



A Framework for Doing Knowledge Translation in Infection and Immunity Research

Background document prepared for the Knowledge Translation Workshop
hosted by the CIHR – Institute of Infection and Immunity

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A Framework for Doing Knowledge Translation (KT)

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Executive Summary

The Canadian Institutes of Health Research's (CIHR) Institute of Infection and Immunity (III) is sponsoring a workshop to seek input to a plan through which the Institute can address its knowledge translation (KT) mandate proactively. This report is a background document intended to support workshop deliberations.

The Institute of Infection and Immunity, as a component of CIHR, is mandated to engage in KT which includes any activity that facilitates or increases the use of knowledge to facilitate progress toward health related outcomes of interest. CIHR describes two types of KT – integrated (i.e. occurs through the research process) and end-of-grant (i.e. occurs upon completion of the research project). The ultimate goal of either is to influence some setting within society where it could be useful in effecting change in health related outcomes.

The Knowledge to Action framework used by CIHR depicts the KT process. Categories from this framework were used to identify examples of KT from within the infection and immunity research communities to date. Examples of the following components were identified: integrated KT; knowledge synthesis, knowledge tools and products, problem identification, knowledge adaptation processes, assessment of barriers to KT selection; and tailoring of interventions and knowledge exchange opportunities.

A framework to assist in doing knowledge translation in the infection and immunity communities is proposed. The framework includes: a high level description of knowledge generation and KT in the specific context of infection and immunity research; a description of the outcomes (and related outputs) with which KT in infection and immunity research is concerned; an overview of KT as viewed by CIHR; commercialization as a special case of KT; and finally an eight step process through which researchers can think about and plan for knowledge translation as it relates to their own area of research. The eight steps are:

1. Identify the area of need or gap (or opportunity).
2. Identify the ultimate outcome of interest.
3. Assess the current state of knowledge in the area of interest.
4. Describe the context within which the knowledge will be used.
5. Identify possible mechanisms and opportunities that will enable movement toward the target outcome.
6. Identify intermediate outcomes that will move knowledge system towards the target outcomes.
7. Select and implement strategies to advance the use of research knowledge.
8. Assess progress and update approach as needed.

There are four major entities involved in helping to ensure that infection and immunity research knowledge results in benefit to the health system and Canada. These are the communities of researchers themselves, the III that provides strategic leadership in this area, the KT Portfolio of CIHR which assists with advancing KT across the full spectrum of health research and last, but not least, a wide ranging group of organizations across Canada that use research knowledge to advance their own objectives related to immune mediated and infectious diseases.

I. Introduction

The Canadian Institutes of Health Research (CIHR) is the major federal agency responsible for funding health research in Canada. It aims to excel in the creation of new health knowledge, and to translate that knowledge from the research setting into real world applications¹. It has thirteen virtual Institutes, each one dedicated to a specific area of focus, linking and supporting researchers pursuing common goals. They are intended to coordinate, focus, and integrate health research in areas of importance to the health of Canadians.

On September 24 and 25, 2008, CIHR's Institute of Infection and Immunity (III) is hosting a workshop in Ottawa on knowledge translation (KT). The workshop is intended to provide an opportunity for key stakeholders to provide input and recommendations to a plan through which the Institute can address its KT mandate proactively.

The purpose of this paper is to serve as a background document to help inform discussions during the workshop.

II. CIHR and the Institute of Infection and Immunity: Mandates for KT

Knowledge translation was embedded as a key component of the health research enterprise in Canada when it was specifically included in the legislation that created the Canadian Institutes of Health Research (CIHR). CIHR defines knowledge translation as **a dynamic and iterative process that includes synthesis, dissemination, exchange and ethically sound application of knowledge**. The legislation includes the following objectives that relate to using health research to benefit Canada and Canadians:

- addressing emerging health opportunities, threats and challenges and accelerating the discovery of cures, treatments and improvements to health care, prevention and wellness strategies;
- promoting the dissemination of knowledge and the application of health research to improve the health of Canadians;
- encouraging innovation, facilitating the commercialization of health research in Canada and promoting economic development through health research in Canada².

¹ <http://www.cihr-irsc.gc.ca/e/7263.html>

² Government of Canada Bill c-13. Accessed June 17, 2008
<http://www2.parl.gc.ca/HousePublications/Publication.aspx?pub=bill&doc=C-13&parl=36&ses=2&File=28&Language=E>

The **mandate** of the Institute of Infection and Immunity (III) is to support research to enhance immune-mediated health and to reduce the burden of infectious disease, immune-mediated disease and allergy through prevention strategies, screening, diagnosis, treatment, support systems and palliation. In the most recent Strategic Plan³ the III identified five areas in which to focus⁴ as well as five goals, one of which is to '**encourage and facilitate knowledge translation in all fields and sectors related to the Institute mandate**'. The III identified three objectives through which to address that goal:

- Build capacity and provide support to assist in translating and communicating new infection and immunity research knowledge
- Support KT initiatives for improved human health outcomes
- Increase opportunities to enhance the international recognition of Canadian infection and immunity research

It is clear that knowledge translation is a central component of the Institute's mandate and that the focus is across the health spectrum from prevention to palliation. A brief description of KT activities to date in infection and immunity are included in Appendix 1.

III. A Framework for KT in Infection and Immunity

A. *What is a Framework? How Will It Be Used?*

A framework presents a structure within which activities, projects or initiatives can be planned, organized and developed. It describes a set of variables and relationships that are helpful in explaining the phenomena under scrutiny⁵. It will help to ensure that research generated within the infection and immunity research communities in Canada leads to benefit for society. A framework will help:

- researchers and III have a common language with which to talk about KT
- to communicate about KT to those groups who use research knowledge generated within the infection and immunity communities to accomplish their own objectives
- III plan strategies to identify and address future priorities and to facilitate and support KT in infection and immunity research
- III position itself to move forward to address the KT imperative within CIHR

³ <http://www.cihr-irsc.gc.ca/e/35161.html#4> Accessed June 16, 2008

⁴ These five areas are: Emerging infections and microbial resistance, HIV/Aids, pandemic flu preparedness, immunotherapy and vaccines of the 21st century.

⁵ Kitson and Bisby (2008) Speeding up the Spread. Putting KT research into practice and developing an integrated KT collaborative research agenda. AHFMR Working document. Available at www.ahfmr.ab.ca.

- to identify mechanisms through which III can facilitate KT within the community of researchers (including funding mechanisms, influencing other entities inside and outside CIHR)
- III to assess KT outcomes and impacts in future
- researchers to assess their KT activities and outputs

A framework is particularly important given the fact that most of the researchers that align with III are either basic biomedical or clinical researchers, yet much of the attention and focus when KT is discussed is on those activities more aligned with Themes 3 and 4 (health services and policy, population and public health) within the CIHR descriptions.

The framework proposed here includes: a high level description of knowledge generation and KT in the specific context of infection and immunity research; a description of the outcomes (and related outputs) with which KT in infection and immunity research is concerned; an overview of KT as viewed by CIHR and commercialization as a special case of KT; and finally an eight step process through which researchers can think about and plan for knowledge translation as it relates to their own area of research.

B. Knowledge Generation and Translation in Infection and Immunity

Knowledge translation most often implies research knowledge generated in one setting being used in a different setting, or context. The concept of knowledge movement, adaptation and use is central. It is important to take as a starting point the specific contexts within which research is done, and also to consider those settings where the knowledge will be used both in the immediate future and in the longer term.

The infection and immunity research communities do research across the entire spectrum, or knowledge trajectory, of health research – biomedical, clinical, health services and policy, and population and public health. This trajectory is further delineated in Figure 1 below and put together with key concepts relevant to knowledge translation.

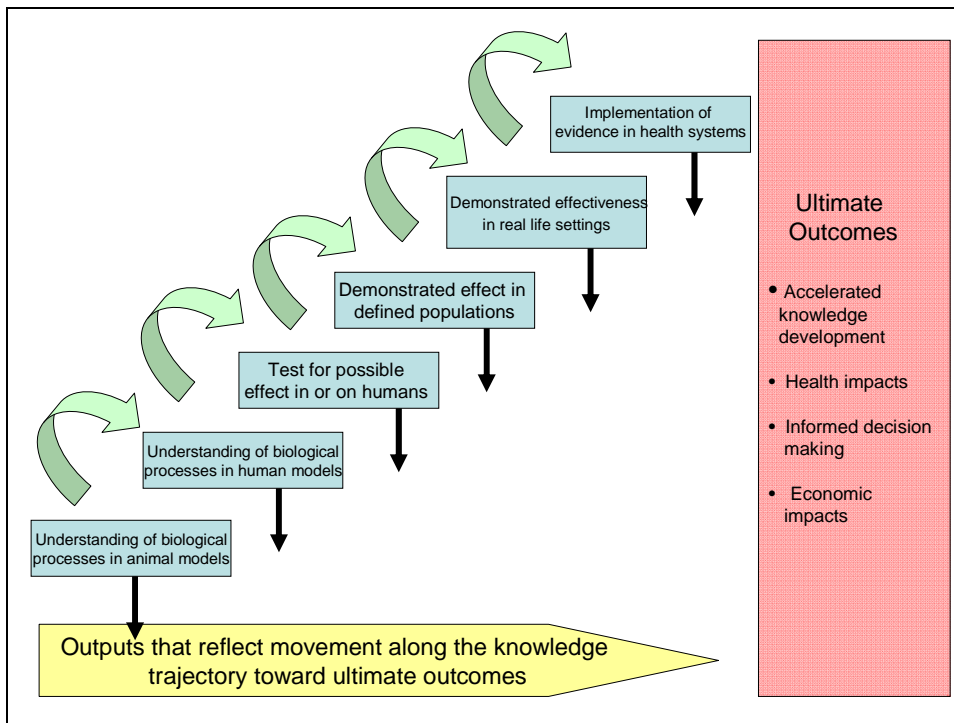
In this figure, research is described as increasing our understanding in six different stages comprising the knowledge trajectory:

- biological processes in animal models
- biological⁶ processes in human models

⁶ For simplicity purposes, language is limited to biological dimensions. This is not meant to be restrictive. Understanding of psychological and social processes is also important. Also there is basic or fundamental research needed to enable the demonstration of effectiveness in real life settings. All along the spectrum of knowledge generation there are types of knowledge that are

- effects in or on humans
- effects in defined populations
- effectiveness of approaches or interventions in real life settings
- use of research evidence in health systems

Figure 1: Knowledge trajectory, outputs and outcomes



Knowledge translation is ultimately about affecting health outcomes. Figure 1 depicts examples of types of knowledge, identifies the ultimate outcomes of interest and presents graphically a way of thinking about intermediate (KT related) outputs that can signal progress towards impact on ultimate outcomes.

Much of the research done within the infection and immunity research communities in Canada falls toward the bottom of the knowledge trajectory in Figure 1; that is, it relates to understanding of biological processes (in animal and humans). Wolf⁷, in considering the spectrum of translational research activities (which by his definition is more-or-less equivalent to KT activities) recognizes two types. The first, called T1, refers to 'bench-to-bedside' research that harnesses

helpful in a general way but not necessarily instrumental in the short term with respect to influencing health outcomes.

⁷ Steven H. Wolf The meaning of translational research and why it matters. JAMA 299(2):211-213,2008

knowledge from basic scientists to produce new drugs, devices and treatment options for patients. The second, T2, begins where T1 ends and refers to translating research to practice or ensuring that new treatments, interventions and relevant research knowledge actually reach the populations for which they are intended, and are implemented correctly. By this definition, much of the work done in Themes 1 and 2 (biomedical and clinical) are T1 KT and, in Themes 3 and 4 (health services and policy; and population and public health) are T2 KT. It is unlikely that much of T1 research will *directly* impact ultimate outcomes. However, biomedical and clinical research can logically be linked to progress towards ultimate outcomes through a series of intermediate steps or outputs.

The downward facing arrows in the diagram represent a wide variety of KT outputs that can be observed. These outputs can be health related, decision support related, or economic in nature. Examples of KT outputs include such things as⁸:

- **a new therapeutic target** of potential interest to pharmaceutical companies; (Research demonstrated a new cell-signaling pathway relevant to allergic inflammation in a pre-clinical model⁹. Hence this is a new therapeutic target of potential interest to pharmaceutical companies.)
- **a patent** being sought for a viral screening kit designed for use in primary care; (The research enabling this could be a combination of research done first in animal or human models, then tested in humans to ensure efficacy in actual subjects. Once the method has been proven, commercializing it will make it available for use [and ultimate health impact] in a much wider range of subjects).
- **presentations** made to infection control practitioners re control of *C. difficile*. (Research done in several hospitals [defined populations] showed that hand-washing with soap and water reduced infection with *C. difficile*. Presentations to many hospitals and infection control committees are examples of a KT related activity arising from this research. The ultimate outcome of interest is a health outcome i.e. fewer infections.)
- **a website** to serve as a gateway to evidence about Hepatitis C for policy makers and practitioners in Atlantic Canada
- **a report** 'Stand on Guard for Thee' (Ethical issues arising from the SARS outbreak were presented in a way appropriate for policy makers and translated into several languages).
- **a tool for tracking bacteria** in water. (This tool is being used by water regulators to help create better land management practices.)

These outputs (or intermediate outcomes) reflect activity at various stages of the knowledge trajectory as shown in Figure 1. These outputs, when taken up or

⁸ To the extent possible, these examples are actual examples from infection and immunity research

⁹ CIHR National Training Program (U. Manitoba) Pilot Project Grant. (Marshall et al)

used by an individual or organization or company that will take application of the knowledge to the next stage, all exemplify KT activities and outputs.

It would be expected that economic outcomes (particularly those of a commercial nature) would be more prevalent at the earlier stages of the knowledge trajectory while population health outcomes would be more probable when evidence is introduced into whole systems.

C. What is KT Designed to Affect? Outcomes of Interest

Knowledge translation is designed ultimately to affect health, health system and economic outcomes in Canada. However, it is difficult to attribute ultimate outcomes to any specific KT activities or interventions, so it is helpful to have some 'intermediate outcomes' or outputs that can be directly attributable to KT efforts and can logically be expected to contribute to changed outcomes. Four categories of ultimate outcomes are identified in the Health Research Impact Measurement Framework under development by CIHR (See Table 1 below). These four categories are: the advancement of knowledge, informed decision making, health impacts and economic impacts. These ultimate outcomes are included in the vertical column on the right of Figure 1 (Knowledge Trajectory Output and Outcomes) on page 7. With respect to knowledge translation and infection and immunity research, it is likely that the indicators will have more or less relevance. For example, there is evidence to date that infection and immunity researchers are able to influence policy (an indicator of informed decision making) and it is very clear that research agendas have been influenced by the pressures of public health challenges (another indicator of informed decision making). Given the primary focus of infection and immunity researchers, it is perhaps less likely that they will be directly able to influence health (e.g. potential years of life lost; health related quality of life). Given the predominance of biomedical and clinical research, it is quite feasible there will be patents, licensing arrangements or other evidence of commercialization. Commercialization is an important variant of KT and its outputs - drugs, devices, and other products - are one important aspect of economic outcomes in the CIHR Health Research Impact Framework.

In the CIHR Health Research Impact Measurement Framework, the developers acknowledge that there are different levels of effects. This acknowledges that some indicators will be under direct control of those doing or directing research. Others will be of a higher order or more distal and, for those, it will be impossible to attribute change directly and solely to groups of researchers. The fact that there are different levels of effects is important to remember as the infection and immunity research communities identify dimensions that will reflect their influence on ultimate outcomes.

Table 1: Preliminary Indicators of Health Research Impact¹⁰

Advancing Knowledge
<ol style="list-style-type: none"> 1. Number of discoveries/breakthroughs resulting from CIHR-supported research 2. Number of Canadian health research publications 3. Number of publications resulting from CIHR-supported research 4. Percentage of Canada Research Chair (CRC) holders attracted to or retained in Canada 5. Number and type of Ph.D. graduates in Canada by year 6. Percentage of Ph.D. graduates in Canada planning post-doctoral work in health
Informing Decision-Making
<ol style="list-style-type: none"> 1. Public policies informed by CIHR and CIHR-funded research 2. Clinical practice informed by CIHR-funded research 3. Health system management decisions informed by CIHR-funded research 4. Research, policy and/or practice agendas influenced by funded research and/or CIHR institutes 5. Impact of Canadian health research publications 6. Impact of publications resulting from CIHR-supported research
Health Impacts
<ol style="list-style-type: none"> 1. Research study participants' health status affected by participating in CIHR-funded research 2. Population health status influenced by CIHR-funded research 3. Potential years of life lost (PYLL) for target disease categories (e.g., cancer, circulatory disease) influenced by CIHR-funded research 4. Health-related quality of life influenced by CIHR-funded research
Economic Impacts
<ol style="list-style-type: none"> 1. Number and nature of patents, spin-off companies and IP licenses influenced by CIHR-funded research 2. Income from IP commercialization 3. Commercial use of research funded by CIHR's commercialization programs 4. Cost savings influenced by CIHR-funded research 5. Human capital gains, including productivity influenced by CIHR-funded research

The mandate of III implies that the health outcomes of relevance to it are reduced burden of infectious and immune-mediated disease and allergy across the entire disease spectrum from prevention through to palliation.

An example of research and KT related activities and how they contribute to improved health outcomes that has occurred largely within the auspices of III (safe food and water) is described in Appendix 2. Activities occurring over several years in a progressive fashion for the purposes of helping Canada to achieve safe food and water are described from the point of view of identifying intermediate outcomes or outputs that can be linked indirectly to an ultimate outcome of safe food and water.

¹⁰ CIHR (Undated) A framework to measure the impact of health research (Internal document)

Work is currently underway within CIHR to identify a set of indicators that are relevant to KT across the spectrum of CIHR activities. The three general areas deemed as key indicators of KT activity are:

- methodology to identify the gaps between research, policy and practice and of opportunities to close the gaps through appropriate knowledge translation activities;
- creation and/or support of opportunities to fund, or facilitate the synthesis, dissemination exchange and ethically sound application of knowledge to translate new knowledge into improved health for Canadians, more effective health services and products and a strengthened health care system;
- successful linkage and exchange with potential users of the research funded by the institute.

These three activities could be expected to help achieve the outcomes described in Table 1 above and of specific interest to III given its mandate.

