Challenges in the Antimicrobial Business Model and Potential Incentives to Increase Access and Promote Innovation

Best Brains Exchange Summary Report

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Acronyms

AMR	Antimicrobial resistance
AMU	Antimicrobial use
BBE	Best Brains Exchange
CADTH	Canadian Agency for Drugs and Technologies in Health
CAIC	Canadian Antimicrobial Innovation Coalition
CCA	Council of Canadian Academies
CIHR	Canadian Institutes of Health Research
DISARM	Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms (Act) (US)
EC	European Commission
EU-JAMRAI	EU Joint Action on AMR and Healthcare-Associated Infections
FDA	U.S. Food and Drug Administration
FPT	federal/provincial/territorial
GDP	Gross Domestic Product
GLASS	Global Antimicrobial Resistance Surveillance System (WHO)
GoC	Government of Canada
HTA	Health Technology Assessment
IDPB	Infectious Disease Program Branch
INESSS	Institut national d'excellence en santé et services sociaux
NAPS	National Antimicrobial Prescribing Survey (Australia)
NHS	National Health Service (UK)
NICE	The National Institute for Health and Care Excellence (UK)
NRC	National Research Council Canada
pCPA	pan-Canadian Pharmaceutical Alliance
PHAC	Public Health Agency of Canada
PMPRB	Patented Medicines Price Review Board
PTs	provinces/territories
QIDP	Qualified Infectious Disease Product
R&D	research and development
SAP	Special Access Program
SMEs	small- and medium-sized enterprises
STEDI	spectrum, transmission, enablement, diversity and insurance value
TPP	target product profile
UN	United Nations
WHO	World Health Organization

1. Executive Summary

1.1 Purpose and objectives

This Best Brains Exchange (BBE) was a virtual meeting held on October 12 and 13, 2021. The goal of the BBE was to bring together senior policy makers, subject matter experts and industry stakeholders to discuss the following topics:

- Challenges with the antimicrobial business model in Canada and their impact on antimicrobial resistance (AMR)
- Options for pull incentive models and how they are being implemented by international counterparts
- How pull incentives models might be applied in the Canadian context

1.2 Background

Antimicrobials (antibiotics, antifungals, antivirals and antiparasitics) are essential to the delivery of modern healthcare. Antimicrobial resistance (AMR) is a serious threat to public health in Canada and around the world. AMR occurs when bacteria, viruses, fungi and parasites that cause infections change over time and develop the ability to resist the antimicrobial drugs designed to kill them.

As resistance to antimicrobials increases, our ability to treat even minor infections effectively is at risk. Researching and developing new antimicrobials is important to combat AMR. That said, recent assessments of the global antimicrobial pipeline show that there are not enough drugs being researched and developed to meet the current and anticipated needs to treat resistant infections.

The market failure of antimicrobials is contributing to the fragile pipeline. Market failure happens when the cost of developing a new health product and/or maintaining it on the market exceeds the revenues generated from its sale. Market failure of new antimicrobials is prevalent because they are expensive to develop and generally have low sales. The low sales is because of the need to use them sparingly to preserve their effectiveness and slow the development of AMR.

Several international reports recommend pull incentives as part of a suite of complementary strategies to address the market failure of antimicrobials and strengthen the pipeline. Pull incentives are mechanisms that reward successful innovation of a health product by providing a known return on investment and creating a viable market. Many countries have developed and/or implemented a range of pull incentive models for antimicrobials. The work of Canada's international counterparts can help inform Canada's AMR policies, including information on:

- different kinds of pull incentives that can be used
- how pull incentives were designed and piloted or adopted
- the challenges faced during policy development and implementation

1.3 Overview of presentations

Over the course of the two day meeting, Canadian and international policy makers, subject matter experts and industry stakeholders spoke on the following topics:

- the overarching challenges of AMR globally and where Canada fits
- Canada's pharmaceutical management system
- access to antimicrobials for resistant infections being treated in Canadian hospitals
- the challenges that small- to medium-sized companies developing antimicrobials face in Canada
- the challenges with the antimicrobial business model specific to Canada
- the importance of a viable market, business environment and industry-government relationships for sustained antimicrobial access
- the role of health technology appraisal bodies in the pharmaceutical business model and assessing the value of health products
- pull incentive models being piloted by the UK and Sweden and under development by the US, EU, and WHO, as well as their opportunities and challenges
- considerations for a pull incentive model tailored to Canada's needs and context

1.4 Summary of themes from discussion

Participants generally agreed that Canada should explore a pull incentive model to support antimicrobial access and innovation. During meeting discussions, participants provided the following recommendations and considerations for next steps on the issue:

- Set goals and timelines for the development and implementation of a Canadian antimicrobial pull incentive model.
- Develop and implement a pilot project and evaluate its success to help establish a long-term strategy for sustained antimicrobial access and innovation in Canada.
- Engage all relevant stakeholders across Canada's pharmaceutical management landscape in the design of the pilot project.
- In the early stages of engagement, educate stakeholders on the nature of the problem, clearly articulating why antimicrobials should be considered differently than other classes of drugs and why pull incentives are needed.
- Ideally, Canada's pull incentive model would prioritize new and innovative antimicrobials that address an unmet medical need and/or anticipate the unmet clinical needs for antimicrobials in the next 5, 10 or 15 years.
- Consider the following elements in the design of Canada's pull incentive model:
  - stewardship principles to preserve the effectiveness of high value antimicrobials
  - health equity, including centering Indigenous health needs, considerations for equitable access, and infrastructure supports in rural/remote communities and for marginalized populations
  - the role for diagnostics to support stewardship of antimicrobials and how a pull incentive model could to contribute to their innovation
  - distribution, supply chain and biomanufacturing capacities in Canada to complement pull incentive models and further improve patient access to antimicrobials
- Clarify the roles and responsibilities for the governance and implementation of a pull incentive model within Canada's federated healthcare system.
- Conduct further engagement and work to determine the mechanisms for valuation and reimbursement of antimicrobials for the Canadian-specific model.
- Explore opportunities for federal government leadership to invest in a pilot project, given the cost estimates presented by subject matter experts were relatively modest, depending on the model and scale of the pull incentive.

1.5 Key takeaways and next steps

- AMR is a global problem that knows no borders and Canada has the opportunity now to show leadership by actively supporting international efforts to address the market failure of antimicrobials.
- There is a need to broaden the understanding in Canada, among the public and across stakeholder groups, as to why antimicrobials pose unique economic challenges compared to other drugs which makes the case for why pull incentives are needed.
- The pull incentive design needs to be strong and suit the unique Canadian context and federated healthcare system. Continued engagement and collaboration with subject matter experts, key stakeholders and PT partners will guide the next steps and will help address the unanswered questions that remain related to roles and responsibilities, data availability and sharing, infrastructure, regulations, legal frameworks, stewardship guidelines, and other relevant elements of pull incentive design for antimicrobials in Canada.
- Canada has the opportunity to build off the experience of international counterparts that have already undertaken work to develop and test pull incentive models for antimicrobials. Canada can take advantage of the lessons learned to adopt a pull incentive model that suits its domestic landscape.
- The cost estimates for pull incentive model options presented in the meeting are considerably reasonable for the potential public health value they could provide. Federal government leadership in this area in the near-term could serve as a much-needed foundation for a longer-term pan-Canadian strategy to improve access and support innovation of antimicrobials with pull incentives.
- The momentum on the discussion on pull incentive for antimicrobials in Canada generated from this BBE should be maintained and work on the overall strategy to address AMR in Canada should continue.

2. Purpose and objectives & background

2.1 Purpose and objectives

The Canadian Institutes of Health Research (CIHR) Best Brains Exchanges (BBE) program hosts invitation-only meetings to bring together leading experts with senior policymakers and other stakeholders to discuss high priority, health-related topics of shared interest. The aim of this BBE, held virtually October 12 and 13, 2021, was to convene relevant senior policymakers, subject matter experts and industry stakeholders to achieve the following objectives:

- Gain a shared understanding of the challenges in the antimicrobial business model specific to Canada, including:
  - the current and potential future impact of these challenges as they relate to antimicrobial resistance (AMR), and
  - characterizing the opportunities to address these challenges by supporting innovation and increasing access to antimicrobials for Canadians.
- Examine options for designs of pull incentives and how they are being implemented by international counterparts.
- Discuss how these pull incentive options might be applied in the Canadian context, identify priorities for future consideration and gather perspectives on next steps to advance progress on this issue.

This report provides a summary of the BBE's proceedings. Please see the Annexes for the agenda (Annex A), the list of participants (Annex B), the biographies for the presenters and the chair (Annex C), and a list of supplementary resources (Annex D).

2.2 Background

AMR is among the most serious threats to public health in Canada and around the world. Antimicrobials (antibiotics, antifungals, antivirals and antiparasitics) are essential to the delivery of modern healthcare. As resistance to antimicrobials increases, our ability to effectively treat even minor infections is threatened. The 2019 study by the Canadian Council of Academies (CCA)1 estimated that the deaths of 5,400 Canadians were directly attributable to AMR in 2018, and that each resistant infection costs the healthcare system approximately $18,000. Left unabated, the cumulative impact in Canada through 2050 is projected to be massive — as many as 396,000 deaths, $120 billion in hospital costs, and $388 billion in lost Gross Domestic Product (GDP).

In order to alter this trajectory, coordinated and concerted effort is required to address the complex, multi-faceted issues of AMR. This need was emphasized in the 2019 mandate letter and 2021 supplemental mandate letter for the Minister of Health, which directs the Minister to work with the Ministers of Innovation, Science and Industry, Agriculture and Agri-Food, and Environment and Climate Change to address the serious and growing public health threat of AMRs by developing and implementing actions with partners to preserve the effectiveness of the antimicrobials Canadians rely on every day. The Government of Canada's approach to AMR, along with those of its partners at the Provincial/Territorial (PT) level and of other stakeholders, is outlined in the pan-Canadian Framework on AMR2 and will be further elaborated as plans for pan-Canadian action on AMR and antimicrobial use (AMU) continue to unfold.

The discovery of new antimicrobials to counteract the evolution of resistance to the existing arsenal of antimicrobials is a critical area for action. Yet, recent assessments of the global antimicrobial pipeline have demonstrated that the state of antimicrobial research and development (R&D) is not sufficient, with too few drugs in development to meet the current and anticipated needs to treat resistant infections.3,4 Discovery of new antimicrobials is challenging scientifically and economically.5 As recognition of the challenges of the antimicrobial business model grows, both public and private interests have taken important actions to bolster the antimicrobial pipeline, although to date much of the focus has been upstream, on drug discovery and clinical development. These upstream measures (i.e., push incentives) provide working capital for companies to attract and support R&D efforts but do not address the downstream market conditions after regulatory approval. Mechanisms that motivate private sector engagement by creating a viable market or rewarding innovation (i.e., pull incentives) are needed in order to generate revenues that can sustain small- and medium-sized enterprises (SMEs) and attract reinvestment from large companies with the definitive goal of strengthening the antimicrobial pipeline. The level of investment required to adequately finance a pull incentive is not insignificant but is also an investment worth weighing against the projected impact of AMR on the economy, healthcare system and loss of life.

The COVID-19 pandemic has demonstrated the potential impacts that untreatable or difficult-to- treat infections can have on health and the global economy and provides lessons on the importance of preparedness and the insurance value of accessible and effective treatments. It is essential that the Government of Canada seek to understand the challenges in the Canadian antimicrobial business model and to examine models and approaches that could help address these challenges. Internationally, there have been calls from prominent groups and agencies to examine this issue including the United Nations (UN), the World Health Organization (WHO), and the G20, and international pressure specific to pull incentives is building. Most recently, under the UK's Presidency of the 2021 G7, both the Health and Finance Ministers' Declarations included AMR commitments related to exploring incentive options to bring new antimicrobials to market.

Several international studies and reports substantiate the role of pull incentives as part of a suite of complementary strategies to strengthen the antimicrobial pipeline1,6,7,8, and several countries have made progress in developing and/or implementing a range of pull incentive models (e.g. the UK, Sweden, US, Germany, France, Norway). Canada can learn a great deal from the work of international counterparts, including the differences in these initiatives, how they were designed and selected, and the challenges faced during implementation. As it stands, the challenges with the antimicrobial business model and the potential role for pull incentives has not yet been sufficiently examined in Canada. There is a need to stimulate discussion of the issues, and on the pull incentive options that have the most potential for success in addressing them, within the unique Canadian context. This is an important step in building a foundation for further examination of the issue and future initiatives.

3. Overview of proceedings

3.1 Introduction and opening remarks

3.1.1. Welcome from CIHR

Dr. Tammy Clifford, Vice-President, Research – Health Learning Systems at CIHR welcomed participants and opened with an Indigenous land acknowledgement. She noted that the COVID-19 pandemic has brought to the fore the importance of knowledge mobilization in protecting and improving health. Much of CIHR's work in the last one and a half years has focused on connecting Government of Canada policy makers with researchers and other stakeholders including people with lived experiences, through a variety of mechanisms including the BBE program, where the topic is driven by policy partners.

