



INSTITUTE OF INFECTION AND IMMUNITY

ANNUAL REPORT 2003-2004



CIHR IRSC

Institut des maladies
infectieuses et immunitaires
Institute of Infection and Immunity

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Message from the Scientific Director

CIHR was created to be responsive to the health needs of Canadians. The Institute's efforts and successes in implementing this vision are an indicator of the success of CIHR, only four years after its creation. It is both an honour and a tremendous responsibility to coordinate the Institute's response to the emerging research challenges of Severe Acute Respiratory Syndrome (SARS), West Nile virus and mad cow (prion) diseases relating to a single BSE case in Canada, while maintaining the Institute's commitment to support and develop research in our other priority areas.

The appearance in Canada of the highly contagious and mysterious disease now known as SARS was a testing ground for the Institute. Underlining the need for a central clearinghouse of information and leadership in infectious disease, within the first month of SARS appearance in Toronto both the media and members of the infection and immunity communities - research, volunteer, industry and professional society - looked to the Institute of Infection and Immunity for information, guidance and partnership. The emergence of SARS has reminded us that the scope of new diseases is not finite. In order to fulfill its mandate of improved health for Canadians, more effective health services and a strengthened Canadian health care system, CIHR must demonstrate and maintain an ability to rapidly develop programs to invest in research critical to the under-

standing and control of novel viral diseases. To this end the Institute undertook the creation of the Canadian SARS Research Consortium (CSRC) that has engaged stakeholders in the coordination, promotion and support of SARS research in Canada. This resulted in the engagement of industry, voluntary health organizations and government departments in CIHR research programs. As we look to the future, the Institute is developing a Canadian Rapid Research Response Team (C3RT), a virtual network of stakeholders and global partners to be engaged if the need arises to develop rapid research responses to future infectious disease outbreaks. This will allow the Institute to develop better international links with many of our programs as infection and immunity research has global impact.

The Institute is working to fulfill its commitments to research in all priority areas. We are supporting a strategic initiative in Microbial Contamination of Food and Water and Antimicrobial Resistance in the Food Chain involving five federal departments. We have been closely involved in developing new research areas in HIV and hepatitis C, including socio-behavioural research. In addition, we have maintained our commitment to build and support our infection and immunity research communities through strategic funding for operating grants and pilot projects.



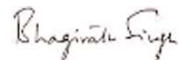
To make the Institute a living and breathing network, we continue to interact with the research community in all areas of our mandate, attending meetings, conferences and workshops and participating in direction-setting exercises across the country. In addition, the Institute hosted innovative events for the community including meetings in autoimmune and prion diseases. To create a forum for feedback and discussion, we also continue to meet with our research community in conjunction with our Institute Advisory Board (IAB) meetings across the country.

We thank our many partners over the past three years, whose interest and commitment in working with us to design and support research initiatives has increased the magnitude and potential impact of our programs and will contribute to the development of future initiatives. Our community continues to grow and to become more involved in the Institute's operation as evidenced by the strong response to our priorities and progress survey. We look forward to extending our communications with our stakeholder communities through electronic links.

In addition, I would like to thank everyone who has contributed to ensuring the Institute's vision for health research is realized, bringing us closer to alleviating the burden of disease. The IAB, composed of 16 highly successful and influential members of the infection and immunity communities, has been exceptional in assisting with the allocation of our resources over an ever-expanding range of research needs.

I would like to take this opportunity to sincerely thank the Institute staff and CIHR staff both in London and Ottawa for their dedication and commitment to the mission of the Institute; it has allowed us to excel during crises. I thank Dr. Lorne Babiuk for his continued leadership in his role as chair of the IAB. I am grateful to CIHR President Dr. Alan Bernstein for

his unwavering support for our Institute and his vision and leadership during the SARS crisis, and thank the CIHR Governing Council for its dedication to upholding the CIHR vision and our place in that vision. Finally, I would like to express my gratitude to Dr. Judy Bray for preparing this Annual Report in a professional manner.



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—Profile of the Institute

As one of the 13 Institutes of CIHR, the goals of the Institute of Infection and Immunity (III) align with the CIHR mandate of supporting and encouraging excellent, multidisciplinary research across the full spectrum of health research: basic, clinical, health services and policy, and the health of populations. III, like other CIHR Institutes, is responsible for identifying the research areas within the Institute mandate that would derive the greatest benefit from targeted research programs designed to build capacity, promote research in areas of identified need, provide innovative programs and create a culture of collaboration and partnership. An additional Institute responsibility, clearly demonstrated during 2003-2004, is the capacity to respond rapidly to infectious disease outbreaks, particularly those that are caused by new, emerging pathogens.

The Institute, located at the Siebens-Drake Research Institute at the University of Western Ontario, is supported by a small staff based both in London and Ottawa and has strong links to staff in other CIHR portfolios. This team, under the leadership of the Institute's Scientific Director, Dr. Bhagirath Singh, benefits from the advice and support of an excellent Institute Advisory Board (IAB). At meetings held three times a year, Institute staff and IAB members plan the Institute strategic agenda and liaise with researchers and community members at the regular receptions held during these meetings.

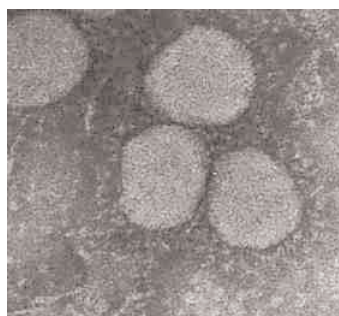
During 2003-2004, III was one of the most prolific of the CIHR Institutes in terms of media coverage and the Institute's Scientific Director was in great demand to speak on issues such as Canada's response to SARS and other emerging health threats. III also continued to produce its regular newsletter covering Institute events and achievements and was a contributing sponsor of 14 research workshops and symposia relevant to infection and immunity. Institute staff members attended these workshops whenever possible to represent Institute interests and identify potential opportunities for **partnership and public engagement**. These activities enabled III to reach out to both scientists and the general public.

III continues to strive for **organizational excellence** through the identification, development and evaluation of strategic research initiatives, the creation and maintenance of links with the research community, the identification and maintenance of partnerships, the support of an active communications strategy, and the ability to deal with the day-to-day issues that arise in the



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Institute's management. During 2003-2004, III created and managed the SARS Consortium, coordinated activities within the Safe Food and Water Coalition, took the lead on strategic research planning in HIV/AIDS through the creation of the CIHR HIV/AIDS Research Advisory Committee (CHARAC) and organized two major meetings, a conference on prion diseases and a symposium on autoimmunity.