D. KT as Viewed by CIHR

What exactly is KT? For our purposes it is any activity that facilitates or increases the use of knowledge, or the likelihood that it will be used to impact outcomes of interest. A list of terminology used within the CIHR community is included in Appendix 3. There is no commonly accepted and shared use of language around the world with respect to KT. In fact, ‘knowledge translation’ is a particular Canadian label, albeit one that is gaining in use. The terminology and language in this report reflects that used by the KT portfolio at CIHR as the starting point. **Knowledge** can be newly generated, or synthesized from and with existing knowledge, or it can be old knowledge that has previously not been used at all. In any event there is a process involved with **generating** it, **synthesizing** it with what is known, and/or **tailoring** it for use. This is illustrated in the central triangle of the Knowledge to Action Process framework (Figure 2, below).

CIHR describes two types of KT¹¹. **Integrated KT** describes a situation where knowledge use and knowledge generation are intertwined. At a minimum, to be integrated KT, researchers and research users work together to shape the research question, decide on methodology, be involved in data collection, interpreting study findings, crafting messaging around them and moving the results into practice. Through close collaboration throughout the research-KT process, research findings are more likely to be adopted by users of the knowledge. **End of grant KT** is carried out after the knowledge generation process is complete. This typically includes many of the activities through which researchers share their results (e.g. publications, presentations at conferences)

¹¹ For more information on KT at CIHR, see <http://www.cihr-irsc.gc.ca/1/29418.html>.

but can also include targeting of particular audiences for particular purposes with the attendant synthesis and tailoring of knowledge or **dissemination**.

Knowledge exchange involves interaction between researchers and decision-makers and results in mutual learning. These descriptions are helpful in gaining a beginning understanding of KT, but like many straightforward explanations, the 'devil is in the detail'. In reality, many KT activities are part or a combination of several strategies. Examples of KT funding initiatives at CIHR are shown in Appendix 4.

The ultimate goal of KT within the CIHR community is to influence some setting within society where it could be useful in effecting change in health related outcomes (either in the near future or longer term, but with clear intent to ultimately affect specific outcomes). The outer circle of the 'Knowledge to Action' process in 2 captures the phases in the implementation of knowledge use in a particular setting (e.g. hospital or community health agency).

There is a wide range of 'enablers' or situations that make KT more likely to be successful and knowledge use more likely. Some of these are captured in the steps depicted on the left hand of the cycle.

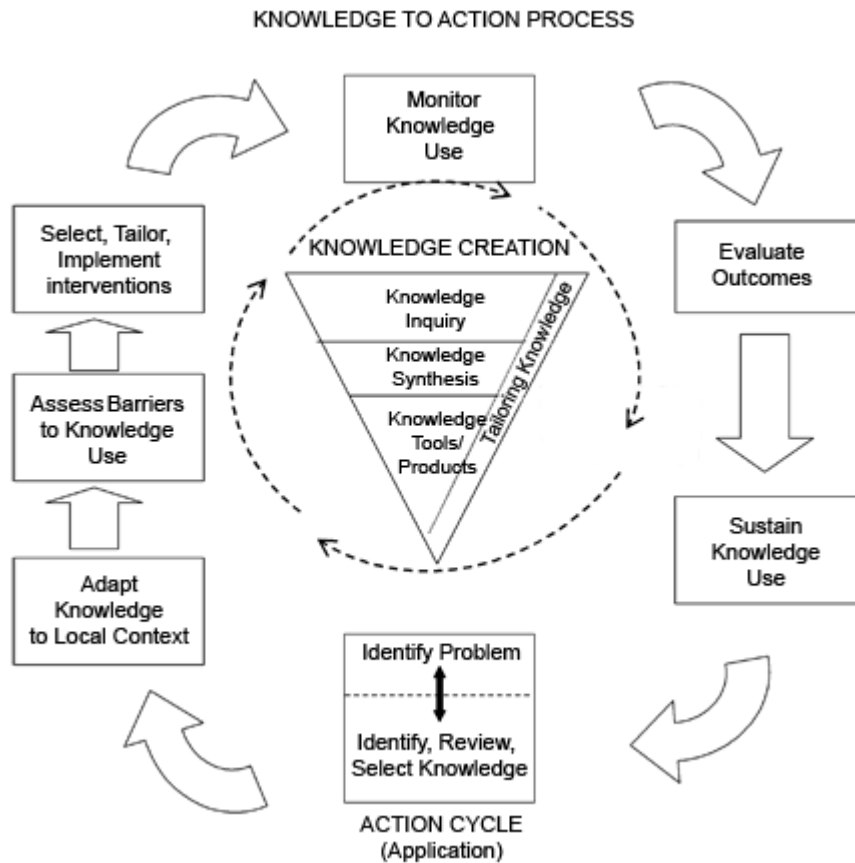


Figure 2: CIHR Knowledge to Action Process¹²

What can be inferred from the Knowledge to Action Process¹³ illustrated in Figure 2 is a series of activities or mechanisms that relate to intermediate outcomes and reflect progress on the path to changed outcomes.

- Collaboration of researchers and users in the research process
- Knowledge synthesis processes and products
- Knowledge tools and products (e.g. clinical practice guidelines; use of PDAs to have clinical information easily available at point of care; media interviews; websites; product suitable for commercialization).
- Problem identification (i.e. the gap between what is needed and what is known)
- Processes to adapt knowledge to context where it will be used
- Assessment of barriers to knowledge use in a particular setting
- Selection and tailoring of interventions through which research knowledge is applied
- Assessment of the impact of KT interventions or the use of knowledge
- Establishment and nurturing of relationships between knowledge generators and knowledge users (policy makers, decision makers in health system; industry)¹⁴
- Knowledge exchange opportunities (workshops, meetings with policy makers, etc)

For specific examples of these KT activities from the infection and immunity communities, see Appendix 1.

The Knowledge to Action Process (above, Figure 2) is one heuristic to help think about the various aspects of KT. Use of research results happens in different **contexts** and strives for different outcomes (economic, evidence informed decisions; health). While there can be an almost unlimited number of settings where KT and/or knowledge use is of interest, some of the major ones with relevance to infection and immunity include:

- Biomedical laboratories
- Everyday health behaviour of Canadians

¹² Referenced in many places; at <http://www.cihr-irsc.gc.ca/e/29418.html> (Accessed June 1, 2008); and in Graham and Tetroe (2007)

¹³ Referenced in many places; at <http://www.cihr-irsc.gc.ca/e/29418.html> (Accessed June 1, 2008)

¹⁴ Rejean Landry and colleagues at Laval University have done many studies that show the importance of exchange and relationships. See for example Belkhodja, O., Amara, N., Landry, R. and Ouimet, M., 2007. "The Extent and Organizational Determinants of Knowledge Utilization in Canadian Health Services Organizations", *Science Communication*, 28 (3), 377-417. and other publications by Rejean Landry and colleagues. See <http://kuuc.chair.ulaval.ca/english/index.php>

- Care provision to individuals by health professionals
- Government departments
- Hospitals and health regions
- Industry

The mandate of III infers that its focus of interest spans the health experience from prevention of infectious and immune-mediated diseases to palliation. This suggests knowledge translation activities in many varied settings.

The Knowledge to Action Process is clearly relevant to many of these contexts. The relevance to others, for example for KT in biomedical or industrial settings in which commercialization is the by-product or goal, has not yet been elaborated.

E. Commercialization: A Special Case of KT

As indicated earlier, the majority of infection and immunity researchers do T1 type activities, working in areas described by the lowest four boxes on the knowledge trajectory (Figure 1, page 7). Their contributions to ultimate health outcomes are likely to be indirect and these contributions will, in many cases, take the form of intermediate outputs such as products that can be used as diagnostic tests, medical devices or candidate drugs that must be tested through specific lab-based and clinical protocols. This is clearly a specialized context for KT.

Although knowledge translation and commercialization are viewed separately on the CIHR website, they can be seen as variations on the same theme. For many potential treatments and diagnostic reagents or tests, health outcomes can only be achieved through commercialization. In other cases, there can be commercial and economic benefits that are not directly related to improved health outcomes, but are of value to the country nevertheless. An example of this might be when a reagent or medium used in biomedical research is developed and produced in Canada and sold around the world. There could be significant benefit to Canada that isn't primarily related to health outcomes.

Several graphical depictions of the commercialization process (including one given on the CIHR website) are included in Appendix 5. For illustrative purposes, Table 2 below presents key elements from the KT process when a health or health system impact is the desired outcome compared to when a commercialization impact is the intended outcome. It should be noted that with respect to commercialization there are other major players besides researchers and CIHR. All research intensive universities have some mechanism through which to support researchers in their institutions with the protection of intellectual property and steps toward commercialization. Industry also plays a major role in moving research knowledge into use.

