Report on the Pandemic Preparedness Strategic Research Initiative

Institute of Infection and Immunity

Canadian Institutes of Health Research

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Table of Contents

Executive Summary

Influenza is an infectious disease that generally causes fever, sore throat, muscle pain, headache and malaise. But, infections can be severe and result in several thousand deaths worldwide each year. New strains of the influenza virus occasionally emerge to cause an influenza pandemic that, in the past, has resulted in several million deaths. Most experts agree that the next pandemic is overdue. An influenza pandemic could have severe health, economic and social consequences. Worldwide, between 2 million and 7.4 million people could die including 11,000 to 58,000 Canadians. It is estimated that 4.5 to 10.6 million Canadians could become ill.

Surprisingly, given the potentially devastating health, economic and social consequences of a pandemic, there are large gaps in knowledge concerning influenza. More research is needed to effectively meet the challenges of a highly virulent strain of influenza. This research will help develop new healthcare strategies, policies and products that could be used to prevent or respond to a pandemic. Many countries are conducting influenza research, but it is essential to develop research capacity in Canada to meet the unique needs of this country and to have local experts available in the event of a pandemic. New research knowledge will be an essential component of an effective national annual and pandemic influenza response plan.

Recognizing the need to develop a coordinated and focused research effort and to build research capacity in pandemic influenza in Canada, the Canadian Institutes of Health Research Institute of Infection and Immunity (CIHR-III) has established the Pandemic Preparedness Strategic Research Initiative (PPSRI). The mandate of the PPSRI is to identify strategic research priorities and support pandemic preparedness research. PPSRI is guided by the Pandemic Preparedness Strategic Research Initiative Task Group. The Task Group has representatives who will carry out pandemic research as well as members who will apply the new research knowledge. The PPSRI is supported by the Canadian federal government which announced in May 2006 that it will provide $21.5 million over five years to support pandemic influenza research.

The purpose of this report is to provide background information about the PPSRI and to summarize its activities, accomplishments and future plans. Significant progress has already been made. In September 2005, CIHR-III in collaboration with the Public Health Agency of Canada organized an Influenza Research Priorities Workshop to identify areas of influenza research requiring support. To direct the future activities of the PPSRI, the Task Group has refined, developed and further prioritized the research areas first identified during the Workshop. These draft priorities were sent to stakeholders for feedback, and the comments were used to revise the priorities. The key areas identified are: i) vaccines and immunization programs ii) the influenza virus, iii) prevention and treatment, and iv) ethics, legal and social research.

It is critical that research that addresses the strategic priorities is funded in a timely manner. To this end, CIHR-III has taken a lead role and has also collaborated with other CIHR Institutes and organizations to launch several requests for applications to support pandemic preparedness research. For example, in June 2006, CIHR-III launched a Request for Applications for pandemic preparedness research operating grants with emphasis on disease control, prevention measures and the healthcare system. CIHR-III received a strong response to the request with the receipt of 60 applications. In July 2006, CIHR-III and the CIHR International Relations Branch, as part of the International Opportunity Program, launched requests for applications for seed and other collaborative research grants to encourage and support international research collaborations in the area of pandemic preparedness research .

A major round of requests for applications was launched in December 2006 by CIHR-III and partners. One request, launched in collaboration with the Public Health Agency of Canada and other partners, was for applications for operating grants to support research that addresses influenza diagnostics, transmission, ethics review and antivirals. A second request was for applications for funding to support team grants in influenza biology, vaccines, ethics, legal and social research. A third request was for applications for team grants to support influenza transmission and prevention research was launched in partnership with the International Development Research Centre and others. To support individuals with an interest in applying for these grants and to foster collaborations between them, a grantsmanship workshop was held in Ottawa on March 1-2, 2007

It is anticipated that research supported through these and other initiatives will help to identify strategies to prevent or mitigate a pandemic outbreak as well as methods and procedures to control disease spread (both human to human and from animals to humans) and to treat affected individuals. In addition, the international research collaborations established and supported through the International Opportunities Program and the Team Grants will enhance linkages between Canadian and international researchers. This is important because the threat of an influenza pandemic is global. Established linkages will be especially useful if a pandemic strain of influenza were to emerge from Southeast Asia, China or other parts of the world.

Funding decisions for the June 2006 Request for Applications for pandemic preparedness research operating grants were announced in February 2007. Twenty-six of the 60 applications that were received were funded. The funded research is wide-ranging, innovative and will assist Canada and the rest of the world to prepare for a pandemic. Highlights of the proposed projects include studies to discover novel antivirals, to develop vaccines that would protect individuals from multiple strains of the virus, to determine the best methods to respond to a pandemic and to identify ethical issues pertaining to a pandemic and to determine how they should be addressed**.**

Results of the International Opportunity Program competition for seed and other collaborative research grants were announced in March, 2007. The researchers who received these grants plan to engage in international research in areas such as determining risk factors for emerging diseases, understanding the genetic changes in influenza viruses that take place in children in different countries, determining the factors that protect individuals against influenza and the development of broad spectrum antivirals.