III is committed to the support of the five CIHR strategic outcomes, described in the CIHR Blueprint document as **outstanding research, outstanding researchers in innovative environments, translating health research into action, effective partnerships and public engagement, and organizational excellence**. These five themes are represented in all III major research programs and initiatives and will be highlighted in this report.

Institute Strategic Research Priorities

Through a continuous process of discussion and consultation, both with the research community and the Institute Advisory Board, III continues to validate the relevance of the priority research areas identified during the Institute's inaugural year. III has identified two strategic research priority areas, infectious diseases and host response. Within each of these areas, the Institute has developed programs addressing the following specific priority areas, listed below in alphabetical order:

Infectious Diseases

- Antimicrobial Resistance
- Emerging Infectious Diseases
- HIV/AIDS and Hepatitis C
- Microbiologically Safe Food and Water
- Novel Vaccine Development

Host Response

- Asthma and Allergy
- Autoimmune Diseases
- Innate Immunity
- Organ Transplantation and Regeneration

During fiscal year 2003-2004, III was active in all these priority areas either through the development/funding of research initiatives, or community/capacity building among researchers and a wide variety of stakeholder organizations. The Institute was particularly active in those priority areas highlighted in this year's Annual Report.



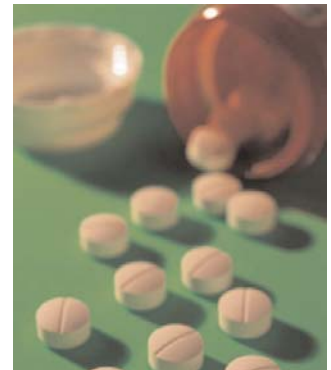
Infectious Diseases

Because of the fear provoked by infectious disease outbreaks and their potential for massive global impact, much of the Institute's effort during 2003-2004 focused on developing strategic research initiatives and programs to address emerging health threats caused by a variety of human pathogens, including those that cause food- and waterborne illness, SARS, HIV/AIDS and hepatitis C. However, research on host immunity is frequently embedded in projects focused on infectious disease. The ability of the host to overcome disease and respond to vaccines and treatment is governed in part by the effectiveness of cellular and humoral immune responses and levels of innate immunity.

—Antimicrobial Resistance

Antimicrobial resistance is becoming a major global crisis as increasing numbers of bacteria and viruses become unresponsive to traditional treatments. The rise in anti-bacterial resistance poses a serious health threat as many common pathogens are already demonstrating resistance to even the latest generations of antibiotic drugs. The problem has been exacerbated by the use of antibiotics in animal husbandry and agriculture, both to treat disease and as growth promoters. Many of the antibiotics used in agriculture are structurally related to classes of antibiotics used in humans, generating cross-resistance. Concomitant with this increasing drug resistance, industry is curtailing its investment in the discovery of new antibiotics, partly because of the rapidity with which resistance arises, but also because profit margins are larger for drugs taken on a continuous basis over the course of many years, such as those used to treat chronic conditions like arthritis and heart disease.

In 2003-2004, III addressed both areas of concern through funded projects under the Safe Food and Water initiative and also through the funding of two New Emerging Team (NET) programs focusing on clinical aspects of antimicrobial resistance. In the first of these, a team of **outstanding researchers** led by Dr. Mark Loeb, of McMaster University will investigate patterns of antimicrobial use and resistance in seniors housed in acute care, long-term care and community environments. This program, funded in **partnership** with the Institute of Aging (IA) will build research capacity to study optimum use of antimicrobials across the continuum of care for the elderly. In the second program, a team of **outstanding researchers** led by Dr. Michael Mulvey, of the National Microbiology Laboratory at Health Canada will study the patterns of antimicrobial resistance in northern Canadian communities. This project, funded in **partnership** with the Institute of Population and Public Health (IPPH), will specifically investigate methicillin-resistant *Staphylococcus aureus* to determine risk factors and antimicrobial prescribing patterns.



The rise in anti-bacterial resistance poses a serious health threat.

— Emerging Infectious Diseases

Severe Acute Respiratory Syndrome (SARS)

The SARS outbreak of early 2003 took the world by surprise and provided a global wake-up call in terms of how we deal with infectious disease outbreaks in the 21st century. For Canada, the impact of SARS on the public health system, particularly in Toronto, prompted the entire health care community to re-examine its infection control practices and public health policies. Despite the international crisis, compounded initially by the unknown nature of the pathogen, and although battered both from the adverse economic effects and the public health consequences, Canada emerged better prepared for similar crises in the future. SARS precipitated the formation of a new agency, the Public Health Agency of Canada, and an increased awareness of the actions necessary to address weaknesses in our public health care system. Together, these will result in an improved level of preparedness for the next infectious disease outbreak.

Table 1

Projects funded under the 'Host Response to Severe Acute Respiratory Syndrome' RFP		
Team Lead	Host Institution	Title of Project
Bergeron, M.	Centre hospitalier de l'Université Laval	The development of a rapid multiplex SARS assay
Dennis, J.	Samuel Lunenfeld Research Institute and University of Toronto	Molecular markers of immunity and outcome for SARS
Loeb, M.	McMaster University	Towards an understanding of SARS: The Canadian SARS Research Network
Skowronski, D.	University of British Columbia	SARS: A scientific collaboration to support public health response through vaccination

SARS was a problem that spanned all areas of health research and the solution required unprecedented collaboration and coordination among Canadian researchers, clinicians, hospital administrators, the Canadian public and provincial and federal government officials at all levels. The research requirements were such that Canada's research funding agencies were ill equipped to provide adequate research funding in the necessary time frame. IHI assumed the lead in orchestrating a rapid research response unprecedented in Canadian health research. The Institute took advantage of its development budget to launch a request for proposals (RFP) in April 2003, entitled "Host Response to Severe Acute Respiratory Syndrome". Eighteen

applications were received within two weeks and were peer reviewed in the record time of just three weeks. Four teams of **outstanding researchers**, comprising more than 30 of Canada's top scientists, received one year funding in May 2003 (Table 1).