Table 2. Comparison of selected key dimensions between effort to influence health outcomes and commercial outcomes

Key dimensions	Health outcomes	Commercial outcomes
Identification of gap or opportunity	What is the health issue that could be better addressed by use of research evidence?	What product would your finding replace? Or what is the unsatisfied need that could be met through a commercial product?
Pre-cursors to dissemination to users	Often publication in peer reviewed outlets	Intellectual property protection; patent; copyright; trademarks; etc.
Typical dissemination processes	Written reports; presentations of evidence; face to face discussion with potential users; IT mediated sharing of research findings (websites, Personal Data Assistants, etc).	Proof of principle demonstrations; assessment of the size of the opportunity;
Typical 'users' of the research knowledge	Health professionals; managers in the health system; policy makers; public.	Private industry (existing companies or start ups)
Typical assessment of context	Examine opportunities and barriers to knowledge use;	Scope industry supply chains
Typical linkage and exchange activities	Workshops; meetings between researchers and users; educational events.	Private funders, angel investors, government assistance programs, business mentors
Typical 'enablers' of linkage and exchange	Money to enable meetings; organizational culture that expects use of research knowledge; influence organizations (e.g. CIHR institutes; health charities; professional bodies).	Venture capital forums; marketing studies; support from investors
Processes through which the knowledge is used by users	Organizational decision making; use of incentives	Purchase of product; license to use product,
Role of universities / employing institutions	Typically 'hands off'. Researchers undertake their own negotiations and discussions with users (sometimes mediated by a third party).	Most universities have intellectual property policies as well as agencies to help researchers with this process.

It is helpful to think about how the 'Knowledge to Action' process as presented by CIHR (Figure 2 above) can be used when thinking about commercialization as a special case of KT. Although there are important differences when comparing commercialization to other forms of knowledge translation, parallels can be drawn. Table 3 below presents specifics of how the various general components of the 'Knowledge to Action' process are operationalized within a commercialization context.

Table 3: Commercialization viewed through the ‘Knowledge to Action’ process

Component of Knowledge to Action Process	Adaptation for Commercialization	Typical activities
Knowledge Creation		
Knowledge inquiry	Research	
Knowledge synthesis	Proof of concept	Research at progressive stages of knowledge development: in vitro animal models; in vitro human models; in vivo animal models; in vivo humans
Knowledge, tools and products	Technologies, tools and products (TTP)	Protection of intellectual property through patents or other mechanisms.
Action Cycle		
Identify problem	Identify opportunities and potential uses for TTP	Participation in industry/science forum; scientific meetings; professional meetings Identification of potential investors;
Identify, review, select knowledge	Identify, review, select TTP	Technology assessment by industry, government departments, health regions
Adapt knowledge to local context*	Adapt TTP to local context	Market testing; usability testing
Assess barriers to knowledge use*	Assess barriers to use of the TTP	Determine freedom to operate; assess competing technologies
Select, tailor, implement interventions	Select, tailor, implement interventions	Identify distribution or sales mechanism
Monitor knowledge use	Monitor use of the TTP	Track sales and/or profit.
Evaluate outcomes	Evaluate outcomes	Assessment of return on investment;
Sustain knowledge use	Sustain use of the TTP	

* These two processes may be done in reverse order in a commercialization context.

While the various components and actions are presented in the ‘Knowledge to Action’ process and in the table above as being quite linear, in reality it is more of

an iterative and fluid cycle, with various factors influencing the order of actions, particularly in the earlier phases.

F. Process for Planning KT Activities

This process is designed for use by researchers in planning KT activities in the future. Eight components of the process are described along with typical questions that could be asked by a researcher or research group to assist with accomplishing that part of the process. Although the steps are presented separately for illustration and clarity, they may in reality be overlapping or concurrent and if actions are opportunistic the entry point may be anywhere along this spectrum.

1. Identify area of need or gap (or opportunity).

- Is there a compelling need to address an issue raised by a powerful stakeholder (e.g. federal government)?
- Does Canada rank very low on a measure related to infectious disease or immunity outcomes relative to other developed countries?
- Do policy statements or positions from expert bodies identify a gap between what we know and what we do?
- Can the Canadian public be assured that the results of research funded by CIHR through the open grants competition are being used in an optimal way?
- Is there a clear gap in our knowledge with respect to how to proceed to impact an outcome of interest?
- Is there an opportunity to commercialize a product that has emerged from biomedical research that will help researchers or enable widespread use of something known to be effective?

2. Identify the ultimate outcome of interest.

- Is it advancing knowledge so that application of findings to the other three outcomes (health impact, informed decision making, economic impact) are more likely?
- What is the health impact that could be influenced by a defined path?
- What are the economic outcomes that may be possible?
- What are the decisions made by a defined body that ideally are informed by research evidence?

3. Assess the current state of knowledge in the area of interest.

- What knowledge is available that could inform or guide action toward the outcome?
- Is the knowledge in an appropriate form for the user?

- What is the nature of the message or intervention that may be appropriate (e.g. simple, complex)
- Is the existing knowledge synthesized in such a way as to be useful to inform the next steps necessary to make progress towards the outcome?

4. Describe the context within which progress towards the outcome of interest will occur.

- Identify the 'actors' (organizations, individuals, professional groups) who will need to be involved if research findings are to be used? What are the motivations of the various actors?
- What are the barriers to uptake of the research knowledge?
- What are the opportunities for KT? What organizations are already working in this area (e.g. professional societies; non-profit organizations; patient groups)? Are there opportunities for partnerships?
- Who (or what organization) is in a position to influence activities and decisions?
- What is the current view of the venture capital community regarding outputs in infection and immunity? What are the views of the biotechnology and pharmaceutical industries? Is there potential value of research discoveries to private interests?
- Is there a risk for duplication of efforts?

5. Identify possible mechanisms and opportunities through which to achieve intermediate outcomes that will move knowledge system toward the target outcome.

- Are there sustained and positive relationships between research generators and users at various levels?
- What are the opportunities for Interpersonal exchange? e.g. workshops, meetings with senior policy makers,
- What knowledge exchange tools are needed? e.g. websites, reports, clinical practice guidelines, talk shows,
- Do we have a good understanding of the state of knowledge, or do we need a synthesis? e.g. systematic reviews, state of science reviews, expert panels
- What organizations are already active in this area or have identified this topic as a priority?
- What are the usual methods through which the user of the focal research knowledge seeks for information?

6. Identify intermediate outcomes that will move knowledge system towards the target outcomes.

- Proactive mechanisms to identify where gaps exist between what is known and what is done

- Established relationships between research generators and influential organizations
- Knowledge synthesized and in a form acceptable by user community
- Process established to assess the 'state of knowledge' in a specific field.
- Venture capital attracted

7. Select and implement strategies to advance the use of research knowledge.

- Given the routes through which change will likely occur, what techniques are needed? (Relevant examples from different contexts are included in Table 3 below).
- Given the nature of the outcomes desired, what actions are needed and by whom to promote the use of research knowledge?

Table 4: Common KT Strategies in Different Contexts

Setting	Interpersonal	Mediated
Citizen behaviour	Seek information from peer informants, e.g. family members and friends	Health information provided on internet by a wide range of groups
Professional care giving	Issue 'champions' influence colleagues; Pharmaceutical salesmen visit physicians in office	Clinical practice guidelines available on Personal Data Assistants
Service delivery in health organizations	Hallway talk	Audit and feedback provided with respect to key processes (e.g. infection rates)
Government	Advocacy groups meet with politicians	Briefing papers written for senior decision makers
Small and medium businesses	Researchers involved in NCEs invite industry reps to their meetings and to sit on committees	Website scan to determine sources of government agency start-up assistance.
Biomedical laboratories	Researchers working in mouse models consult researchers working with humans	Researchers access quality controlled samples of stem cells from reference labs

8. Assess progress and update approach as needed.

- What activities have you done to identify gaps between what we know from research and what we as a society do to use those results for societal benefit?
- What opportunities have you created (or influenced) to facilitate the synthesis of research knowledge?
- What activities have you done to disseminate results of research to groups that could use it to help support movement toward outcomes of interest?
- What meetings and/or relationships have you created or supported with potential users of research results?
- What activities have you done to support an individual, group or organization to incorporate the results of your research into work that will take steps toward influencing a health (or economic) outcome?
- What have been the intermediate outcomes (those that enabled tangible progress towards an important health outcome?)
- Which of the mechanisms and strategies that you have used seem to have had most effect? In what circumstances?

IV. Key Challenges for KT in Infection and Immunity

In addition to the fact that KT is a complex and multi-faceted process as described above, there are other challenges. Key stakeholders of III were interviewed with respect to key trends or factors in the environment that influence future actions of III with respect to KT. This input helped define some challenges related to KT in infection and immunity both inside and beyond CIHR.

- It is not clear what the capacity in Canada is to 'use' evidence. It is not clear if the system contains the necessary elements and attributes to enact the 'uptake' end of the research use activity. The varied roles that other organizations play in knowledge use in Canada need to be understood and embraced.
- KT must be global in scope, particularly with respect to infection. Bugs know no borders.
- New leadership in the KT portfolio at CIHR has provided numerous new frameworks and tools and there will be increased level of activity on this front for the foreseeable future. Internalizing the relevance and application of the various tools etc for infection and immunity requires time and focused attention.
- The desire to have economic benefits from research is great. Government policy and priorities and politics are major influences on KT. There is a current preoccupation with return on research investments and a focus on knowledge based economies.