CIHR and partners plan to establish a network of influenza researchers in Canada to further enhance research collaboration and build research capacity. Members of the network will include successful recipients of pandemic preparedness research grants awarded by CIHR and partners.

Introduction

Canadian Institutes of Health Research Institute of Infection and Immunity (CIHR-III) is leading the Pandemic Preparedness Strategic Research Initiative (PPSRI) to develop a coordinated and focused research effort and to build influenza and pandemic preparedness research capacity in Canada. Work includes identifying current gaps in knowledge and supporting research training, operating grants, teams and multidisciplinary approaches to pandemic preparedness. The ultimate goal is that the new knowledge will allow Canada and others around the world to prevent or mitigate an influenza pandemic or to be better prepared to respond to a pandemic should one arise. The purpose of this report is to provide background information about the Initiative and to summarize the activities, accomplishments and future plans of the PPSRI.

Background

Influenza is an infectious viral disease that generally causes fever, sore throat, muscle pain, headache and malaise, but infections can be severe and result in several thousand deaths worldwide each year. Occasionally, a new strain of influenza virus emerges to cause an influenza pandemic that has resulted in several million deaths. There were three pandemics in the last century. The worst was the Spanish flu in 1918-1919 that killed 20 to 40 million people worldwide. The last pandemic occurred in 1968-69.

It is difficult to predict the timing of the next influenza pandemic, but most experts agree that one is overdue. An additional cause of concern is the human deaths caused by a new highly pathogenic strain of influenza A virus (H5N1) that emerged in south-east Asia in recent years, which has spread widely in birds, the natural reservoir for the virus. By August 2006, the World Health Organization had confirmed 241 cases of human H5N1 infection and 141 deaths. It is not known whether H5N1, or some other strain, will be the cause of the next pandemic.

The Public Health Agency of Canada has estimated that, in the event of an influenza pandemic, 4.5 to 10.6 million Canadians will become clinically ill, 2 to 5 million will require outpatient care, 34,000 to 138,000 will require hospitalization and that 11,000 to 58,000 will die. The World Health Organization has suggested that worldwide between 2 million and 7.4 million people could die from a global influenza pandemic.

The World Health Organization and public health agencies in many countries have developed plans to prevent and prepare for a pandemic. Canada was one of the first countries to develop a preparedness and response strategy, the Canadian Pandemic Influenza Plan. The Plan was developed to assist with the main components of planning, including surveillance, vaccine programs, use of antivirals, health services, emergency services, public health measures and communications.

Surprisingly, considering the scope of the potential health, economic and social consequences of pandemic influenza, there are severe gaps in knowledge about the virus. For example, questions remain about the prevention and treatment of influenza. There has also been a lack of discussion and consensus concerning ethical and social issues, such as the allocation of scarce resources during a pandemic. Acquiring knowledge in these and other areas will facilitate development of new healthcare system strategies, policies and products for pandemic preparedness. Therefore, in addition to public health planning, it is critical to mount a comprehensive influenza research initiative. Ultimately this knowledge will be an essential component of an effective national annual influenza and pandemic influenza response plan.

Other countries have, and continue to develop, research responses to pandemic influenza. In the USA, for example, influenza pandemic preparedness research is a priority of the American government. Examples of current research projects include H5N1 vaccine clinical trials being run by National Institutes of Health (NIH) vaccine treatment and evaluation units, as well as the National Institute of Allergy and Infectious Diseases' (NIAID) influenza genome project. Additionally, the NIH and NIAID Cooperative Research Partnership for Influenza Product Development supports research leading to the discovery and development of therapeutics, diagnostics and vaccines for influenza.

The Medical Research Council in the United Kingdom is also supporting research in several identified priority areas. These include the modes of transmission of avian flu to humans, the molecular and cellular mechanisms of virulence and pathogenicity, mechanisms of immune protection, creation of improved vaccines, effective use of antivirals, development of rapid diagnostics and determination of methods to prevent the spread of infection.

In Canada, CIHR-III has led the way in developing and supporting pandemic influenza preparedness research. CIHR-III established the Pandemic Preparedness Strategic Research Initiative (PPSRI) to support research that will improve Canada's ability to prevent and/or respond to an influenza pandemic. It is essential to build a network of researchers in Canada, to address issues unique to this country and so that local experts and knowledge will be available in the event of a pandemic. In addition, Canada's healthcare system and expertise make researchers in this country ideally suited to address specific research questions concerning pandemic influenza.