Table 2

Members of the Canadian SARS Research Consortium
Aventis Pasteur
Canadian Institutes of Health Research
Canadian Lung Association
Canadian Network for Vaccines and Immunotherapeutics
Fonds de la recherche en santé du Québec
GlaxoSmithKline
Health Canada
Mathematics of Information Technology and Complex Systems
Michael Smith Foundation for Health Research
Ontario Research and Development Challenge Fund
Protein Engineering Network of Centres of Excellence

To fund the four successful projects described in Table 1, collectively worth \$1.7 million, III once again took the lead by engaging partners to collaborate on the support of the SARS research response. A **partnership** was formed between III, the Ontario Research and Development Challenge Fund, the Canadian Network for Vaccines and Immunotherapeutics, le Fonds de la recherche en santé du Québec and Health Canada. As a further example of the effectiveness of CIHR Institutes in mobilizing both the research community and stakeholder organizations to collaborate in research planning, co-ordination and funding, III went on to form the Canadian SARS Research Consortium (CSRC). CSRC was created to coordinate, promote and support SARS research in Canada through a focus on diagnostics, vaccine development, therapeutics, epidemiology and databases, and public health and community impact. Members of the Consortium are listed in Table 2.

The CSRC has met regularly by teleconference throughout the year to monitor the progression of SARS research, facilitate the distribution of SARS samples, establish national research platforms and provide information and advice to national public health bodies and the media.

Within weeks of the eruption of the SARS crisis in Canada, a team of 58 Canadian researchers was the first to publish the genome sequence of the human coronavirus believed to cause SARS. In a further example of **outstanding research**, the SARS teams funded by III and partners began producing results in the areas of diagnostics, pathology, modeling, host immune response, immunopathogenesis, treatment and vaccination. One team of **excellent researchers** led by Dr. James Dennis at the University Health Network in Toronto evaluated the clinical benefit and safety of the anti-viral drug Infergen (interferon alfacon-1) in SARS treatment. Another group led by Dr. Jack Gaudie at McMaster University, in collaboration with researchers from the SARS Vaccine Initiative (SAVI) of British Columbia, developed two potential SARS vaccines, currently being tested in mice and ferrets.



Canadian researchers were the first to publish the genome sequence of the human SARS coronavirus.

In a further example of **partnership and public engagement**, a Request for Applications (RFA) entitled "Public Health and Health Preparedness and Response to Severe Acute Respiratory Syndrome (SARS): Evaluation and Lessons Learned" was launched in September 2003. The purpose of this RFA was to assess the effects of SARS on the Canadian public health and health care systems. The control measures taken to contain the SARS outbreak had economic, social, ethical, psychological, legal and health-related consequences for the affected populations that extended way beyond the infected patient population. This research initiative was designed to address ways to improve the response to, and mitigate the effects of, future infectious disease outbreaks on the Canadian public health and health care systems. Launched by IPPH, partners included III, the Institute of Health Services and Policy Research (IHSPR), the Institute of Circulatory and Respiratory Health (ICRH) and the Canadian Lung Association. The ability of the CIHR Institutes to rapidly form the partnerships necessary to address the SARS crisis from the perspective of all domains of health research is a prime example of the versatility of the CIHR model in responding to health challenges.

Canadian Rapid Research Response Team (C3RT)

As a result of the SARS crisis and to build on partnerships already created, III once again took the lead in planning the creation of a rapid research response team drawn from Canadian and international infectious disease experts. C3RT will be responsible for maintaining a database of scientists who can be called upon to advise on the need to launch a rapid research response to new infectious agents. C3RT will also assist in coordinating the mobilization and funding of a national rapid research effort.



The ability of the CIHR Institutes to rapidly form the partnerships necessary to address the SARS crisis from the perspective of all domains of health research is a prime example of the versatility of the CIHR model in responding to health challenges.

C3RT was discussed at the January 2004 Institute Advisory Board meeting in Quebec City.



UBC Training Program for Translational Research in Infectious Diseases

One of the three strategic training programs funded by III in 2003 focused on translational research in infectious disease, led by Dr. Anthony Chow (Table 6, page 21). In response to the increasing challenges posed by the re-emergence of “old” diseases such as anthrax, tuberculosis and smallpox, either as potential biological weapons or multi-drug resistant organisms, and the emergence of new pathogens such as SARS, this **outstanding team of researchers** will recruit and train future leaders in the fields of infectious diseases, microbiology, communicable disease epidemiology and public health.

Priority Announcement on Emerging Infectious Diseases

Although CIHR already funds **outstanding research** in infectious disease through its regular grants programs, there is currently no priority given to research projects involving emerging pathogens. In a proactive move, III issued a priority announcement calling for innovative three-year projects that focus on new and emerging infectious agents and the diseases they cause. The best of these projects will be funded by CIHR as part of the regular operating grants funding, giving III the opportunity to support additional excellent research that falls below the CIHR funding cut-off. Ongoing research and capacity building in this area are likely to increase Canada’s ability to respond to new health crises caused by infectious agents.

Grand Challenges in Global Health

III supplied application development grants to teams of **outstanding researchers** responding to the call for applications issued by the Bill and Melinda Gates Foundation on Grand Challenges in Global Health, most of which related to infectious diseases. With the assistance of IPPH and the Institute of Gender and Health (IGH), III offered to support 15 projects that were successful at the Letter-of-Intent stage and approved to progress to full application.



Ongoing research and capacity building in the area of emerging infectious diseases are likely to increase Canada’s ability to respond to new health crises caused by infectious agents.

—HIV/AIDS and Hepatitis C

HIV/AIDS

Worldwide, HIV/AIDS continues to be an escalating health, social and economic problem, particularly in Africa and Asia, causing millions of deaths every year. In Canada, the overall incidence of HIV/AIDS and HIV/AIDS-related deaths among the general population has plateaued. Despite this trend however, there

has been an alarming increase in infection rates in certain populations, such as aboriginal youth and intravenous drug users. Research is the key to the successful prevention and treatment of HIV/AIDS and the results of decades of **excellent research** have, for many infected people, transformed HIV/AIDS from a certain death threat into a chronic, manageable disease.



Dr. Karl Tibelius and Ms. Jennifer Gunning of CIHR attend the Canadian Association for HIV Research (CAHR) 2003 annual meeting in Halifax, Nova Scotia.

In 1988, the Canadian Strategy on HIV/AIDS (CSHA) was established by the federal government and supported by an annual, budget of \$42.2 million. The CSHA was created to address a comprehensive range of HIV/AIDS-related issues, with research being a major component. The CSHA encompasses community organizations, Aboriginal groups, the private sector, academia, health and social service providers, governments and people living with HIV/AIDS. CIHR has a partnership with Health Canada under the CSHA and has the administrative responsibility for the biomedical,

clinical, health services and population health research programs and the Canadian HIV Trials Network.

