Submission to Advisory Panel on Healthcare Innovation 2014

Research Canada: An Alliance for Health Discovery
December 4, 2014
RESPONSE TO QUESTION 1:

Canada’s health system—and the population it serves—lies at the heart of our health innovation system. It is both the driver of discovery and the receptor—the end-user or customer—for innovative knowledge, services and products whose relative value is ultimately measured in terms of patient benefit. However, notwithstanding its centrality to health innovation, our health system is a somewhat ambiguous partner, in part due to a narrow definition of innovation that rewards disruptive products and services (those offering dramatic benefits vis-à-vis the standard of care) over the process of incremental improvement—continuous innovation—that lies at the heart of a functional, discovery-driven health innovation system.

There has been much discussion in recent years about the imperative of strengthening our health system as a receptor for innovation; as the primary customer for the majority of health innovations, the health system creates the market incentive—or ‘pull’—essential to the translation and commercialization of health innovation. However, not all innovation is perceived as equal: a first-in-class health technology is often—and increasingly—regarded as the only ‘true’ innovation, whereas the value of a ‘follow-on’ or incrementally innovative technology is often challenged. Critics of incrementally innovative health technologies protest that the additional marginal cost is not justified; the private sector should be encouraged to redirect investment toward ‘true innovation’; and follow-on development allows industry to reap market reward without risk. At a time when the health system is coping with severe financial pressures, incremental innovation has become an easy and misguided target of the cost-containment ethos.

This characterization of incremental innovation misunderstands the process of innovation, overlooks significant benefits to patients and to society, and underestimates the enormous value of the associated discovery and development process.

The research funding and policy framework within which our health system operates—from investments in basic science to the decision-making framework that sets standards for pricing, formulary listing, product procurement, health economics, calculation of health, social and cost benefit—must recognize biomedical discovery, commercialization and product development not simply as outcomes, but more importantly as a process of continuous innovation.

RESPONSE TO QUESTION 2

**Statin: A Case Study in Continuous Innovation**

With approximately 3 million Canadians currently on a prescription statin, this class of drugs has become one of the most common interventions for cholesterol management—and provides an illuminating example of the criticality of continuous innovation, including the accumulation of evidence through continuous clinical trials, to industry, the health system and patients.

Decades before the discovery of statins—whose significance was established through years of scientific study of the biological mechanisms implicated in cholesterol synthesis and metabolism—the link between cholesterol and heart disease had led to the hypothesis that patients would greatly benefit from a cholesterol-lowering drug. More than a decade after the discovery of a statin in 1973, Merck brought the first statin, MEVACOR, to market. While it is often assumed that other pharmaceutical players simply piggybacked on Merck’s success, the reality is that the majority of statin development programs began long before the clinical and commercial potential of statins was known. For example, LIPITOR, the most successful drug in history, reached the market a decade later, though development activities began before

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1 It is important to distinguish between generics (exact copies of a medicine) and compounds resulting from continuous innovation, which have a distinctive chemical or biological structure and, as a new and original compound, require full clinical testing.

MEVACOR’s launch. In the years preceding commercial launch of the first statins, confidence in the cholesterol-lowering effect of this class was shaky, clinical trials were inconclusive and safety concerns were rampant. *The lucrative outlook of the statins market was by no means certain when development of many statins was underway. (See Appendix 1, Figure 1)*

The evidence also refutes the notion that Merck’s pioneering product ‘de-risked’ future development. The reality is that many statins failed technically and commercially, succumbing to the unpredictability of drug development. Later entrants gained valuable lessons from product failures, adjusting programs to ensure value-added benefits were delivered by new therapies. Given that development costs for each of these statins were in the hundreds of millions of dollars over more than a decade, risks were significant—and showed developers’ commitment to bringing more competitive products to market.