The Initiative is funded by the Canadian federal government which announced in May 2006 that it would provide $21.5 million over five years to CIHR to support pandemic preparedness activities.

Report on Activities

Influenza Research Priorities Workshop

CIHR-III collaborated with the Public Health Agency of Canada (PHAC) to organize the Influenza Research Priorities Workshop in Ottawa in September 2005. Ten research areas were identified by national and international influenza experts attending the Workshop. Pandemic influenza was recommended as a major research focus in the short term. Participants discussed gaps in knowledge, research activities to help bridge the gaps and infrastructure and capacity requirements that are currently lacking. See the Institute website (www.cihr-irsc.gc.ca/e/30967.html) for the Workshop report.

Request for Applications for Pandemic Preparedness Operating Grants

In June 2006, in response to the recommendations made during the Influenza Research Priorities Workshop, CIHR-III launched a Request for Applications (www.cihr-irsc.gc.ca/e/31297.html) for operating grants to support pandemic preparedness research. The purpose of the Request for Applications was to further strengthen Canadian influenza research in preparation for a potential pandemic outbreak by funding two-year projects to conduct critical research on disease control, prevention measures and healthcare system preparedness. It is expected that this targeted investment will lead to new diagnostic methodologies, evaluation of vaccines, new antivirals, mechanisms to control disease spread, outbreak modelling and design, assessment of optimal health system strategies and an understanding of ethical issues pertaining to a pandemic and how they should be addressed. CIHR-III received a strong response to the request with the receipt of 60 applications. Funding decisions (www.cihr-irsc.gc.ca/e/33490.html) were announced in February 2007.

Pandemic Preparedness Strategic Research Initiative Task Group

To develop and guide the Pandemic Preparedness Initiative, CIHR-III formed the Pandemic Preparedness Strategic Research Initiative Task Group. The Task Group includes members carrying out pandemic research as well as members who will apply the new research knowledge to help Canada prepare for a pandemic (see Appendix 1 for a list of members and their expertise). The mandate of the Task Group encompasses the following objectives: to make recommendations on strategic research priorities and mechanisms to support these areas; to develop outcome indicators/measures for research; to facilitate research linkages; to identify national and international experts to act as peer reviewers; and to identify partners and obtain funding to support necessary research activities.

Draft Pandemic Preparedness Strategic Research Priorities

To support the PPSRI and direct its future activities, the Task Group refined, developed and further prioritized the research areas first identified during the Influenza Research Priorities Workshop. The objective of the Task Group was to identify areas in which Canadian researchers could obtain results that would have a significant impact on the ability to prevent and/or respond to an influenza pandemic. The Task Group considered current pandemic and annual influenza research in progress in Canada and internationally, and identified gaps in research that Canadian researchers are well positioned to fill. The implications of potential research results in specific areas were also considered.

The Task Group felt that vaccine research should form the cornerstone of an influenza pandemic preparedness research effort, because an effective vaccine will be key to stopping a pandemic. To develop vaccines and assist in the prevention of infection and treatment of influenza, fundamental knowledge about the influenza virus and molecular mechanisms of transmission is needed. And, in the event that a vaccine for a new strain of influenza is not available at the start of a pandemic, methods to prevent the spread of the virus and to treat affected individuals will also be critical. The Task Group determined that preparing for and responding to a pandemic raises many ethical, legal, social and societal issues, many of which relate to the other broad research areas. They also noted that research carried out under the PPSRI will also impact and inform future responses to annual influenza outbreaks. Detailed descriptions of each priority are contained in the next section of the report.

The research priorities identified by the Task Group reflect areas which require investment through strategic initiatives such as targeted requests for applications. The priorities are not intended to lessen the importance of other areas of influenza and infectious disease research which remain eligible for funding through the CIHR regular grant programs and other targeted initiatives.

Consultation Process with Stakeholders

The draft of the Pandemic Preparedness Strategic Research Priorities was sent to the Canadian Rapid Research Response Team and additional stakeholders in pandemic-related fields. For a list of those who received the document, see Appendix 2. The purpose of the consultation was to give stakeholders an opportunity to review the draft priorities and provide feedback. The consultation also helped create of linkages with organizations working in areas related to pandemic preparedness, as well as users of research knowledge nationally and internationally.