3.1.2. Welcome from BBE Chair

Dr. Gerry Wright, Lead, Canada's Global Nexus for Pandemics and Biological Threats from McMaster University, welcomed participants as the BBE Chair. He remarked that he had been working in the area of AMR and antibiotics for all of his professional life, and looks forward to providing momentum in this BBE to what is widely regarded as one of the most critical issues in the fight against AMR. He noted that the BBE was an opportunity to hear from experts in Canada and from around the world and encouraged participants to engage in the discussion.. He thanked the partners for putting this BBE together, noting that it is critical for Canada to "get this right" on the international scene. While Canada is a small country, we are seen as leaders across the world and hence it is important for us to step up in this field.

3.1.3. AMR as a global problem and where Canada fits

Dr. Howard Njoo, Deputy Chief Public Health Officer and Chief Medical Advisor, Infectious Disease Program Branch (IDPB) of the Public Health Agency of Canada (PHAC) then provided a brief overview of the Canadian policy context for AMR. He started by outlining that AMR is a global problem, and the WHO identifies AMR as one of the top threats for health care and public health. Many reports, including the report written by CCA, have identified the high direct and indirect costs of AMR.

Dr. Njoo remarked that Canada is small relative to other countries and punches above its weight on the international stages. He underlined that with COVID-19 he has seen the many ways that Canada has been working through challenges in terms of global supply chains for personal protective equipment, changing technologies, and the vaccine rollout, ultimately resulting in Canada being respected even more for expertise in vaccinology and immunology. Canada can leverage this COVID-19 experience and apply it to make progress in the fight against AMR.

Dr. Njoo observed that AMR is a challenging problem that must be addressed using a One Health approach that recognizes the intersections between human and animal health and our shared environment. Such an approach must involve the active engagement and participation of multiple sectors, different levels of government, and a variety of stakeholders. The focal point for a coordinated AMR response at the federal level is PHAC, which can continue to play a convener role as it has with COVID-19. He reinforced PHAC's commitment with the announcement of PHAC's AMR Taskforce which officially launched on October 18, 2021. This Taskforce will enhance the Government of Canada's ability to work across other federal departments, PTs, academics and other stakeholders.

3.1.4. Purpose and objectives of the BBE

Mr. Pierre Sabourin, Assistant Deputy Minister, Health Products and Food Branch at Health Canada, remarked that the market failure surrounding antimicrobials, and antibiotics in particular, presents a major challenge in our ability to combat AMR and that it is an economic issue that cannot be ignored. Mr. Sabourin noted that he is the head of Canada's health regulatory agency, which includes in its responsibilities the regulatory review and approval of antibiotics. He has observed first hand that there are not enough new antibiotics in the pipeline and that it is something that urgently needs to be addressed. Mr. Sabourin stated that compared with other high-income countries, Canada has not had success in attracting and sustaining novel antimicrobials to its market and that Canada needs to improve in this area. He identified that work had been done to engage companies to try to encourage the introduction of new products to Canada but with limited success. He acknowledged the encouraging work being done by international experts and counterparts to draw attention and develop solutions to this problem and concluded his remarks by outlining the purpose and objectives of the meeting (provided in section 1.1 of this report).

3.2 Setting the scene

3.2.1. Challenges with the antimicrobial business model

Dr. John Rex, Chief Medical Officer, F2G Ltd, Operating Partner, Advent Life Sciences and Adjunct Professor of Medicine at McGovern Medical School set the scene by providing an overview of the challenges with the antimicrobial business model including the insurance value of antibiotics, the fragility of the antibiotic pipeline, and what is known about solutions (push and pull incentives).

Dr. Rex outlined that antibiotics are the safety net of modern medicine. Antibiotics have value even when not in use in a given patient, as illustrated by the STEDI acronym: spectrum (replacing broad-spectrum drugs), transmission, enablement, diversity, and insurance. This public health value is why it is critical to think of delinked pull incentives for antibiotics. As an example, if a drug to treat beta coronavirus had been developed and approved in 2019, there would have been no sales in 2019. This would have changed in January 2020, and would have helped to prevent millions of illnesses, but would not have resulted in high sales of product. The value to society, and to the economy, of preventing COVID-19 would have been enormous.

Push funding can be used to stimulate research and generate ideas. Pull funding helps to create a level economic playing field and is paid on approval, not per use. He used the analogy of firefighters — we do not pay firefighters per fire; they are paid to be ready for a fire. Setting the parameters for pull funding can provide direction for the future.

Dr. Rex observed that the reward must match the required risk, as drug development takes time and is costly especially for novel antibiotics. Demonstrating safety is often the point of failure. Usage-based income will not recover costs, and hence delinked pull rewards that are independent of use should be supported. Truly novel antibiotics require years of effort from discovery to usable drug. The average cost until approval is $1.3 billion, as not all companies and products are successful. Then, the cost for the next 10 years to keep the drug available (e.g. post-approval commitments) is $350 million. Hence, the total cost is approximately $1.7 billion.

In terms of models, the AMR Action Fund was created by medium and large pharmaceutical companies. He noted that several pilots are under way and can be used as an inspiration for Canada. The UK “Netflix” model is a model whereby the UK will purchase two new antibiotics at approximately 10m GBP/year whether the drugs are used or not. Over a 10-year period and recognizing that the UK is approximately 3% of the G20, this implies a value of $4 billion from the G20 for each new antibiotic. Dr. Rex argued that if you have an effective pull incentive, which is a “prize”, people will go to work and venture capital will flow, as this levels the playing field and ensures that antibiotics are just as profitable as drugs for other diseases. Investment will occur if the reward is consistent and sufficient. The United States’ Pasteur Act is another example he offered.

Dr. Rex concluded by outlining that R&D takes time, and it takes many years to develop a new drug. Pull awards are needed. The UK's pilot Netflix model and the proposed terms of the PASTEUR Act in the US would both contribute a proportionate share relative to each country's economy to address this global challenge. The Swedish model is small but could be scaled up. Canada has an opportunity to model good behaviour globally by implementing a pull incentive similar to what the US and UK are doing.

3.2.2. Canada's pharmaceutical management system

Lawrence Cheung, Director of the Pharmaceutical Policy Division presented on behalf of Michelle Boudreau, Executive Director, Office of Pharmaceuticals Management Strategies at Health Canada, on how Canada's pharmaceutical management system works.

He started by outlining that Canada's pharmaceutical management system is very complex with many players involved in the process, from a drug's authorization for sale (Health Canada approval takes 180 days for priority review, or 300 days in normal circumstances) to its formulary listing by insurance plans. Following approval, a drug undergoes a Health Technology Assessment (HTA) by Canadian Agency for Drugs and Technologies in Health (CADTH) or Institut national d'excellence en santé et services sociaux (INESSS) to assess its value to the existing healthcare system and provide listing recommendations. The drug then may be considered for listing on private drug plan formularies; however, for each provincial and territorial government's public drug plan, it must go through a separate reimbursement process, including individual PT Expert Advisory Committees that assess the impact of listing a drug on each PT before it is covered under public drug plans. The pan-Canadian Pharmaceutical Alliance (pCPA) then undertakes pricing negotiations with the manufacturer on behalf of each PT, referencing the HTA and formulary listing recommendation by CADTH or INESSS. The Patented Medicine Prices Review Board (PMPRB) also plays a role in setting a ceiling price of patented drugs in an effort to support drugs remaining available and accessible to patients.

In community settings, PTs determine which drugs are reimbursed and under what conditions. The federal government is in charge of reimbursing drug costs for eligible groups (e.g. First Nations and Inuit Peoples, veterans, members of the Canadian Armed Forces, resettled refugees and refugee claimants, RCMP, federal inmates). In hospital settings, PTs fund hospitals' fixed global budgets and generally drugs provided in the hospital are provided at no cost to the patient as per the Canada Health Act. Some hospitals have their own formularies that list drugs they deem eligible for coverage, and hospitals may purchase drugs, equipment, supplies and services on their own, as part of a buying group, or through group purchasing organizations. Hospitals may rely on bulk purchasing organizations to negotiate drug prices. Due to the complex nature of this process, and the federated nature of the health system, altering the pricing of antimicrobials will need close collaboration with PTs as this will have an impact on their health care budgets, and with other health system partners.

Mr. Cheung noted current AMR work underway and opportunities, including:

- Engaging in ongoing work, such as the Pathogen of Interest list that informs sponsors and manufacturers of the pathogens that require innovative antimicrobials most urgently, and hence access to a priority regulatory approval process
- The international collaboration underway at the G7, G20, and bilaterally with peer nations including the UK, US, and Swedish models
- The potential to learn from lessons from the COVID-19 Critical Drug Reserve process and the overall COVID-19 response in terms of federal procurement in a federated health system, including collaboration with PTs and other key stakeholders
- Possibly exploring a continuation of the 2019 work of the CCA to examine market incentives in Canada's unique context

In response to this session, participants noted that a similar rationale could be used for AMR based on the federal procurement role in COVID-19 vaccines and therapeutics. In addition, the Canadian Malaria Network is another example of a federal/provincial/territorial (FPT) program that could inform an AMR program. However, others noted that this would be a challenge given current drug formularies are managed at the PT level, and that many challenges were identified in the COVID-19 process with federal purchase/approval and PT use/deployment. Any policy reforms would need to consider both hospital and community use, including proper stewardship and data gaps are a major challenge in a federated system.

3.3 Canadian perspective on the challenges with the antimicrobial business model

Stakeholders from clinical, industry and academic backgrounds were invited to join an armchair discussion moderated by Dr. Gerry Wright. To start, each panelist was asked to briefly describe the challenges of antimicrobials in Canada from their perspective. The themes that emerged from the ensuing discussion are summarized in section 3 of this report.

Dr. Andrew Morris, Medical Director, Antimicrobial Stewardship Program, Sinai Health System/University Health Network; Professor, Department of Medicine, Faculty of Medicine at the University of Toronto described the challenges with antimicrobial access from the hospital perspective. He outlined that although most of the antimicrobial use is outside of the hospital setting, there is an important need in hospitals for antimicrobials. There are many challenges with inpatient use, which sees little attention in this area, given a rise in patients with drug resistant infections and limited access to drugs and therapeutics especially in comparison to other countries. Although the Special Access Program (SAP) is in place to obtain certain drugs that are not available in Canada, the delay can be problematic in acute or critical care scenarios. The shortage of novel treatments is most acutely felt in hospitals. The access to novel therapies is not as good in Canada compared to other countries like the United States or some European countries. Over the past few decades, the rise in resistance without corresponding rise in availability of effective antimicrobials presents a challenge. He argued that 25 years ago, physicians rarely encountered drug resistance, but this is now a common issue.

Ms. Suzanne McGurn, President and Chief Executive Officer at Canadian Agency for Drugs and Technologies in Health (CADTH) spoke about the raison d'etre of health technology assessment (HTA) bodies, like CADTH, whose role is to provide analysis of available evidence to support healthcare decision making. The process that HTA bodies use includes a comparative assessment of a health technology against existing treatments and considers, among many factors, the potential trade-offs or opportunity costs in light of the finite nature of healthcare resources. The process also importantly includes stakeholder, clinician, patient and industry input and examines ethical, environmental and other concerns. Ms. McGurn then expanded the HTA concept to speak briefly about the role of health technology management. She described health technology management as a process of continual reassessment and management of technologies and noted that it is actually intended to enable access to clinically effective products rather than, as has been suggested in the literature for antimicrobial products, to act as a potential barrier. Ms. McGurn then raised several important questions including: whether Canada's approach to addressing the challenge of the current AMR situation will be national, jurisdictional or institution-based; and whether it will reflect a whole of system commitment including not only regulatory and HTA but also reimbursement models and approaches. She also reinforced the importance of understanding whether products will be procured and paid for by the federal government or jurisdictions as the impact on HTA agencies, or rather their place in the identification and implementation of solutions, will be different depending on the answer. She reinforced the

importance of carefully considering and supporting implementation, highlighting a potential role for CADTH's Implementation Support and Knowledge Mobilization team as well as the potential value of clinical implementation panels.

In CADTH's experience, clinical implementation panels can be an effective and timely way of developing recommendations to assess system readiness, confirming specific clinical criteria to support optimal use, and may support evaluation of different approaches to assessing value of a new product. Finally, but importantly, Ms. McGurn spoke about the importance of engaging decision-makers. CADTH has played a key convenor role, particularly in the pharmaceutical ecosystem, working with provinces, territories and the federal government. Developing trusting relationships amongst stakeholders is key, and we can do more together than we can apart. She concluded by saying that she hoped HTA can be seen as part of the solution for AMR and not, as it has been portrayed, as a barrier.