**Continuous innovation improves performance and addresses unmet needs.** The first drug in a class is often perceived as sufficiently efficacious to achieve desired outcomes. MEVACOR did indeed reduce cholesterol in patients. However, with increased emphasis on aggressive cholesterol lowering, the potency of that pioneering statin became insufficient to treat high-risk patients safely. Through continuous innovation, industry has developed far superior compounds. LIPITOR and CRESTOR, which entered the market 5th and 7th, respectively, reduce cholesterol and LDL-C far more effectively than the first-in-class compound (see Appendix 1 figure 2). A greater number of patients can now safely reach their recommended cholesterol targets, translating into better outcomes. By addressing unmet medical needs, **continuous innovation has redefined the gold standard in the class.**

Follow-on statins are also safer. Early entrants are associated with a greater rate of adverse events, particularly at high doses. Today’s statins are far more potent, allowing physicians to achieve therapeutic objectives at lower doses with fewer side-effects; for example, LIPITOR has an 80% lower rate of fatal rhabdomyolysis (breakdown of muscle fibres). Continuous innovation has reduced adverse events, patients achieve desired outcomes safely, resulting in healthcare savings.

**Continuous innovation advances knowledge.** While the cholesterol hypothesis was postulated in the 1950s, it was statin research that cemented our understanding of cholesterol’s pivotal role, informed new treatment algorithms and expanded the benefits of cholesterol management to new patient populations. *In expanding the reach and maximizing the value of statins, continuous innovation has transformed our understanding of cholesterol and uncovered new approaches to heart health (See Appendix 1, Figure 3).* More recently, the process of continuous innovation has uncovered statins’ potential role in the prevention of Alzheimer’s disease—an unexpected development made possible by the incremental accretion of clinical and population-level data.

**Continuous innovation creates options for patient and doctor.** As medicine transitions toward a focus on the individual patient, the healthcare system can no longer take a ‘one-drug-fits-all’ approach. It must be armed with the ability to tailor treatments based on individual patient characteristics and needs. Indeed, **precision and personalized medicine are partially dependent on continuous innovation**, introducing material modifications to existing medicines in order to treat specific patient segments, provide options for

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1 The National Cholesterol Education Program recommends Low Density Lipoprotein cholesterol levels below 100mg/dl. High-risk patients present with levels > 190mg/dl.
2 Low Density Lipoprotein-Cholesterol, often referred to as ‘bad’ cholesterol
unresponsive or at-risk patient segments and reflect the population diversity, allowing a larger patient cohort to benefit.

**RESPONSE TO QUESTION 3:**
Canada’s current approach to healthcare innovation lacks organization and has resulted in its extremely slow progress. The current approach to how the system supports innovation has many weaknesses. There is no organized or integrated approach and only small siloed efforts. The system is focused almost entirely on containment of healthcare dollars and outcomes rather than recognizing innovation as a continuous process that warrants an environment within which there is permission to experiment and fail. A lot of innovation will take place on the front lines of care every day, and without recognition of its incremental nature and the mechanisms to support it, healthcare will continue not to invest in itself.

Yet despite its numerous limitations, there are small pockets of strengths inherent in its structure. Canada has tremendous strength in clinical trials, and it is fundamental to our innovation system that the country is a leader in this area. The fact that we have a single-payer healthcare system means we can learn more from our clinical trials because the system enables the monitoring of patients across the continuum of care and over long periods of time. Furthermore, Canada has a highly educated patient population that is easily engaged in advancing healthcare through innovation. Moreover, the current system has a few programs that support innovation to a certain degree (see Appendix 2).

What is required to reverse the innovation deficit in healthcare is an organized network of research-based health institutions—an integrated innovation system across the continuum of care anchored by the excellence within our strong academic-based medical centres and committed to a continuous process of knowledge translation and exchange in which all healthcare partners are both drivers of and receptors for innovation. Academic medical centres are nodes of innovation—‘living laboratories’ whose government-funded base infrastructure enables a culture of experimentation, supports scientific inquiry and drives the systematic analysis of healthcare services and patient outcomes. Community-based healthcare organizations and frontline professionals are essential to—and must increasingly become an integral part of—this system of innovation given their proximity to the daily experience of patients as consumers of healthcare.

The efficiency and impact of health innovation in Canada have been hampered by fragmentation across our academic nodes and the community-based networks they serve; integrating this complex constellation of actors is essential to Canadian leadership in health research and innovation.

**RESPONSE TO QUESTION 4**
Policy and financial support of initiatives that recognize the interdependencies among key sectors is a key step for increased investment in R&D and health innovation. Moreover, improvements in regulatory environments and tax policy make Canada an attractive destination for investment in R&D and health innovation.