- It is impossible to predict exactly the nature of the infectious challenges that will arise. Given the nature and uncertainty of infectious diseases, there may be potential impact if an event that is planned for and resourced (such as pandemic flu) does NOT happen.
- The Federal-Provincial dynamics within Canada require particular knowledge and skill in negotiating.
- There is increasing expectation that societal benefit from research be apparent. The free flow of health related information results in high awareness and expectations by the public. KT is not synonymous with communications, but instead is a suite of processes that will integrate researchers with the consumers of research.
- III needs to adopt a position relating to promoting research and uptake of findings that address rare diseases.
- The activities of the 'Big 13' research intensive universities in Canada with respect to KT (particularly commercialization) will influence what can and should be done.
- Much of infection and immunity research is done within Theme 1 (biomedical) and Theme 2 (clinical) areas; much of the focus in KT to date within CIHR has been on policy, service delivery and population and public health. Is KT within Theme 1 limited to commercialization; or is there more?
- The mandate of III states that their interests extend from prevention of infectious and immune-mediated disease to palliation and all the stages in between. However, the majority of researchers aligned with III focus their attention on research related to the biomedical aspects of disease. Addressing some aspects of the mandate of III requires deep knowledge and partnership with other groups and organizations with the requisite knowledge and expertise.

V. Several Lenses Through Which to View KT

There are at least four perspectives or groups that must be integrally engaged in the KT discussion and activities if research knowledge is to be applied to greatest advantage. These four perspectives are the community of researchers themselves, the Institute of Infection and Immunity that provides strategic leadership in this area, CIHR (with specific emphasis on the KT Portfolio) and last, but not least, a wide ranging group of organizations across Canada that use research knowledge to advance their own objectives related to immune mediated and infectious diseases.

This paper suggests a process through which an **individual researcher or a group of researchers** may think through their role in KT, but it is clear that KT is not an individual pursuit, but rather one that is done interactively and often in collaboration with others. Knowledge translation is by definition a process that is dynamic and involves ongoing interaction among many parties, including those

that generate research knowledge and those that influence its use. Often those that generate research work independently or in small groups with no formal connection to those organizations or individuals that use or influence the use of research knowledge. Often research knowledge that is suitable for use does not arise from one research group's work, but rather is a synthesis of the work of many. Knowledge translation is a complex process.

At a high level, researchers are involved in facilitating KT through doing research in ways such that use is inherent in the research (integrated KT); by thinking strategically about various actions and roles they could undertake (such as suggested in the eight step process in this document); by interacting and exchanging information with users to support the achievement of a specific goal.

The **Institute of Infection and Immunity** acts as a bridging organization between the targeted research community and CIHR. The III has a specific role to play in supporting KT within its area of influence. Its role may include such things as **funding mechanisms; strategic action by III personnel, creation of an enabling and supportive environment for KT¹⁵ and collaboration with others (partnering)**. The funding mechanism is just one mechanism employed by research funding organizations such as CIHR. In addition to funding mechanisms, Institute staff are in unique positions to take strategic action (identify areas needing attention; maintain relationships with key agencies and individuals; convene meetings, etc.) that enhance the chances of successful knowledge translation. This approach has been evident in many of the strategic initiatives supported by III to date.

The last two strategies above (creation of a supportive environment and collaboration) are worthy of mention as they too, like strategic action by Institute staff, are generally relevant and not just within a specific project or issue area. In a sense they are both enabling for KT. A **supportive environment** is one where those who are involved in KT understand what it is about, the necessary infrastructure is in place to support the use of research knowledge in many instances, and generally people and systems have capacity to actually use research findings. The nurturing and maintenance of ongoing relationships with key policy agencies (such as provincial Centres for Disease Control or the Public Health Agency of Canada) is an example of a dimension that typifies a supportive environment. If the relationship exists and a public health challenge emerges, the parties working in concert are in a much better position to move into action more quickly. The creation of a rapid response mechanism by III as a

¹⁵ For example, in a recent commentary, Hayday and Peakman (Nature Immunology 9(6), 2008) suggest that to improve knowledge translation of basic immunology research, there needs to be a shifting emphasis in research from animal models to human cells, tissues, organs and whole organisms. A supportive environment for this would provide access to more human, tissue and organ cultures, standardized culture protocols, the availability of more biostatistical and trial design expertise in molecular immunology, increasing numbers of small, independent clinical trials, and facilitation of long-term studies to establish the parameters of a healthy immune system.

result of one of the earlier challenges is another example of a supportive environment. With respect to collaborative action or partnering: aside from the fact that partnering has been identified as a key strategy across the board at CIHR and given the unique requirements of working with many other parties to ensure research knowledge is used, identifying partnering or collaboration as a key strategy seems self evident.

Of course, **CIHR as a whole** has KT as an integral part of its mandate and within its various programs provides initiatives that support KT (See Appendix 4). As the majority of research done is under the Open Competition program, this is an important focus for KT activity.

The **varied population of potential research users** is by definition an integral part of a process aiming to enhance the application of knowledge for benefit to Canadians. The focus of the workshop in September is to identify key priorities for KT within the infection and immunity focal area and actions through which to address those priorities. All of the entities above will ultimately be involved in KT activities to reduce the burden of infectious and immune-mediated diseases. During the workshop, the intent is to identify specific actions within the infection and immunity research communities that are needed to help enable KT, and to provide input to III and partners about how they can support those actions.

VI. Summary

This report describes a framework for KT within infection and immunity research and provides examples. Several things are highlighted.

First, given the fact that most of the infection and immunity research communities are in Themes 1 (biomedical) and 2 (clinical), this needs to be accommodated in this plan. In other words, there needs to be a greater focus on those KT activities that are important facilitators or enablers of the ultimate aim to improve health, health services and products. These include all of those activities that lead to all the activities identified in the CIHR Knowledge to Action process. These include: knowledge synthesis and tailoring of knowledge for ultimate use, knowledge exchange between researchers and others whose primary interest is in using knowledge to achieve long term outcomes or intermediate steps that will support achievement of longer term outcomes. In other words, the elaboration of KT in this framework is sufficiently broad to include the various activities engaged in by a community that is largely composed of biomedical and clinical researchers.

Second, the eight step framework, as written, is a tool that can be used for analysis of research initiatives, programs and projects that have already been completed or put in place, but also, and more importantly going forward, as part of the planning exercise prior to development or implementation of future research. If KT is a deliberate part of thought processes from the beginning, it should lead to a situation where KT is enabled and more effective in future steps.

Third, following from this, it should be more possible to discuss how III (on behalf of the community of researchers it represents) can assess the impact that KT is having on infection and immune mediated disease in Canada, especially in relation to those areas it has identified as priorities. It will continue to be increasingly important to be able to explain the difference that investment in research is making to Canada and Canadians.

Fourth and finally is the realization that III is an important 'influence organization' when it comes to moving the infection and immunity research and research-using communities to a greater appreciation of incorporating aims and outputs indirectly (and sometimes directly) relevant to the long-term improvement of health, health care delivery and health-related activity. The framework can be taken as a guide to making this explicit in both funding applications and grant reporting and as a self-assessment tool for all those engaged in planning strategy and engaging in research.

The III has stated three objectives relating to KT. They are to

- Build capacity and provide support to assist in translating and communicating new infection and immunity research knowledge
- Support KT initiatives for improved human health outcomes
- Increase opportunities to enhance the international recognition of Canadian infection and immunity research.

The workshop in September will provide important input into how to achieve these three objectives.

Appendix 1. Examples of KT to Date in Infection and Immunity

Introduction:

This appendix has been written to provide a snapshot of KT activities in the infection and immunity communities since the creation of CIHR. This summary has been influenced in a significant way by the data that was available to the writers. Although most resources have been invested by CIHR through the open-competition program, there is no consistent data through which to review KT activities resulting or initiated through that program. So, although we have attempted to describe KT activities in the infection and immunity communities, we can make no claim with respect to the comprehensiveness of this description. However, we hope that it gives a sense of the type of KT activities done.

Past KT activities within these communities are described in three sections:

- Examples of KT through strategic programs

- Examples of projects with high KT potential summarized on the CIHR website

- Examples of KT activities and projects described by members of the infection and immunity communities in a survey done during the summer of 2008

Examples of KT through strategic programs

The examples given below are organized under the eight mechanisms inferred from the CIHR Knowledge to Action process described in Section IIID above. They include examples from both T1 and T2 categories as articulated by Wolf. Most are from infection and immunity research projects that were responses to funding opportunities arising from strategic priorities identified by CIHR or by the III. This is simply a matter of expediency, since KT activities within strategic programs are well tracked. It must be emphasized that KT takes place through planning of strategic initiatives and programs within the Institutes of CIHR but responses to funding opportunities elaborated through these strategic programs are articulated by researchers and funded through competitive, peer reviewed processes.

Co-production of knowledge / Collaborative research processes

An excellent example comes from the HIV/AIDS Community-Based Research Program which forms part of the larger Canadian HIV/AIDS Initiative. In this program, research is directed by the community through their involvement with researchers in all stages of the process from elaboration of the research question to dissemination of results to affected individuals. Community leaders can serve

as principal investigators or co-investigators and funds can flow directly to community organizations. There is a variety of funding programs available to serve this program. One example, an operating grant entitled “The Diagnosis and Care of HIV Infection in Aboriginal Youth”¹⁶ and its companion piece the “Community Solutions Workshop: HIV Testing and Care for Aboriginal Youth” illustrates this kind of integrated KT.

Knowledge synthesis

Surveys, workshops and consensus conferences are important strategies for enabling knowledge synthesis. A survey of Canadian vaccine-related organizations, vaccine researchers and vaccine funding organizations identified significant research investments, and important Canadian discoveries, challenges and opportunities. The results, summarized in a report entitled “Vaccines of the 21st Century: Taking Canada to the Next Level”¹⁷ represents an important pooling and synthesis of knowledge by significant stakeholders in the vaccine community. The report was aimed at policy-makers, researchers and research-funders, and end-users of vaccines and immunization programs. It included a series of recommendations and represents not only important knowledge synthesis but also knowledge tailoring and tool development for use in developing vaccine priorities and policy.