Ms. Pamela Fralick, President of Innovative Medicines Canada (IMC) highlighted AMR is a global problem and mentioned the work that members of the G7, G20, and WHO have been doing to address this threat. However, Ms. Fralick noted that we need more and better antimicrobials, and COVID-19 has exacerbated the issue. Canada lags behind other countries in the area of incentives to address the challenge of antimicrobials. She outlined two overarching themes that can help move us forward as we develop solutions: (1) the viable business environment and (2) industry-government relationships. She presented the challenges including:

- Canada's administrative mechanisms like PMPRB pCPA, CADTH, INESSS which need to be optimized to incentivize the introduction of novel antibiotics in Canada to fulfil unmet public health needs
- The lack of appropriate market incentives for business. Fueling a robust pipeline of antibiotics that have a high level of investment and limited use is often a deterrent for companies and governments to provide the resources required for the development of AMR therapeutics. Additionally, these therapeutics must be used judiciously to preserve their effectiveness, making it very difficult for antibiotic innovators to earn the reasonable return on investment necessary to sustain the antibiotic pipeline
- The value proposition of new therapeutics needs to be considered, as it is not a priority to invest in R&D for new antibiotics
- The reimbursement systems often discourage the use of new antibiotics due to cost, even if it is the most appropriate treatment choice. Many antibiotics reserved for 'line of last usage', to preserve clinical options for patients who fail on existing antibiotics, remain in place until another new antibiotic is introduced and this leads to almost insurmountable financial challenges for companies
- Diagnostics are a critical tool in managing AMR; however, they are underfunded and under-attended. The decisions to prescribe antibiotics is rarely based on confirmed diagnosis. Effective and rapid diagnostic tools are needed for guiding optimal use and can limit unnecessary use of antimicrobials by eliminating inappropriate prescriptions for infections which are caused by viruses – for which an antibiotic can do nothing

Addressing these challenges requires dedicated new resources. Internationally, there has been focus on these challenges, with the Davos Declaration in 2016, then the Industry Roadmap for Progress on Combatting AMR in 2016, and the AMR Industry Alliance being launched. More recently, industry launched the AMR Action Fund, with $1 billion committed to create 4 novel antibiotics by the end of the decade. The AMR Action Fund provides temporary sustenance of the fragile pipeline - allowing governments the time to make the necessary economic policy reforms needed to build a sustainable pipeline including the investment into antibiotic R&D, reducing inappropriate use of antibiotics, improving global access, and reducing environmental discharge from manufacturing.

Ms. Fralick offered recommendations for moving forward, including:

- The release of Canada's Pan-Canadian Action Plan on AMR as soon as possible
- A clear global roadmap with annual progress updates, and meaningful action and progress
- Using a whole of multi-government approach
- Valuing antibiotics and rapid diagnostics more accurately and appropriately
- Valuing collaboration including with non-profit partners
- Developing new economic incentives and a unique HTA value assessment and reimbursement plan for antibiotics, with a faster regulatory review, and new funding models
- Consideration for global non-profit partnerships
- Acknowledging the value of rapid diagnostics
- Changing the January 2022 PMPRB approach for a more balanced approach
- Applying an end-to-end life science strategy for Canada, similar to the one for COVID-19

Mr. Ryan Lock, Director, Federal Affairs, Policy and Public Health at GlaxoSmithKline Canada Inc. remarked that there were very few companies left working on new and novel antibiotics to bring more treatment options for patients and clinicians. The AMR Action Fund mentioned is a push incentive, which are critical. But new research dollars alone will not fix global and local issues, including in Canada where currently few antimicrobials reach the market. The pull incentive discussion is timely as market access is a missing piece of the puzzle.

He observed that the current HTA system does not account for the societal or insurance value of the reserved antimicrobials. If there is a new, innovative antibiotic, the new drug will be compared to a drug that has established efficacy on the market, likely a generic that has been on the market for decades. The price comparison for a novel antibiotic which will command a pricing premium will be compared to an older drug that may be only "pennies a dose". There are lessons that can be learned from other jurisdictions on pull incentives (e.g. US, UK) and on HTA (e.g. Germany). However, we have to recognize that the Canadian federated health system is unique, and we need a "made-in Canada" solution. He concluded by stating that Canada has demonstrated through COVID-19 the willingness and ability to be adaptable and agile in terms of treatment and vaccines, and the same frame of mind could be applied to AMR.

Dr. Sameeh Salama, Chief Scientific Officer, Fedora Pharmaceuticals Inc. noted that Fedora Pharmaceuticals is developing a new class of antibiotic that targets gram-negative bacteria, and also have some beta lactamase inhibitors at Phase 2 or 3 clinical trials. He argued that Canada has much to be proud about and described the long history of antibiotic discovery in Canada. One success story was Tazobactam which was discovered in Edmonton by the team he worked with, and is now sold by Pfizer. One of the principal scientists that discovered Tazobactam still works at Fedora.

He observed that a report by the WHO in 2020 found that 86% of biotechnology companies developing antibiotics worldwide are small companies, and 75% have 50 employees or less. Small biotechnology firms bring big value to the discovery of antibiotics. However, the last few years have been difficult, and antibiotic biotechnology companies are an "endangered species".

He highlighted that due to the broken market for antibiotics, the return on investment in antibiotic R&D is simply not there, and this means that companies see little incentive to continue developing new antibiotics. He noted that in past years, biotechnology companies like Fedora either did the early development only and then handed over the new antibiotics to a big pharmaceutical company to continue development and commercialization, or in a few cases, took the new antibiotics to market by themselves. Recently, and in the absence of private investments and lack of interest by big pharma, these small companies are now forced to take the antibiotic through the full development cycle. There is, therefore, an urgent need for push and pull incentives to support companies to continue to innovate, otherwise they will face big challenges bringing their innovative products to market.

These challenges also result in a loss of talent, where antibiotic researchers are going to other disease areas where there is more funding. The longer the gap is in terms of R&D, the more damage will be done and the longer it will take to restore this capacity. Push incentives are equally important to pull incentives, and he expressed that he is hoping this discussion will examine push and pull incentives hand-in-hand.

Dr. Salama remarked that the focus for the target product profile (TPP) is on new classes of antibiotics and new mechanisms of action, not simply 3rd or 4th generation antibiotics. He observed that the WHO Priority Pathogens List has been useful for his company to target their research to design drugs. However, since these novel drugs will only be used in an emergency setting, there will be very little revenue so incentives are needed, or it is not worth it for companies to invest. He closed by highlighting that he is looking forward to seeing the Canadian framework and action plan for AMR, and that as chair of the Canadian AMR Innovation Coalition (CAIC), he looks forward to continuing to work with the Government of Canada on this important topic.

Dr. Lori Burrows, Interim Director, Michael G. DeGroote Institute for Infectious Disease Research; Professor, Biochemistry and Biomedical Sciences at McMaster University explained that there is an access issue to current antibiotics. Getting antibiotics to patients is challenging, whether it is antibiotics that are approved in Canada or those that are not. She noted that pull incentives are important, but not enough. Consideration must also be given to the fact that hospitals must pay for the antimicrobials for their patients, and this should be taken into account in the HTA. Antibiotics are unique medicines, and have to be considered uniquely as a class. She reiterated that companion diagnostics for novel antibiotics are essential.

She provided recommendations from the pull incentive perspective, including: waiving market approval costs, signing off on exclusions to existing HTA processes, guaranteeing manufacturers some revenue, and establishing a separate funding envelope for antimicrobials. Stewardship must also be kept front and centre; she elaborated that this is not a given in Canadian hospitals, especially for smaller hospitals. Dr. Burrows offered that a solution could be to create a body that can oversee the delivery of antimicrobials (including both responding to requests in a timely fashion and the stewardship pieces), modelled on the Canadian Malaria Network or Canadian Blood Services.

3.4 Spotlight presentations

3.4.1. Pull incentive options to increase access and promote innovation

Prof. Kevin Outterson, Professor, Boston University, and Executive Director of CARB-X provided the spotlight presentation on pull incentives to increase access and promote innovation. He outlined that it is important to reward for the societal and preparedness value of antibacterials. The market fails to reward antibacterials correctly, and incentives should not be linked to sales volumes. He reported U.S. Food and Drug Administration (FDA) data that shows that clinical development is slower and riskier and conducted in smaller companies than in the past, with almost double the chance of failure compared to the past. It is largely small and medium sized companies who are filling the antibacterial clinical pipeline, not big pharmaceutical companies.

The access issue for antibiotics is not just for low income countries. In Canada, there are three companies that went through the Canadian process to approval but chose not to commercially launch their product yet, as incremental costs exceed the revenue that they expect. He noted that both push and pull incentives are needed for sustainable and robust antibacterial drug development. Sustainability requires 3 legs of the stool – access, stewardship and innovation; all three are needed and they need to be balanced. Pull incentives will allow the ability to reward highly unique and innovative drugs. It is important to pay for value, and then also address access and stewardship.

Prof. Outterson outlined the reasons that the market is not working in the case of antibiotics. First, it is difficult to reimburse for population-level benefits in a patient-level market (the prevention of spread). Governments should pay for preparedness — antibiotics that are not currently used. It is difficult to ascertain the per-pill economic value of safer, less dangerous bacterial evolution. As well, he reiterated that antibacterials are essential as a safety net for many medical procedures, yet these areas are not paying for antibacterial R&D, but benefit from antibacterials nonetheless.

Prof. Outterson reported in detail on the modelling he has done. He estimates that $3.1 billion (with a range of $2.2 to $4.8 billion) is needed per drug over 10 years, in a fully delinked global subscription model. The global amounts implied in the UK pilot and US PASTEUR Act are in this range. Canada's share is estimated to be about CAN$11 million per drug per year for about a decade, which is potentially very affordable given that only a few innovative drugs are needed. He noted that Canada could follow the Swedish model, which might solve the access problem, but does not contribute to the global R&D for AMR.

Some prior estimates of pull incentives were lower, around $1 billion. However, these estimates are partially delinked market entry awards, not subscriptions. Most assume increased push incentives, and post-approval costs are underestimated. These older estimates also assume much higher sales than may be realistic, given stewardship concerns. The data from this model will be released in the public domain, and the article will be published on November 1, 2021 in Health Affairs.[9]

In conclusion, he summarized that push incentives are a good value, and decreasing these would increase the cost of pull incentives by more than a billion dollars. The costs he provided should be considered as ranges, as more valuable drugs may be worth more, and some may be worth less. International coordination is needed, and Canada could take a remarkable leadership place on the global stage for a relatively affordable amount of money, piloting a few drugs.

Participants noted that the overall price of CAN$11 million for Canada's share is lower than they anticipated and worth it for Canada to avert a public health disaster. One participant cited that understanding stewardship and underlying enablers and constraints (e.g. data, diagnostics, human resources) will be important at the outset.

Participants noted that innovation on its own is irrelevant if the antimicrobial does not address an unmet need. The WHO assessed many antibiotics as not being truly innovative, which may have resulted in lower sales however there is potential for value of products even if they do not meet the innovation bar. A point system may be useful to incentivize pulls for novel products over the next generation, same-mechanism drugs. There is no incentive to take big chances (high risk should equal high reward), as a bad new antibiotic and a spectacular new antibiotic both will have little sales if proper stewardship is in place.

3.4.2. Considerations for applying pull incentive options in the Canadian context

Dr. Aidan Hollis, Professor, Economics at University of Calgary spoke next on the considerations for applying pull incentive options in the Canadian context. He noted that Canada is a small market, representing only 0.3% of the total global revenues for the 10 novel antibiotics launched between 2008 and 2018. Many drugs are not submitted to Health Canada for approval, mostly due to the complexity of the Canadian market. This, in addition to physicians not asking for products even with the SAP due to insurance considerations, creates a negative feedback loop. Hospitals are the main buyers of antibiotics and they have binding budget constraints. Canada shows lower antibiotic use and AMR, thus lower sales, than the United States. Therefore, a risk exists of Canada paying for drugs that will not be used in Canada given this lower AMR incidence. Hence, Canada cannot do this on our own — we have to have a number of countries supporting the development of novel antibiotics.

Fully delinked incentives can sustain development and demand, and ensure stronger stewardship than partially delinked incentives. Dr. Hollis observed that most antibiotics will not be superstars in Canada or anywhere else immediately, but will offer incremental improvements with changing resistance patterns over time. Other considerations include the public perception — so that the new approach also has the appearance of being successful, in addition to actually being successful. It is critical to also find the right balance between overpaying for low values versus not investing enough and hence the reward not being adequately attractive.

Dr. Hollis noted that the UK model is a promising one for Canada. Consideration could be given to having a fixed amount of funding that Canada can divide across drugs, perhaps providing a wider scope and added flexibility. He recommended collective action without too many different mechanisms than what is being done abroad, as this adds administrative burden to innovators. Paying the $11 million per drug per year is recommended, as this is reasonable given the ask is to innovate brand new classes of products to ensure societal benefit/insurance value. (For comparison, the cost for Canada to cover Vertex's Trikafta for cystic fibrosis could be up to $1 billion annually.) Similar to the UK, the highest value drugs should be granted the full amount, $11 million. Any lower-value drugs (graded lower per a scale of value, for example) should receive proportionally less. This way, a fixed budget amount would be divided amongst different drugs according to its graded value. Hence, he concluded that Canada can still provide meaningful compensation to innovators, while getting access to more drugs for the set budget, thereby widening the scope of drugs that can be used to address AMR.

3.5 International perspectives on pull incentive models

Dr. Colm Leonard, Consultant Clinical Adviser, Centre for Health Technology Evaluation, National Institute for Health and Clinical Excellence (NICE) provided an overview of the UK's novel value assessment and reimbursement of antibiotics ('subscription-style') pilot project. He began by illustrating the need to act by comparing the pipeline between immune-oncology agents in phases 1 to 3 (around 10,000) with the number of antibiotics in these phases (less than 100). He highlighted that pull incentives that ensure income at the point of marketing, and push incentives that support R&D, are needed. The UK project is sponsored by NICE and NHS England & NHS Improvement. The aim of the project is to demonstrate the feasibility of innovative models that pay companies for antimicrobials based primarily on a HTA of their public health value to the NHS as opposed to the volumes sold. This is fully delinked reimbursement, providing fixed payments to companies to provide a level of certainty for when drugs come to market.