Innovation is ultimately a social process in which new products and processes emerge from the ongoing interaction of a range of actors. What is essential for effectively upgrading an innovation system is to ‘embed’ the business sector in a broader system of continuous innovation involving greater complexity of interaction and stronger links between the actors.⁹

In other words, improving business R&D in Canada requires integrated solutions that harness and strengthen the interdependencies across government, academia, industry and the not-for-profit/charitable

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sector; recognize that innovations in health technology cannot flourish without innovations in the structure of the healthcare system and the context in which care is delivered; and take a balanced approach to investment in fundamental and applied health research across the discovery to practice continuum.¹⁰

Health systems that are good receptors for innovation invest in it. For example, in the UK, the National Health Service commits 2% of its budget to biomedical and health innovation. In Canada, we are seeing the seeds of such an investment through initiatives like CIHR’s Strategy for Patient Oriented Research (SPOR), which integrates actors across the continuum of research, development and delivery; however, this investment as a fraction of our total healthcare spend is negligible, and the opportunity to engage industry and support economic development remains under-developed.

To make it possible for private sector partners to engage in initiatives like SPOR, we require improvements in the regulatory environment, intellectual property regime and tax policy. The federal government should:

- Improve the quality and timeliness of regulatory approval times through enhanced reliance on established relationships with other leading regulatory jurisdictions; and
- Introduce tax policy incentives to stimulate private sector and charitable investments in health research, innovation and commercialization. Further incentives for charitable giving by increasing the federal charitable tax credit from 29% to 39% could result in an upsurge of giving. Government should also consider removing the tax barrier for charitable gifts of private company shares and real estate.

Attracting pharmaceutical investment to Canada through changes to tax and regulatory policy is an important strategy to enhance business investment; however, it must be complimented by a plan that creates health innovation incentives through a favourable procurement and reimbursement environment. Governments, for example, can adopt financial incentives, such as “proof-of-concept” funding that can stimulate and support the adoption of health innovation. Such incentives are a key ingredient for creating a culture of health innovation in Canada. In this regard, and cognizant of the stringent economic times, the Government of Canada might, nonetheless, consider increased investment in proof-of-concept funding through the launch of a federal matching program, analogous to the funding algorithm adopted by CFI. Given the growing provincial interest in extracting economic value from the investments made in discovery research, the time may be right for a federal-provincial partnership in supporting proof-of-concept, with strategies for adopting successful practices.

Longer-term, government-funded programs (see Appendix 3) support continuous innovation and provide funding to de-risk discoveries emerging from healthcare system labs that will allow unimpeded uptake by private sector investors and/or companies.

A robust health innovation system requires a strong foundation of multi-sectoral partnerships. Partnerships promote collaboration, support shared responsibility and accountability and enable important efficiencies on the road to innovation.

RESPONSE TO QUESTION 5:
Health Technology Assessment (HTA) is widely seen as an area that should be given priority. HTA can inform decision-making by systematically examining the effects of a particular program/drug with respect to its safety, efficacy, effectiveness and cost-effectiveness, as well as its social, economic and ethical implications. However, it must be used as a tool to encourage more piloting within a continuous and incremental innovation environment. An enormous component of the inefficiency in healthcare is that we do a lot of

things we don't need to do. In the absence of strong recommendations / policy such as can be generated through the HTA approach, little changes.

More emphasis on HTA would significantly improve return on investment by identifying those services/drugs/devices that are good value and those that are not. Studies on the use of diagnostics and drugs will likely show that there is significant overuse. (See Appendix 4 for Areas of Relevance)

**Workforce management** has the greatest value-for-money. A huge proportion of healthcare costs are in paying people. The workforce - physicians, nurses, allied health - is not well managed and tends to be poorly distributed. Canada needs a healthcare workforce management plan. There is an overall trend to have some tasks performed by less-trained personnel such as physician assistants doing some work that physicians did in the past. Nurse-led models of care are also more affordable improving access and optimizing health by enabling patients with complex chronic conditions to be effectively and appropriately cared for in the community. Nurse-led primary health-care services are helping manage the ever increasing number of Canadians with chronic conditions and helping them understand how to reduce the risks of acquiring chronic disease and better manage disease.