This **partnership** has been very effective in promoting innovative research and attracting **excellent researchers** to the field. In 2003-2004, the CSHA funds supported a total of 93 research grants, 3 group grants, 5 randomized controlled trials, 15 salary awards and 46 training awards. Examples of some of the **outstanding research** occurring in Canadian laboratories include the work of Dr. Julio Montaner from the University of British Columbia on the optimal time to begin HIV treatment; the development of a vaginal gel containing microbicide as a preventive measure, by Dr. Michel Bergeron of Laval University; the testing of the effectiveness of a new drug, originally developed for cancer treatment, in the treatment of HIV-associated dementia, by Dr. Chris Power of the University of Calgary; the studies of Dr. Mark Wainberg on ways to counteract the growing resistance to antiretroviral therapy; and studies on the effectiveness of innovative combination drug therapy being conducted by Dr. Jonathon Angel of the University of Ottawa.

Internationally, CIHR has been active through its Global Health Research Initiative. This **partnership**, currently funding 13 health research HIV/AIDS projects, is a collaboration with the Canadian International Development Agency, the International Development Research Centre and Health Canada.

CIHR HIV/AIDS Research Advisory Committee (CHARAC)

From the beginning, III recognized HIV/AIDS as an important research priority and assumed the responsibility for identifying strategic research priorities for HIV/AIDS. In 2003-2004, III established the CIHR HIV/AIDS Research Advisory Committee (CHARAC) as a sub-committee of the Institute Advisory Board and held the first meeting of the newly formed committee in November 2003. CHARAC brings together researchers from all areas of health research, five CIHR Institutes, community representatives, Health Canada and the Ministerial Council on HIV/AIDS. The inaugural chair of the committee is Dr. Michel Bergeron, the vice-chair of the III Advisory Board. CHARAC will advise III and CIHR on appropriate research initiatives that address identified priorities. In consultation with CIHR staff, III will plan and deliver strategic research initiatives based on the recommendations of CHARAC. This committee is another example of **effective partnerships and public engagement** applied to an extremely complex health issue in order to develop appropriate research strategies through national coordination. Members of the CHARAC Committee for 2003-2004 are listed in Table 3.

Table 3

Members of CHARAC in 2003-2004	
Member	Affiliation
Michel Bergeron, chair	IAB, Institute of Infection and Immunity
Jonathan Angel	Researcher, University of Ottawa
Paula Braitstein	HIV/AIDS Community Representative
Liviana Calzavara	Researcher, University of Toronto
Catherine Hankins	IAB, Institute of Population and Public Health
René Lavoie	Ministerial Council on HIV/AIDS
Earl Nowgesic	Assistant Director, Institute of Aboriginal Peoples' Health
Christopher Power	Researcher, University of Calgary
Rémi Quirion	Scientific Director, Institute of Neurosciences, Mental Health and Addiction
Paul Sandstrom	Director, National HIV and Retrovirology Laboratories, Health Canada
Martin Schechter	IAB, Institute of Health Services and Policy Research
Robb Travers	HIV/AIDS Community Representative
Mark Wainberg	Researcher, University of McGill
Ex officio	
Bhagirath Singh	Scientific Director, III
Jennifer Gunning	Team Lead, HIV/AIDS Research Program CIHR
Bruce Moor	Assistant Director, III
Karl Tibelius	Director, Research Capacity Development CIHR

Hepatitis C

Hepatitis C is probably best known as an infection resulting from contaminated blood transfusions, but more recently hepatitis C has become prevalent among high-risk or socio-economically disadvantaged populations, such as prison inmates, aboriginal youth and intravenous drug users. Infection with the hepatitis C virus generally leads to development of chronic disease characterized by liver cirrhosis, leading to liver failure and/or liver cancer. It is estimated that almost 1% of Canadians are infected with hepatitis C and, despite a latent period of up to 30 years, up to a third of infected individuals eventually die of the disease.

In recent years, hepatitis C research has benefited from the funding provided by the Health Canada/CIHR Research Initiative on Hepatitis C, a **partnership** designed to build research capacity in Canadian hepatitis research in areas such as pathogenesis, modes of transmission, treatment, access to care and prevention through interventions in risk behaviours. One example of the **excellent research** being conducted is that of Dr. Denis Leclerc's laboratory at the University of Laval, where researchers have produced a new tool to study the assembly of hepatitis C virus in yeast. Dr. Leclerc's team is also working on using the papaya mosaic virus as a potential powerful adjuvant in the preparation of vaccines against hepatitis C.

In conjunction with the Joint Advisory Committee for Hepatitis C research, III continues to work to identify strategic research priorities in hepatitis C and to encourage research applications to regular CIHR programs and relevant Institute RFA. III is also contributing to the strategic planning for a renewed Health Canada/CIHR Hepatitis C Initiative that will stimulate hepatitis C research and lead to the development of a National Hepatitis C Prevention/Care/Research Outcomes Network.

In 2003-2004, III funded a strategic training program, focussed on hepatitis C led by Dr. Elizabeth Heathcote at the University Health Network in Toronto (Table 6, page 21). This team of **outstanding researchers** spans a number of disciplines, including basic, clinical and social sciences research. Their network will recruit and train students to address the diverse and complex issues posed by chronic hepatitis C.

It is estimated that almost 1% of Canadians are infected with hepatitis C and, despite a latent period of up to 30 years, up to a third of infected individuals eventually die of the disease.



In June 2003, III launched an RFA entitled “Social and Behavioural Research Issues in HIV/AIDS and Hepatitis C”. This RFA was developed in response to an identified need to address fundamental gaps in knowledge related to the implementation and maintenance of positive behavioural changes in population groups at highest risk of acquiring both HIV/AIDS and hepatitis C. These objectives will be realized through the Interdisciplinary Capacity Enhancement (ICE) Teams Program, a program specifically designed to increase research capacity, encourage multidisciplinary research and promote the integration of **knowledge translation** to ensure the immediate application and uptake of research findings. This initiative is supported by the CIHR/Health Canada HIV/AIDS Research Program, the Canadian Strategy on HIV/AIDS and the Health Canada/CIHR Research Initiative on Hepatitis C.

In **partnership** with a total of five other CIHR Institutes, III has supported a number of strategic research programs and Requests for Applications (RFAs) related to HIV/AIDS and hepatitis C including HIV/AIDS RFA, Global Health Research Pilot Project Grants, Global Health Research Program Development and Planning Grants and Improving Access to Appropriate Services for Marginalized Groups.