He identified the modelling challenges, which include:

- Broad marketing authorizations, equivalent to multiple 'standard' NICE technology appraisals if everything is modelled
- Unique and overlapping additional attributes of value (STEDI: spectrum, transmission, enablement, diversity and insurance value).
- Variability of standard care across hospitals
- Uncertain evidence base and difficultly predicting usage and emergence of resistance

He outlined the qualification and selection criteria for the two products that the UK is using to test this approach. Qualification requirements include technical and professional ability, financial and economic standing, grounds for exclusion, and project specific requirements for new and existing antimicrobials. Selection requirements include unmet need (based on WHO priority pathogen list, UK unmet need, performance against key determinants of AMR, and the severity of the clinical setting for the disease area covered by the licensed indications), degree of novelty, surety of supply, antimicrobial stewardship and surveillance, and cost.

The model that is being used will forecast the value of health benefits provided by a new antimicrobial. The value will be estimated by NICE through an adapted HTA with information (health economic modelling and expert elicitation). The model will capture value not just from the direct health gain to patients treated, but additional elements including insurance value, diversity value, transmission value and enablement value. The value forecast will be used to inform commercial negotiations, leading to payments to the company in instalments. He noted that a 'one size fits all' model is unlikely as the model may need to be tailored to suit particular medicines, pathogens and settings including unmet needs and future threats.

The payment model that is being used by the UK is a subscription type, independent of the quantity supplied. The contract value is set based on the value to NHS, with a cap of £10 million annually over 3 years, with an option to extend to 10 years. There are individual purchase prices for hospitals with top ups to meet payments. There are key performance requirements on availability, as well as surveillance and minimum stock holds and other requirements. Another similar style of subscription-style payment are the Pandemic Readiness Contracts for the pandemic flu, with a 10 year length and a 'keep warm' fee (up front) and a 'pandemic' fee.

Dr. Leonard outlined that two antibiotics (ceftazidime with avibactam and cefiderocol) were chosen with high value clinical scenarios that lend themselves to detailed modelling. Published economic evaluations, expert clinical opinion, and extrapolations from high value clinical scenarios will capture the benefits outside of the high value clinical scenarios. The project is nearing the end of stage 3, where HTAs will be completed for the two products. Then, the NICE committee will meet to evaluate these assessments and produce a document that will inform commercial discussions, with the first payments in April 2022.

In terms of incorporating stewardship programs into incentive model design and delivery, Dr. Leonard noted that the NICE committee will take the HTA assessment and comment on plausible range of quality adjusted life years benefit and also give firm stewardship advice on appropriate usage. The company contracts mandate that any marketing must emphasise that products only be used within this stewardship advice framework. Dr. Leonard stated that diagnostic tests are available for both of the products included in the pilot.

He concluded by highlighting elements that would define success of the pilot:

- An agreed HTA valuation framework and complete value assessment of two products
- An agreed payment framework that leads to successful negotiation of payments for the two products, supporting good stewardship
- Other countries testing models that, together, achieve pull incentives for antimicrobials and stimulate companies to increase investment. A global pull incentive is needed.

More details are available on the project website.

Ms. Jenny Hellman, Analyst at the Public Health Agency of Sweden spoke about Sweden's pilot to improve access to existing antibiotics to the Swedish market by keeping or bringing new (existing) antibiotics of special market value. She outlined that Sweden has low resistance rates, good stewardship, a small population (10 million), and hence is a small market for antibiotics. A pilot study started in 2018 of a new alternative proposed reimbursement model uses a partially delinked reimbursement model. The model includes testing contracting processes and legal aspects, and evaluating the effect on availability and cost-benefit.

She noted that the goal is at the end of 2022 to provide the government with recommendations on the model and if it should be extended in Sweden. The model does not focus on incentives for R&D for new development, but this is also important and Sweden is working on this too. The model provides a guaranteed annual minimum revenue at the national level, and in return, availability of the product is guaranteed to be delivered to the hospital within 24 hours. If revenue is lower, the difference is paid at the national level. The healthcare system pays for use. The revenue is determined using a predictable formula. Antibiotics for the pilot study were identified via open tender based on an algorithm from specific criteria (e.g. medical needs, expert opinion, number of clinical infections, number of market authorization holders, ecological profile, role in treatment guidelines, compliance with WHO priority pathogen list, market exclusivity). The guaranteed annual revenue was calculated as the price per package (average price for included products) multiplied by security stock and multiplied by 150% (for assurance of availability within 24 hours). This also helps to compensate for administrative overheads. The goal of the pilot study is to contract for all antibiotics that fulfill the requirements. Contracts were developed for five products, three that are new for the Swedish market.

Ms. Hellman concluded that the pilot is a learning process, with many insights arising from turning theory into practice. It is a complex context, and there are national laws and European Union laws to comply with. There are legal, practical, and organizational aspects, including the Procurement Act and the current structure and laws for drug ordering and delivery. Dialogue with pharmaceutical companies within the procurement and with the regions was helpful. The pilot will be evaluated and monitored over time. She remarked that it is important to share experiences from across countries. Challenges for the future include selection of products, the level of annual revenue, and financing. More pilot studies are needed, and this pilot could be adjusted for application in other countries. The pilot could also be used for different categories of antibiotics. She concluded by highlighting that additional incentives for R&D, as well as mechanisms to secure the fragile supply chain, are critical, along with political commitment.

Prof. Kevin Outterson, Professor, Boston University, Executive Director at CARB-X presented an overview of two proposed US initiatives, neither currently implemented nor piloted.

He outlined that the proposed Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms (DISARM) Act which would enable hospitals to use new antibacterials without financial penalty. He noted that this would drive up sales, as Alan Carr modelled 50% market penetration would result in $3.7 billion in additional US revenues across all relevant drugs over ten years. This raises questions of stewardship, as it is not delinked, and is entirely based on sales.

Prof. Outterson then spoke to the proposed US PASTEUR Act. This would be a subscription, similar to the UK plans, but adapted to the US system**.** If this Act was enacted, Prof. Outterson argued that it would be large enough to move the needle on global innovation. In terms of addressing state versus national issues under the PASTEUR Act, all sales occur under normal conditions in place now, and then at the end of the year, the reconciliation reduces the subscription payment by market purchases by covered federal entities. The company has a guarantee, and they receive a top up to meet normal revenues over the annual subscription value. Technically, all sales occur through normal market channels.

He then outlined the positive features when evaluating pull incentive proposals, including: the focus on high quality, high impact new drugs; delinking revenues from sales volumes; a transparent process so developers know the TPPs and can act accordingly including judging feasibility; and ease of administration without disrupting health systems. The pull incentives must be sufficiently large to incentivize innovation, with each G7 country paying their "fair share".

Looking at delinkage, TPP clarity, and R&D impact, he argued that PASTEUR has clear TPP, is fully delinked, and has the largest plausible ten-year impact on revenues to support R&D for one product. Others, such as Germany's reimbursement reforms, are not delinked. He closed by outlining that pull incentives should focus on high quality and high impact new drugs. Companies should be guided as to governmental priorities with TPPs so they can plan the innovation. Pull incentives need to be large enough yet also administrable. Wealthy countries should each pay their fair share of the R&D bill.

A few clarifying questions were asked in the chat or in the group discussion.

- On whether CARB-X advises developers on what may be in demand in 10 years, Prof. Outterson responded that CARB-X focuses on clinical need in the appropriate time frame (usually 10+ years) but if there were subscriptions like PASTEUR, everyone (companies and investors) would aim for these targets. In essence, subscriptions replace the commercial uncertainty with guaranteed revenues based on social value.

- On if there is a project on the quantity and quality of new antibiotics available under DISARM compared to the PASTEUR scenario, Prof. Outterson outlined that DISARM covers Qualified Infectious Disease Product (QIDP) drugs, which is essentially every antibiotic approved by the FDA. On the other hand, PASTEUR is funded with the expectation that between three and five high-quality drugs per decade would get the subscription.
- On whether the PASTEUR Act is a legally binding contract given at IND, Prof. Outterson advised that it is if and only if the company reaches targets at FDA approval or thereafter. The company retains the science, technical, and regulatory risk.
- On how stewardship was included in CARB-X initiatives, Prof. Outterson noted that CARB-X-funded product developers are contractually obligated to develop a Stewardship and Access Plan for their funded product, outlining what strategies they will employ to ensure responsible stewardship and appropriate access. These stewardship obligations follow the product and these remain in place until the patent expires, noting that additional stewardship can be applied as needed.

Maarten van der Heijden, Project Lead, WHO's SECURE Project spoke on behalf of Dr. Peter Beyer (Team Lead, Antimicrobial Resistance, WHO) provided an update on the SECURE project, which has as its aim to expand access to essential antibiotics to prepare countries in addressing the silent pandemic of drug-resistant bacterial infections. Access to new antibiotics is a challenge given many new antibiotics are only registered in a few countries. Challenges to accessing existing antibiotics include shortages and supply chain interruptions; this is a challenge in Canada as well. SECURE is a project still in development, at the tender phase, with implementation likely to start in a few years. SECURE is being led by the WHO and GARDP, in collaboration with CHAI and UNICEF. SECURE will provide member countries with sustainable access to new and existing antibiotics, establishing a quality assured portfolio that is driven by clinical and public health needs. Key interventions will include generating evidence around antimicrobials including their use in neonates and children, extending registration, enhancing clinical practice and forecasting, and contributing to guidelines for use, training and stewardship efforts. SECURE can align with and complement a country's pull incentives and is intended to have a positive impact on other pull incentives. WHO is engaging stakeholders now, and working on SECURE's business plan that will be out later this year.

On how will SECURE regulate stewardship practices is dependent on the stage of antibiotic stewardship, it was noted that many countries have good programs in place. For countries that express a need for support, SECURE's main aim is to enhance use through a sustainable market introduction including training and marketing that is focused on conservation and including national guidelines. In addition, through a needs-based assessment, SECURE aims to guide countries on the antibiotics actually needed. In particular for Reserve antibiotics, SECURE is considering specialized stewardship programmes and systems to limit use. If reserve antibiotics are used in a limited way, an assessment could be made by a trained focal point on a case-by-case basis. It is dependent also on a country's individual existing systems.

It was noted that it is hard to assess at this point if SECURE will be able to contribute toward R&D and innovation of antimicrobials as it depends on the size of the markets of countries that join SECURE. SECURE aims to open up markets that would probably not access these drugs otherwise and will be dependent on the willingness of the manufacturers to opt in. This issue is a global issue, and the market is broken. Even countries manufacturing antimicrobials can experience shortages. Hence, countries need to work together to find solutions at national and global levels.

Dr. Christine Årdal, Senior Researcher, Norwegian Institute of Public Health then spoke to the European perspective. She noted that the European Commission (EC) uses Joint Actions, like the EU Joint Action on AMR and Healthcare-Associated Infections (EU-JAMRAI) as a tool to leverage cooperation and collaboration among EU/EEA countries. The EC also uses its ongoing competitive platforms to tender out pieces of work. The design of a European pull incentive was put out to tender recently; hence, implementation will likely not start until 2024 or after. The main challenge to antibiotic innovation in the EU is low sales and low prices. In many countries, novel antimicrobials cannot enter the market above the price ceiling of the current comparator when no additional benefit is demonstrated through clinical trials, which is often the case for new antibiotics. Therefore, many countries are not seeing a high value in the current pipeline of antibiotics for public health needs. At the same time, there are frequent shortages of current essential antibiotics. She outlined that most of the countries that EU-JAMRAI interviewed expressed support for new incentives for antibiotics and understand the need for delinked incentives. They found that EU countries would prefer a common multinational incentive, recognizing that implementation may be complex. Countries would also prefer an incentive that can improve access to both old and new antibiotics.

Dr. Årdal presented a proposed pull incentive (recommended by EU-JAMRAI) that would align with other pull incentives, where the EC would implement a pan-European revenue guarantee through a joint tender. The intention of the model is to ensure access to important antibiotics meeting public health needs, including both old and new ones. The model is designed to ensure access with flexible guarantee amounts so that novel antibiotics meeting unmet public health need would be awarded attractive amounts. By design, governments and companies can opt in, and the company must service all countries that opt in. At the end of the specified period, the EC would calculate each governments' amount due, as per expectations, and each country would then pay the company directly. She noted that an important area is matching countries' perceptions of the value of unmet public health need against companies' profitability expectations.

Panelists were asked to comment on what Canada can learn from the development and implementation of pull incentives in their jurisdictions and the following four points were raised:

Public perception: It is important to have clear communication to the public to support the understanding that providing a financial incentive is not about providing funding to large pharmaceutical companies but antibiotics are different than other types of medicines and these types of pull incentives are required to ensure access to an arsenal of treatments to avert a public health crisis.

Unmet medical need and valuing: Innovation on its own is not relevant if the antibiotic does not meet an unmet medical need. It is critical to find the methodology that allows for the pull incentive to send the signal to industry for what clinical indications are needed and will be rewarded for antimicrobial innovation.