**Public health**, with a focus on prevention and chronic disease management, is critically important, but to date, has been surprisingly limited in its implementation strategies; however, the potential for long-term impact and cost saving are ample with the right interventions. It ultimately comes down to manipulating context (environment) and consequences so that people make the desirable choices from a health perspective. Becoming more serious about consumer incentives might make a difference e.g. taxes and increasing patient engagement, e.g. exercise. Engaging people, like marketers, who know how to make people want things could be a way towards engendering outcomes with impact, e.g. the social innovation strategy that is being discussed in Alberta might provide some interesting points of intersection with the healthcare system. (See Appendix 4 for other public health approaches).

**Disruptive changes in treatment** will always have the greatest potential for radically changing care models e.g. HIV/Hep C. While once lethal diseases with expensive treatments, HIV and Hep C are now treated effectively and cheaply. In this field some of the areas most susceptible to sudden discoveries include autoimmune disease, brain and mental health and obesity because of a better understanding of the microbiome. (See Appendix 4 for Priorities for Research Supportive of Disruptive Changes)

**Analytics** is an important enabler of research/innovation that will allow better value for health dollars spent. Canada has not invested enough in the physical infrastructure, personnel, data and legislation/policy needed to unlock this value. We perform poorly compared with other countries and we are not well positioned for the future.

**CONCLUSION**
Incremental innovation is an integral part and an inevitable result of an essential healthcare innovation process that leads to new knowledge, better technologies and expanded, more cost-effective options for the health system and patients. The research funding and policy framework within which our health system operates must recognize biomedical discovery, commercialization and product development not simply as outcomes, but more importantly as a process of **continuous innovation**. Recognizing the enormous value of the discovery and development process within healthcare innovation reinforces the imperative of supporting all aspects of the innovation ecosystem, including funding discovery research consistently and sufficiently over time.
Specific statins show variable benefit across populations. In 2005, Health Canada issued a warning for CRESTOR due to a higher rate of rhabdomyolysis in the Asian population, later found to be caused by differences in drug metabolism. Although the genetics have not been uncovered, options in the statin class now allow for treatment in this population.
Appendix 2

- **Council of Academic Hospitals of Ontario’s (CAHO) Adopting Research to Improve Care (ARTIC) program**: This program was launched to accelerate and support the implementation of research evidence into practice across the health care system to drive quality care. It has launched six projects since 2010.

- **MaRS Excellence in Clinical Innovation Technology Evaluation (EXCITE)**: This program is a collaboration between a range of stakeholders in the health system that work together to help innovative health technologies get to market faster and improve patient outcomes.

- **Ontario’s Institute for Clinical Evaluative Sciences (ICES)**: ICES is a not-for-profit research institute encompassing a community of research, data and clinical experts, and a secure and accessible array of Ontario’s health-related data. Its goal is to achieve research excellence resulting in trusted evidence that makes policy better, health care stronger and people healthier.

- **The Centre for Drug Research and Development**: CDRD is Canada’s national, not-for-profit drug development and commercialization centre. Its mandate is to de-risk discoveries stemming from publicly funded research to create viable investment opportunities for the private sector— thereby bridging the commercialization gap between early-stage academic research and industry. CDRD is the only fully-integrated centre of its kind in the country — and one of a handful in the world — with the full expertise and infrastructure to source, evaluate, develop and commercialize both small molecule and biologic innovative technologies in virtually any therapeutic area.

- **Toronto Health Economics and Technology Assessment Collaborative (THETA)**: This multidisciplinary research collaboration is dedicated to providing evidence informed decision support to health technology policy makers and advancing the science of health technology assessment (HTA).

- **Ward of the 21st Century**: W21C began in 2004 with the creation and opening of a state-of-the-art Medical Unit which functions as a "Living Laboratory" at the Foothills Medical Centre (FMC) in Calgary. W21C enables both researchers and industry experts to bring new ideas, prototypes, or health care products for testing in pre-clinical and clinical environments - to enhance patient safety and quality of care both now and in the future.
Appendix 3

CECR, POP and S²B Programs

Designed to bridge the challenging gap between innovation and commercialization, the Centres of Excellence for Commercialization and Research (CECR) program brokers the dynamic partnerships that match clusters of research expertise with the business community to share the knowledge and resources that bring innovations to market faster.