The PPSRI received 16 responses to the consultation request. The overwhelming majority agreed that each of the draft areas identified by the Task Group were a priority for Canadian research. The comments were incorporated and are presented below in a summary of the strategic research priority areas. The following organizations indicated they would like to partner in supporting one or more of the research areas:

- American Red Cross
- Canadian Food Inspection Agency
- Association of Medical Microbiology and Infectious Disease Canada / Canadian Foundation for Infectious Diseases
- Canadian International Development Agency
- Emerging Infectious Disease Research Network
- First Nations and Inuit Health Branch, Health Canada
- Rx&D (an association of Canada's research-based pharmaceutical companies) Health Research Foundation
- International Development Research Centre
- Public Health Agency of Canada

Pandemic Preparedness Strategic Research Priorities

The following is a summary of the Pandemic Preparedness Strategic Research Priorities that were developed by the Task Group in consultation with stakeholders. These priorities will direct future activities of the PPSRI.

Capacity Building

An overarching theme is the need to build capacity in pandemic influenza research in Canada. It is essential for Canada to build research expertise now so that it will have expert researchers to call on during a pandemic outbreak. The Task Group felt that the best way to achieve this is to support training in influenza research, such as doctoral and fellowship support, as a component of operating and team grants.

Vaccines and immunization programs: optimal use and efficiency of existing vaccines and development of new pandemic vaccines

Research is needed to further our understanding of immune response and protection as well as to devise new vaccine technologies. Effective vaccination strategies would greatly reduce the impact of a new strain of influenza.

Research is required to: optimize existing vaccination programs; aid in the discovery of novel means of vaccine delivery; examine scheduling and dosing; and address issues of safety.

Research is required to further our understanding of immune response and protection. Proposed projects would: study human and animal immune responses to immunization and indicators of protective immunity; assess the carry-over and cross-protection by vaccines; develop cross-protective vaccines; study the effectiveness of human vaccines to prevent reassortment of animal and human influenza; and develop novel influenza virus vaccine technologies and new vaccine platforms.

Research is also needed to: develop better assessments of the potential benefits and short- and long-term safety of influenza vaccines in specific populations, studies to measure the economic benefits of immunization, the development of methodologies and capacity for annual assessment of program effectiveness.

The virus: biology of the influenza virus and rapid diagnostics

Much more information is needed about the influenza virus, and reliable and rapid diagnostic tests for influenza are currently not available.

Research is needed on: the biology of the influenza virus; the human and animal host response to infection such as the innate and acquired immune response; and the role of mucosal immunity and correlates (predictors) of protection. Recommended research would also include: studies to investigate the genetics of influenza; analysis of influenza evolution in avian and mammalian species; and assessment of disease production and immune response using animal and human models.

Research is required to develop and evaluate rapid diagnostic tests for hospital laboratories and “point-of-care” applications which, at the present time, are not available. Research would also evaluate the utility and impact of optimized diagnostic testing.

Prevention and treatment: modes of transmission, use of antivirals and alternate strategies for prevention

In the event of a pandemic, knowledge of ways to prevent the spread of the virus and to treat infected individuals will be critical. Further knowledge is needed on how influenza spreads in different settings.

Research is required to: study the molecular basis for transmission of the influenza virus between humans as well as from animals; the mechanisms involved in pathogenesis; the mode of transmission including influenza shedding patterns; and the risk factors for infection. Research is also required to determining optimal methods of preventing transmission at the individual, institutional and community level. Research areas include comparison of protective equipment such as masks, the utility of vaccination of specific populations and the value of increasing social distancing and containment.

There is a need for new antivirals in light of the limited number that are currently available, but discovery of new drug targets and development of new antivirals are a long-term project. In a pandemic, it will be critical to optimally use existing limited supplies of antiviral drugs such as Tamiflu. Research is needed to determine the optimal dosing, effects on various influenza strains, usage in a variety of settings and degree of development of viral resistance to antivirals. Research might also include discovery of innovative uses of existing antivirals, as well as discovery of existing drugs that have an antiviral effect.

Ethics, legal and social contract: research in risk communication, prioritization and the regulatory approval process

It is essential that research and discussions that aid in the planning of how to prevent and respond to a pandemic are in place before a pandemic starts. Research is needed to develop and optimize communication strategies, determine effective means to educate health care providers in the application of care guidelines and to identify effective protective measures in the Canadian context. There is a need for research to address the issues of surge capacity in pandemic situations. Research into prioritization and resource allocation could address global, hospital, and bedside requirements, fairness of distribution of limited resources and would take into account ethical issues. Ethics research is needed to examine the perceptions among health care providers and the public on the scope and extent of obligations and duty to care during a pandemic. Research is needed to understand the social, economic, cultural and secondary impact of such measures and examine the needs of vulnerable populations and children in pandemic outbreaks.

In the event of a pandemic, new therapeutics and diagnostics will require expeditious approval in a manner that protects human subjects. Research is needed into ways to improve efficiency of the ethics review process. This would include development of models, processes, guidelines and standard operating procedures to allow the research community and research ethics review boards to submit and process applications related to public health threats quickly.