Complexity of laws and regulation: There are various laws and regulations (e.g. procurement, trade) that need to be considered in implementing a pull incentive. Involving experts from beyond public health at the planning stage is critical.

Commitment from champions: In the UK, momentum from Lord O'Neill's AMR Review, championing by Dame Sally Davis, and lobbying by industry were key drivers. While countries like Canada may have low AMR rates, guaranteed access is still key. Politicians need to be engaged and committed to addressing this issue.

3.6 Breakout groups and plenary session

To stimulate discussion and exchange of ideas, participants were divided into breakout rooms to discuss the questions below, followed by a plenary discussion which is thematically summarized in section 3 of this report.

- Are there any other challenges with the antimicrobial business model in Canada that have not been raised or that merit further elaboration?
- Are any of the pull incentive models presented in the panel session applicable in Canada? And if yes, how would they need to be adapted?
- Are there any other ideas for pull incentives models that should be considered as options?
- What impact would a pull incentive model have on the antimicrobial business model in Canada?

3.7 Conclusions and reflections

Ms. Bersabel Ephrem, Director General, Infectious Disease Prevention and Control Branch at PHAC thanked everyone for their participation and sharing their expertise, thanked Health Canada for their leadership in this BBE, and thanked CIHR for hosting the session. She remarked that this meeting is an important first step to address the market failure of antimicrobials. In collaboration with partners, she highlighted that more work needs to be done, and work will continue to build on the many great ideas identified. She noted that the outcomes of this meeting will be used to inform the development of a proposal to the Council of Canadian Academies aimed at continuing to advance progress on this issue. She said that she felt encouraged by the discussion and the commitment expressed across the various stakeholder groups to collaborate moving forward. She reiterated that we need to sustain access to antimicrobials to help protect Canadians and the global citizenry in the face of AMR.

Dr. John Patrick Stewart, Director General, Therapeutic Products Directorate at Health Canada provided final words by reiterating thanks to the participants, speakers and the BBE Chair for their time and valuable contributions. He noted that the discussion provided a better understanding of the barriers to marketing of antimicrobials as well as pull incentives that could strengthen Canada's access to new antimicrobials and contribute to reinvigorating the pipeline. He added that a report will be produced from this meeting and shared publicly and invited continued engagement to work together to address the challenges discussed. He concluded the meeting by remarking that there has been tremendous energy in Canada and internationally to raise attention to the market failure of antimicrobials and that he is left hopeful for concrete actions in the future that will improve access and drive innovation of antimicrobials in Canada and across the globe.

4. Summary of themes from discussions

4.1 Key principles for designing pull incentives

There was general agreement by participants that Canada should explore a pull incentive model to support antimicrobial access and innovation. Throughout the discussion, participants raised a number of key principles, considerations and recommendations for designing a pull incentive.

As a starting point, it was suggested that Canada set objectives, timelines, and aspirational goals for its pull incentive model. This vision would help define a clear scope and should aim to anticipate the unmet clinical needs for antimicrobials in the next 5, 10 or 15 years. It was observed that the bar should not be set too high, nor too low but at an appropriate level to attract market entry and drive innovation for antimicrobials that are and will be needed to address AMR in Canada.

Developing a pilot and conducting a thoughtful evaluation its outcomes is an important step to establishing Canada's longer term strategy. The pilot work should be informed through appropriate engagement of all the relevant stakeholders across Canada's pharmaceutical management landscape. Part of this engagement in the early stages should include socializing the nature of the problem and its potential solutions, clearly articulating why antimicrobials need to be considered differently than other classes of drugs.

When considering what antimicrobials to include in the pull incentive model, new and innovative products that meet an unmet medical need should be prioritized. Clearly identifying criteria and defining the TPP early in the process The Pathogens of Interest List from Health Canada was mentioned as a start to inform what target product profiles are important in the Canadian environment and the WHO's Priority Pathogens List, among other sources, should also be consulted. David Shlaes has recently provided some suggestions[10] for what might constitute innovation and hence what could then be eligible for pull incentives.

A number of participants highlighted that stewardship principles should be built into any pull incentive model as there is a need to preserve the effectiveness of the high value antimicrobials. A core design element that supports good stewardship is delinking revenue from sales volume. The France and Germany models were mentioned, which are not delinked but rather allow for higher unit prices based on clinical merit, as elements that can be considered as part of a broader pull incentive strategy. Suggestions were made that

a partially delinked system may be more feasible given Canada's federated system, with federal income guarantees, and year-end reimbursement. This way, federal intervention would not disrupt the PT role in procurement, and PTs would have the ability to adapt their model to pathogen resistance patterns and priorities. The UK model could also be adapted, with the federal level providing the top-up.

In the UK, surveillance and sharing of information of emerging resistant pathogens are key pillars of the future contracts that will be signed by the two companies included in their pilot (once assessment of the two antimicrobial products is complete). In addition, a company's past behaviour and planned future behaviour in the areas of surveillance and stewardship were key to the scoring system when selecting the products to be included in the UK project.

It was noted that many other models for pull incentives are dependent on maximizing revenues based on the volume of antimicrobials sold (e.g. patent extensions, new technology advance payments) which challenges stewardship. Transferable exclusivity vouchers were another model discussed but its drawbacks were also raised. Companies with a drug that has high value or meets a high unmet could sell their voucher to another company for profit and this is not palatable to many citizens. Vouchers could also be used to extend the patent for another drug, but then costs are being transferred to other patients/diseases as there is a delay in generic entry, which can be viewed unethical. Delinking sales volume from revenue protects companies by providing a known return on investment, which in turn, encourages private investment, while also focusing on stewardship.

It was argued that a suite of products, including vaccines, diagnostics and alternative therapies, could be considered for pull incentives to address AMR in Canada, although it was also recognized that these products do not face the same economic challenge as antimicrobials. It was expressed that push incentives, such as the US's CARB-X (in which Canada does not currently participate) are also needed in Canada to complement the pull incentives to enable sustainable innovation of antimicrobials.

4.1.1. FPT Dynamics

The federated context of Canada's healthcare system has implications in the design of any pull incentive model. Participants noted that discussions are needed between FPT stakeholders on data sharing, trust, and fiscal accountability to enable a pull incentive strategy. Not every province or territory has the same healthcare delivery model (i.e., hospital, regional). Payers have a unique perspective and set of considerations that should also be socialized as part of this discussion on pull incentives to complement discussions from the public health perspective. Hence, when looking at incentive models, it is important that early discussions involve the implementers in different provinces and territories (e.g. hospital-based pharmacists, people delivering the programs). It was noted that the EU model may be interesting when considering complexities related to provinces and territories. Sweden also had similar issues of local/regional differences, although uses a different approach than the EU. The experience from Sweden highlights the importance of setting the goals of the initiative and discussing these many considerations early in the process.

4.1.2. Scope

Participants cautioned that care should be taken to ensure that the objectives of the pull incentive are met (improving availability and innovation of antimicrobials) and to avoid conflation with related but separate issues that do not face the same economic constraints (other AMR-related products, distribution, procurement and manufacturing). Decisions will need to be made on if the incentive will target existing drugs that have not yet been brought to market in Canada or novel drugs that are under development, and if the focus will be on hospital based or community-based drugs, recognizing that the largest impact may be achieved in hospitals. Flexibility is also needed to address unforeseen events, while also focusing on products that target the Pathogen of Interest List and other public health priorities.

4.1.3. Distribution, procurement and manufacturing capacity

Participants recommended that consideration be given to distribution oversight, as Canada is a large country with low population density. From an industry perspective, a procurement system for antimicrobials could make sense as then smaller companies would not have to invest in sales representatives across Canada. This type of distribution oversight could entail a single place for the drugs to come in to the country, and the Canadian government would be responsible for distribution. Considerations for supply chain, include expiry dates, local distribution, and speed of access when a need is identified, could also be considered. It was noted that SAP has challenges, and mechanisms need to be considered to remove barriers to access. Creating a separate hospital funding envelopes for critical antibiotics, along with consistent antimicrobial stewardship programs across hospitals and jurisdictions, was a suggestion raised by participants as a way to help with patient access as it removes the barriers the hospitals face with procurement, distribution and resources. There were also questions raised related to security of supply and production that were identified during COVID-19. Biomanufacturing in Canada is not extensive and consideration may be given to subsidize the establishment of facilities with a tied commitment to manufacture and distribute certain drugs. It was noted that Norway is taking this approach of domestic production for older narrow-spectrum antibiotics but the cost is very high.

4.1.4. Indigenous health and other equity/access measures

Participants identified that considering equity throughout the development of incentives, including the needs for access for those in rural and remote areas and reaching the most marginalized populations, was critical. Centering Indigenous health needs and expertise, to ensure equitable access to appropriate drugs at the appropriate time with appropriate infrastructure and support, was also noted. This includes considering the health-related Truth and Reconciliation Commission of Canada Calls to Action 18 to 24.

4.2 Roles and responsibilities

4.2.1. HTA and pricing

There was general agreement that there is a role for HTA in pull incentive strategies for antimicrobials. The challenge is that the current HTA process might not include the information that would be needed to assess the public health value of antimicrobials. Another consideration is that in the Canadian healthcare system and unlike in other countries like the UK, hospitals sit outside of the HTA processes and have their own internal processes for making formulary decisions. Implementing a HTA process for antimicrobials that is consistent across jurisdictions is important. Other options discussed include disconnecting antimicrobials from the regular HTA or adapting that process to a model that was used during COVID-19. It was also noted that the Patented Medicines Regulations can be viewed as a barrier for manufacturers to pursue approval for drugs in Canada and having exceptions for antibiotics within these regulations was recommended as a means to help diminish those barriers.

4.2.2. Governance of pull incentive program

Questions were raised on governance of a pull incentive program including responsibilities between orders of governments for decision-making and financing. Recognizing that Canada is a federated system, and the pilot costs are estimated at amounts not beyond the reasonably possible ($11M/drug/year), some noted that it would be easier to coordinate at a federal level given the relatively low investment for a pilot.

4.2.3. Potential role for Government of Canada

There is an opportunity for PHAC and other federal partners to carry the mandate of setting up the pull incentive mechanism including clearly defining the TPPs and other criteria for product selection, and providing a clearinghouse for approval, which could come with a contract and negotiating a price to satisfy the procurement side. There is an option to impose stewardship requirements/standards and track how products are being used. One challenge identified with the federal lead is the lack of clinical expertise which could be mitigated by consulting relevant experts.

4.3 Complimentary considerations

4.3.1. Parallels with models for other health issues to draw from

From within Canada, inspiration for addressing some of the issues raised, including the federated system, supply chain and procurement, could be gleaned from the models used by Canadian Malaria Network, Canadian Blood Services and lessons learned from the procurement and distribution of COVID-19 vaccines and therapeutics. A comparison was made between the economic challenges for antimicrobials and treatments for rare disorders. It was observed that often rare disorders have a focused lobby because the receiving population is readily identifiable. In addition, the eligible population is unlikely to increase significantly, compared to the AMR population which is projected to steadily increase over time. It was also noted that compared to drugs for rare diseases, new antibiotics tend to be paid for and delivered mainly in hospital while drugs for rare diseases are in many cases delivered in the community. Also, novel antibiotics tend to be prescribed for the treatment of short-term, acute infections while rare disease drugs can extend to be treatments for longer-term or chronic illness. Hospital formularies can make it difficult to justify high prices for novel antibiotics. In the hospital, “broad” antimicrobials are often initiated prior to knowing sensitivity results which also highlights the very important role of the lab and diagnostics to help steward antimicrobials. However, in a rare disease, the patient has been diagnosed with the rare disease before initiating therapy. This adds another layer of complexity to AMR.

4.3.2. Surveillance

It was recognized that there are many gaps in surveillance in Canada to inform the development of an appropriate pull incentive. Surveillance is needed on the incidence of clinically-relevant drug-resistant infections and antimicrobial use. Integrated surveillance is needed for Canada and there is currently variability in surveillance data across provinces and territories. Integrated surveillance at the global level is also needed and the WHO’s Global Antimicrobial Resistance Surveillance System (GLASS) may be one approach to consider. Another model discussed is Australia’s National Antimicrobial Prescribing Survey (NAPS). These improvements of surveillance were raised as important to inform stewardship practices and product selection. The development of a national-level list of reserve antimicrobials was also raised as a possible complimentary measure.

5. Key takeaways and next steps

A number of **key takeaways** from the meeting were identified. There was general agreement from participants that Canada must show global leadership in AMR and that the timing is right to take action with respect to pull incentives to improve access and support innovation of antimicrobials. AMR knows no borders and Canada has a key role to play and should not wait for other countries to do the work to address the market failure of antimicrobials on their own. Participants noted that the costs estimates presented in the meeting representing Canada's share of the global pharmaceutical market are reasonable for what could has the potential to provide benefits with high public health value. Federal government leadership in investing in this area in the near-term could serve as a much needed foundation for a longer-term pan-Canadian strategy. The pull incentive design needs to be strong and suit the unique Canadian context and federated healthcare system. Stakeholders and experts from across sectors and governments should be engaged in the consideration of options and design process. Important elements of the pull incentive design are prioritizing the type of antimicrobials to target with incentives, building in stewardship principles, factoring in health equity and Indigenous health, and considering the role for other AMR-relevant products like diagnostics. Canada has the opportunity to build off the work of international counterparts to develop and test pull incentive models and take advantage of the lessons learned to adopt a pull incentive model that suits its domestic landscape.