—Microbiologically Safe Food and Water

Safe Food and Water Initiative

Food- and water-borne illness represents a significant health threat for Canadians. In addition to the short- and long-term health effects of such illnesses, there is also a substantial cost to the Canadian economy in terms of work days lost and the potential impact of a contamination incident on international trade. These points have been well illustrated in Canada, by outbreaks of water contamination such as occurred in Walkerton, by numerous food-borne outbreaks and, more recently by the finding of a single cow with bovine spongiform encephalitis (BSE), better known as ‘mad cow disease’. It has been estimated that more than 200 known diseases are caused by food- and/or water- borne transmission of pathogens or their toxins. In reality, this number is likely much higher as the causative agent is often never identified. Because of changing patterns in demographics, globalization, emerging pathogens and antimicrobial use in agriculture, food- and/or water-borne illness is likely to become an increasing problem. In order to best protect our food and water supplies, strategic national food and water safety policies need to be developed that are flexible enough to respond to changing conditions and that are based on the latest scientific evidence.



Dr. Krystyna Miedzybrodzka, Dr. Lorne Babiuk and Dr. Bhagirath Singh at the 2003 Safe Food and Water Annual Meeting.

Prior to the creation of CIHR a series of opportunities workshops were funded to provide research recommendations in priority areas likely to be of interest to the newly created Institutes. One of these, led by Dr. Brett Finlay of the University of British Columbia, focused on the microbial contamination of food and water and the use of antimicrobials in agriculture. Based on the recommendations coming out of this workshop, III took a leadership position in the development of multiple **partnerships** with both the government and private sector to coordinate a national research agenda on microbiologically safe food and water. The result was the creation of a 17-member Canadian Research Coalition for Safe Food and Water. In 2003-2004 an additional organization, Aquanet – one of the Networks of Centres of Excellence – joined the Coalition, bringing the number of members to 18 (Table 4).

Table 4
Members of the Canadian Research Coalition for Safe Food and Water

Aquanet
Agriculture and Agri-Food Canada
Canadian Agri-Food Research Council
Canadian Aquaculture Industry Alliance
Canadian Bacterial Diseases Network
Canadian Cattlemen's Association
Canadian Food Inspection Agency
Canadian Institutes of Health Research
Canadian Pork Council
Canadian Veterinary Medical Association
Canadian Water Network
Chicken Farmers of Canada
Dairy Farmers of Canada
Environment Canada
Genome Canada
Health Canada
National Research Council of Canada
Natural Sciences and Engineering Research Council

In May 2002, following a series of meetings, the Coalition launched its first RFA, a Needs, Gaps and Opportunities Assessment, funded by III, the Canadian Water Network (CWN) and the Natural Sciences and Engineering Research Council (NSERC). The one funded project, led by Dr. Mansell Griffiths of the University of Guelph, produced a comprehensive document entitled “Microbial Risk Assessment as a Foundation for Informed Decision Making”, released in March 2004.

In December 2002, the five federal department members of the Coalition, Agriculture and Agri-food Canada, Environment Canada, Canadian Food Inspection Agency, Health Canada and the National Research Council formed a **partnership** with III to launch the second RFA, entitled “Microbial Contamination of Food and Water and Antimicrobial Resistance in the Food Chain-Phase II – Establishing a Framework”. One of the primary goals of this RFA was to promote the formation of new research teams, or to expand existing teams, in which academic and federal government-funded researchers would combine their skills and resources in order to more efficiently and effectively address important research questions.



This initiative achieved its goal of bringing together **excellent researchers** from two very different worlds, university and government research laboratories. From the 24 full applications received, seven were funded in February 2004. Each of the seven teams comprises a mix of university and government scientists from a total of ten universities and five different government departments. The projects are summarized in Table 5.

The Safe Food and Water Initiative, led by III, is one of the best examples of the role of the CIHR Institutes in changing the nature of collaborative research through **partnership**. By combining the expertise and experience of researchers from diverse backgrounds, it has been possible to create new research teams that span the country and combine the strengths of both university and government environments. Innovative teams of **excellent researchers** such as those funded in this initiative add new perspectives to addressing research problems and **translating research into action** by facilitating the uptake of results by government policy makers, setting an example for other countries striving to achieve the same goal.

Table 5

Projects Funded Under the Safe Food and Water Initiative		
Team Lead	Host Institution	Title of Project
Cashman, Neil	University of British Columbia	The Canadian Prion Disease Network: Meeting the challenge
Issac-Renton, Judith	University of British Columbia	Safe Drinking Water Through Source Surveillance: Assessing impacts of environmental factors and microbial contamination of watersheds on community health
Karmali, Mohammed	University of Guelph	Comparative pathogenesis and public health significance of verocytotoxin-producing <i>Escherichia coli</i> serotypes
Louie, Marie	Sunnybrook and Women's College Health Sciences Centre	Prospective multi-province surveillance for antimicrobial-resistant <i>Escherichia coli</i> in drinking and recreational source waters: Impact on humans and the environment
Mazumder, Asit	University of Victoria	Source tracking and environmental determinants of coliform bacteria in source water under various land-use in British Columbia
Sad, Subash	University of Ottawa	Modulation of immunity and development of therapeutics against <i>Salmonella</i>
Taylor, Diane	University of Alberta	Pathogenesis and antibiotic resistance in <i>Campylobacter</i>

The creation and continued management of the Coalition by III serves as another example of **organizational excellence**. In October 2003, the Coalition held its third annual meeting to update members on the progress of the Safe Food and Water Initiative and to plan for future projects. To our knowledge, this is the only group of its kind that has so many diverse member organizations working towards a common research goal in the area of food and water safety. It is an excellent vehicle for the coordination of research and the setting of a national research agenda.

Travelling Museum Exhibit – Food for Health

Food- and water-borne pathogens can emerge at any point in the food chain starting with the agricultural environment in which the food is grown, continuing through harvesting, processing and packaging procedures to storage, retail and food handling methods. In addition, the continuum from watershed to tap provides many opportunities for the introduction of pathogens to the water supply. This may, in turn, have implications for the food supply chain. Consumer knowledge and practice, in the handling and preparing of food plays a significant role in food safety and food-borne illness. There is, therefore, a need for public education, taking the results of the research on food- and water-borne illness and **translating this research into action** by applying it to public practice.