There are opportunities to learn from the research work carried out in this area during the Severe Acute Respiratory Syndrome (SARS) outbreak. As a starting point, research could take the form of analysis of funded SARS research and lessons learned from that research.

Request for Applications that Address Pandemic Preparedness Strategic Research Priorities

It is critical that the strategic research priorities identified during the Influenza Research Priorities Workshop and by the PPSRI Task Group are funded in a timely manner. To this end, CIHR-III has taken a lead role and has also collaborated with other CIHR Institutes and organizations to launch several requests for applications to support pandemic preparedness research. These requests for applications are summarized below.

Operating Grants: Pandemic Preparedness
(www.cihr-irsc.gc.ca/e/31297.html)
June 2006
CIHR-III launched this request for applications to address the recommendations made at the Influenza Research Priorities Workshop. The purpose is to further strengthen Canadian influenza research in preparation for a potential pandemic outbreak by funding two-year projects to conduct critical research on disease control, prevention measures and healthcare system preparedness. It is expected that this targeted investment will lead to new diagnostic methodologies, evaluation of vaccines, new antivirals, mechanisms to control disease spread, outbreak modelling and design, assessment of optimal health system strategies and an understanding of ethical issues pertaining to a pandemic and how they should be addressed. In August 2006, CIHR-III received a strong response to the request with 65 letters of registration submitted by researchers. The deadline for full applications was October 2006 and grants will start in March 2007.

CIHR International Opportunity Program: Seed and *Other Grants*
(www.cihr-irsc.gc.ca/e/32585.html and www.cihr-irsc.gc.ca/e/30802.html)
July and October 2006
CIHR-III and the CIHR International Relations Branch issued a joint call for requests for applications to the International Opportunity Program for both seed and collaborative research project grants that are relevant to pandemic preparedness. The purpose of the seed grants is to assist Canadian researchers to explore, develop and establish new international collaborations with foreign researchers. These one-time grants support Canadian participation in the pre-research stages that will lead to new international research collaborations. The Other Grant enables Canadian researchers to participate in international research projects approved for funding by foreign entities in which the Canadian participants must secure their own funding.

The importance that CIHR-III places on establishing international collaborations is evidenced by its participation in a re-launch of the request for applications for *International Opportunity Program Seed Grants* (www.cihr-irsc.gc.ca/e/30812.html) to develop international pandemic preparedness research collaborations in October 2006.

Operating Grants: Partnerships for Health System Improvement
(www.cihr-irsc.gc.ca/e/32476.html)
October 2006

In the event of a pandemic, many issues will arise that relate to health systems and services. Research is needed to create new knowledge for informed decision making in pandemic planning and policies. To encourage this research, CIHR-III partnered with the CIHR Institutes of Health Services and Policy Research and Population and Public Health to launch this request for applications. The purpose is to support teams of researchers and decision-makers interested in conducting applied health research in the area of pandemic preparedness useful to health system managers and/or policy makers.

Operating Grants: Influenza Diagnostics, Transmission, Ethics Review and Antivirals
(www.cihr-irsc.gc.ca/e/32803.html)
December 2006

CIHR-III launched this request for applications in collaboration with the Public Health Agency of Canada and in partnership with CIHR Institute of Aboriginal Peoples' Health, Canadian Foundation for Infectious Diseases and Association of Medical Microbiology and Infectious Disease Canada. The purpose is to fund three-year research projects that will examine optimal use of existing antivirals, disease transmission, rapid diagnostics and the ethics review process. It is expected that the funded research will lead to increased knowledge, better methods for responding to an influenza pandemic, controlling disease spread and treating affected individuals, as well as improving the ethics review process for research proposals during a possible outbreak.

Team Grants: Influenza Biology, Vaccines, Ethics, Legal and Social Research
(www.cihr-irsc.gc.ca/e/32804.html)
December 2006

CIHR-III launched this request for applications in collaboration with the Public Health Agency of Canada and in partnership with CIHR Institute of Aboriginal Peoples' Health and the Canadian Food Inspection Agency. The purpose is to fund three-year team grants on vaccines, the biology of the influenza virus, including the animal-human interface, and the social, ethical and legal issues related to preventing and responding to a pandemic. Expected outcomes of funded research are the identification of strategies to prevent or mitigate a pandemic outbreak, as well as methods and procedures to control disease spread between humans and from animals to humans, and to treat affected individuals.