In terms of **next steps**, it was agreed upon that the nature of the problem needs to be further socialized across stakeholder groups (including the public, FPT governments, healthcare system and industry partners) to broaden the understanding of why antimicrobials unique economic challenges compared to other drugs and to make the case for why pull incentives are needed. Continued collaboration and consultation with experts, key stakeholders and PT partners will guide next steps and help address the unanswered questions that remain related to roles and responsibilities, data availability and sharing, infrastructure, regulations, legal frameworks, national stewardship guidelines on antimicrobials, and other relevant elements of pull incentive design. There was a general sense that momentum should be maintained on the issue and it also reinforced the importance of the continued work on the overall strategy to address AMR in Canada.

6. ANNEX A: Meeting agenda

Best Brains Exchange (BBE) – Agenda

Challenges in the Antimicrobial Business Model and Potential Incentives to Increase Access and Promote Innovation

Hosted by the Canadian Institutes of Health Research (CIHR) in collaboration with Health Canada (HC) and the Public Health Agency of Canada (PHAC) and in consultation with the National Research Council Canada

October 12-13, 2021 12:30-3:30 PM EDT both days

Day 1 – October 12, 2021	
Time (EDT)	**Agenda Item**
12:30 **12:35**	**Opening Remarks** ▶ Welcome from CIHR – *Dr. Tammy Clifford, Vice-President, Research – Learning Health Systems* ▶ Welcome from the BBE Chair – *Dr. Gerry Wright, Lead, Canada's Global Nexus for Pandemics and Biological Threats, McMaster University*
12:45 **12:50**	**Canada's Stake in antimicrobial resistance (AMR)** ▶ AMR as a global problem and where Canada fits – *Dr. Howard Njoo, Deputy Chief Public Health Officer and Interim Vice-President, Infectious Disease Programs Branch (IDPB), PHAC* ▶ Overview of BBE objectives – *Mr. Pierre Sabourin, Assistant Deputy Minister, Health Products and Food Branch, HC*
13:00 **13:15**	**Scene Setting** ▶ What are the challenges with the antimicrobial business model? – *John Rex, Chief Medical Officer, F2G Ltd.; Editor-in-Chief, AMR.Solutions; Operating Partner, Advent Life Sciences; Adjunct Professor of Medicine, McGovern Medical School, Houston, Texas* ▶ Canadian respondent: How does Canada's pharmaceutical management system work? – *Michelle Boudreau, Executive Director, Office of Pharmaceuticals Management Strategies, HC*
13:25	**Health Break**

Day 1 – October 12, 2021

Time (EDT)	Agenda Item
13:30	**Armchair Discussion - Moderated by Dr. Gerry Wright** ▶ **Defining the Problem: Challenges with the antimicrobial business model in Canada** ▪ Panelists will be given five minutes to elaborate on the challenges from the antimicrobial business model in Canada from their perspectives. Panelists were chosen to represent a range of perspectives, including industry, clinical, buyer and academic views. ▪ Following panelists' initial perspectives, there will be a 30-minute interview-style armchair discussion guided by the questions below, with interventions from participants encouraged. **Panelists** ▶ Dr. Lori Burrows, Interim Director, Michael G. DeGroote Institute for Infectious Disease Research; Professor, Biochemistry and Biomedical Sciences, McMaster University ▶ Ms. Pamela Fralick, President, Innovative Medicines Canada (IMC) ▶ Mr. Ryan Lock, Director, Federal Affairs, Policy and Public Health, GlaxoSmithKline Canada Inc. ▶ Ms. Suzanne McGurn, President and Chief Executive Officer, Canadian Agency for Drugs and Technologies in Health (CADTH) ▶ Dr. Andrew Morris, Medical Director, Antimicrobial Stewardship Program, Sinai Health System/University Health Network; Professor, Department of Medicine, Faculty of Medicine, University of Toronto ▶ Dr. Sameeh Salama, Chief Scientific Officer, Fedora Pharmaceuticals Inc. **Discussion Questions** ▶ From your perspective, what are the challenges in the antimicrobial business model in Canada? ▶ What are the risks if these challenges are not sufficiently addressed (i.e. public health, economic, and/or biomedical innovation risks)?
14:30	**Health Break**
14:40	**Spotlight Presentation** ▶ Pull Incentive Options to Increase Access and Promote Innovation – *Dr. Kevin Outterson, Professor and N. Neal Pike Scholar in Health and Disability Law, Boston University; Executive Director & Principal Investigator, CARB-X*
15:05	▶ Canadian Respondent: Considerations for Applying Pull Incentive Options in the Canadian Context – *Dr. Aidan Hollis, Professor of Economics, University of Calgary; President, Incentives for Global Health*
15:15	**Closing Remarks** ▶ Day 1 Recap and Preview of Day 2 – *Dr. Gerry Wright*
15:30	**Adjournment of Day 1**

Day 2 – October 13, 2021

Time (EDT)	Agenda Item
12:30	**Opening Remarks and Panel Introductions – *Dr. Gerry Wright***
12:35	**Panel Discussion – *Moderated by Dr. Christine Årdal, Senior Researcher, Norwegian Institute of Public Health*** ▶ An International Perspective on Pull Incentive Models ▪ Panelists will be given five to seven minutes to elaborate on the design and/or implementation of pull incentives in their jurisdiction. Panelists were chosen to represent a range of pull incentive models being considered, piloted or implemented in the European Union, Norway, Sweden, United Kingdom, United States and globally. ▪ Following 30 minutes of presentations from panelists there will be a 30 minute moderated discussion, with interventions from participants encouraged. **Panelists** ▶ Dr. Peter Beyer, Unit Head a.i., AMR Global Coordination Department, World Health Organization ▶ Ms. Jenny Hellman, Project Leader, Swedish Pilot Study; Assistant Head of Unit Antibiotics and Infection Control, Public Health Agency of Sweden ▶ Dr. Colm Leonard, Consultant Clinical Adviser, Centre for Health Technology Evaluation, National Institute for Health and Clinical Excellence (NICE) ▶ Dr. Kevin Outterson, Professor and N. Neal Pike Scholar in Health and Disability Law, Boston University; Executive Director & Principal Investigator, CARB-X **Discussion Questions** ▶ What were the most important factors that influenced the ultimate design and/or implementation of the pull incentive in your jurisdiction? ▶ What has been the most unexpected challenge to putting pull incentives in place? Have there been any unexpected benefits?
13:35	**Health Break / Instructions and Transition for Breakout Groups – *Dr. Gerry Wright***

Day 2 – October 13, 2021

Time (EDT)	Agenda Item
13:45	**Concurrent Breakout Groups** **Moderators** ▶ Dr. Charu Kaushic, Scientific Director, CIHR Institute of Infection and Immunity ▶ Dr. John Patrick Stewart, Director General, Therapeutic Products Directorate, HC ▶ Mr. Lawrence Cheung, Director, Office of Pharmaceuticals Management Strategies, HC ▶ Ms. Jacqueline Arthur, A/Executive Director, AMR Policy Coordination Team, IDPB, PHAC **Discussion Questions** ▶ Are there any other challenges with the antimicrobial business model in Canada that have not been raised or that merit further elaboration? ▶ Are any of the pull incentive models presented in the panel session applicable in Canada? And if yes, how would they need to be adapted? ▶ Are there any other ideas for pull incentives models that should be considered as options? ▶ What impact would a pull incentive model have on the antimicrobial business model in Canada?
14:25	**Health Break / Transition to Plenary**
14:30	**Report Back & Discussion** **Moderator: Dr. Gerry Wright**
15:15	**BBE Evaluation**
15:20	**Wrap-up** ▶ **Short summary/reflection – *Dr. Gerry Wright*** ▶ **Closing remarks – *Ms. Bersabel Ephrem, Director General, IDPB, PHAC & Dr. John Patrick Stewart, Director General, Therapeutic Products Directorate, HC***
15:30	**Adjournment of Day 2**

7. ANNEX B: List of attendees

Name	Title	Organization
Chair:		
Gerry Wright	Lead, Canada's Global Nexus for Pandemics and Biological Threats	McMaster University
Welcoming Remarks:		
Tammy Clifford	Vice-President, Research – Learning Health Systems	Canadian Institutes of Health Research
Howard Njoo	Deputy Chief Public Health Officer and Interim Vice-President	Public Health Agency of Canada – Infectious Diseases Programs Branch
Pierre Sabourin	Assistant Deputy Minister	Health Canada – Health Products and Food Branch
Presenters:		
Christine Årdal	Senior Researcher	Norwegian Institute of Public Health
Maarten van der Heijden	Project Lead, SECURE Project	World Health Organization
Michelle Boudreau	Executive Director, Office of Pharmaceuticals Management Strategies	Health Canada – Strategic Policy Branch
Lori Burrows	Professor of Microbiology and Interim Director, Michael G. DeGroote Institute for Infectious Disease Research	McMaster University
Pamela Fralick	President	Innovative Medicines Canada
Jenny Hellman	Project Leader, Swedish Pilot Study; Assistant Head of Unit Antibiotics and Infection Control	Public Health Agency of Sweden
Aidan Hollis	Professor of Economics; President	University of Calgary; Incentives for Global Health

Name	Title	Organization
Colm Leonard	Consultant Clinical Adviser, Centre for Health Technology Evaluation	National Institute for Health and Care Excellence
Ryan Lock	Director, Federal Affairs, Policy and Public Health	GlaxoSmithKline Canada Inc.
Suzanne McGurn	President and Chief Executive Officer	Canadian Agency for Drugs and Technologies in Health
Andrew Morris	Medical Director, Antimicrobial Stewardship Program; Professor, Department of Medicine, Faculty of Medicine,	Sinai Health System /University Health Network; University of Toronto
Kevin Outterson	Professor and N. Neal Pike Scholar in Health and Disability Law; Executive Director & Principal Investigator	Boston University; CARB-X
John Rex	Chief Medical Officer; Editor-in-Chie; Operating Partner; Adjunct Professor of Medicine	F2G Ltd.; AMR.Solutions; Advent Life Sciences; McGovern Medical School, Houston, Texas
Sameeh Salama	Chief Scientific Officer	Fedora Pharmaceuticals Inc.
Breakout Group Moderators:		
Jackie Arthur	Acting Executive Director, AMR Policy Coordination Team	Public Health Agency of Canada – Infectious Diseases Programs Branch
Lawrence Cheung	Director, Office of Pharmaceuticals Management Strategies	Health Canada – Strategic Policy Branch
Charu Kaushic	Scientific Director	CIHR Institute of Infection and Immunity
John Patrick Stewart	Director General, Therapeutic Products Directorate	Health Canada – Health Products and Food Branch
Participants:		
Lama Abi Khaled	Executive Director, Ethics, Legal and Regulatory	Innovative Medicines Canada
Christina Adams	Chief Pharmacy Officer	Canadian Association of Hospital Pharmacists
Enis Baris	Sector Manager for Health, Nutrition and Population, Europe and Central Asia	World Bank
Peter Beyer	Unit Head a.i., AMR Global Coordination Department	World Health Organization
Yad Bhuller	Director, Health Effects Division	Health Canada – Pest Management Regulatory Authority

Name	Title	Organization
Manon Bombardier	Associate Assistant Deputy Minister	Health Canada – Health Products and Food Branch
Eric Brown	Professor of Biochemistry	McMaster University
Wangxue Chen	Team Leader, Human Health Therapeutics	National Research Council Canada
Daniel Chiasson	President and Chief Executive Officer	Canadian Association for Pharmacy Distribution Management (CAPDM)
Siri Chunduri	Policy and Research Analyst	HealthCareCAN
Eric Costen	Assistant Deputy Minister	Innovation, Science and Economic Development Canada – Manufacturing and Life Sciences Branch
Joël Denis	Director General, Strategic Policy Directorate	Public Health Agency of Canada – Strategic Policy Branch
Christina Donaldson	Vice-President, Pharmacy	HealthPro Canada
Bersabel Ephrem	Director General, Centre for Communicable Diseases and Infection Control	Public Health Agency of Canada – Infectious Diseases Programs Branch
Karen Gallant	Deputy Executive Director	CARB-X
Sean Hillier	Professor, School of Health Policy & Management	York University
Nabil Kanji	Senior Pharmacist, Brand Drugs	pan-Canadian Pharmaceutical Alliance
Julian Karaguesian	Special Advisor, International Trade and Finance Branch	Department of Finance Canada
Rhonda Kuo Lee	Executive Advisor to Vice-President, Life Sciences	National Research Council of Canada
Elizabeth Leung	Clinical Pharmacy Specialist Lead – Infectious Disease; Antimicrobial Stewardship Program	St. Michael's Hospital; Unity Health Toronto
Jerome Leis	Medical Director of Infection Prevention & Control; Associate Professor in the Department of Medicine	Sunnybrook Health Sciences Centre; University of Toronto Representing Choosing Wisely Canada
Wendy Levinson	Professor of Medicine, Department of Medicine; Chair	University of Toronto; Choosing Wisely Canada
Heather Logan	Vice-President of Pharmaceutical Reviews	Canadian Agency for Drugs and Technologies in Health
Elena Lungu	Manager, Policy	Patented Medicine Prices Review Board
Sarah Lutes	Provincial Antimicrobial Stewardship Pharmacist	Health Prince Edward Island