MaRS Innovation was among the first CECRs to be created in 2008, largely based on the founding belief of its members that Toronto is a fertile research land for precisely this kind of translational activity.

The Pan-Provincial Vaccine Enterprise Inc. (PREVENT) is a Centre of Excellence for Commercialization and Research (CERC) as well, established in February, 2008 through the Networks of Centres of Excellence program. It has a mandate to fast-track veterinary and human vaccine development for diseases of major public health concern, and to address the commercialization challenges faced by Canada’s biotechnology industry. As a unique pan-Canadian vaccine commercialization platform, PREVENT accelerates the most promising Canadian vaccine discoveries through preclinical and early clinical evaluation, catalyzing the commercially viable development of products that address significant public health needs. This reduces the risk shouldered by industry through the facilitation of time and labour intensive critical mid-stage vaccine development. PREVENT further supports this development as vaccine candidates are passed into the hands of receptor organizations, either in the private or public sector.

Through Research Canada’s membership we have direct experience with the Centres of Excellence in Commercialization and Research (CECR) program, as well as CIHR’s Proof of Principal (PoP) program. Both of these programs promise to accelerate the process of extracting economic value from knowledge through impressive centres such as MaRs Innovation and PREVENT.

The PoP program is an innovative approach to meeting the challenge of commercializing and mobilizing knowledge from research discoveries; at only $5.7 million in grants for successful applicants; however, it is far from adequate to meet even current needs.

The S²B (Science to Business) program is also an excellent start to provide scientists with the business training to support the commercialization of their research and ongoing support is urgently needed.

Clearly, these programs have inherent sustainability challenges and it is not realistic to expect the new initiatives they fund to achieve financial independence within five years. Even if they do, they are more likely, in such a short period, to have become a Contract Research Organization (CRO), which was not the original intent of the program. Research Canada encourages the Government of Canada to invest in these programs using a longer-term funding approach that reflects the temporal realities of knowledge translation and commercialization and the tremendous opportunity cost we will incur if we take a narrow and short-term view.

Research Canada recommends that the CECR program continue to be extended, selecting those that have achieved commercialization and other high-impact milestones for continued support.
Research Canada recommends a federal-provincial matching grant program that could amplify support for the PoP program.

**Industrial Research Assistance Program (IRAP)**

A large gap exists in the funding of companies as they enter the order-fulfillment cycle. Changes to the IRAP program to reflect features of programs such as New York State’s Strategic Partnership for Industrial Resurgence (SPIR) would be valuable. Encouraging investors through tax credits would be an innovative approach to ensuring SMEs have the capital they need to grow.

In addition, aligning various programs would be important; a great deal of time is currently required to put together applications that are similar in nature, but different enough to require significantly more work than is truly necessary. As well, many timelines are not appropriate for fast-growing businesses. Support in marketing Canadian innovative companies through awards or other forms of publicity can also be helpful.

**SR&ED**

The SR&ED tax credit, and in particular the refundable credit, is the lifeblood for small companies to conduct research investments in Canada. The continued investment that results from the SR&ED tax credit is essential in ensuring that a company can engage in research to extend and expand their product lines, thus ensuring a given company’s sustainability.

The current structure, while encouraging investment for small and medium-sized companies (SMEs), cuts off investment once a company grows past a certain size or when a company loses its Canadian-controlled private company status, resulting in reduced investment at an artificial point. The loss of the tax credit, once a company can no longer benefit from it, has a detrimental impact on the amount of future investment in R&D. The loss of the refundable credit simply due to loss of a “Canadian-controlled” status is particularly troubling as the focus on the incentive should be to stimulate investments in research in Canada irrespective of the ownership status.

