadian Institutes for Health Research), and a member of The BMJ's Patient Panel Reviewers, and was the first Patient Advisor of the Canadian Medical Association's Wait Time Alliance. She advocates for arthritis awareness, access to treatment, the inclusion of patients in decision-making and as research collaborators, and the importance of research.

Frédéric Lavoie

Frédéric Lavoie obtained his Master's Degree in Economics in 1995 from Université du Québec à Montréal. Until 1998, he worked as a health economist at the Centre for the Analysis of Cost-Effective Care within the Division of Clinical Epidemiology, a research unit affiliated to McGill University. In this position, he worked on and authored different papers on economic evaluation of pharmaceuticals. In 1997, Frederic was part of a working group of researchers mandated by the Government of Quebec to evaluate the economic impact of the proposed tobacco legislation.

Frederic began his career in the pharmaceutical industry when he joined Pfizer Canada in 1998, where he occupied various roles of increasing responsibilities. He joined Novartis Oncology in October 2014 as Head of Health Policy and Patient Access, and returned to Pfizer as Vice President of Access & Government Relations in March 2016.

Frederic graduated in 2007 as a PhD in Biomedical Sciences under the supervision of Dr. Jacques LeLorier at Universite de Montreal. He also serves on the editorial board of the *International Journal of Technology Assessment in Health Care*.

Eric Lun

In his current role within the Medical Beneficiary and Pharmaceutical Services Division (MBPSD) in British Columbia, Eric Lun leads the Drug Intelligence and Optimization branch of the British Columbia Ministry of Health. The branch is responsible for determining which drugs are included in the BC PharmaCare formulary through the national Common Drug Review (CDR-CADTH) process, the pan-Canadian Pharmaceutical Alliance (pCPA) negotiation process, and the provincial Drug Benefit Council (DBC) review process. The branch also is responsible for adjudicating drug funding requests through Special Authority, supporting the optimal and appropriate use of drugs in BC (e.g., supporting prescribing guidelines and academic detailing), and leading other specialty programs and initiatives.

Prior to joining MBPSD in 2007, Eric worked with the Vancouver Coastal Health Authority as Regional Coordinator, Medication Use Management. Eric has also worked as a financial research analyst for the biotech and healthcare sector (TD Securities), as a clinical pharmacist (Vancouver General Hospital), a Drug Use Evaluation pharmacist (University of Alberta Hospital), and a pharmacy lecturer (University of Technology, Jamaica).

Julia Brown

Julia Brown has been with Janssen Inc. for 14 years and is currently the Vice President of Government Affairs and Market Access. Previous roles at Janssen include National Director of Government and Community Relations, Director of Health Economics and Reimbursement, and Director of Government Relations, Ontario/Atlantic.

Julia also serves as the Past-President of the Canadian Association for Healthcare Reimbursement (CAHR) and has sat on the CAHR Board of Directors for 12 years. She served as a Chief of Staff in the Ontario Provincial Government from 1997 to 2003 in the portfolios of Municipal Affairs and Housing, Management Board and Natural Resources, and as an Executive Assistant to the Member from Bruce-Grey from 1995 to 1997. Julia has additional experience in the Federal Government, the not-for-profit sector, and a manufacturing firm, and holds a BA in Political Science from Carleton University.

Dr. Sandy Sehdev

Dr. Sehdev attended medical school at the University of Ottawa and had subsequent training in medical oncology at the University of Toronto and The Princess Margaret Cancer Centre (1991).

He worked at The William Osler Health System, serving a large Toronto area suburban community for 25 years (until 2016), and while there was chief of the Pharmacy & Therapeutics Committee (5 years), and long term lead of the clinical trials program (oncology) and continuing medical education (oncology). He was a past lead of CME for the Community Oncologists of Metropolitan Toronto (COMET), and a past Director of the Cancer Advocacy Coalition of Canada. He is a current co-director and founding member of the Physician Alliance for Cancer Control and Treatment (Canada), an oncologist led advocacy coalition.

Dr. Sehdev is currently a medical oncologist at The Ottawa Hospital Cancer Centre and Lecturer at the University of Ottawa, focusing on the treatment of breast, genitourinary cancers, and melanoma. His interests included advocacy, medical education, and applications of technology in medicine.

Appendix B: Forum Registrant Affiliations

No.	Registrant Affiliation	No.	Registrant Affiliation
1	AbbVie	40	Innovative Medicines Canada
2	Abbvie	41	Institute of Health Economics
3	AbbVie	42	Janssen Inc.
4	Alberta Health	43	Janssen Inc.
5	Alberta Health	44	Janssen Inc.
6	Alberta Health Services	45	Lymphoma Canada
7	Amgen Canada Inc.	46	McGill University
8	ApoBiologix Inc	47	McKesson Canada
9	BC MInistry of Health	48	McMaster University (PATH)
10	Biosimilars Canada	49	Merck Canada Inc.
11	BIOTECanada	50	Mylan
12	CADTH	51	NHS Scotland
13	CADTH	52	NIHB Health Canada
14	Canadian Arthritis Patient Alliance	53	Ontario Ministry of Health and Long-Term Care
15	Canadian Council of the Blind	54	Pfizer
16	Canadian Dermatology Associati	55	Provincial Drug Programs, Manitoba Health
17	Canadian Dermatology Association	56	Roche Canada
18	Canadian Dermatology Association	57	Roche Canada
19	Canadian Organization for Rare Disorders	58	Sandoz Canada
20	Canadian Organization for Rare Disorders	59	Sanofi
21	Canadian Psoriasis Network	60	Santis Health
22	Canadian Rheumatology Association (CRA)	61	Saskatchewan Health
23	Canadian Society of Hospital Pharmacists	62	Save Your Skin Foundation
24	Canadian Spondylitis Association	63	Takeda Canada
25	CARNA	64	Takeda Canada
26	Chair	65	The Alliance for Safe Biologic Medicines
27	Eli Lilly	66	The Arthritis Society
28	Gastrointestinal Society	67	The Arthritis Society
29	Global Public Affairs	68	The Ottawa Hospital Cancer Centre
30	Government of BC	69	Université de Montréal
31	Government of Prince Edward Island	70	University of Alberta
32	Great-West Life	71	University of Calgary
33	Health Canada	72	University of Calgary
34	Health Canada	73	University of Toronto
35	Health Canada		
36	Health Canada		
37	HealthCareCAN		
38	INESSS		
39	INESSS		

This report provides a summary of the IHE Biosimilars Forum engagement exercise that took place on April 23, 2017 in Ottawa, Ontario. The intent of the forum was to identify:
options to categorize and consider biosimilars;
a process to engage stakeholders to identify place in therapy and further evidence development that may be required;
and an approach to knowledge exchange that will enable a common view and shared agreement amongst stakeholders regarding appropriate and intended use of biosimilars.

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