Team Grants: Influenza Transmission and Prevention

(www.cihr-irsc.gc.ca/e/32802.html)

December 2006

CIHR-III and CIHR/Rx&D Collaborative Research Program launched the request for applications in partnership with Canada's Research-Based Pharmaceutical Companies (Rx&D) Health Research Foundation 2006, the Canadian Food Inspection Agency, CIHR Institute of Aboriginal Peoples' Health and the International Development Research Centre. The purpose is to fund three-year team grants to study the modes of transmission of the influenza virus and alternative strategies for prevention of infections. Canadian-based researchers may apply with researchers in low or middle income countries in SE Asia or with researchers in China. The objective of the joint funding of Canada-SE Asia or China grants is to strengthen cooperation between scientists in these countries, and foster the development and exchange of knowledge relevant to pandemic preparedness. Established linkages will be especially useful if a pandemic strain of influenza were to emerge from SE Asia or China and also because most of the human infections with the H5N1 strain that is of current concern originated in this part of the world.

Research Syntheses: Knowledge Translation

(www.cihr-irsc.gc.ca/e/32856.html)

December 2006

CIHR-III launched this request for applications in partnership with the CIHR Knowledge Translation Branch. The purpose is to strengthen knowledge translation by funding research syntheses related to preparing for and responding to an influenza pandemic. There are opportunities to learn from research work carried out during the Severe Acute Respiratory Syndrome (SARS) and other disease outbreaks. It is expected that the funded research will summarize this information and develop recommendations that will contribute to pandemic preparedness planning and control.

Workshop/Symposia Support In collaboration with Knowledge Translation Branch

(www.cihr-irsc.gc.ca/e/24244.html)

December 2006

CIHR-III and the CIHR Knowledge Translation Branch will provide partial support of workshops and symposia, which either support knowledge translation research and/or contribute to building networks relevant to pandemic research and that will contribute to pandemic preparedness planning and control.

Application Development Workshop

(www.cihr-irsc.gc.ca/e/33173.html)

March 2007

A grantsmanship workshop for researchers with an interest in submitting applications to the December 2006 requests for applications was held in Ottawa on March 1-2, 2007.

The purpose of the workshop was to assist researchers in the application process, review the relevant research areas, discuss the goals of the organizations collaborating to fund this research and highlight key components of writing a successful grant application. The workshop also allowed researchers to meet each other to discuss areas of common interest and will facilitate the preparation of joint applications.

Research Supported Under the Pandemic Preparedness Strategic Research Initiative

Operating Grants: Pandemic Preparedness

(www.cihr-irsc.gc.ca/e/33490.html)

Awarded February 2007

CIHR-III received a strong response to its June 2006 request for applications for two-year operating grants to conduct critical research on pandemic influenza disease control, prevention measures and healthcare system preparedness. Twenty-six of the 60 applications that were received were funded (Table1). The research proposed by the successful applicants is wide-ranging and innovative, and will be vital to help Canada and the rest of the world prepare for a potential pandemic outbreak. For example, it is anticipated that the research will lead to novel methods to detect pandemic strains of influenza, to a universal influenza vaccine that would protect against multiple strains of influenza, to new ways to prevent the spread of the virus and to treat people with influenza infections, to improved healthcare strategies and to a better understanding of ethical issues pertaining to a pandemic and how they should be addressed. The funding also supports and helps to build influenza research capacity in Canada, which is essential to meet the unique needs of this country and to ensure that local experts are available in the event of a pandemic.

Table 1: Projects funded under the Pandemic Preparedness Operating Grants RFA

Principal Investigator	Institution	Project Title
BOIVIN, Guy	Université Laval	Mechanisms of resistance of influenza to antiviral agents and evaluation of new therapeutic modalities
BUCKERIDGE, David L	McGill University	Understanding epidemics in special populations: Guiding intervention and planning
COOMBS, Kevin M	University of Manitoba	Proteomics of influenza virus-infected human cells
DASCAL, André	Sir Mortimer B. Davis Jewish General Hospital-Montreal	Ability and willingness of health care workers to report for work in an influenza pandemic
DAY, Robert	Université de Sherbrooke	Antiviral inhibitors of furin and related convertases. Inhibiteurs antiviraux ciblant la furine et les proprotéines convertases
EARN, David J	McMaster University	Consequences of evolution for pandemic preparedness