Name	Title	Organization
Ian Mackay	Manager, Special Access Programme	Health Canada – Health Products and Food Branch
Nicole Mittman	Chief Scientist and Vice-President of Evidence Standards	Canadian Agency for Drugs and Technologies in Health
Wes Miyai	Manager, Public Health	Merck Canada
Angela Nguyen	Scientific Director	Pharmacy Strategy, Sandoz Representing Canadian Generic Pharmaceutical Association
Madhav Panday	Analyst/Economist, Federal-Provincial Relations and Social Policy Branch	Department of Finance Canada
Danielle Paes	Chief Pharmacist Officer	Canadian Pharmacists Association
Susan Pierce	Manager, Pharmacy Policy Development Division	Indigenous Services Canada
Supriya Sharma	Chief Medical Advisor	Health Canada – Health Products and Food Branch
Don Sheppard	Director, McGill Interdisciplinary Initiative in Infection and Immunity; Chair, Department of Microbiology & Immunology, Professor, Departments of Medicine; Microbiology & Immunology	McGill University
Chelsea Smallwood	Government Relations & Public Policy Director	BD Canada
Evelyn Soo	Director, Bureau of Gastroenterology, Infection and Viral Disease, Therapeutics Products Directorate	Health Canada – Health Products and Food Branch
Roman Szumski	Vice-President, Life Sciences	National Research Council Canada
Observers:		
Edith Brochu	Project Manager, Strategic Initiatives	CIHR Institute of Infection and Immunity
Elizabeth Dyke	Report Writer	External Consultant
Barry Jones	Senior Policy Advisor, Office of Pharmaceuticals Management Strategies	Health Canada – Strategic Policy Branch
Suzanne Loney	Senior Research Associate	Council of Canadian Academies
Selina Manji	Policy Analyst, Office of Pharmaceuticals Management Strategies	Health Canada – Strategic Policy Branch
Anita Melnyk	Project Director	Council of Canadian Academies

Name	Title	Organization
Dani Peters	Consultant to the Canadian Antimicrobial Innovation Coalition	Magnet Strategy Group
Pablo Romero-Barrios	Epidemiologist, Food Directorate	Health Canada – Health Products and Food Branch
Mitchell Rowe	Senior Policy Analyst, Office of Pharmaceuticals Management Strategies	Health Canada – Strategic Policy Branch
Melanie Whiteside	Senior Advisor, Bureau of Gastroenterology, Infection and Viral Diseases, Therapeutic Products Directorate	Health Canada – Health Product and Food Branch
BBE Planning Team:		
Grace Alessi	Acting Analyst, Knowledge Translation Strategies, Science Policy Branch	Canadian Institutes of Health Research
Joseph Cavallari	Project Officer	CIHR Institute of Infection and Immunity
Mary Coughlin	Senior Regulatory Policy Advisor, Bureau of Gastroenterology and Viral Diseases, Therapeutic Products Directorate	Health Canada – Health Product and Food Branch
Kiera Keown	Senior Advisor, Knowledge Translation Strategies, Science Policy Branch	Canadian Institutes of Health Research
Janet Lalonde	Initiatives Officer, Knowledge Translation Strategies, Science Policy Branch	Canadian Institutes of Health Research
Morgan Lay	Senior Policy Advisor	CIHR Institute of Population and Public Health
N'Kem Odita	Policy Analyst, Office of Pharmaceuticals Management Strategies, Strategic Policy Branch	Health Canada – Strategic Policy Branch
Sharon Thomas	Senior Policy Analyst, AMR Policy Coordination Team	Public Health Agency of Canada – Infectious Diseases Programs Branch

8. ANNEX C: Biographies of presenters and chair

Dr. John Rex

**Chief Medical Officer, F2G Ltd. Editor-in-Chief, AMR.Solutions
Operating Partner, Advent Life Sciences, Adjunct Professor of Medicine, McGovern Medical School, Houston, Texas**

Dr. Rex is a physician and drug developer with more than 30 years of development and policy experience focused on antimicrobial agents. He is currently CMO for F2G, Ltd. (an antifungal biotech), is an operating partner with a venture capital group (Advent Life Sciences), is Chair of the Scientific Advisory Board of the $1b AMR Action

Fund, and was (2015-2019) a voting member on the US Presidential Advisory Council on Combating Antibiotic Resistant Bacteria (PACCARB). He also blogs regularly at http://amr.solutions/blog.html.

His experience includes moving compounds from preclinical development through all development phases via academic positions (NIH, Bethesda, MD; McGovern Medical School-Houston) and VP-level roles at a multinational pharmaceutical firm (AstraZeneca). Other past activities include advancing novel regulatory paradigms for antibacterials, publications on novel reimbursement models for antibiotics, co-founding of a public-private partnership (CARB-X), co-founding the New Drugs for Bad Bugs (ND4BB) program of Europe's Innovative Medicines Initiative (IMI), and a 4-year term as Industry Representative on the FDA Anti-Infective Drugs Advisory Committee (AIDAC, 2007–2011).

Dr. Lori Burrows

Interim Director, Michael G. DeGroote Institute for Infectious Disease Research Professor, Biochemistry and Biomedical Sciences, McMaster University

Professor Lori Burrows is a microbiologist, Fellow of the American Academy of Microbiology, and expert on the structure, function, and regulation of type IV pili (T4P), ubiquitous bacterial virulence factors used for adherence, DNA uptake, biofilm formation, and twitching motility. Using the opportunistic pathogen *Pseudomonas aeruginosa* as a model, her group studies its pilin repertoire and glycosylation systems involved in bacteriophage defense; structure-function of the pilus assembly system and its integration into the cell envelope; and the complex regulation underlying T4P function. Her group also studies biofilm formation and antibiotic resistance, with particular interests in stimulation of biofilm development by sub-inhibitory antibiotic concentrations and exploitation of that stimulation phenotype to find new antimicrobials for multidrug-resistant gram-negative bacteria. Burrows' research is funded by the Canadian Institutes of Health Research (CIHR), the Natural Sciences and Engineering Research Council of Canada, the Canadian Glycomics Network, the Ontario Research Fund, and industrial support. She has published over 120 peer reviewed papers, reviews, and book chapters (h-index 52). She is the Interim Director of McMaster University's Michael G. DeGroote Institute for Infectious Diseases Research, on the Advisory Board for the Canadian Institutes of Health Research's Institute for Infection and Immunity, and serves on the Editorial Boards of the Journal of Bacteriology (ASM), the Journal of Biochemistry (ASBMB), and ACS Infectious Diseases.

Ms. Pamela Fralick

President, Innovative Medicines Canada (IMC)

Driven by a life-long commitment to improving Canadians' health and well-being, Pamela works with the country's research-based pharmaceutical companies to ensure that all Canadians have access to the medicines they need, when they need them, and that Canada remains an attractive place to invest in the life sciences. Her unique perspective on the policy issues of the day is informed by her decades of working closely with patients and researchers to find solutions to some of our most pressing healthcare challenges.

Prior to IMC, Pamela was President and CEO of the Canadian Cancer Society, where she led the transformation of the organization's operational and governance structures, helping to strengthen its position as the country's leading cancer-fighting charity.

Her patient-centric perspective is also shaped by past leadership roles at the Canadian Healthcare Association (now HealthCareCAN), the Canadian Physiotherapy Association, the Health Action Lobby (HEAL), the Health Charities Coalition of Canada (HCCC), CAMH (Centre for Addiction and Mental Health) and the Canadian Centre on Substance Abuse.

Mr. Ryan Lock

Director, Federal Affairs, Policy and Public Health, GlaxoSmithKline (GSK) Canada

Ryan W. Lock is Director, Federal Affairs and Public Policy for GSK Canada. Leading a small team within GSK's Government Affairs and Market Access department, Ryan is responsible for developing GSK policy positions on market access and reimbursement issues and implementing evidence -driven national advocacy campaigns. Ryan is also responsible for GSK's publicly-tendered vaccines portfolio, which includes managing relationships with the Public Health Agency of Canada and provincial public health departments.

Previously, Ryan was the Sr. Manager – External Affairs (Ontario).Prior to joining GSK in February 2016, Ryan was a member of the Ontario Public Service for sixteen years,

including over ten years at the senior management level. His varied roles included Director of the Access to Capital and Business Development Branch for the Ministry of Research and Innovation; Director of Strategic Policy for the Ministry of Consumer and Business Services; and Director of the Office for Social Enterprise with the Ministry of Economic Development, Employment and Infrastructure.

Ryan has extensive policy experience, both in industry and in government. In industry, Ryan was active in helping to shape and inform Ontario's Bill 160 health transparency legislation. During his time with the Ontario Government, working closely with industry and other key stakeholders, Ryan led the development of leading-edge policies, programs and marketing initiatives to help reinforce Ontario's position as a Top Five life sciences cluster internationally. This included:

- Launching a $161 million *Life Sciences Commercialization Strategy* that is helping to make Ontario a preferred destination for global clinical trials (e.g. establishment of Clinical Trials Ontario);
- Through the *Biopharmaceutical Investment Program* (BIP), leveraging over $140 million in new investment by the innovative pharmaceutical industry to Ontario, and creating 500 new jobs;
- Partnering with industry, academia and the Province of Quebec to help lay the foundations for the
- *Ontario – Quebec Life Sciences Innovation Corridor*, announced in 2012 at BIO in Washington.
- In 2013, Ryan was also a key architect of Ontario's award-winning $25 million Social Enterprise Strategy, a first-of-its-kind in Canada.

Ryan has a Master's in Public Administration from the University of Western Ontario, and a Bachelor of Arts (Hons.), Political Science and French (minor) from Wilfrid Laurier University in Waterloo, Ontario.

Ms. Suzanne McGurn

President and Chief Executive Officer
Canadian Agency for Drugs and Technologies in Health (CADTH)

Ms. Suzanne McGurn joined CADTH in July 2020 as its President and Chief Executive Officer. She brings to the role a deep understanding of the complex issues surrounding the management of pharmaceuticals, medical devices, and clinical interventions in Canadian health systems.

Prior to joining CADTH, Ms. McGurn's distinguished career spanned clinical practice, patient support, and senior roles in government. Within the Ontario Ministry of Health, she served as the Assistant Deputy Minister of the Drugs and Devices Division and the Executive Officer of the Ontario Public Drug Programs. She also led the implementation of the pan-Canadian Pharmaceutical Alliance and served as its first chair.

Dr. Andrew Morris

Medical Director, Antimicrobial Stewardship Program Sinai Health System/University Health Network Professor, Department of Medicine

Faculty of Medicine, University of Toronto

Dr. Morris is a Professor of Medicine at the University of Toronto and the Medical Director of the Sinai Health System-University Health Network Antimicrobial Stewardship Program. He is currently Chair of the Antimicrobial Stewardship Committee for the Society for Hospital Epidemiology of America (SHEA) and chairs the Antimicrobial Stewardship Working Group for Accreditation Canada. He was appointed to the Canadian Government's Expert Advisory Group on Antimicrobial Resistance (EAGAR) in 2015.

Dr. Morris obtained his medical degree from the University of Toronto, where he subsequently completed specialty training in Internal Medicine and subspecialty training in Infectious Diseases. He went on to complete a Masters of Science degree in Epidemiology from the Harvard School of Public Health, while completing a Canadian Infectious Diseases Society (now AMMI Canada) research fellowship. He often says that his primary job is coaching basketball, which he started doing over 30 years ago.

Dr. Morris has worked closely with regional, provincial, and federal governments and interprovincial organizations to help develop and coordinate antimicrobial stewardship efforts. He is widely sought as a speaker and consultant on antimicrobial stewardship, behaviour change, implementation, and quality improvement. He is an author of over 100 peer-reviewed publications.

Dr. Sameeh Salama

Chief Scientific Officer, Fedora Pharmaceuticals Inc.

Dr. Salama has more than 25 years drug discovery experience across several disciplines including the discovery and development of new antibacterial and antifungal agents. In addition to being the Chief Scientific Officer (CSO) of Fedora Pharmaceuticals Inc. (fedorapharma.com), he is also the CSO of Brass Dome Ventures Ltd. (brassdomeventures.com); an active member of the Multi-sectoral Federal, Provincial and Territorial Task Group on Antimicrobial Resistance for the Government of Canada; GARDP REVIVE Endorsing Expert, Chairman of the Steering Committee of the Canadian Antimicrobial (AMR) Resistance Innovation Coalition (CAIC); Director on the Board of Directors of BioAlberta (bioalberta.com), a biotechnology advocacy group representing the biotechnology sector of the Province of Alberta, Canada; Chairman of the Board of Al Rashid

Education Foundation (alrashideducation.com), a not-for-profit organization promoting post-secondary education of

marginalized communities; and involved in a number of not-for-profit organizations. He also held several C-Level positions in both the drug discovery and contract research sectors.