As part of a broader education and outreach program, III is a major supporter of a travelling museum exhibit with a working title of “Food for Health”, currently being developed by the Canada Agriculture Museum. III was instrumental in developing the partnership of sponsors for this exhibit which includes four CIHR Institutes and seven members of the Canadian Research Coalition for Safe Food and Water. During 2003-2004, work began on the project brief and the interpretive plan. The exhibit is scheduled to open at the Canada Agriculture Museum in Ottawa in March 2006 and, over the following four years, will travel to many venues across Canada, including Canada’s major agricultural fairs. It will serve as an educational outreach tool that will reach millions of children and their families across Canada with information and practical advice on food safety and the links between diet, exercise and susceptibility to chronic diseases such as diabetes, heart disease and cancer.

Meeting the Challenge of Prion Diseases

In September 2003, in **partnership** with Health Canada and IPPH, III organized a conference entitled “Meeting the Challenge of Prion Diseases”. This international meeting brought together researchers, clinicians and decision-makers from universities, institutions and governments in Canada, the United States and Europe. The conference was followed by an invitational research planning workshop which examined needs, gaps and opportunities in Canadian research related to prions and prion diseases. Many of the workshop recommendations were used in drafting the call for applications for a Network of Centres of Excellence (NCE) on prion diseases.



The 2003 Prions conference was held at the Hotel MacDonald in Edmonton, Alberta.

—Novel Vaccine Development

The topic of vaccine development overlaps with many of the Institute's research priorities including efforts to develop vaccines against SARS and HIV/AIDS, and vaccines to induce mucosal immunity, the topic of a research program funded by III in 2002. One excellent example of the **outstanding research** in this area is that of a team of investigators led by Dr. Brett Finlay of the University of British Columbia and funded in part by CIHR, who have developed a vaccine that could significantly reduce human disease associated with E. coli outbreaks. The vaccine, when given to cattle, significantly reduces the level of E. coli O157 shedding into the environment.

III has been actively engaged in the preparation of a request for funding for the National Immunization Strategy and is a strong supporter of collaborative research in the area of vaccine development, working with many groups and organizations, including industry, to promote national coordination and to engage in international partnerships where appropriate.

Host Response

—Asthma and Allergy

III has been active in previous years in the area of asthma and allergy through the funding of NETs and Strategic Training Programs. During 2003-2004, the Institute paused to take stock of results achieved and to decide on future directions that will build on research projects previously funded. IAB members with a strong interest in this area of research have committed to working with III staff to develop a strategic research initiative for launch in 2004 that will focus on host immunity and increase our understanding of the causes and underlying disease mechanisms responsible for the onset of asthma and allergies.

—Autoimmune Diseases

Autoimmune disease occurs when the cells of the body's immune defense system attack normal tissues, organs and cells causing inflammation and damage. There are more than 80 diseases that involve autoimmune responses, including multiple sclerosis, rheumatoid arthritis, lupus erythematosus and type 1 diabetes. Autoimmune diseases can strike at any time in the life span and are more prevalent in women. Many of the diseases are chronic and debilitating and, although some can be treated symptomatically, few have been cured. It is thought that the onset of autoimmunity in a genetically predisposed individual is triggered by extraneous environmental factors such as infectious agents. Autoimmune diseases tend to cluster, so that a given patient may have more than one disease and members of the same at-risk family may present with a variety of different diseases. The recent revolution in molecular biology has created new research platforms that offer the potential for improved understanding of the causes and biological processes involved in many diseases including autoimmune diseases.

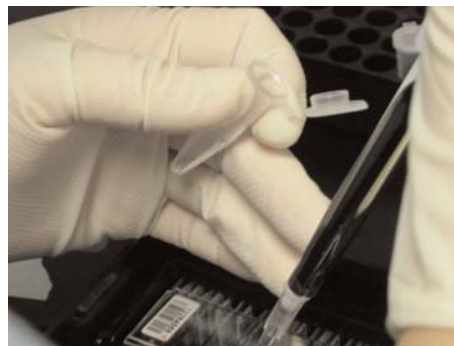
In December 2003, III organized a research symposium, entitled “Integrating Discovery Platforms in Autoimmune Diseases”, which was designed to develop a framework for a Canadian health research agenda in autoimmune diseases. The focus of the symposium was on the examination of the basic mechanisms leading to these diseases and investigation of the commonalities between them. This meeting brought together national and international researchers, health policy makers and representatives from voluntary associations. The Institute is now working to develop partnerships with a view to developing a research initiative in this area during 2004-2005.

Also in 2003-2004, III **partnered** with the Institute of Neurosciences, Mental Health and Addiction (INMHA) on a strategic training program entitled “Integrated Training Program in Basic and Clinical Aspects of Neuroinflammation” (Table 6, page 21) that focuses on multiple sclerosis. This team of basic and clinical researchers brings together expertise in genomics, proteomics, immunology, biochemistry, neurobiology and population biology.

—Innate Immunity

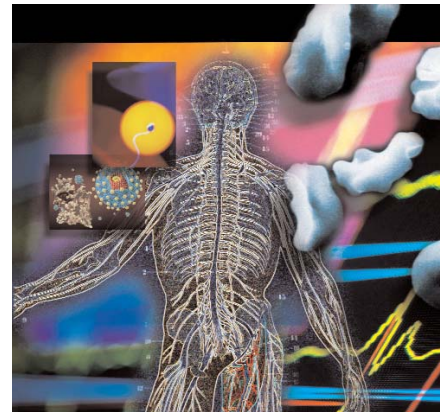
Although III did not launch or fund any research initiatives in 2003-2004 that specifically focused on innate immunity, this topic is important to many III-funded projects and initiatives currently under development. For example, innate or natural immunity plays a large part in resistance to all infectious diseases, in susceptibility to autoimmune diseases, in the development of asthma and allergy and also in organ transplantation and tissue regeneration. It is also an important element in the host response to cystic fibrosis and, in 2003, III participated in a \$6 million research program on cystic fibrosis entitled Basic Research and Therapy (BREATHE), launched in **partnership** with the Canadian Cystic Fibrosis Foundation and ICRH. Innate immunity is, therefore, an extremely broad subject with relevance to most, if not all, of the Institute research priorities and will likely become the focus of future initiatives.

In 2003, III participated in a \$6 million research program on cystic fibrosis entitled Basic Research and Therapy (BREATHE), launched in partnership with the Canadian Cystic Fibrosis Foundation and ICRH.