An international conference in 2003 on “Meeting the Challenge of Prion Diseases” was followed by a prion planning workshop in which researchers met to consider the sum of prion research knowledge and expertise and to elaborate needs, gaps and opportunities in this area. Recommendations from this workshop formed the basis for a successful application to the Networks of Centres of Excellence program, resulting in the creation of the pan-Canadian Prionet, jointly funded by Health Canada, CIHR and Industry Canada.

Knowledge tools and products

Important outputs of fundamental research are the production of chemicals, cellular products, genetic information, etc., which only have health or economic impacts after they are available through the marketplace. Knowledge is translated through industrial partnerships, technology transfer, patenting, proof-of-principle and the later components of commercialization. The Novel Technology Applications in Health Research Program funded multidisciplinary teams of scientists with the aim of bringing technologies from the natural and physical sciences to biomedical research. Several patents emerged from this program. The results from one team included the production of a parasite screening tool based on the ability of specific antibodies to recognize human proteins that had been altered by parasitic proteins and detected by mass

¹⁶ Judy Mills, Principal Investigator

¹⁷ Report prepared for the Institute of Infection and Immunity, 2008

spectrometry. This tool has the potential for use in the mass screening of blood samples for parasitic infections.

Problem identification

This is exemplified in the planning of large strategic research initiatives where groups of researchers, researchers and partners, or researchers and stakeholders/research users came together to establish priorities and funding opportunities. At the researcher level, many team grantees pooled their expertise to shape general research questions and the role of each expert in the research team. One early example was a group led by the Institute of Human Development, Child and Youth Health, that included expertise across four Themes, epidemiology and population health, clinical science, genetics, immunology, and environmental health in order to address the question of gene-environmental interactions in childhood asthma¹⁸.

Processes to adapt knowledge to the context in which it will be used

A project conducted by Dr. Ross Upshur examined ethical issues related to quarantine, priority-setting, duty of care and global governance during the SARS outbreak¹⁹. A report written as a practical framework, “Stand on Guard for Thee”, received extensive media interest and uptake by planners and policy-makers locally, nationally and globally.

Assessment of barriers to knowledge use in a particular setting

In a project entitled “Barriers and Facilitators to Implementing Protective Measures Against SARS for Healthcare Workers”²⁰, the investigators used questionnaires and workplace assessments to address barriers to the use of infection control practices. They examined compliance and non-compliance of healthcare workers in high risk areas and what tools healthcare workers perceived to be available and what was actually available to them in a SARS-like event. The investigators were able to distinguish the demographics which described the least compliant workers. Outputs of the study included the development of a framework for assessment of the factors that influence intent to comply with specific behaviours relevant to infection control and safety. Based on the results, they created an accessible, web-based training module and relevant results were disseminated through newsletters and websites with targeted messages to specific audiences.

Selection and tailoring of interventions

¹⁸ Allan Becker PI. Origins of asthma in childhood.

¹⁹ Ross E.G. Upshur, PI. Ethical challenges in the preparedness and response to SARS.

²⁰ Annalee Yassi, PI

The infection and immunity communities include researchers whose primary role is to generate new knowledge from research and to synthesize it with knowledge that already exists. Thus ‘interventions’ usually take the form of researcher-to-researcher communications through scholarly meetings, presentations and papers, less frequently of researcher-to-stakeholder (funder, industrial partner) communications and occasionally researcher-to-knowledge user communications. Aside from these traditional means, ‘interventions’ are usually targeted verbal presentations. The CIHR Partnerships for Health Systems Improvement Program provides support for projects on emerging health needs, research that is relevant to decision-makers, with provincial partners and knowledge dissemination plans. One such project²¹ was able to demonstrate control of *C. difficile* in health workers by hand-washing with soap and water – a method shown to be more effective than alcohol-based hand cleaners. The investigators presented their results at relevant conferences but also to local infection control groups in order to inform infection control guidelines.

Relationships between knowledge generators and knowledge users

An early Opportunity Fund Workshop defined the foci of the Safe Food and Water Initiative as microbial contamination of food and water and the use of antimicrobials in agriculture. This led to the creation, facilitated by the Institute of Infection and Immunity, of a national, multi-sector partnership of academics, government and industry of the 17-member Canadian Research Coalition for Safe Food and Water that included five federal government departments or regulatory agencies, several universities, food industry associations. Through the activities of the Coalition, multiple funding opportunities were launched. This has been a sustained partnership which has built research capacity and facilitated outputs in applied food and water research, encouraged government-academia research collaboration and fostered public education.

Knowledge exchange opportunities

Knowledge exchange among researchers and between researchers and stakeholders is a key strategy throughout CIHR through conferences, workshops, symposia, consensus conferences and various other groups. In one example, a Canada-UK Workshop, “Beating the Bugs” brought together researchers from universities and public health agencies in both countries specifically to exchange information, and to explore opportunities for partnerships and collaboration and for sharing complementary expertise.

Examples of projects with high KT potential as summarized on the CIHR website

²¹ Michael Libman, PI. Efficacy of alcohol-based hand disinfection versus liquid soap for the removal of *C. difficile* from the hands

Outside of projects funded through strategic initiatives, there is very little information available about KT activities associated with infection and immunity research projects. A scan of the News Section of the CIHR website for 2006-2008 generated a list of projects with high potential for translation from basic research to new therapies²². It should be noted that these are projects selected as newsworthy for the CIHR website. Also it was not possible to determine the source of funding, open competition or strategic programs for these projects. They do provide a sense of the translational research activities in the investigator-initiated research community. A selection of these research projects is quoted here:

Moses et al: A randomized controlled trial done in Kenya but funded by CIHR showed that male circumcision reduced HIV incidence in young men. The trial was halted before completion because there had been sufficient evidence accumulated to show the risk reduction. The results from this study will inform international guidelines for HIV prevention. The study was cited by Time magazine as first place in their list of top 2007 medical breakthroughs.

Berghuis et al: A new way in which *Staphylococcus aureus*, a multi-drug resistant 'superbug', inactivates one of the latest drugs used to fight It has potential to be used to develop strategies to counteract drug resistance.

Chadee et al: A vaccine developed to prevent infection by *Entamoeba histolytica* prevents the parasite from attaching to the lining of the intestine. The researchers tested the vaccine on gerbils and found that it provided 100 per cent protection against the parasite. These findings may lead to the development of a vaccine for humans.

Cameron et al: This team demonstrated that during the early stages of the SARS infection patients produced two different immune responses. The researchers found they could predict how severe the disease would be by determining which type of immune response the patients had. Patients who would later experience only mild SARS symptoms had a different immune system response from those who would later suffer severe symptoms or death. This study, partially funded by CIHR, provides information about how the immune system reacts to SARS. It may be used to target patients who need extra medical care.

Cohen: A specific HIV protein suppresses the immune system by preventing cells from the immune system from replicating and thereby reducing the ability of HIV-infected persons to fight the infection. These findings could lead to the development of new drugs to combat HIV.

²² <http://www.cihr-irsc.gc.ca/e/20452.html> (2008), <http://www.cihr-irsc.gc.ca/e/35578> (2007), <http://www.cihr-irsc.gc.ca/e/33166> (2006)

Kotra et al: A synthetic compound has been identified that binds to and inhibits a key enzyme required for the malarial parasite to reproduce and survive. This has the potential for a new anti-malarial drug effective in drug-resistant strains.

Cashman and Lehto: Amorfix founded with a grant from the CIHR Proof of Principle program and focussing on the diagnosis and treatment of neurodegenerative diseases such as Alzheimer's, Parkinson's and Bovine Spongiform Encephalopathy (or mad-cow disease), all diseases where aggregated, misfolded proteins (AMPs) are prevalent. Amorfix was the only Canadian company of 47 nominees to be named a Technology Pioneer 2007.

Finlay et al: A vaccine to E. coli 0157.H7 has been authorized for use in Canada. The vaccine is administer to Canadian cattle to stop attachment of E. coli to the intestinal surface of cattle so that meat and produce exposed to cattle products will be less likely to transmit the pathogen.

Madrenas et al: Flesh-eating disease, food poisoning and toxic shock syndrome are caused by superantigens or toxins secreted by some bacteria. These toxins trigger massive activation of immune cells that sets off damaging events. This systemic immune response then sets off its own chain of damaging biochemical events that can lead multiple organ failure and death. This research will provide important information for the development of targeted drug therapies for these devastating diseases.

Singh et al: Diabetics are at greater risk of recurrent infections. This compromised immunity exists because their dendritic cells fail to produce enough interferon-alpha. This information emphasizes the importance of strategies such as vaccines to reduce the incidence or severity of infection.

Coulton and Pawelek: By successfully producing the first known 3-D structure of a complex involved in bacterial iron uptake, processes have been identified by which bacteria access essential nutrients such as iron. This could lead to better drugs to combat antibiotic resistance.

Saleh et al: A protein caspase-12 has been identified. It blocks the body's response to life-threatening infection by preventing another protein from working properly. This knowledge will guide the development of treatments that could strengthen the immune systems of those with the defective protein.