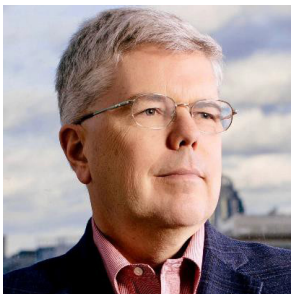
In his scientific capacity, Dr. Salama played a senior role in the discovery and development of several antibiotics including beta-lactmas, beta-lactamase inhibitors, fluoroquinolones, azoles, polyenes, as well as several natural products.

Additionally, Dr. Salama is business development professional with nearly 20-year experience in strategic planning, evaluation of new business and scientific opportunities, partnership establishment and management, contract negotiations, as well as in-licensing and out-licensing of assets. He was actively involved in dozens of licensing and partnership agreements, including the licensing of Fedora's Beta-lactamase inhibitors to F. Hoffman La Roche in a US$750 million license deal.

Dr. Salama received his Ph.D. in Microbiology from the University of Salford, UK, and published over 50 original research articles and presentations at international congresses. He is also an inventor on several original patents in the anti-infective and anti-inflammatory disease areas.

Dr. Kevin Outterson

Professor and N. Neal Pike Scholar in Health and Disability Law, Boston University
Executive Director & Principal Investigator, CARB-X



Professor Outterson teaches health care law at Boston University, where he co-directs the Health Law Program. He serves as the founding Executive Director and Principal Investigator for CARB-X, a $480M international public-private partnership to accelerate global antibacterial innovation. Key partners in CARB-X include the US Government (BARDA & NIAID), the Wellcome Trust, the German Federal Ministry of Education and Research (BMBF), the UK Government (GAMRIF), and the Bill & Melinda Gates Foundation.

Professor Outterson's research work focuses on the law and economics of antimicrobial resistance (available at Google Scholar). He served as a senior author on many key research reports on antibiotic innovation, including Chatham House, ERG, DRIVE-AB, and the Lancet Commission. Professor Outterson was given the 2015 Leadership Award by the Alliance for the Prudent Use of Antibiotics for his research and advocacy work. He has testified before Congress, Parliamentary working groups, WHO, and state legislatures. Since August 2016, he leads CARB-X, the world's largest and most innovative antibiotic accelerator.

Dr. Aidan Hollis

Professor of Economics, University of Calgary President, Incentives for Global Health

Aidan Hollis is Professor of Economics at the University of Calgary, and President of Incentives for Global Health, a US-based NGO focused on the development of the Health Impact Fund proposal. Hollis studied at Cambridge University and the University of Toronto, where he obtained a PhD in economics. His research focuses on innovation and competition in pharmaceutical markets, and he has published over eighty peer-reviewed articles and two books in a range of fields of economics.

He has provided expert reports and testimony in a variety of pharmaceutical-related

cases in Federal, Appeals and Supreme Court cases in Canada, and has advised companies and governments. He served on the WHO Guideline Development Group on Antimicrobial Use in Food Animals and the Expert Advisory Group for the Global AMR R&D Hub. In recent years, he has made invited presentations at (among others) OECD, UNESCO, UN, World Bank, Harvard, Yale, Université Paris Descartes, and LSE.

Dr. Christine Årdal

Senior Researcher, Norwegian Institute of Public Health

Christine Årdal MBA PhD has worked for over 20 years on access to medicines through different sectors, including research institutes, governmental development assistance, pharmacy, national health service and insurance. At the Norwegian Institute of Public Health, her research focuses on the policy aspects of antimicrobial access and innovation. Årdal was a co-lead of the research and innovation work package for the European Union's Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU- JAMRAI), working to detail European strategies to implement mechanisms to increase antibiotic and alternative therapeutic innovation. She was also a co-lead in the DRIVE-AB research project which aimed to transform the way policymakers stimulate innovation,

the sustainable use, and the equitable availability of novel antibiotics to meet unmet public health needs. Previously she was a member of the World Health Organization expert review panel for the overall programme review of the Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property. She led the Norwegian Agency for Development Cooperation's (Norad) efforts within the UN Commission on Life-Saving Commodities for Women and Children.

Dr. Peter Beyer

Unit Head a.i., AMR Global Coordination Department, World Health Organization

Peter Beyer, a trained lawyer, is a Senior Advisor with the World Health Organization (WHO) in Geneva where he leads a team working on global initiatives on antimicrobial resistance. He focuses on developing global instruments to combat antimicrobial resistance and to foster the development of new antimicrobial treatments. Peter was instrumental in setting up the Global Antibiotic R&D Partnership (GARDP), a foundation

that is developing new antibacterial treatments as well as the trilateral collaboration among the World Intellectual Property Organization (WIPO), the World Trade Organization (WTO) and WHO. Previously, Peter Beyer was a Legal Advisor to the Swiss Federal Institute of Intellectual Property in Berne. He negotiated bilateral free trade agreements for the European Free Trade Association (EFTA) and was responsible for the bilateral dialogue between Switzerland and China on intellectual property. Prior to joining the Swiss civil service, Peter Beyer worked with the Ecologic Institute in Berlin on environmental law and policy.

Ms. Jenny Hellman

Project Leader, Swedish Pilot Study
Assistant Head of Unit Antibiotics and Infection Control, Public Health Agency of Sweden

I have a Master of Science of Pharmacy. I work as an analyst and Assistant

Head of Unit Antibiotics and Infection Control at the Public Health Agency of Sweden (PHAS). I have been working at national level within the antibiotic resistance and antibiotic use area since 2009. I started my career at the national STRAMA office, with focuses on rational use of antibiotic

and antibiotic stewardship programs. Since 2014, I have also been the project leader for the PHAS´s work regarding availability of antibiotics at the Swedish market. Now I´m the project leader of the Swedish pilot study of a new reimbursement model to ensure the availability of antibiotics in Sweden.

Dr. Colm Leonard Consultant Clinical Adviser

Centre for Health Technology Evaluation,
National Institute for Health and Clinical Excellence (NICE)

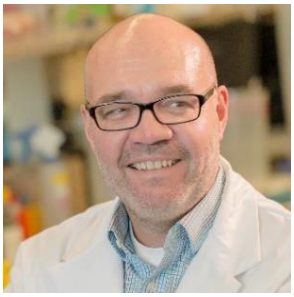
Prof Colm Leonard is a Consultant Thoracic Physician at Manchester University NHS Foundation Trust since October 2000, and is an honorary professor of respiratory medicine at the Manchester Academic Health Sciences Centre. Since 2008 has been on part-time secondment to the Centre for Health Technology Evaluation at NICE as consultant clinical adviser.

Prof Leonard went to Medical School at the University of Dublin, Trinity College, graduating in 1991. In 1994 Prof Leonard commenced his respiratory specialty training & in 1995 was awarded a British Council Research Fellowship grant to carry out work on Asthma Immunology. In 1997 Prof Leonard commenced a three-year fellowship in Pulmonary & Critical Care Medicine at Stanford University Medical Center, California. During this time Prof Leonard subspecialised in interstitial lung disease (ILD) and lung transplantation. Prof Leonard joined the Stanford faculty after his fellowship but relocated to Manchester in October 2000 to take up the post of Consultant Thoracic Physician and medical lead for lung transplantation and ILD.

Prof Leonard has been involved in basic science research, animal model work, clinical trials and his horizon scanning work with NICE is across all specialties. Since 2016 Prof Leonard has been clinical lead for the UK project on novel evaluation & delinked reimbursement of antimicrobials, a joint project between NICE, NHS England & Improvement and Department of Health and Social Care with the aim of incentivising the antimicrobial pipeline.

Dr. Gerry Wright – Chair

Lead, Canada's Global Nexus for Pandemics and Biological Threats, McMaster University



Gerard (Gerry) Wright is the lead of Canada' Global Nexus for Pandemics and Biological Threats at McMaster University. He is a Professor in the Department of Biochemistry and Biomedical Sciences and holds the Michael G. DeGroote Chair in Infection and Anti-Infective Research and a Tier 1 Canada Research Chair in Antibiotic Biochemistry. He was elected as a Fellow of the Royal Society of Canada and a fellow of the American Academy of Microbiology and is the recipient of a Killam Research Fellowship, Murray Award for Career Achievement of the Canadian Society of Microbiologists among other awards. He has trained over 70 graduate students and postdocs and is the author of over 280 manuscripts. His research interests are in the origins and mechanisms of antibiotic resistance and the discovery of new anti-infective strategies, focusing on the application of microbial natural products and synthetic biology towards this goal.

9. ANNEX D: List of recommended resources from presenters

1. Signatories (2016). Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial Resistance. Industry_Declaration_on_Combating_Antimicrobial_Resistance_UPDATED- SIGNATORIES_MAY_2016.pdf (ifpma.org)

2. Årdal, C. Lacotte, Y., & Ploy, M. (2021). Policy Brief: Improving access to essential antibiotics. Joint Action Antimicrobial Resistance and Healthcare-Associated Infections. 1.3.1_Policy_brief_Improving_access_to_essential_antibiotic.pdf (jazmp.si)

3. Colson, A. R., Morton, A., Årdal, C., Chalkidou, K., Davies, S. C., Garrison, L. P., ... & Xiao, Y. (2021). Antimicrobial resistance: is health technology assessment part of the solution or part of the problem?. Value in Health.

4. Hollis, A. (2021). Policy Brief: Increasing Canada's support for the development of new antimicrobials. Antimicrobial Resistance- One Health Consortium.

5. Morel, C. M., Lindahl, O., Harbarth, S., de Kraker, M. E., Edwards, S., & Hollis, A. (2020). Industry incentives and antibiotic resistance: an introduction to the antibiotic susceptibility bonus. The Journal of Antibiotics, 73(7), 421-428. https://doi.org/10.1038/s41429-020-0300-y

6. National Institute for Health and Care Excellence (NICE) website: Models for the evaluation and purchase of antimicrobials | Scientific advice | Life sciences | What we do | About | NICE

7. O'Neill, J. (2016). Tackling drug-resistant infections globally: final report and recommendations. https://apo.org.au/sites/default/files/resource-files/2016-05/apo-nid63983.pdf

8. Outterson, K. (2019). A shot in the arm for new antibiotics. Nature biotechnology, 37(10), 1110-1112.

9. Outterson, K., Orubu, E. S., Rex, J. H., Årdal, C., & Zaman, M. H. (2010). Patient Access in Fourteen High-Income Countries to New Antibacterials Approved by the FDA, EMA, PMDA, or Health Canada, 2010-2020. EMA, PMDA, or Health Canada, 2020. http://dx.doi.org/10.2139/ssrn.3825520

10. Rahman, S., Lindahl, O., Morel, C. M., & Hollis, A. (2021). Market concentration of new antibiotic sales. The Journal of Antibiotics, 74(6), 421-423.

11. Rex, John. (2021). “Astonishing Mismatch”: Market Potential Of AMR Tools Vs. Patient Needs. “Astonishing mismatch”: Market potential of AMR tools vs. patient needs. AMR.Solutions. https://amr.solutions/2021/08/20/astonishing-mismatch-market-potential-of-amr-tools-vs-patient-needs/

12. Rex, J. and Outterson, K. (2020). Pull Incentives For Antibiotics: How Much And Why? — A Literature Survey. AMR.Solutions. https://amr.solutions/2020/04/14/pull-incentives-for-antibiotics-how-much-and-why/

13. Strathdee, S. A., Davies, S. C., & Marcelin, J. R. (2020). Confronting antimicrobial resistance beyond the COVID-19 pandemic and the 2020 US election. The Lancet, 396(10257), 1050-1053. https://doi.org/10.1016/S0140-6736(20)32063-8

14. Theuretzbacher, U., Outterson, K., Engel, A., & Karlén, A. (2020). The global preclinical antibacterial pipeline. Nature Reviews Microbiology, 18(5), 275-285. https://doi.org/10.1038/s41579-019-0288-0

15. World Health Organization. (2021). 2020 antibacterial agents in clinical and preclinical development: an overview and analysis. https://www.who.int/publications/i/item/9789240021303

Endnotes

1. Council of Canadian Academies, 2019. When Antibiotics Fail: The Expert Panel on the Potential Socio-Economic Impacts of Antimicrobial Resistance in Canada, Council of Canadian Academies: Ottawa (ON).

2. Government of Canada, 2017. Tackling Antimicrobial Resistance and Antimicrobial Use: A Pan-Canadian Framework for Action.

3. The PEW Charitable Trust, 2021. Tracking the Global Pipeline of Antibiotics in Development.

4. World Health Organization, 2019. Antibacterial agents in clinical development: an analysis of the antibacterial clinical development pipeline.

5. Wellcome Trust, 2020. Why is it so hard to develop new antibiotics?.

6. O'Neill, 2016. Tackling drug-resistant infections globally: final report and recommendations.

7. Duke-Margolis Center for Health Policy, 2017. Value-based strategies for encouraging development of new antimicrobial drugs.

8. Driving reinvestment in R&D for antibiotics and advocating their responsible use (DRIVE-AB), 2018. Revitalizing the antibiotic pipeline.

9. Outterson, Kevin, 2021. Estimating The Appropriate Size Of Global Pull Incentives For Antibacterial Medicines: Study examines global antibacterial pull incentives. Health Affairs 40.11 (2021): 1758-1765.

10. Shlaes, David, 2021. Europe, Antibacterials, Pull Incentives and Access. Antibiotics- The Perfect Storm blog.