— Organ Transplantation and Regeneration —

During 2003-2004, III addressed the topic of organ transplantation and regeneration primarily through **partnerships**. III was a partner in the launch of the CIHR multi-Institute strategic initiative entitled “Regenerative Medicine: Innovative Approaches to Health Research”. Regenerative medicine is a field that is poised to take advantage of recent advances in stem cell technologies, nanotechnology, imaging and transplantation. **Outstanding research** already ongoing in this area has provided the first evidence that adult stem cells can induce pancreatic tissue to repair itself, restoring normal insulin production and reversing symptoms associated with diabetes. The study was done by a team of international scientists led by Dr. Mick Bhatia from the Robarts Research Institute at the University of Western Ontario. The integration of this new science into multidisciplinary research has tremendous implications for health research in the 21st century, through the repair or replacement of damaged tissues and organs. Six CIHR Institutes, including III, and nine external organizations with a shared interest in regenerative medicine and nanotechnology came together on the launch of this initiative. Three different funding tools were offered to meet the diverse needs of the research community and several similar Institute RFA with similar objectives were linked to the initiative, including an RFA launched by III, entitled “Novel Technology Applications in Health Research”. This initiative was in response to an increasing demand for research that crosses traditional boundaries and disciplines and facilitates the application of technologies from fields such as mathematics, physics, computational science, nanotechnology and chemistry to the traditional life sciences. The program is designed to create small multidisciplinary teams that will integrate expertise from the natural sciences into biomedical research and enhance our understanding of the molecular basis of disease.



In the area of transplantation, III joined the Kidney Foundation of Canada and the Canadian Society of Transplantation in a **partnership** created to support clinical research fellowships. This program will provide up to three years of support for full-time, postdoctoral training in the kidney transplantation field. The objective of the program is to promote and enhance the development of clinician scientists involved in basic and clinical kidney transplantation research.

III also **partnered** with the Institute of Human Development, Child and Youth Health (IHDCYH) to fund a NET program, entitled “Pancreatic Islet Generation from Human Stem Cells”, which will provide a training program for basic and clinical students and fellows in regenerative medicine and diabetes.

Table 6

Strategic Training Programs Funded by III in 2003-2004			
Principal Investigator(s)	Title of Project	Host Institution	Institute(s)/ Partner(s)
Antel, Jack	Integrated Training Program in Basic and Clinical Aspects of Neuroinflammation	McGill University	III INMHA FRSQ
Chow, Anthony	UBC Training Program for Translational Research in Infectious Diseases	University of British Columbia	III
Heathcote, Elizabeth Jane Lindsay	A National Hepatitis C Research Training Program Grant	University Health Network (Toronto)	III Health Canada (Hepatitis C Initiative)

Additional Institute Achievements in 2003-2004

— Capacity Building

III retains its commitment to training the next generation of health researchers. In 2003-2004, the Institute funded an additional three strategic training programs (Table 6) that fell within the Institute’s mandate, bringing the total to 14 strategic training programs receiving funding from III either as the lead Institute or in partnership with other Institutes and external organizations.

— Community Development

In support for infection and immunity researchers, III provided bridging funding to many excellent fundable, but unfunded operating grants and multi-user equipment and maintenance grants in the areas of the Institute research mandate. This funding frequently contributes to a successful outcome on the resubmission of a grant proposal to a subsequent competition and helps to ensure the continuity of high-quality research programs.

In June 2003, as an example of III’s commitment to the support and encouragement of young investigators in the fields of infection and immunity, the Institute launched an RFA entitled “Pilot Project Grants for New Investigators”. These pilot project grants are intended to support innovative pilot or feasibility research by new investigators in their first five years of an academic appointment. Grants are for a maximum of \$100,000 for one year and will encourage new investigators to further develop their research skills with a goal of obtaining future long-term funding from regular or Institute- specific funding programs. The strong response to the RFA confirmed the need for programs designed to support the early career development of Canada’s **excellent researchers**. Of the 65 applications received, 25 were approved for funding (Appendix 1, page 23-24).



Appendices

—Appendix 1









Projects Funded under the Pilot Projects for New Investigators RFA		
Principal Investigator	Institution Name	Project Title
Ashkar, Ali	McMaster University	Study of human leukocyte function in alymphoid RAG-2/gamma chain null mice in response to human viral infections and cancer
Booth, James	Sunnybrook and Women's College Health Sciences Centre	Cell biology of toll-like receptors
Burrows, Lori	Hospital for Sick Children (Toronto)	Peptidoglycan synthesis and bacterial biofilm formation
Burshtyn, Deborah	University of Alberta	Vaccinia virus modulation of natural killer cells
Cousineau, Benoît	McGill University	Development of a new generation of live vaccines using <i>Lactococcus lactis</i>
Fowke, Keith	University of Manitoba	The role of immune activation and CD4 gene polymorphisms in an HIV seroconversion cohort from Kisumu, Kenya
Glogauer, Michael	University of Toronto	Non-invasive oral rinse assay (NORA) to monitor neutrophil tissue delivery: monitoring susceptibility to infection in neutropenia, neutrophil-related disorders and patients recovering from bone marrow transplantation
Granville, David	St. Paul's Hospital, Vancouver	Protease inhibitor-9/serine protease inhibitor-6: role in heart transplant rejection
Grunebaum, Eyal	Hospital for Sick Children (Toronto)	Correcting purine nucleoside phosphorylase (PNP) deficiency in mice by intracellular delivery of human PNP combined with the HIV-TAT protein transduction domain
Guttman, David	University of Toronto	Functional screen for <i>Pseudomonas aeruginosa</i> type III secreted effector proteins
Heinrichs, David	University of Western Ontario	Methodologies to investigate Gram-positive bacterial pathogenesis
Johnston, Brent	Dalhousie University (Nova Scotia)	Role of the chemokine receptor CXCR6 in inflammatory autoimmune disease
Labrecque, Nathalie	Hôpital Maisonneuve-Rosemount (Montreal)	Regulation of hematopoiesis and memory T cell generation by interleukin-21