Suissa et al: The drugs used to reduce gastric acidity allow C. difficile to develop outside of hospitals. The bacterium can cause fatal bowel infection. The discovery may lead to novel treatments that will prevent C. difficile infections.

It should be noted that that until recently there has been no attempt to understand or systematically 'take stock' of the knowledge that has been created or translated through projects funded through the open competition program.

Recently CIHR has created an end-of-grant reporting program with a requirement for reporting specifically on knowledge translation activities. Analysis of this information will provide the opportunity to better understand how the infection and immunity research community is fulfilling this aspect of the CIHR mandate.

Examples of KT activities and projects described by researchers in the infection and immunity communities in III Survey August 2008

Frequency of Mention	Group 1: Biomedical and Clinical Researchers	Group 2: Health Systems, Services, Population and Public Health Researchers
Frequently	<ul style="list-style-type: none"> • Scholarly publications • Scholarly presentations • Commercialization (patenting, interactions with tech transfer offices, licensing agreements, creation of spinoff company; disclosure through industry university liaison, etc) 	<ul style="list-style-type: none"> • Collaboration with community through roundtables; community based research; development of partnerships for research • Advice and input from community members e.g. Advisory Committees, • Meetings with decision makers – government decision makers, community based organizations, community leaders
Occasionally	<ul style="list-style-type: none"> • Presentations to various audiences (community forums, family physicians, board members; continuing education) • Interactions with others (participation in biotech events, one on one meetings with key industry or government folks, those affected by disease, pharmaceutical companies, other scientists, • Media (through science journalists, • Seek input from those affected • Collaboration with other researchers 	<ul style="list-style-type: none"> • Recommend policies and programs based on research • Presentations at conferences for community organizations
Rarely	<ul style="list-style-type: none"> • Dedicated centres that promote KT • Web-based release of information, software, etc. • Publication for non research audiences • Teaching of future health professionals • Advocacy efforts 	<ul style="list-style-type: none"> • Written products – summaries of research in government publications, editorial commentaries, • CIHR cafes • Scholarly publications – scientific journals, open access journals.

Appendix 2. An Example of KT in Infection and Immunity: Safe Food and Water

Knowledge translation is not a simple or one-dimensional activity. To illustrate the complex and long term nature of much of KT, an example is used from the infection and immunity research communities. It is one that arose as a priority because of several events that caused all Canadians to focus on the safety of our food and water. Although there are many good examples within the infection and immunity communities, this example is used as it is a 'mature' area; one in which there has been time to see a path from research activity to a potential impact on health outcomes.

Figure 4 (Toward Health Impacts...) located in this Appendix (page 35) provides an illustration of how an outcome of interest (safe food and water for the country) has intermediate steps that reflect progress towards a specified goal. An example of how this might be conceptualized through a combined KT lens and an outcome oriented framework²³ is given in this figure. At the bottom of the figure examples of the health outcomes (phrased in the language of the Treasury Board Results Management Accountability Framework) are identified. Ultimately, the hope was to impact the health of the population of Canada in those areas that were related to infection through food and water sources. While the outcome articulated in the figure may never have been explicitly stated by anyone, it is not difficult to imagine that many Canadians hoped that research would lead to a state where no more Canadians died as a result of E.coli contaminated water. In this figure, the Safe Food and Water Initiative²⁴ is used as an example of how within one strategic initiative subsequent actions taken lead to progressively more applied activities, and ultimately to actions that clearly have an influence on health outcomes.

A key event that occurred which influenced these actions included the deaths in Walkerton, Ontario in 2000 as a result of water contamination with E.coli.

While the actions taken by III and others over the past few years can be described in this framework through a backward looking lens, it is safe to say that the evolution of various activities at the time did not seem quite as logical and planned. Some of the key events occurring within this general area²⁵ include:

During the transition to CIHR, there was funding offered for 'opportunity workshops' to help inform future directions of CIHR. One of these

²³ The basic format of this table is that presented by the Treasury Board of Canada in its Results Management Accountability Framework. http://www.tbs-sct.gc.ca/eval/pubs/RMAF-CGRR/RMAF_Guide_e.pdf Accessed July 16, 2008.

²⁴ The Safe Food and Water Initiative was supported by III shortly after its creation.

²⁵ This priority had actually been identified by the Medical Research Council prior to the creation of CIHR although the label of 'Safe Food and Water Initiative' emerged after CIHR was created.

workshops led by Dr. Brett Finlay of UBC focused on the microbial contamination of food and water, and the use of antimicrobials in agriculture.

III responded to this focus and worked to develop partnerships with both the government and private sector. The result was the creation of the 18-member Canadian Research Coalition for Safe Food and Water.

In May 2002 the Coalition launched its first funding opportunity on 'Needs, Gaps and Opportunities Assessment'.

In December 2002 a consortium of Coalition members and others launched a second funding opportunity to promote the formation of new research teams that incorporated academic and federal government researchers. Prior to this launch, there was an 'Application Development Workshop' to bring these diverse groups of researchers together.

Seven projects were funded under the second RFA, including one in which a vaccine was developed that when given to cattle significantly reduces the level of E. coli shed into the environment and exposure to E. coli of produce and meat products.

In June 2003 a funding opportunity was launched on 'Microbial contamination of food and water and antimicrobial resistance in the food chain'.

This example illustrates one strategic initiative of III. Therefore the activities described are those that III took (acting alone or in concert with partners). There are activities that other agencies took that also influenced the outputs and outcomes shown in Figure 3. For example, a Network of Centres of Excellence in Prion research (Prionet) was funded in 2005 through a federal government program²⁶. The Principal Investigator of the NCE had previously received a grant in the June 2003 RFA competition from III on 'The Canadian Prion Disease Network: Meeting the Challenge'. This had clearly been a building block towards funding of a full fledged multi-year NCE program.

Regardless of the activity (meetings, display, research projects done, etc) it is possible to trace the steps to see how activity of the research community could influence ultimate outcomes of interest. Although there is no direct evidence presented with respect to levels of E.coli contamination of water sources and the ultimate health outcomes, the path through which the various activities could influence health outcomes is clear.

The primary reason for presenting at least some of the activities arising from this initiative is to illustrate that KT happens incrementally and in a set of complex

²⁶ www.nce.gc.ca

interactions; hence it is important to think about the incremental steps toward knowledge use so that progress towards the ultimate outcome can be assessed and appreciated (while, of course, focusing on the importance of actually getting to the ultimate outcome). It is a key point that not every step or every research project will produce measurable results at the ultimate health outcome level. It is important to recognize that it is a multi-faceted and sometimes lengthy process in which intermediate mileposts can be identified.

In a very generic sense, some of these relevant mileposts can be derived from the CIHR Knowledge to Action process, and this framework is discussed in Section IIID of this paper.

Figure 4: Toward Health Impacts in Infection and Immunity Through Knowledge Translation: An Example

		PROGRESSIVE COMPONENTS OF ACTION TO ADDRESS STRATEGIC PRIORITY ON ANTIMICROBIAL RESEARCH AND MICRO-BIOLOGICALLY SAFE FOOD AND WATER				
		Strategic Priority: Antimicrobial Resistance and Microbiologically Safe Food and Water	Safe Food and Water Initiative	Canadian Research Coalition for Safe Food and Water	RFA: Microbial Contamination of Food and Water and Antimicrobial Resistance in the Food Chain - Phase II	Research Projects
UNDER DIRECT CONTROL OF III	Inputs	<ul style="list-style-type: none"> - I and I researchers / opinion leaders - Workshop dollars 	<ul style="list-style-type: none"> - Research dollars - Leadership: scientific director, III staff - IAB 	<ul style="list-style-type: none"> - Meeting dollars - Leadership and coordination - RFA dollars - Multi-sector advice - Working groups 	<ul style="list-style-type: none"> - Research projects - Industry / government departments / funding agencies / IPPH funding partnerships 	<ul style="list-style-type: none"> - Grant administration
	Activities	<ul style="list-style-type: none"> - Opportunities workshop (2001) 	<ul style="list-style-type: none"> - Partnership development: Government agencies and labs - IPPH - Industry associations. - Other funding agencies 	<ul style="list-style-type: none"> - RFA May 2002 (Needs, Gaps, Opportunities) - Develop partnership to sponsor museum exhibit 	<ul style="list-style-type: none"> - Application development workshop (December 2002) - RFA launched June 2003 - Research projects funded 	
UNDER INDIRECT CONTROL OF III	Outputs	<ul style="list-style-type: none"> - Report from workshop 		<ul style="list-style-type: none"> - Museum exhibit 'Food for Health' scheduled to travel across Canada for four years starting March 2006 - Media interest 	<ul style="list-style-type: none"> - Creation of new research teams - New research partnerships between government and university scientists 	<ul style="list-style-type: none"> - New knowledge about pathogens, vaccines, surveillance, local water supplies, river water contamination, antibiotics - Development of new vaccine for cattle to reduce E.coli shedding - Results of research projects shared with policy makers
INFLUENCED BY THINGS EXTERNAL TO III	Immediate Outcomes (Direct)	<ul style="list-style-type: none"> - Safe Food and Water Initiative 	<ul style="list-style-type: none"> - Canadian Research Coalition for Safe Food and Water 	<ul style="list-style-type: none"> - Increased public awareness - Links with other relevant sectors / decision-makers - Research programs of local and national importance 	<ul style="list-style-type: none"> - Linkages between government and university scientists 	<ul style="list-style-type: none"> - Creation of Prionet (NCE), e.g. better understanding of regional and local conditions contributing to coliform contamination - Partnerships between researchers and local medical officers of health
	Immediate Outcomes (Indirect)	<ul style="list-style-type: none"> - Public policies informed by CIHR and CIHR-funded research (e.g. regulations re re-routing cattle to reduce river contamination; vaccination encouraged for all cattle to reduce levels of E.coli shed into environment) 				
	Final Outcome (Specific)	<ul style="list-style-type: none"> - A safe and secure food and water supply for Canadians 				
	Ultimate Health Outcome	<ul style="list-style-type: none"> - Population health status influenced by CIHR funded research (e.g. Rates of e.coli infection reduced in those jurisdictions that implemented regulations that reduce cattle proximity to water sources) 				

Appendix 3. Knowledge Translation Terminology

Activity - An operation or work process internal to an organization, intended to produce specific outputs (e.g. products or services). Activities are the primary link in the chain through which outcomes are achieved. (3)

Application of knowledge - The term application is used to refer to the iterative process by which knowledge is put into practice. (4)

End of grant KT - The researcher develops and implements a plan for making knowledge users aware of the knowledge that has been gained from a project.