Principal Investigator	Institution	Project Title
GUTFREUND, Klaus S	University of Alberta	Immunotargeting with CD154 to induce antiviral immunity to avian influenza
KELVIN, David J	University Health Network (Toronto)	The role of complement cascades in pathogenesis of H5N1 disease
KENNY, Nuala P	Dalhousie University	Pandemic Planning and Foundational Ethical Questions of Justice, the Common Good and the Public Interest
KING, Malcolm	University of Alberta	Cough and bioaerosol in influenza pandemic containment
KOBINGER, Gary P	University of Manitoba	In vivo evaluation of conventional and experimental avian influenza A (H5N1) virus vaccines
LAPOINTE, Réjean	Centre Hosp. de l'Université de Montréal	Development of a pan-specific cellular immune response to influenza
LECLERC, Denis	Université Laval	Development of an universal influenza vaccine Candidate
MAGOR, Katherine	University of Alberta	Antiviral responses to influenza in the natural host
MAUNDER, Robert G	Mount Sinai Hospital	Education and support to increase the resilience of healthcare workers facing pandemic influenza: What is the minimum effective dose?
NICHOLAS, David B	Hospital for Sick Children	Pandemic Planning for Paediatric Care
PANTE, Nelly	Capital Health Region (Edmonton, AB)	Toward the development of novel anti-influenza drugs that block nuclear import of influenza
PREDY, Gerald N	University of British Columbia	Feasibility and Effectiveness of a Community Triage Centre to Manage Influenza-like Illness in an Urban Setting
SKOWRONSKI, Danuta M.	University of British Columbia	Influenza Vaccine Effectiveness Against Serious Outcomes
SKOWRONSKI, Danuta M.	University of Alberta	From genotype to Phenotype: Early detection of influenza variants and correlation with variation in vaccine effectiveness
SURESH, Mavanur R	Hospital for Sick Children	Targeted Dendritic Cell Vaccines for Influenza: Providing a vaccine to all 33M Canadians
TELLIER, Raymond	University of Toronto	Early detection of avian influenza isolates with increased affinity for the human sialic acid receptor
UPSHUR, Ross E	INRS - Quebec	Ethics and pandemic planning: Engaging the voices of the public

Principal Investigator	Institution	Project Title
VON MESSLING, Veronika	University of Toronto	Pandemic potential assessment of recent animal influenza isolates
WATTS, Tania H	University of Saskatchewan	Mouse models for evaluating the protective value of increased costimulation of CD8 T cell responses in the lung
ZHOU, Yan	University of Saskatchewan	The role of PI3K/akt pathway in modulating chemokine IP-10/CXCL10 production by influenza A virus infection in human airway epithelial cells

CIHR International Opportunity Program: Seed and *Other Grants*
(www.cihr-irsc.gc.ca/e/34273.html)
Awarded March 2007

Seven seed grants were awarded under this program, which assists Canadian researchers to explore, develop and establish new international collaborations with foreign researchers (Table 2). It is anticipated that the results of the research will improve our ability to prevent and treat pandemic influenza and will foster necessary international research linkages in this important area. Dr. Veronika Von Messling was awarded a collaborative research project grant to support her involvement in international research with the goal to determine whether type 1 interferons can be used for the treatment of influenza and, if so, their mechanism of action.

Table 2 - Projects Funded under the CIHR International Opportunity Program

Seed Grants		
Principal Investigator	**Host Institution**	**Project Title**
BREWER, Timothy F	Centre universitaire de santé de McGill	Risk factors for emerging diseases
BROWN, Earl G	University of Ottawa/ Université d'Ottawa	Evolution of interferon resistance of avian and human influenza viruses.
FISH, Eleanor N	University Health Network (Toronto)	Canada-EU collaboration: Development of broad-spectrum antivirals
MCELHANEY, Janet E	Vancouver Coastal Health Research Institute	The roadmap to improved correlates of protection against influenza
O'CALLAGHAN, Christopher J	Queen's University (Kingston, Ontario)	Building global capacity for evidence-based research in communicable diseases
POURBOHLOUL, Babak	University of British Columbia	Pandemic preparedness: An international modeling exchange

Seed Grants		
Principal Investigator	**Host Institution**	**Project Title**
TRAN, Dat	Hospital for Sick Children (Toronto)	Genetic epidemiology of influenza: A multinational pediatric initiative
Other Grants		
Principal Investigator	**Host Institution**	**Project Title**
VON MESSLING, Veronika	INRS - (Québec, QC)	Characterizing the potential and mechanism of type I interferons as influenza treatment

Summary

Significant progress has been made by CIHR-III in developing a research initiative to prepare for pandemic influenza. Successful applicants to the first request for applications for pandemic preparedness operating grants launched by CIHR-III in June 2006 were announced in February 2007, and critical research projects are underway. The PPSRI Task Group formed by CIHR-III worked with stakeholders over the summer of 2006 to quickly set strategic research priorities that have formed the basis of a second major round of requests for applications for pandemic preparedness research. To enhance the funding available for these grants, the CIHR-III approached and reached agreements with partners that have a mutual interest in influenza pandemic preparedness. The international research collaborations established and supported through the International Opportunities Program and the Team Grants will enhance linkages between Canadian and international researchers. This is important because the threat of an influenza pandemic is global. It is anticipated that the results from research that has been fostered and supported by the PPSRI and the continued activities of the Initiative will have significant outcomes that will help Canada and the rest of the world prepare for influenza outbreaks and a future pandemic.