—Appendix 1









Projects funded under the Pilot Projects for New Investigators RFA		
Principal Investigator	Institution Name	Project Title
Levings, Megan	University of British Columbia	T regulatory cells in Toxoplasma pathogenesis
Liang, Chen	Sir Mortimer B. Davis Jewish General Hospital	Understanding of the interactions between viral vif protein and a cellular factor APOBEC3G: implications for future HIV/AIDS therapies
MacPherson, Paul	Ottawa Health Research Institute	Down regulation of the interleukin-7 receptor on circulating CD8 t-cells during HIV infection
Marshall, Aaron	University of Manitoba	Role of novel signal transduction molecules in regulating the activation and production of allergic mediators by mast cells
Mui, Alice	Vancouver General Hospital	Immunotolerance therapy for transplantation
Neumann, Norman	University of Calgary	Development of advanced multiplexed diagnostic tools for the detection and molecular characterization of waterborne pathogens
Provost, Patrick	Centre hospitalier de l'Université Laval	Significance of the interaction between Dicer and 5-lipoxygenase
Stanford, William	University of Toronto	Sca-1 signalling in hematopoietic stem cells
Vergnolle, Nathalie	University of Calgary	Cleavage of proteinase-activated receptor-2 by proteinases from intestinal pathogens of the escherichia coli family modulates the host inflammatory response
Von Dadelszen, Peter	B.C. Women's Hospital (Vancouver)	The role of Chlamydomphila pneumoniae and cytomegalovirus in pre-eclampsia: a link between pre-eclampsia and later atherosclerosis
Wan, Yonghong	McMaster University	Development of safe and effective genetically engineered dendritic cell-based tuberculosis vaccines
Woo, Minna	Ontario Cancer Institute (Toronto)	Caspase 8 and autoimmune islet destruction

—Appendix 2

Institute Advisory Board of the Institute of Infection and Immunity		
	Dr. Lorne Babiuk (Chair)	Director, Vaccine and Infectious Disease Organization; Professor, Department of Veterinary Microbiology, University of Saskatchewan
	Dr. Michel G. Bergeron (Vice-Chair)	Professor and Director, Division of Microbiology and Infectious Diseases Research Center, University of Laval
	Dr. Chris Bleackley	Professor, Department of Biochemistry, University of Alberta
	Dr. Joseph Cox	Assistant Professor, Family Medicine, McGill University; Public Health Specialty, Montreal Regional Public Health Department
	Dr. Abdallah Daar	Director, Program in Applied Ethics and Biotechnology, Public Health Sciences and Surgery, University of Toronto
	Dr. B. Brett Finlay	Professor, Biotechnology Laboratory, University of British Columbia
	Dr. Jack Gauldie	Professor and Chairman, Department of Pathology and Molecular Medicine, McMaster University
	Dr. Kevin Glasgow	Assistant Clinical Professor, Department of Family Medicine, McMaster University; CEO, Cardiac Care Network of Ontario



—Appendix 2

Institute Advisory Board of the Institute of Infection and Immunity		
	Dr. Warren Hill	Executive Director, Canadian Viral Hepatitis Network; Senior Research Analyst, B.C. Centre for Disease Control
	Dr. Mark Loeb	Associate Professor, Pathology and Molecular Medicine, McMaster University
	Dr. Marc Ouellette	Canada Research Chair in Antimicrobial Resistance; Professor, Microbiology, Université Laval
	Dr. William E. Paul	Chief, Laboratory of Immunology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, USA
	Dr. Kevork Peltekian	Medical Director, Atlantic Liver Transplantation Program; Assistant Professor, Medicine (Gastroenterology), Dalhousie University
	Dr. Francis Plummer	Scientific Director, National Microbiology Laboratory; Canadian Science Centre for Human and Animal Health
	Mrs. Helaine Shiff	Member, Research Partnership Program for Juvenile Diabetes Foundation International; Partner, Focus on You
	Dr. Tania Watts	Professor, Department of Immunology, University of Toronto

—Appendix 3

Institute Support Grant - For the year ending March 31, 2004

Available Funds		\$ 1,724,960
Expenses		
Institute Development		
Conference, Symposia and Workshops	\$ 379,969	
Institute Advisory Board	77,449	
Professional Services	37,623	
Travel Expenditures	1,903	
Expenditures Institute Request for Proposal "SARS"	325,100	
Other Costs	6,000	
		\$ 828,044
Institute Operations		
Salaries and Benefits	\$ 360,749	
Office Accomodations	11,205	
Telephone and Communication Services	13,812	
Supplies, Material and Other Services	33,221	
Office Furniture and Fixtures	375	
Computer Equipment and IT Support	7,531	
Professional Services	1,624	
Travel Expenditures	87,532	
Other Expenditures	1,479	
		\$ 517,528
Total Expenses		\$ 1,345,572
Unspent Balance*		\$ 379,388

Institute Support Grant - SARS Initiative

Available Funds		\$ 578,000
Expenses		
Institute Initiative - SARS		
Grants to Institutions - SARS Project	\$ 578,000	
		\$ 578,000
Total Expenses		\$ 578,000
Unspent Balance*		\$ -

*Note: The unspent balance as at March 31, 2003 is carried forward to the subsequent fiscal year





—Appendix 4

Institute Investments in Strategic Initiatives - For the year ending March 31, 2004

Strategic Initiatives	Number	Contributions through Grants and Awards				Total
		2003-04	2004-05	2005-06	2006 and beyond	
Safe Food and Water	5	536,579	1,041,671	985,686	472,592	\$ 3,036,528
Interdisciplinary Capacity Enhancement Teams	1	15,000	30,000	30,000	52,500	\$ 127,500
Global Health Research	2	143,612	-	-	-	\$ 143,612
Operating Grants to Open Competition	13	755,964	-	-	-	\$ 755,964
Health Research Programs of Excellence	2	746,230	751,480	751,480	563,610	\$ 2,812,800
New Emerging Teams	3	191,379	191,379	191,379	251,326	\$ 825,463
Needs, Gaps and Opportunities	1	30	-	-	-	\$ 30
IAPH Strategic Initiative	2	73,145	58,272	25,000	-	\$ 156,417
Host Susceptibility and Resistance to Pathogens in Health and Disease	2	587,000	587,000	587,000	1,174,000	\$ 2,935,000
Anti-microbial Resistance, Health System Implications and Health Outcomes	2	278,177	390,719	469,787	872,677	\$ 2,011,360
CIHR Training Program Grants	8	1,019,767	1,334,767	1,377,683	3,287,365	\$ 7,019,582
Pilot Project for New Investigators	20	1,629,123	146,400	-	-	\$ 1,775,523
SARS - Evaluation and Lessons Learned	-	-	100,001	-	-	\$ 100,001
	61	\$ 5,976,006	\$ 4,531,688	\$ 4,418,015	\$ 6,674,070	\$ 21,599,779

Note : Grants and awards in respect to these programs are approved for 1 to 6 years. Figures displayed represent CIHR financial commitments for these programs in 2003-04 and subsequent years. Availability of these funds in future years are subject to funding appropriations by Parliament. For some initiatives, partners also contributed to the funding of the grants and awards.