Exchange - The exchange of knowledge refers to the interaction between the knowledge user and the researcher resulting in mutual learning through the process of planning, producing, disseminating, and applying existing or new research in decision-making.

Dissemination - Involves identifying the appropriate audience for the knowledge to be translated and tailoring the message and medium to the audience. (2)

Ethically sound application of knowledge - The iterative process by which knowledge is actually considered, put into practice or used to improve health and the health system. KT activities must be consistent with ethical principles and norms, social values as well as legal and other regulatory frameworks. (4)

Final Outcome - These are generally outcomes that take a longer period to be realized, are subject to influences beyond the policy, program or initiative, and can also be at a more strategic level. (3)

Impact - *Impact* like *effect* is a synonym for *outcome*, although an impact is somewhat more direct than effect. Both terms are commonly used, but neither is a technical term. For technical precision, Treasury Board Secretariat recommends that *outcome* be used instead of *impact*. (3)

Input - Resources (human, material, financial, etc.) used to carry out activities, produce outputs and/or accomplish results. (3)

Integrated KT - stakeholders or potential research users are engaged in the entire research process. (4)

Knowledge translation - a dynamic and iterative process that includes synthesis, dissemination, exchange and ethically sound application of knowledge to improve the health of Canadians, provide more effective health services and products and strengthen the health care system. (1)

Outcome - An external consequence attributed to an organization, policy, program or initiative that is considered significant in relation to its commitments. Outcomes may be described as: immediate, intermediate or final, direct or indirect, intended or unintended. (3)

Output - Direct products or services stemming from the activities of a policy, program or initiative, and delivered to a target group or population. (3)

Synthesis - Synthesis in this context means the contextualization and integration of research findings of individual research studies within the larger body of knowledge on the topic. A synthesis must be reproducible and transparent in its methods, using quantitative and/or qualitative methods. (4)

Sources:

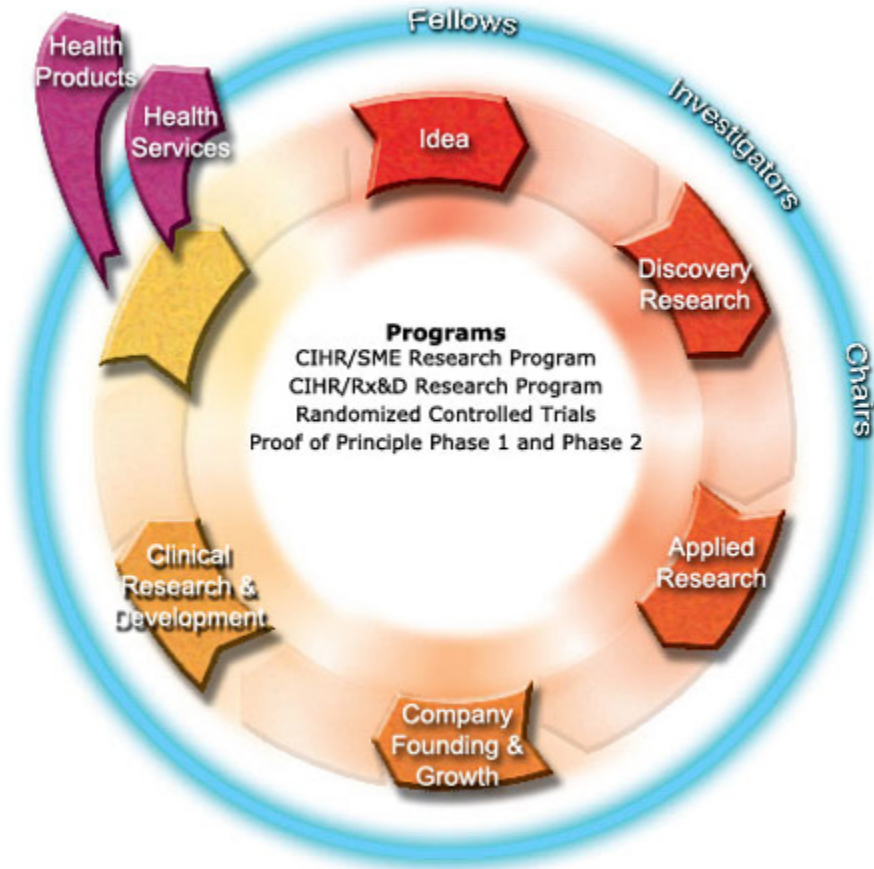
1. Government of Canada (2001) Bill C-13
2. CIHR (2008) Committee on the revision and review of the Common Framework Indicators (May 27, 2008)
3. Treasury Board of Canada Secretariat (2008). Guide for the Development of Results-based Management and Accountability Frameworks
4. About Knowledge Translation (2008). Available from CIHR website <http://www.cihr-irsc.gc.ca/e/29418.html> Accessed April 2008.

Appendix 4. CIHR Funded Initiatives Addressing KT

KT Focus	Initiatives
Synthesis	CIHR funds the Canadian Cochrane Network and Centre Knowledge Synthesis Initiative
Integrated KT (exchange and application)	Partnerships for Health System Improvement (PHSI) Knowledge Synthesis Initiative Knowledge to Action Initiative (integrated KT) Strategic KT initiatives research funded through institutes Proof of Principal (POP) Meeting, Planning and Dissemination grants to develop collaborative relationships and grant proposals
End of Grant KT (exchange and application)	Allowable expense as part of a grant application Knowledge to Action Initiative (end of grant KT) Meeting, Planning and Dissemination grants to disseminate results
Science of KT	Operating grants competition KT Panel Strategic calls from the KSE Branch on theories and methods of KT
Recognizing KT excellence	KT National and Regional Annual Prizes KT Casebook
KT Training and Capacity Building	Health Research Communications Award (HRCA) KT Assessment Project KT Handbook KT training requirements in STIHR (Strategic Training Initiative in Health Research) KT Doctoral Research Awards, Fellowships and New Investigator Awards KT Synthesis Training Modules Commercialization Programs
CIHR KT Policy	Policy on Access to Research Outputs Clinical Research Related Policies Commercialization Policy Evaluating KT at CIHR Integrating KT requirements into initiatives across CIHR Merit Review Policy

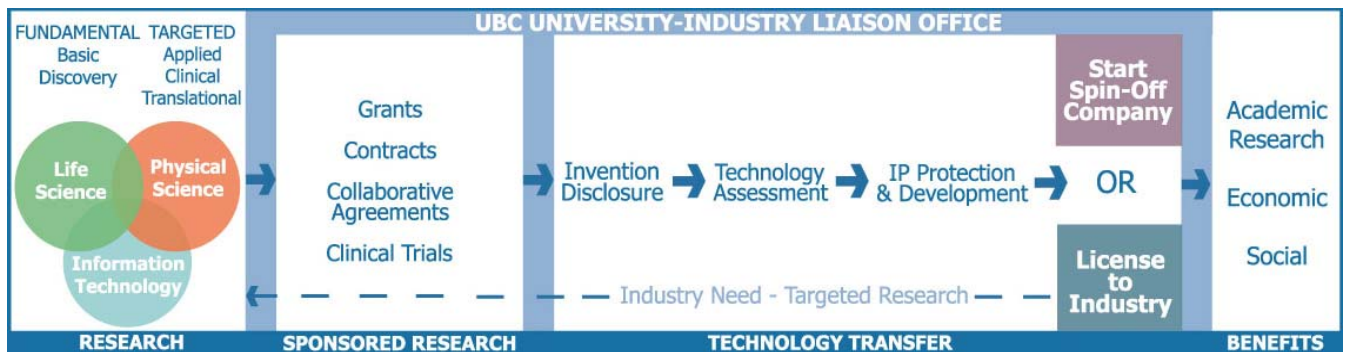
Appendix 5. Graphical Depictions of the Commercialization Process

1. From CIHR (<http://www.cihr-irsc.gc.ca/e/23906.html>)



2. From University of British Columbia

http://www.uilo.ubc.ca/images/Pathway_regular.jpg



3. Adapted from material provided by Annemarie Moseley, Aggregate Therapeutics (Structure depicted for ultimate clinical application)