Next Steps

CIHR-III and partners plan to establish a network of influenza researchers as part of the PPSRI. The Institute believes Canada must have this network in place and ready to respond to an influenza pandemic should one occur. The network will also help to build collaboration amongst influenza researchers and enhance research capacity in Canada. Members of the network will include successful recipients of pandemic preparedness research grants awarded by the CIHR and partners.

Appendix 1: CIHR Pandemic Preparedness Strategic Research Initiative Task Group

Mark Loeb (Chair), CIHR-III Advisory Board, Professor McMaster University

Expertise: Influenza epidemiology, Randomized controlled trials, Health services research, Population health, Influenza surveillance, Observational epidemiology, Pneumonia, Cohort studies

Earl Brown, Professor, University of Ottawa

Expertise: Influenza virus, Viral pathogenesis, Viral pneumonia, Viral genetics, Mouse models, Interferon response, Fusion, Receptor specificity, Influenza virus, RNA viruses, Molecular biology, Reovirus.

Robert Brunham, Director, Centre for Disease Control, University of British Columbia

Expertise: Epidemiology, Immunology of infectious diseases, Public health, Population biology, Mathematical modeling

Theresa Tam, Director, PHAC Centre for Infectious Disease Prevention and Control

Expertise: Influenza virus**,** Immunization**,** Vaccines**,** Epidemiology**,** Paediatrics**,** Vaccine preventable diseases**,** Infectious diseases**,** Influenza pandemic**,** Surveillance**,** Outbreak response**,** Emergency preparedness.

Ross Upshur, Director Primary Care Research Unit, Sunnybrook Health Sciences Centre

Expertise: Respiratory disease epidemiology, Primary care research, Public health ethics, Clinical ethics, Qualitative methodologies, Philosophy of medicine

Bhagirath Singh, (Ex Officio) CIHR Institute of Infection and Immunity (CIHR-III), Scientific Director

Appendix 2: Stakeholders Consulted to Finalize the PPSRI Priorities

Canadian Rapid Research Response Team (C3RT) Members

Lorne Babiuk, Chair, Institute Advisory Board, CIHR Institute of Infection and Immunity

Alan Bernstein, President, Canadian Institutes of Health Research (CIHR)

Judith Bossé, Vice-President, Science, Canadian Food Inspection Agency

Colleen Flood, Scientific Director, CIHR Institute of Health Services and Policy Research

John Frank, Scientific Director, CIHR Institute of Population and Public Health

Jean Marion, Director, Scientific Affairs, Rx&D (Canada's Research Based Pharmaceutical Companies)

Frank Plummer, Director General, Public Health Agency of Canada

Bhagirath Singh, Scientific Director, CIHR Institute of Infection and Immunity

Isaac Sobol, Chief Medical Officer of Health, Council of Chief Medical Officers of Health

Ernest T. Takafuji, Director, Office of Biodefense Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health

Aubrey Tingle, President, Michael Smith Foundation for Health Research

Michael Vandergrift, Director, Health Science Policy Division, Health Canada

C3RT Ad Hoc Members

Sandra Black, Senior Advisor Pandemic Influenza, Canadian International Development Agency

Dominique Charron, Director, International Development Research Centre

Arlene King, Director General for Pandemic Preparedness, Public Health Agency of Canada

Roland Levandowski, Section Chief, Influenza, SARS, and Related Viral Respiratory Diseases Section, Respiratory Diseases Branch, National Institute of Allergy and Infectious

Michael Mackey, Biomedical Sector Theme Leader, Mathematics of Information Technology and Complex Systems (MITACS) Network of Centres of Excellence

Earl Nowgesic, Assistant Director, CIHR Institute of Aboriginal Peoples' Health

Susan Richardson, Past President, Association of Medical Microbiology and Infectious Disease Canada

Elizabeth Stirling, KT Sector Specialist, CIHR Knowledge Translation Branch

Burleigh Trevor-Deutsch, Director, CIHR Ethics Office

Others

Althea House and Jennifer Gray, First Nations and Inuit Health Branch, Health Canada

Ben Schwartz, U.S. Center for Disease Control and Prevention

Harpreet S. Kochhar, Canadian Food Inspection Agency

Paul Gully, World Health Organization

Philip Schwab, BioteCanada

Ray Saginur et Tom Wong, Canadian Foundation for Infectious Diseases and Emerging Infectious Disease Research Network

Robert Pascal, Industry Canada

Shimian Zou, University of Ottawa and American Red Cross

Veronika von Messling, INRS-Institut Armand-Frappier