In addition to the eligibility of companies, the definition of eligible research for credits is similarly limiting. Research undertaken today goes beyond the definition written over 30 years ago. **Research Canada encourages the government to consider broadening SR&ED eligibility to include a broad continuum of health-related research, in alignment with the Organization for Economic Cooperation and Development (OECD). In addition, permitting milestone payments to biotechnology firms acquiring drug or biologic intellectual property rights would be a powerful support to a crucial emerging sector.**

In light of the increasing focus by regulators on the entire life cycle of drugs and biologics, **the federal government should credit research in areas such as health economics; health-care management; studies that address socio-economic factors; pharmaco-economic studies that build on known health outcomes; and studies to develop new methodologies and models for a broad continuum of health-related research.** Further, given the potential commercial impact of the hundreds of millions of dollars spent on R&D by research hospitals, **the federal government should review how SR&EDs apply to them, in particular examining the rules governing both the “expenditure limit” and who is deemed to be an “excluded corporation”.**

These changes to SR&ED would encourage collaborative, interdisciplinary research and attract new capital for Canada’s healthcare sector.
Refundable portion of the SR&ED tax credit and the growth and commercial success of SMEs

In addition to the limitation of which type of company qualifies for refundable credits on research conducted in Canada, the timing of payment is also a problem. For small and medium-sized enterprises in particular, every month counts. Some banks will finance the cheque once certain conditions are met, but that typically happens at a later point. Another issue that has been identified is the capped value of the refund, as it does not encourage very significant investments and the credit does not apply to patent costs. Patenting of concepts should be funded in lock step with the development of technology. A strong intellectual property position is paramount for engaging further investment and defending a firm’s position in the market. A final issue is that the SR&ED cannot be used in conjunction with other programs such as the Industrial Research Assistance Program (IRAP), making application to these programs less beneficial.

The strengths of the refundable credit are that it appears to be audited fairly, does enforce some structure to research programs and the funding is, ultimately, truly essential to maintaining a long-term technology development plan.
Appendix 4

Areas of Relevance for Health Technology Assessment (HTA)

Also of relevance is a systematic review of clinical effectiveness as this would provide a great opportunity for incorporating patient-reported outcomes (quality of life, for example), which are becoming increasingly important.

Another important focus for decision makers, and one that relies on the outcome of HTA, is the process of de-adoption of therapeutic interventions / clinical practices, also known as "disinvestment" (withdrawing resources from existing health care interventions deemed to be ineffective or harmful). There is increasing evidence of de-adoption of many established clinical practices, although the methods/process for this remains poorly defined, and is a key area for further research. This would also align with projects such as "Choosing Wisely Canada" (modeled after that American Board of Internal Medicine Foundation's Choosing Wisely Initiative).

There should be reform of the billing codes for procedures. Why pay for procedures and drugs that have been proven to be useless – de-list those procedures and drugs. Do it in a timely way when the data become clear - be decisive and clear about it. For example,

- Why do we still pay for doxasozin for hypertension? It is harmful.
- Why do we pay for chiropractic spinal adjustment? It is proven to be no better than conservative management.
- Why do we pay for a whole slew of cosmetic surgical procedures?

HTA is principally valuable economically if it is followed by action - disinvestment or investment - are the key outcomes of any HTA strategy. Perhaps obvious, but it is not clear that when we undertake these kinds of tasks (HTA on a drug or device or process) that they necessarily result in action.

Public Health Approaches

A key goal is to delay illness/preserve health until the last 6-12 months of life and even then have adequate palliative care planning so that we don't spend $M during those last 6-12 months. Thus, public policy could have largest effects on the cost of health care.

- Smoking reduction. Tax it hard. Regulate the hell out of it.
- Salt. Tax it hard. Regulate the hell out of it.
- Obesity - make it hard to become obese. Built environment, transit, sugary foods, junk food taxes, subsidize celery (fruits and vegetables), promote fitness everywhere. Make it socially unacceptable and we will see improvements in health care costs.
- Exercise is the panacea for health. Get everyone moving / running / swimming etc.

Priorities for Research Supportive of Disruptive Changes

We should spend research money on the big medical problems in society. These include:

- mental health
- dementia
- vascular disease - stroke and coronary artery disease
- colon, lung, prostate and breast cancer
- diabetes
- trauma
- influenza
Appendix 5

About Research Canada

Research Canada is a national, broad-based alliance dedicated to increasing investments in health research through collaborative advocacy.

We believe health research is a shared benefit, a shared responsibility and in investment in Canada’s future.

We engage government, academia, industry and non-profit sectors to build support for balanced and long-term health research funding—investments that strengthen Canada’s health innovation system and lead to better health, sustainable health care, new commercialization opportunities and skilled jobs for Canadians.

Our Mission

To improve the health and prosperity of all Canadians by championing Canada’s global leadership in health research.